Journal of Fluorine Chemistry 131 (2010) 1013–1024

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

Novel fluoro-substituted benzo- and benzothieno fused pyrano[2,3-*c*]pyrazol-4(1*H*)-ones

Wolfgang Holzer *, Angelika Ebner, Karin Schalle, Gyselle Batezila, Gernot A. Eller

Department of Drug and Natural Product Synthesis, Faculty of Life Sciences, University of Vienna, Althanstrasse 14, A-1090 Vienna, Austria

ARTICLE INFO

Article history:
Received 9 June 2010
Received in revised form 8 July 2010
Accepted 9 July 2010
Available online 16 July 2010

Keywords:
Pyrazolones
Acylation
Ring closure
Chromeno[2,3-*c*]pyrazol-4(1*H*)-one
NMR (^{1}H, ^{13}C, ^{15}N, ^{19}F)

ABSTRACT

A straightforward, two-step synthesis of fluoro substituted chromeno[2,3-*c*]pyrazol- and [1]benzothieno[2′,3′:5,6]pyrano[2,3-*c*]pyrazol-4(1*H*)-ones, respectively, is presented. Hence, treatment of 1-substituted or 1,3-disubstituted 2-pyrazolin-5-ones with fluoro substituted 2-fluorobenzoyl chlorides or 3-chloro-6-fluoro-1-benzothiophene-2-carbonyl chloride using calcium hydroxide in refluxing 1,4-dioxane gave the corresponding 4-aroylpyrazol-5-ols, which were cyclized into the fused ring systems. 5-Fluorochromeno[2,3-*c*]pyrazol-4(1*H*)-one was obtained upon treatment of the 1-(4-methoxybenzyl) protected congener with trifluoroacetic acid. Treatment of 5-fluorochromeno[2,3-*c*]pyrazol-4(1*H*)-ones with methylhydrazine afforded novel tetracyclic ring systems such as 2-methyl-7-phenyl-2,7-dihydropyrazolo[4′,3′:5,6]pyrano[4,3,2-*cd*]indazole. Detailed NMR spectroscopic investigations (^{1}H, ^{13}C, ^{15}N, ^{19}F) with the obtained compounds were undertaken.

1. Introduction

The important role of fluorine in medicinal and pharmaceutical chemistry is indisputable and well reflected by a large number of recent publications, including some excellent reviews [1–4]. Introduction of fluorine into a biologically active molecule often enhances the metabolic stability and modulates physicochemical properties such as basicity or lipophilicity [1,2]. Moreover, the presence of fluorine can enhance the binding affinity of drug molecules to the target protein [1,2]. Considering these facts there is an ongoing interest in the synthesis of fluorinated heterocyclic compounds, which may serve as building blocks or precursors of biologically active fluorine-containing molecules.

In the course of a program aimed to the synthesis of new heterocyclic scaffolds we recently presented a short and generally applicable synthetic approach to various fused pyrano[2,3-*c*]pyrazol-4(1*H*)-ones of type **A**, which can be considered as heterocyclic analogues of xanthone (Fig. 1) [5–11]—the latter representing the core of several biologically active molecules [12]. In compounds **A** one benzene system of the parent xanthone is replaced by a pyrazole system whereas ring H is a heteroaromatic moiety or a benzene ring. Some representatives of the latter chromeno[2,3-*c*]pyrazol-4(1*H*)-ones (*H* = benzene) are already known and have been primarily described by Sarenko et al. [13]. Type **A** compounds are interesting for medicinal chemists, as an example the A_2-subtype specific adenosine receptor antagonist **B** – containing a substituted pyrazole system – may serve (Fig. 1) [14].

Hence, in this paper we want to present the synthesis of fluoro-substituted compounds of type **A**, with the H-ring consisting of benzene or a benzothiophene system. Moreover, extensive NMR spectroscopic studies (^{1}H, ^{13}C, ^{15}N, ^{19}F) with the title compounds are showcased as well as their potential to act as precursors for the synthesis of higher condensed systems of biological interest.

2. Results and discussion

2.1. Chemistry

The synthesis of target compounds of type **A** was accomplished according to the general approach described in Refs. [5–11]. Hence, pyrazolones **1** were reacted with fluoro-substituted 2-fluorobenzoyl chlorides **2–7** under the conditions described by Jensen to achieve selective C-4 acylation of pyrazolones (calcium hydroxide, dioxane, reflux) [15] (Scheme 1). Cyclization of the thus obtained 4-aroylpyrazol-5-ols **8–13** by treatment with sodium hydride in dry DMF or by K_2CO_3 in MeCN afforded the fluorinated pyrano[2,3-*c*]pyrazol-4(1*H*)-ones **14–19** (Scheme 1). In this manner, all ring-H monofluoro products were obtained (compounds **14–17**, F in

* Corresponding author. Tel.: +43 1 4277 55623; fax: +43 1 4277 9556.
E-mail address: wolfgang.holzer@univie.ac.at (W. Holzer).

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doi:10.1016/j.jfluchem.2010.07.007

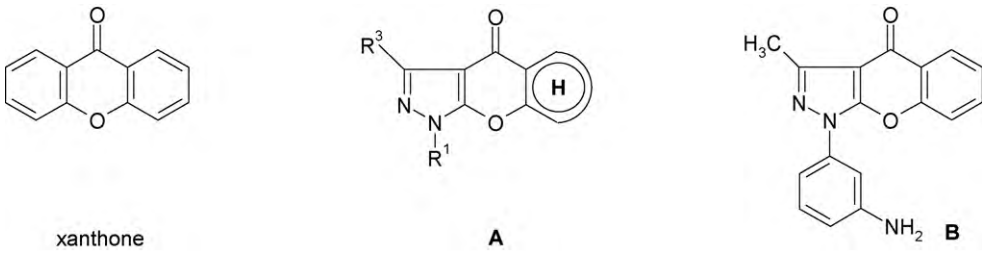


Fig. 1. Xanthone and pyrazole analogues thereof.

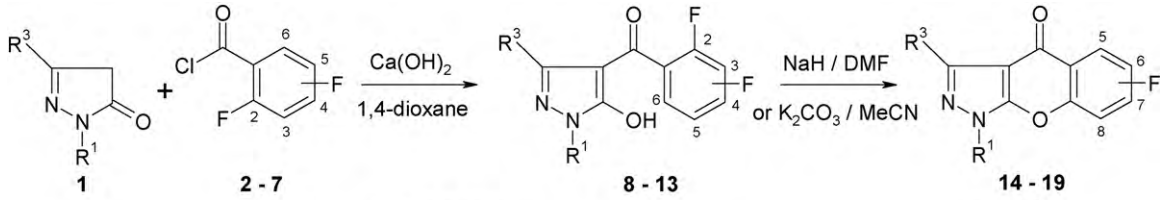
position 5, 6, 7 and 8 at the tricyclic system). Moreover, two difluoro congeners (**18a**, **19a**) were prepared.

The ring closure reaction of the 4-(2,3,6-trifluorobenzoyl)pyrazol-5-ol **12a** theoretically may lead to two different cyclization products, namely the 5,8-difluoro compound **18a** or the isomeric 5,6-difluoro congener **C** (Scheme 2). Nevertheless, only a single product was isolated upon treatment of **12a** with NaH/DMF to which structure **18a** was unequivocally assigned considering the NMR spectra (Scheme 2). Obviously, in the course of the intramolecular nucleophilic substitution reaction the fluoro atom in position 2 of the benzene system of **12a** is more reactive than that in 6-position.

An interesting phenomenon was observed upon the cyclization of the trifluorobenzoylpyrazolol **13a**: conducting the ring closure reaction in the usual way by treatment of **13a** with NaH/DMF led to a mixture of two reaction products (Scheme 3). Besides the desired 5,7-difluorinated tricycle **19a** a second compound was formed in considerable amount which turned out to be the 5-dimethylamino congener **19y**. The formation of **19y** via nucleophilic displacement of the activated fluorine substituent in position 5 can be explained considering the tendency of DMF to slow decomposition at its boiling temperature, leading to the liberation of dimethylamine [16]. The latter process can even occur at lower temperatures and to a higher degree when catalyzed by basic or acidic materials [16]. Thus, in the case of **13a** cyclization using the system K_2CO_3/MeCN turned out to be advantageous as here **19a** resulted as the only isolated reaction product (Scheme 3). In principle, also compounds **14** and **18** carry an activated fluoro substituent in position 5 of the tricyclic system. Indeed, during the synthesis of **14b** upon forced reaction conditions and prolonged heating, formation of some 5-dimethylamino substitution product was observed. Nevertheless, cyclization of **8b** in the system NaH/DMF led to higher yields of **14b** compared to the usage of K_2CO_3/MeCN.

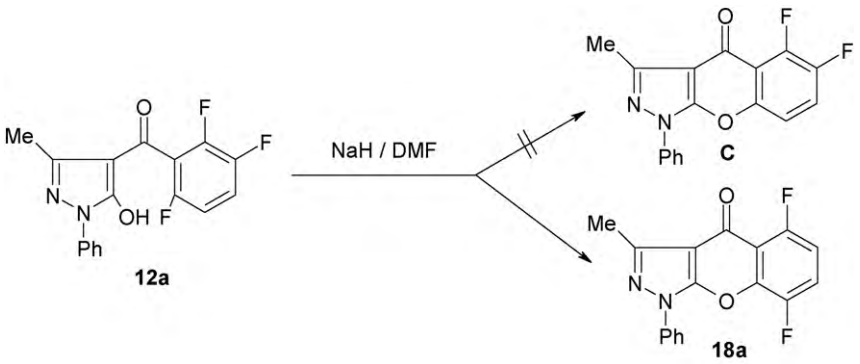
Furthermore, the N-unsubstituted 5-fluorochromeno[2,3-*c*]pyrazol-4(1*H*)-one **14x** was prepared from **14c** *via* removal of the PMB protecting group [17] upon heating with trifluoroacetic acid (Scheme 3) [5–7].

Similarly as described for the synthesis of chromeno[2,3-*c*]pyrazol-4(1*H*)-ones **14**–**19** we also obtained the fluorinated tetracycle **25** (Scheme 4). Reaction of 3-methyl-1-phenyl-2-pyrazolin-5-one (**1a**) with 3-chloro-6-fluoro-1-benzothiophene-2-

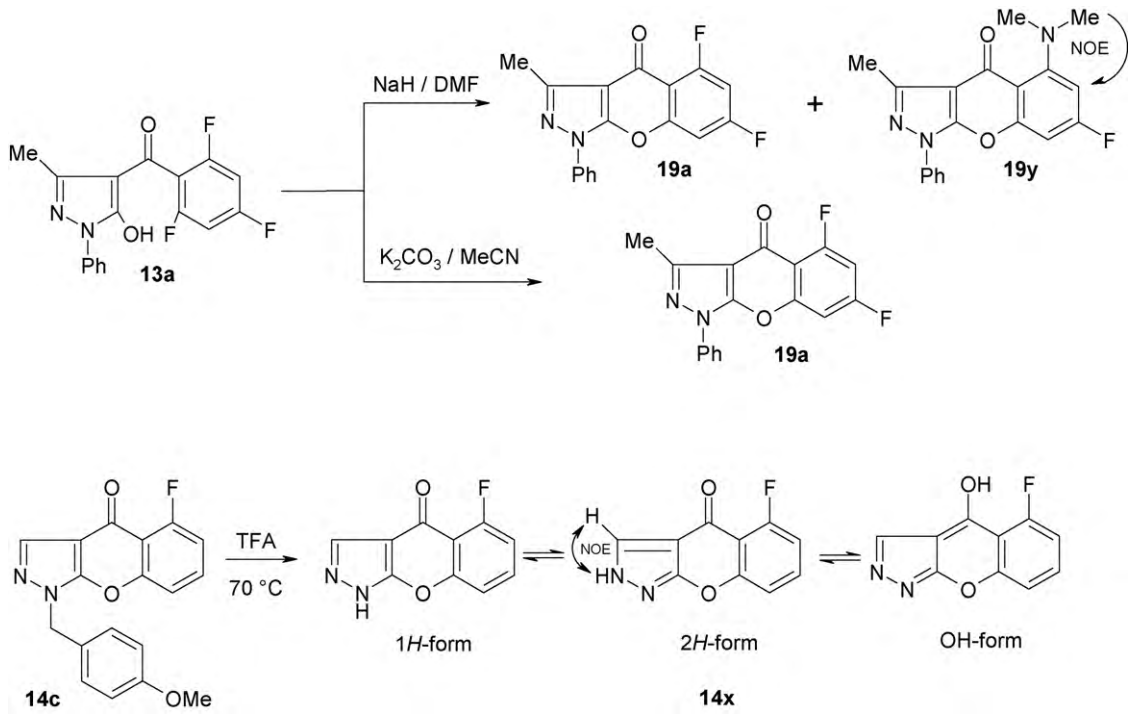


	comp.	F in pos.	comp.	F in pos.
a: R^1 = Ph, R^3 = Me	**2**, **8**	2,6	**14**	5
b: R^1 = Ph, R^3 = H	**3**, **9**	2,5	**15**	6
c: R^1 = PMB, R^3 = H	**4**, **10**	2,4	**16**	7
	5, **11**	2,3	**17**	8
PMB = (4-methoxy)benzyl-	**6**, **12**	2,3,6	**18**	5,8
	7, **13**	2,4,6	**19**	5,7

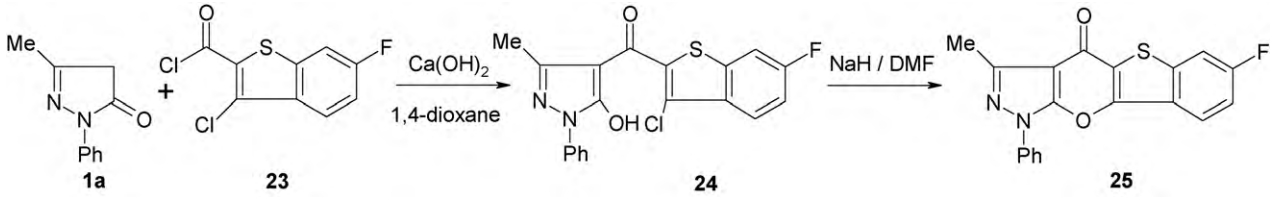
Scheme 1.



Scheme 2.



Scheme 3.

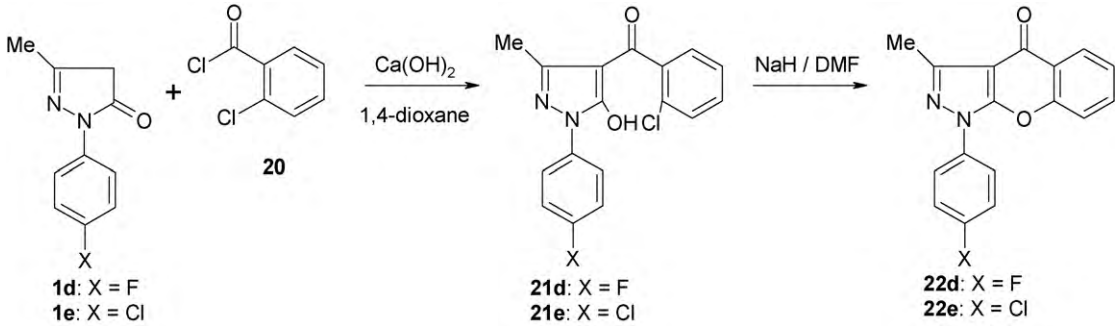


Scheme 4.

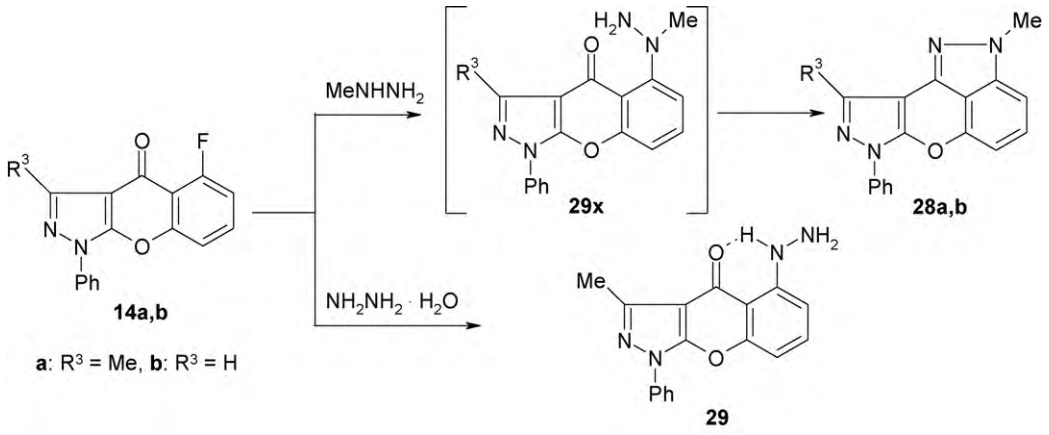
carbonyl chloride (**23**) afforded the aroylation product **24** which was consecutively cyclized into the annelation product **25** with NaH/DMF.

The presented approach also permitted access to products of type **22**, carrying a 4-substituted phenyl ring at position 1 of the chromeno[2,3-*c*]pyrazol-4(1*H*)-one system (Scheme 5). The N-fluorophenyl congener **22d** resulted from reaction of pyrazolone **1d** with 2-chlorobenzoyl chloride (**20**) and subsequent cyclization of the aroylpyrazolol **21d**. For comparison purposes, also the corresponding chloro compound **22e** was prepared in a similar way starting from pyrazolone **1e** (Scheme 5).

Type **14** compounds can be regarded as 1,3-dielectrophiles as they feature an activated fluoro atom and a carbonyl group in 1,3-position. Due to this fact they can act as precursors for the construction of higher anellated systems. This is demonstrated by means of reaction of **14a** or **14b**, respectively, with methylhydrazine leading to tetracycles **28a**,**b**—the latter containing two different condensed pyrazole moieties (Scheme 6). The structure of compounds **28** (methyl group attached to N-2) was explicitly confirmed by NMR experiments (Fig. 4). Compounds structurally related to **28** have been found to exhibit interesting antiproliferative and cytotoxic activity as well as ability to overcome multi-drug resistance [18–21]. In contrast, reaction of **14a** with hydrazine hydrate afforded the hydrazine **29**, which did not cyclize into the corresponding tetracycle even at elevated temperature. However, the formation of **29** demonstrates that in the reaction of **14** with hydrazines the nucleophilic substitution of the fluoro atom – expectedly – proceeds a lot easier than the condensation reaction of



Scheme 5.



Scheme 6.

hydrazine with the pyranone C=O group. The strong intramolecular hydrogen bond between hydrazine NH and C=O in compound **29** (Scheme 6, Fig. 4), which prevents attack of the terminal NH_2 group at the carbonyl C-atom, may serve as a possible explanation why **29** resists cyclization. NMR experiments showed that this hydrogen bond is even fully intact in the strong acceptor solvent $(CD_3)_2SO$, in which such hydrogen bonds are usually broken. From numerous examples it is known that in SN_{Ar} reactions with methylhydrazine the N-atom attached to the methyl group is more nucleophilic than NH_2 [22–24]. Consecutively, the primary substitution products upon reaction of **14a** or **14b** with methylhydrazine are intermediates **29x** (Scheme 6), the latter having no possibility for the formation of such a strong intramolecular hydrogen bond comparable to that in **29**. As a consequence, compounds **29x** readily cyclize into the corresponding tetracycles **28a** and **28b**, respectively.

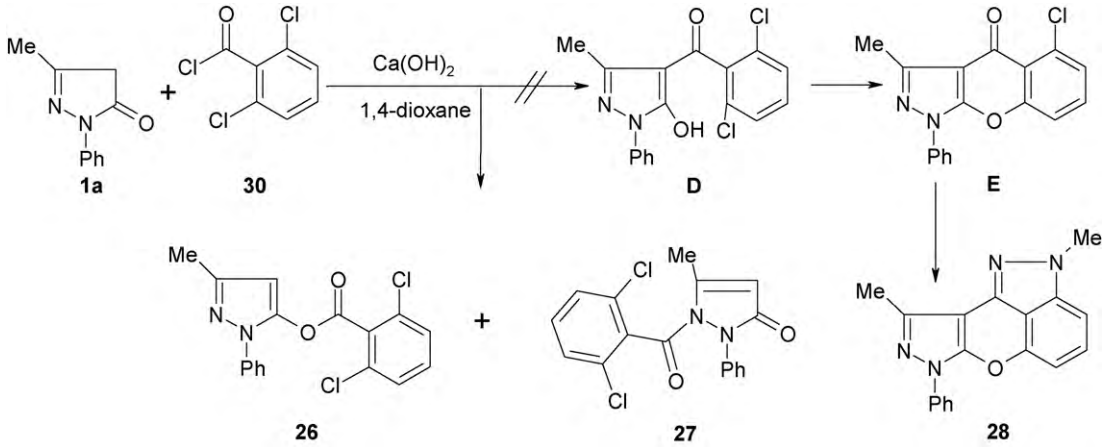
Finally, it should be mentioned that the access to fused systems of type **28** was not possible upon replacement of 2,6-difluorobenzoyl chloride (**2**) by 2,6-dichlorobenzoyl chloride (**30**) (Scheme 7). Thus, treatment of **1a** with **30** under Jensen-conditions did not afford the desired 4-aroylpyrazol-5-ol **D**. Instead, from the complex reaction mixture the isomeric O-aroyl compound **26** was isolated as the main component by column chromatography. Besides, the N-substitution product **27** was obtained in traces (Scheme 7).

2.2. NMR spectroscopic investigations

Full and unambiguous assignment of all ^1H, ^{13}C, ^{15}N and ^{19}F NMR resonances was achieved by combining standard NMR techniques [25], such as fully ^1H-coupled ^{13}C NMR spectra, ^1H-decoupled ^{19}F NMR spectra, APT, HMQC, gs-HSQC, gs-HMBC, COSY, TOCSY, NOESY and NOE-difference spectroscopy. Moreover, experiments with selective excitation (DANTE) of certain ^1H-resonances were performed, such as long-range INEPT [26] and 2D(δ,J) long-range INEPT [27]. The latter experiments were indispensable for the unambiguous mapping of some long-range ^{13}C,^1H coupling constants. The complete analysis of ^1H,^1H and ^{19}F,^1H-spin coupling constants was performed as far as possible, however, due to overlapping of signals and the presence of higher order spin systems this task was unfeasible in some cases. In the numerous compounds carrying a phenyl substituent attached at pyrazole N-1 the phenyl protons establish an AA′BB′C spin systems which cannot be analyzed according to the first order. Nevertheless, assignment of the corresponding resonances is easy as the signals due to Ph H-3,5 and Ph H-4 resemble a triplet, whereas those of Ph H-2,6 have more 'dublet'-character. Even so, these signals are always designated as multiplets (m) in Section 4.

2.2.1. 4-Aroylpyrazol-5-ols (compounds 8–13, 21, 24)

In principle, these compounds are capable of prototropic tautomerism and can exist in several isomeric forms [28–31] (Fig. 2). However, ^{13}C and particularly ^{15}N NMR data reveal them to exist as hydroxypyrazoles B′ in $CDCl_3$ solution. Thus, for instance, pyrazole N-1 and pyrazole N-2 exhibit large differences regarding their ^{15}N NMR chemical shifts (**8a**–**11a**: N1 ∼ −190 ppm, N2 ∼ −100 ppm) what excludes the existence of larger amounts of NH-form C in the overall tautomeric composition. The CH-form A can be ruled out owing to the lack of a pyrazole H-4 signal and the fact that C-4 shows to be a quaternary C-atom in the ^{13}C NMR



Scheme 7.

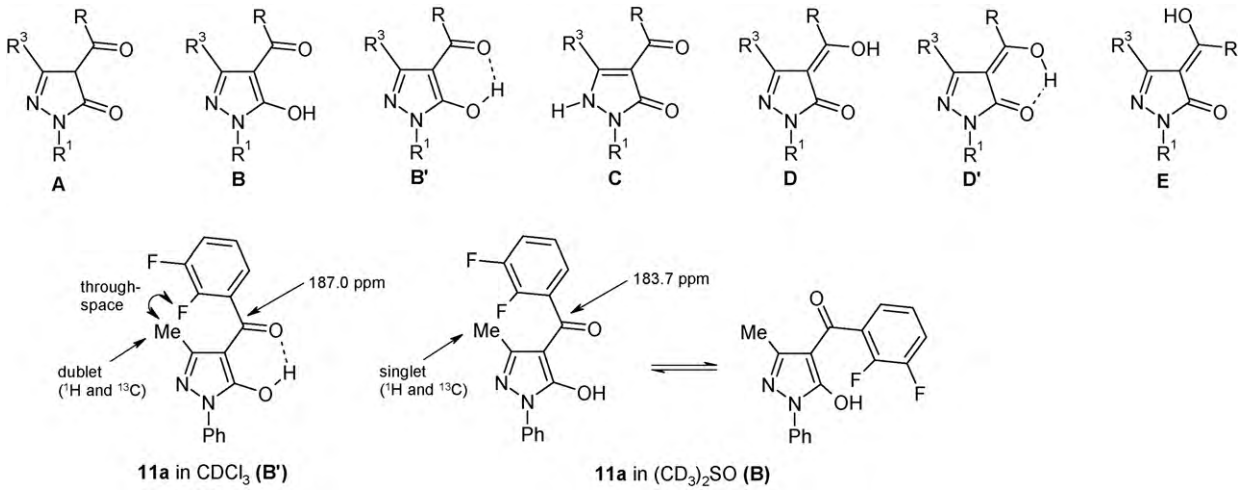


Fig. 2. Possible tautomeric forms of 4-aroylpyrazolones and tautomeric behavior of **11a** in $CDCl_3$ and $(CD_3)_2SO$ solution.

spectra. However, an interesting phenomenon in some of these compounds was observed. For instance, in the ^{1}H-broadband decoupled ^{13}C NMR spectrum of **11a** in $(CD_3)_2SO$ solution the signal due to the methyl-C atom appears as a singlet (δ 13.8 ppm), whereas in $CDCl_3$ solution the corresponding signal is split into a dublet (δ 13.9 ppm, J = 2.0 Hz). In the ^{1}H NMR spectrum of **11a**, the 3-methyl signal appears as a singlet in $(CD_3)_2SO$ (δ 2.37 ppm) and as a dublet in $CDCl_3$ (δ 2.01 ppm, J = 0.9 Hz). This can be explained by the presence of **11a** (in $CDCl_3$) in form B′, where the strong intramolecular hydrogen bond fixes the benzoyl moiety and brings the methyl group close to the fluoro atom F-2 (Fig. 2). In contrast, in $(CD_3)_2SO$ solution (a strong acceptor) the hydrogen bond is obviously broken (predominance of form B) and the average distance between methyl-group and fluoro substituent is now much larger. Similar splittings due to ^{19}F,^{13}C and ^{19}F,^{1}H (through-space) couplings in $CDCl_3$ solution were found in the spectra of **8b**, **8c**, **9a** and **10a**. Moreover, the intramolecular hydrogen bond of **11a** in $CDCl_3$ solution is evidenced by a significant downfield shift for the carbonyl C-atom (δ 187.0 ppm, $CDCl_3$) compared to the corresponding value found in $(CD_3)_2SO$ (δ 183.7 ppm) (Fig. 4) [32]. With congener **8b**, the C=O resonance is shifted from 179.2 ppm (in $(CD_3)_2SO$) to 183.3 ppm upon switching to $CDCl_3$ solution. Similar phenomena have been described by us for 4-acyl-3-trifluoromethylpyrazol-5-ols [33].

In the spectra of **8**–**13**, **21a** and **24** the typical influences of fluoro substituents on ^{13}C and ^{1}H NMR chemical shifts could be observed [32,34]. Thus, protons located in ortho-position to a fluorine atom receive a significant upfield shift, which becomes larger for protons between two F-atoms in ortho-position (**10a**: δ CPh H-3 = 6.96 ppm, **13a**: δ CPh H-3,5 = 6.80 ppm). ^{13}C NMR signals of carbons being in ortho or para-position to a fluoro substituent are significantly shifted to lower frequencies, whereas ipso C-atoms are characterized by a marked downfield shift. Compounds **8**–**13** feature a di- or trifluoro substituted benzene ring. Here the ^{19}F chemical shifts agree well with those found in correspondingly substituted di- or trifluorobenzenes, this is also the case for ^{19}F,^{19}F coupling constants [35–37]. The unambiguous determination of ^{19}F,^{19}F couplings was facilitated by recording ^{1}H-decoupled ^{19}F spectra, whereas the ^{19}F,^{13}C spin coupling constants could be easily derived from the ^{1}H-decoupled ^{13}C NMR spectra.

2.2.2. *Chromeno[2,3-c]pyrazol-4(1H)-ones* 14–19

Tricycles **14**–**17** with one fluoro atom attached to the condensed benzene ring exhibit complex splitting patterns in the ^{1}H and ^{19}F NMR spectra, which in some cases could be completely analyzed according to the first order. Again, here the typical influences of the fluorine's −I and +M effect on ^{1}H and ^{13}C chemical shifts are present. A comparison of the ^{19}F shifts in isomeric compounds **14a**–**17a** clearly exhibits the marked influence of the pyrane-ring O-atom, most notably in ortho (**17a**: δ F-8 = −133.6 ppm) and – weakened – in para position (**15a**: δ F-6 = −115.4 ppm), whereas the shifts in **14a** (δ F-5 = −110.6 ppm) and **16a** (δ F-7 = −102.8 ppm) are the least affected (meta-position of O and F). The pyrane O-atom and the C=O function impair the one-bond ^{19}F,^{13}C couplings as well, the latter ranging from 246.6 Hz (^1J(C6,F6) in **15a**) to 265.6 Hz (^1J(C5,F5) in **14a**).

As described in the chemistry part, cyclization of **12a** exclusively leads to the 5,8-difluoro compound **18a** and not to the 5,6-difluoro isomer **C** (Scheme 2). Unequivocal assignment of structure **18a** and thus discrimination from **C** can be achieved considering the ^{19}F,^{13}C coupling constants of C-5 (157.3 ppm) and C-8 (147.2 ppm): apart from the large direct C,F couplings (^1J(C5,F5) = 262.4 Hz, ^1J(C8,F8) = 249.4 Hz) the C-signals are additionally split by a second, but small coupling, namely ^4J(C5,F8) = 3.1 Hz and ^4J(C8,F5) = 4.3 Hz. In structure **C**, where the two fluoro atoms are in ortho-position at the benzene ring, much larger long-range C,F couplings (^3J(C,F) ~ 12–14 Hz, compare corresponding couplings in **11a**) have to be expected. Moreover, many other ^{13}C,^{19}F couplings found do not fit for structure **C**. In **18a**, also the F,F coupling of 17.7 Hz perfectly matches the ^5J coupling in 1,4-difluorobenzene (^5J(F,F) = 17.6 Hz [35,36]), whereupon ^3J(F,F) as present in **C** should be larger (~21 Hz in 1,2-difluorobenzene [35,36], 21.6 Hz in **11a**). As a typical example, some important chemical shift and coupling data are displayed for **14a** in $CDCl_3$ solution (Fig. 3).

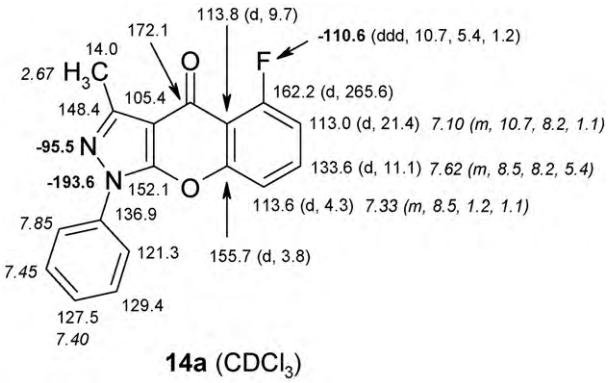


Fig. 3. ^{1}H (in italics), ^{13}C, ^{15}N (in bold) and ^{19}F NMR (in bold) chemical shifts (δ, ppm) and spin coupling constants (in parentheses, Hz) of **14a** (in $CDCl_3$).

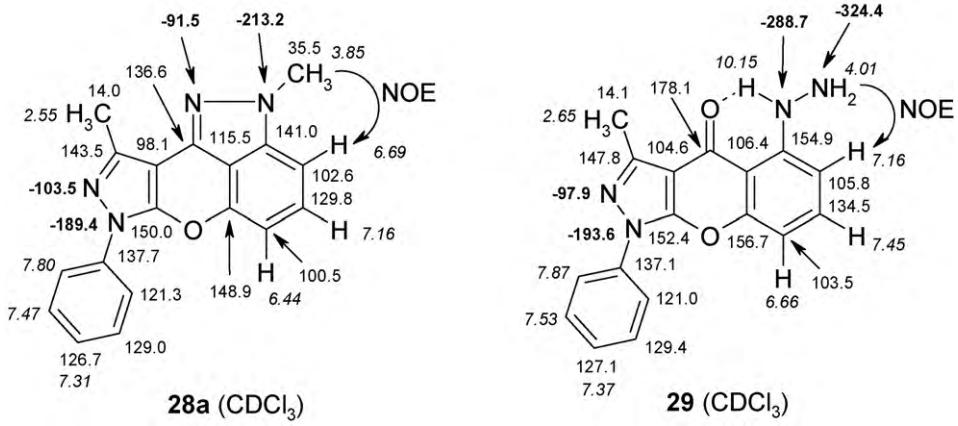


Fig. 4. ^{1}H (in italics), ^{13}C, and ^{15}N NMR (in bold) chemical shifts (δ, ppm) of **28a** and **29** (in $CDCl_3$).

Tricycle **14x**, carrying no substituent at pyrazole N-1 can be present in three tautomeric forms (Scheme 3). Considering the chemical shifts of C-3 (δ 129.0 ppm) and C-9a (δ 160.2 ppm), the diagnostic coupling constant ^{2}J(C3a,H3) = 8.3 Hz [31] as well as the results of NOE-experiments (NOE on H-3 upon irradiation of NH) it is assumed that **14x** exists in an equilibrium of the 1*H* and 2*H*-form in $(CD_3)_2SO$ solution (Scheme 3), as found with related compounds [5–8].

The substitution pattern in the N,N-dimethlylamino product **19y** clearly results from an NOE-difference experiment: irradiation of the NMe_2 resonance (2.97 ppm) gives the H-6 signal an explicit NOE, whereas the signal of H-8 remains unaffected (Scheme 3). This unequivocally assigns the 5-NMe_2-7-F substitution pattern of **19y**. In case of a reverse 5-F-7-NMe_2 substitution an NOE on both H-6 as well as H-8 has to be expected after irradiation of the NMe_2 transition.

2.2.3. Other compounds

Products **26** and **27** resulting from reaction of **1a** with 2,6-dichlorobenzoyl chloride (Scheme 7) can be easily distinguished on basis of their NMR data. The ester **26** exhibits a C–H moiety incorporated in the pyrazole system which can be only attributed to pyrazole C-4 with the H-4 singlet resonating at 6.34 ppm and C-4 at 95.7 ppm (^{1}J(C4,H4) = 181.7 Hz). Moreover, the small chemical shift of pyrazole C-5 (143.6 ppm) is typical for such a structure [38]. The large differences regarding the ^{15}N chemical shifts of pyrazole N-1 ($-\delta$ 183.1 ppm) and N-2 (δ −95.1 ppm) hint to two different types of N-atoms and thus to an 'aromatic' pyrazole system. In contrast, the N-benzoyl derivative **27** shows two much more similar N-atoms (δ N-1 = −190.7 ppm, δ N-2 = −211.5 ppm; reverse numbering of ring atoms compared to **26**!) and a pyrazole C-3 (δ 168.0 ppm) typical for a pyrazolone structure.

Reaction of **14a,b** with methyl hydrazine can principally lead to two regioisomeric anellation products. Attachment of the methyl group at N-2 (and hence presence of **28a,b**) was confirmed by NOE-difference experiments. Irradiation of the N-methyl resonance (NMe) clearly enhanced the signal due to H-3 (6.69 ppm) (Fig. 4). For a possible isomeric structure (methyl group attached to N-1) an NOE to the signal of C-9-methyl has to be expected. In Fig. 4, important chemical shifts (mainly assigned via HSQC and HMBC experiments) and NOE correlations unequivocally confirming structure **28** are given. According to its NMR spectra (^{1}H NMR: 3 protons exchangeable with D_2O; ^{13}C NMR: signal at δ 178.1 ppm; ^{15}N NMR: signals at −324.4 ppm and −288.7 ppm), MS, IR and microanalytical data the reaction product of **14a** with hydrazine (compound **29**) cannot be a tetracyclic system similar to **28** but must be the substituted hydrazine **29**. In $CDCl_3$ solution the hydrazine NH-proton has a marked downfield shift (δ 10.15 ppm) indicating its involvement into an intramolecular hydrogen bond to the pyranone carbonyl O-atom (Fig. 4). In contrast, the terminal NH_2 protons exhibit a much smaller chemical shift (δ 4.01 ppm). Similar chemical shifts (δ NH 9.91 ppm, δ NH_2 4.46 ppm) were found in $(CD_3)_2SO$ solution. Moreover, it should be mentioned that in both solvents a marked NOE between NH_2 and H-6 (Fig. 4) and no NOE between NH and H-6 was observed, providing an additional hint for the strong fixation via the intramolecular hydrogen bond.

3. Conclusions

In summary we have presented a simple and straightforward synthesis of fluoro-substituted benzo- and benzothieno fused pyrano[2,3-*c*]pyrazol-4(1*H*)-ones starting from commercially available or easily accessible pyrazolones and aroyl chlorides. It was demonstrated that representatives of type **14** can be used as precursors for further anellation reactions. Furthermore, we have presented extensive NMR studies with all compounds obtained, providing full and unambiguous assignment of all ^{1}H, ^{13}C, ^{15}N and ^{19}F resonances as well as an ambitious analysis of homo- and heteronuclear spin coupling constants. We continue to explore related compounds with biologically relevant side-chains attached to the tricyclic or tetracyclic cores—these results will be published elsewhere.

4. Experimental

4.1. General

Melting points were determined on a Reichert–Kofler hot-stage microscope and are uncorrected. Mass spectra were obtained on a Shimadzu QP 1000 instrument (EI, 70 eV) and on a Finnigan MAT 8230 instrument (EI, 70 eV, HRMS). IR spectra were recorded on a Perkin-Elmer FTIR 1605 spectrophotometer or on a Perkin-Elmer FTIR spectrum 1000 spectrometer. Elemental analyses (C, H, N) were performed at the Microanalytical Laboratory, University of Vienna, and were in good agreement (±0.4%) with the calculated values. ^{1}H and ^{13}C NMR spectra were recorded on a Varian UnityPlus 300 spectrometer (299.95 MHz for ^{1}H, 75.43 MHz for ^{13}C) or on a Bruker Avance 500 spectrometer (500.13 MHz for ^{1}H, 125.77 MHz for ^{13}C) at 25 °C. The centre of the solvent signal was used as an internal standard which was related to TMS with δ 7.26 ppm (^{1}H in $CDCl_3$), δ 2.49 ppm (^{1}H in $(CD_3)_2SO$), δ 77.0 ppm (^{13}C in $CDCl_3$), and δ 39.5 ppm (^{13}C in $(CD_3)_2SO$). ^{15}N NMR spectra (50.68 MHz, referenced against external nitromethane) and ^{19}F NMR spectra (470.56 MHz, absolute referencing via Ξ ratio) were

obtained on a Bruker Avance 500 instrument with a 'directly' detecting broadband observe probe (BBFO). Digital resolutions were 0.2 Hz/data point in the ^{1}H and ^{19}F NMR spectra and 0.4 Hz/data point in the ^{1}H coupled ^{13}C NMR spectra (gated decoupling). Systematic names according to IUPAC recommendations were generated with ACD/Name [39] and subsequently proved manually to ensure correct nomenclature within this publication [40]. Pyrazolone **1c** was prepared according to Ref. [17], all other starting materials are commercially available.

4.2. General procedure for the 4-aroylation of pyrazolones 1: synthesis of compounds 8–13, 21 and 24

Under anhydrous conditions, to a suspension of pyrazolone **1a–d** and $Ca(OH)_2$ (2 equiv) in dry 1,4-dioxane (2 mL per mmol of pyrazolone) a solution/suspension of the corresponding acid chloride **2–7**, **20**, **23** (1 equiv) in dry 1,4-dioxane (2 mL per mmol) was added. The reaction mixture was heated at reflux for 3 h under stirring. After cooling to room temperature, the mixture was treated with 2 N HCl (4 mL per mmol), stirred for 15 min, and poured into H_2O (10 mL per mmol). After 30 min, the solid products were filtered off, washed with H_2O, and recrystallized from the solvent given below.

4.2.1. (2,6-Difluorophenyl)(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)methanone (8a)

Yield 81%; colorless solid; mp 176–180 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.98 (3*H*, s, 3-Me), 7.04 (2*H*, m, CPh H-3,5), 7.32 (1*H*, m, NPh H-4), 7.47 (1*H*, m, CPh H-4), 7.48 (2*H*, m, NPh H-3,5), 7.84 (2*H*, m, NPh H-2,6), 9.64 (1*H*, br s, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.2 (3-Me, ^{1}J = 128.9 Hz), 105.5 (pyraz C-4, ^{3}J(C4,3Me) = 2.7 Hz), 112.0 (m, CPh C-3,5), 116.4 (CPh C-1, ^{2}J(C1,F2,6) = 21.5 Hz), 121.1 (NPh C-2,6), 127.0 (NPh C-4), 129.1 (NPh C-3,5), 132.3 (CPh C-4, ^{1}J = 164.7 Hz, ^{3}J(C4,F2,6) = 9.7 Hz), 136.9 (NPh C-1), 148.3 (pyraz C-3, ^{2}J(C3,3Me) = 6.9 Hz), 159.1 (CPh C-2,6, ^{1}J(C,F) = 252.0 Hz, ^{3}J(C,F) = 7.2 Hz), 159.7 (pyraz C-5), 183.6 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −190.3 (pyraz N-1), −100.7 (pyraz N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −113.1 (CPh F-2,6). IR (KBr): ν (cm^{-1}) 1628 (C=O). MS (*m/z*, %): 314 (M^+, 53), 200 (71), 141 (100), 132 (20), 113 (23), 91 (57), 77 (59), 67 (37), 51 (39), 63 (21). Anal. Calcd for $C_{17}H_{12}F_2N_2O_2 \cdot 0.1\ H_2O$: C, 64.60; H, 3.89; N, 8.86. Found: C, 64.51; H, 4.00; N, 8.84.

4.2.2. (2,6-Difluorophenyl)(5-hydroxy-1-phenyl-1H-pyrazol-4-yl)methanone (8b)

Yield 50%; yellowish solid; mp 140–144 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.03 (2*H*, m, CPh H-3,5), 7.34 (1*H*, m, NPh H-4), 7.48 (3*H*, m, CPh H-4 and NPh H-3,5), 7.63 (1*H*, t, pyraz H-3, *J*(H3,F2,6) = 1.6 Hz), 7.85 (2*H*, m, NPh H-2,6), 10.69 (1*H*, OH). ^{1}H NMR (300 MHz, $(CD_3)_2SO$): δ 7.22 (2*H*, m, CPh H-3,5), 7.35 (1*H*, m, NPh H-4), 7.49 (2*H*, m, NPh H-3,5), 7.58 (1*H*, m, CPh H-4), 7.69 (2*H*, m, NPh H-2,6), 7.75 (1*H*, s, pyraz H-3), 7.98 (1*H*, br s OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 106.0 (pyraz C-4, ^{2}J(C4,H3) = 10.5 Hz), 112.2 (CPh C-3,5), 115.6 (CPh C-1, ^{2}J(C1,F2,6) = 19.6 Hz), 121.2 (NPh C-2,6), 127.3 (NPh C-4), 129.1 (NPh C-3,5), 132.8 (CPh C-4, ^{1}J = 165.0 Hz, ^{3}J(C4,F2,6) = 10.2 Hz), 137.0 (NPh C-1), 139.8 (pyraz C-3, ^{1}J = 191.2 Hz, *J*(C3,F2,6) = 2.9 Hz), 158.3 (pyraz C-5, ^{3}J(C5,H3) = 4.6 Hz), 159.7 (CPh C-2,6, ^{1}J(C,F) = 254.2 Hz, ^{3}J(C,F) = 6.8 Hz), 183.3 (C=O). ^{13}C NMR (75 MHz, $(CD_3)_2SO$): δ 106.8 (pyraz C-4, ^{2}J(C4,H3) = 9.2 Hz), 112.1 (m, CPh C-3,5), 117.7 (t, CPh C-1, ^{2}J(C1,F2,6) = 22.6 Hz), 122.2 (NPh C-2,6), 127.0 (NPh C-4), 129.0 (NPh C-3,5), 132.1 (t, CPh C-4, ^{3}J(C4,F2,6) = 10.1 Hz), 137.1 (NPh C-1), 141.2 (pyraz C-3, ^{1}J = 189.3 Hz), 155.6 (pyraz C-5, ^{3}J(C5,H3) = 4.9 Hz), 158.7 (CPh C-2,6, ^{1}J(C,F) = 248.0 Hz, ^{3}J(C,F) = 8.1 Hz), 179.2 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −185.0 (pyraz N-1), −96.6 (pyraz N-2). ^{15}N NMR (50 MHz, $(CD_3)_2SO$): δ −181.9 (pyraz N-1), pyraz N-2 was not found. ^{19}F NMR (470 MHz, $CDCl_3$): δ −111.3 (CPh F-2,6). ^{19}F NMR (470 MHz, $(CD_3)_2SO$): δ −114.4 (CPh F-2,6). IR (KBr): ν (cm^{-1}) 1623.0 (C=O). MS (*m/z*, %): 301 (M^++1, 13), 300 (M^+, 78), 186 (85), 141 (100), 113 (22), 91 (22), 77 (63), 53 (20), 51 (31). Anal. Calcd for $C_{16}H_{10}F_2N_2O_2$: C, 64.00; H, 3.36; N, 9.33. Found: C, 63.99; H, 3.21; N, 9.49.

4.2.3. (2,6-Difluorophenyl)[5-hydroxy-1-(4-methoxybenzyl)-1H-pyrazol-4-yl]methanone (8c)

Yield 62%; brownish crystals; mp 146–148 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78 (3*H*, s, OMe), 5.11 (2*H*, s, NCH_2), 6.88 (2*H*, m, CH_2Ph H-3,5), 6.99 (m, CPh H-3,5), 7.30 (2*H*, m, CH_2Ph H-2,6), 7.41 (1*H*, m, CPh H-4), 7.43 (1*H*, t, pyraz H-3, *J*(H3,F2,6) = 1.6 = Hz), 9.50 (1*H*, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 49.8 (NCH_2, ^{1}J = 140.6 Hz, ^{3}J = 4.5 Hz), 55.2 (OMe, ^{1}J = 143.9 Hz), 105.2 (pyraz C-4, ^{2}J(C4,H3) = 10.5 Hz), 112.1 (m, CPh C-3,5), 114.1 (CH_2Ph C-3,5), 115.9 (CPh C-1, ^{2}J(C1,F2,6) = 20.0 Hz, ^{3}J(C1,H-3,5) = 4.6 Hz), 127.2 (CH_2Ph C-1), 129.5 (CH_2Ph C-2,6), 132.4 (CPh C-4, ^{1}J = 164.7 Hz, ^{3}J(C4,F2,6) = 10.1 Hz), 139.2 (pyraz C-3, ^{1}J = 190.7 Hz, *J*(C3,F2,6) = 2.7 Hz), 157.6 (pyraz C-5), 159.5 (CH_2Ph C-4), 159.6 (CPh C-2,6, ^{1}J(C,F) = 253.7 Hz, ^{3}J(C,F) = 6.8 Hz), 183.0 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −189.0 (pyraz N-1), −97.0 (pyraz N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −111.5 (CPh F-2,6). IR (KBr): ν (cm^{-1}) 1660.0 (C=O). MS (*m/z*, %): 344 (M^+, 19), 141 (19), 121 (100). Anal. Calcd for $C_{18}H_{14}F_2N_2O_3$: C, 62.79; H, 4.10; N, 8.14. Found: C, 62.70; H, 4.08; N, 8.18.

4.2.4. (2,5-Difluorophenyl)(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)methanone (9a)

Yield 55%; colorless solid; mp 168 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): 2.04 (3*H*, s, 3-Me), 7.17 (1*H*, m, CPh H-6), 7.19 (1*H*, m, CPh H-3), 7.20 (1*H*, m, CPh H-4), 7.33 (1*H*, m, NPh H-4), 7.48 (2*H*, m, NPh H-3,5), 7.84 (2*H*, m, NPh H-2,6), 6–9 (1*H*, very br s, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9 (3-Me, ^{1}J = 128.9 Hz, *J*(Me,F) = 2.6 Hz), 104.6 (pyraz C-4, ^{3}J(C4,3Me) = 2.7 Hz), 115.5 (CPh C-6, ^{2}J(C6,F5) = 25.4 Hz, ^{3}J(C6,F2) = 3.5 Hz), 117.7 (CPh C-3, ^{2}J(C3,F2) = 24.3 Hz, ^{3}J(C3,F5) = 8.3 Hz), 119.3 (CPh C-4, ^{2}J(C4,F5) = 24.1 Hz, ^{3}J(C4,F2) = 8.5 Hz), 121.0 (NPh C-2,6), 127.1 (NPh C-4), 127.8 (CPh C-1, ^{2}J(C1,F2) = 19.1 Hz, ^{3}J(C1,F5) = 7.1 Hz), 129.2 (NPh C-3,5), 136.9 (NPh C-1), 148.2 (pyraz C-3, ^{2}J(C3,3Me) = 6.8 Hz), 154.5 (CPh C-5, ^{1}J(C5,F5) = 246.3 Hz, ^{4}J(C5,F2) = 2.6 Hz), 158.5 (CPh C-2, ^{1}J(C2,F2) = 245.5 Hz, ^{4}J(C2,F5) = 2.5 Hz), 160.0 (pyraz C-5), 186.9 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −190.3 (pyraz N-1), −100.6 (pyraz N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −120.6 (CPh F-5), −117.1 (CPh F-2). IR (KBr): ν (cm^{-1}) 1628 (C=O). MS (*m/z*, %): 314 (M^+, 37), 200 (33), 141 (100), 113 (40), 91 (39), 77 (73), 67 (40), 63 (24), 51 (39). Anal. Calcd for $C_{17}H_{12}F_2N_2O_2$: C, 64.97; H, 3.85; N, 8.91. Found: C, 64.65; H, 3.75; N, 8.75.

4.2.5. (2,4-Difluorophenyl)(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)methanone (10a)

Yield 71%; colorless solid; mp 145 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.04 (3*H*, d, 3-Me, *J*(Me,F) = 1.1 Hz), 6.96 (1*H*, m, CPh H-3), 7.04 (1*H*, m, CPh H-5), 7.32 (1*H*, m, NPh H-4), 7.47 (2*H*, m, NPh H-3,5), 7.49 (1*H*, m, CPh H-6), 7.85 (2*H*, m, NPh H-2,6), 9.92 (1*H*, s, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 (3-Me, ^{1}J = 128.8 Hz, *J*(Me,F) = 2.7 Hz), 104.7 (CPh C-3, ^{1}J(C3,H3) = 167.4 Hz, ^{2}J(C3,F2) = 25.3 Hz, ^{2}J(C3,F4) = 25.3 Hz, ^{3}J(C3,H5) = 4.3 Hz, ^{4}J(C3,H6) = 1.5 Hz), 104.8 (pyraz C-4, ^{3}J(C4,3Me) = 2.8 Hz), 112.1 (CPh C-5, ^{1}J(C5,H5) = 167.5 Hz, ^{2}J(C5,F4) = 21.7 Hz, ^{3}J(C5,H3) = 3.8 Hz, ^{4}J(C5,F2) = 3.7 Hz), 121.0 (NPh C-2,6), 123.2 (CPh C-1, ^{2}J(C1,F2) = 16.1 Hz, ^{3}J(C1,H3) = 4.2 Hz, ^{3}J(C1,H5) = 7.3 Hz, ^{4}J(C1,F4) = 3.9 Hz), 126.9 (NPh C-4), 129.1 (NPh C-3,5), 130.6 (CPh C-6, ^{1}J(C6,H6) = 165.5 Hz, ^{3}J(C6,F2) = 4.6 Hz, ^{3}J(C6,F4) = 10.0 Hz), 137.0

(NPh C-1), 148.2 (pyraz C-3, ^2J(C3,3Me) = 6.9 Hz), 159.6 (CPh C-2*, ^1J(C2,F2) = 253.7 Hz, ^3J(C2,F4) = 12.4 Hz), 160.2 (pyraz C-5), 164.6 (CPh C-4*, ^1J(C4,F4) = 254.5 Hz, ^3J(C4,F2) = 11.6 Hz), 187.1 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −190.5 (pyraz N-1), −100.7 (pyraz N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −109.9 (CPh F-2), −104.0 (CPh F-4). IR (KBr): ν (cm^{-1}) 1637 (C=O). MS (*m/z*, %): 314 (M^+, 26), 200 (55), 141 (100), 113 (32), 91 (41), 67 (26), 51 (37). Anal. Calcd for $C_{17}H_{12}F_2N_2O_2$: C, 64.97; H, 3.85; N, 8.91. Found: C, 64.80; H, 3.89; N, 8.77.

4.2.6. (2,3-Difluorophenyl)(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)methanone (**11a**)

Yield 56%; colorless solid; mp 110 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.01 (3*H*, d, 3-Me, *J*(Me,F) = 0.9 Hz), 7.22 (1*H*, m, CPh H-6), 7.24 (1*H*, m, CPh H-5), 7.33 (1*H*, m, NPh H-4), 7.36 (1*H*, m, CPh H-4), 7.48 (2*H*, m, NPh H-3,5), 7.84 (2*H*, m, NPh H-2,6), 10.50 (1*H*, br s, OH). ^{1}H NMR (300 MHz, $(CD_3)_2SO$): δ 2.37 (3*H*, s, 3-Me), 7.24 (1*H*, m, CPh H-6), 7.25 (1*H*, m, CPh H-5), 7.28 (1*H*, m, NPh H-4), 7.46 (2*H*, m, NPh H-3,5), 7.52 (1*H*, m, CPh H-4), 7.61 (2*H*, m, NPh H-2,6), 6-10 (1*H*, br s, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9 (3-Me, ^1J = 128.9 Hz, *J*(Me,F) = 2.0 Hz), 104.6 (pyraz C-4, ^3J(C4,3Me) = 2.7 Hz), 119.7 (CPh C-4, ^2J(C4,F3) = 17.3 Hz), 121.0 (NPh C-2,6), 123.6 (CPh C-6, *J*(C6,F) = 3.9 and 1.7 Hz), 124.9 (CPh C-5, *J*(C5,F) = 6.5 and 4.6 Hz), 127.1 (NPh C-4), 128.8 (CPh C-1, ^2J(C1,F2) = 12.9 Hz), 129.2 (NPh C-3,5), 136.9 (NPh C-1), 147.1 (CPh C-2, ^1J(C2,F2) = 253.0 Hz, ^2J(C2,F3) = 14.0 Hz), 148.2 (pyraz C-3, ^2J(C3,3Me) = 7.0 Hz), 150.4 (CPh C-3, ^1J(C3,F3) = 251.1 Hz, ^2J(C3,F2) = 12.5 Hz), 159.9 (pyraz C-5), 187.0 (C=O, ^3J(CO,F2) = 2.7 Hz). ^{13}C NMR (75 MHz, $(CD_3)_2SO$): δ 13.8 (3-Me, ^1J = 129.9 Hz), 104.6 (pyraz C-4, ^3J(C4,3Me) = 2.4 Hz), 118.7 (CPh C-4, ^2J(C4,F3) = 17.1 Hz), 121.1 (NPh C-2,6), 124.4 (CPh C-6), 124.7 (CPh C-5, *J*(C5,F) = 6.7 and 4.3 Hz), 126.2 (NPh C-4), 129.0 (NPh C-3,5), 131.2 (CPh C-1, ^2J(C1,F2) = 12.9 Hz), 136.2 (NPh C-1), 147.0 (CPh C-2, ^1J(C2,F2) = 249.0 Hz, ^2J(C2,F3) = 13.4 Hz), 149.3 (CPh C-3, ^1J(C3,F3) = 245.7 Hz, ^2J(C3,F2) = 13.1 Hz), 150.6 (pyraz C-3), 158.4 (pyraz C-5), 183.7 (C=O, ^3J(CO,F2) = 2.5 Hz) ^{15}N NMR (50 MHz, $CDCl_3$): δ −190.1 (pyraz N-1), −100.5 (pyraz N-2). ^{15}N NMR (50 MHz, $(CD_3)_2SO$): δ pyraz N-1 not found, −93.3 (pyraz N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −139.8 (m, CPh F-2), −136.1 (m, CPh F-3), ^3J(F2,F3) = 21.6 Hz. ^{19}F NMR (470 MHz, $(CD_3)_2SO$): δ −142.3 (m, CPh F-3*), −139.3 (m, CPh F-2*), ^3J(F2,F3) = 22.6 Hz. IR (KBr): ν (cm^{-1}) 1628 (C=O). MS (*m/z*, %): 315 (M^++1, 18), 314 (M^+, 83), 295 (25), 200 (40), 141 (100), 113 (49), 91 (65), 77 (92), 69 (45), 67 (80), 63 (33), 51 (58). Anal. Calcd for $C_{17}H_{12}F_2N_2O_2$: C, 64.97; H, 3.85; N, 8.91. Found: C, 64.67; H, 3.60; N, 8.84.

4.2.7. (5-Hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)(2,3,6-trifluorophenyl)methanone (**12a**)

Yield 71%; colorless solid; mp 157–158 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.00 (3*H*, s, 3-Me), 7.00 (1*H*, m, CPh H-5, ^3J(H5,H4) = 9.3 Hz, ^3J(H5,F6) = 7.9 Hz, ^4J(H5,F3) = 3.4 Hz, ^5J(H5,F2) = 2.0 Hz), 7.31 (1*H*, m, CPh H-4, ^3J(H4,F3) = 9.4 Hz, ^3J(H4,H5) = 9.3 Hz, ^4J(H4,F2) = 8.6 Hz, ^4J(H4,F6) = 5.0 Hz), 7.34 (1*H*, m, NPh H-4), 7.49 (2*H*, m, NPh H-3,5), 7.83 (2*H*, m, NPh H-2,6), 9.57 (1*H*, br s, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.3 (3-Me, ^1J = 129.0 Hz), 105.3 (pyraz C-4, ^3J(C4,3Me) = 2.7 Hz), 111.8 (CPh C-5, ^2J(C5,F6) = 23.8 Hz, ^3J(C5,F3) = 6.1 Hz*, ^4J(C5,F2) = 4.2 Hz*), 118.0 (CPh C-1, ^2J(C1,F) = 23.9 and 17.8 Hz), 119.1 (CPh C-4), 121.2 (NPh C-2,6), 127.3 (NPh C-4), 129.2 (NPh C-3,5), 136.7 (NPh C-1), 146.9 (CPh C-2, ^1J(C2,F2) = 254.5 Hz, ^2J(C2,F3) = 15.7 Hz, ^3J(C2,F6) = 8.1 Hz), 147.1 (CPh C-3, ^1J(C3,F3) = 248.3 Hz, ^2J(C3,F2) = 12.5 Hz, ^4J(C3,F6) = 4.0 Hz), 148.1 (pyraz C-3, ^2J(C3,3Me) = 6.9 Hz), 154.1 (CPh C-6, ^1J(C6,F6) = 248.7 Hz), 159.5 (pyraz C-5), 182.4 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −190.0 (pyraz N-1), −100.3 (pyraz N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −140.4 (m, CPh F-3, ^3J(F3,F2) = 21.7 Hz, ^5J(F3,F6) = 15.5 Hz, ^3J(F3,H4) = 9.4 Hz, ^4J(F3,H5) = 3.4 Hz), −136.0 (m, CPh F-2, ^3J(F2,F3) = 21.7 Hz, ^4J(F2,H4) = 8.6 Hz, ^5J(F2,H5) = 1.8 Hz), −118.3 (m, CPh F-6, ^5J(F6;F3) = 15.5 Hz, ^3J(F6,H5) = 7.9 Hz, ^4J(F6,H4) = 5.0 Hz). IR (KBr): ν (cm^{-1}) 1635 (C=O). MS (*m/z*, %): 333 (M^++1, 19), 332 (M^+, 100), 313 (33), 201 (19), 200 (57), 159 (49), 91 (47), 77 (59), 67 (26). Anal. Calcd for $C_{17}H_{11}F_3N_2O_2 \cdot 0.2\ H_2O$: C, 60.79; H, 3.42; N, 8.34. Found: C, 60.74; H, 3.19; N, 8.34.

4.2.8. (5-Hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)(2,4,6-trifluorophenyl)methanone (**13a**)

Yield 71%; colorless solid; mp 160 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.01 (3*H*, s, 3-Me), 6.80 (2*H*, m, CPh H-3,5, ^3J(H3,F2) = 7.5 Hz, ^3J(H3,F4) = 8.5 Hz), 7.32 (1*H*, m, NPh H-4), 7.47 (2*H*, m, NPh H-3,5), 7.82 (2*H*, m, NPh H-2,6), 10.05 (1*H*, br s, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.3 (3-Me, ^1J = 128.7 Hz), 101.1 (CPh C-3,5, ^2J(C,F) = 26.0 Hz, ^4J(C,F) = 3.8 Hz), 105.5 (pyraz C-4, ^3J(C4,3Me) = 2.7 Hz), 113.2 (CPh C-1, ^2J(C1,F2,6) = 22.1 Hz, ^4J(C1,F4) = 4.4 Hz), 121.1 (NPh C-2,6), 127.2 (NPh C-4), 129.2 (NPh C-3,5), 136.8 (NPh C-1), 148.1 (pyraz C-3, ^2J(C3,3Me) = 6.9 Hz), 159.6 (pyraz C-5), 159.7 (CPh C-2,6 ^1J(C,F) = 253.1 Hz, ^3J(C,F) = 14.9 and 10.0 Hz), 163.9 (CPh C-4, ^1J(C4,F4) = 254.2 Hz, ^3J(C4,F2,6) = 14.9 Hz), 182.6 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −190.2 (pyraz N-1), −100.5 (pyraz N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −109.7 (m, CPh F-2,6, ^3J(F2,H3) = 7.5 Hz, ^4J(F2/6,F4) = 7.5 Hz,), −102.8 (m, CPh F-4, ^3J(F4,H3/5) = 8.5 Hz, ^4J(F4,F2/6) = 7.5 Hz). IR (KBr): ν (cm^{-1}) 1640 (C=O). MS (*m/z*, %): 333 (M^++1, 11), 332 (M^+, 56), 201 (16), 200 (99), 159 (100), 132 (47), 131 (27), 91 (78), 77 (63), 67 (32), 51 (41). Anal. Calcd for $C_{17}H_{11}F_3N_2O_2 \cdot 0.1\ H_2O$: C, 61.12; H, 3.38; N, 8.39. Found: C, 60.96; H, 3.12; N, 8.46.

4.2.9. (2-Chlorophenyl)[1-(4-fluorophenyl)-5-hydroxy-3-methyl-1H-pyrazol-4-yl]methanone (**21d**)

Yield 60%; colorless solid; mp 122–124 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.84 (3*H*, s, 3-Me), 7.16 (2*H*, m, NPh H-3,5), 7.36 (1*H*, m, CPh H-6), 7.41 (1*H*, m, CPh H-5), 7.46 (1*H*, m, CPh H-4), 7.49 (1*H*, m, CPh H-3), 7.83 (2*H*, m, NPh H-2,6), 8.78 (1*H*, br s, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.7 (3-Me, ^1J = 129.0 Hz), 104.4 (pyraz C-4, ^3J(C4,3Me) = 2.7 Hz), 116.0 (NPh C-3,5, ^2J(C,F4) = 23.0 Hz), 122.7 (NPh C-2,6, ^3J(C,F4) = 8.4 Hz), 127.1 (CPh C-5), 127.8 (CPh C-6), 130.0 (CPh C-3), 130.4 (CPh C-2), 131.4 (CPh C-4), 133.2 (NPh C-1, ^4J(C1,F4) = 3.0 Hz), 137.6 (CPh C-1), 148.6 (pyraz C-3, ^2J(C3,3Me) = 6.9 Hz), 159.9 (pyraz C-5), 161.1 (NPh C-4, ^1J(C4,F4) = 247.2 Hz), 190.5 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −192.1 (pyraz N-1), −101.1 (pyraz N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −114.6 (F-4, ^3J(F4,H3,5) = 8.2 Hz, ^4J(F4,H2,6) = 4.8 Hz). IR (KBr): ν (cm^{-1}) 1624 (C=O). MS (*m/z*, %): 330/332 (M^+, 45/16), 296 (20), 295 (M^+−Cl, 100), 218 (32), 139/141 (2-chlorobenzoyl, 70/27), 95 (FC_6H_4, 64), 82 (48), 75 (65), 66 (78). Anal. Calcd for $C_{17}H_{12}ClFN_2O_2$: C, 61.73; H, 3.66; N, 8.47. Found: C, 61.71; H, 3.47; N, 8.46.

4.2.10. (2-Chlorophenyl)[1-(4-chlorophenyl)-5-hydroxy-3-methyl-1H-pyrazol-4-yl]methanone (**21e**)

ield 88%; colorless solid; mp 141–142 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.84 (3*H*, s, 3-Me), 7.36 (1*H*, m, CPh H-6), 7.41 (1*H*, m, CPh H-5), 7.43 (2*H*, m, NPh H-3,5), 7.46 (1*H*, m, CPh H-4), 7.50 (1*H*, m, CPh H-3), 7.83 (2*H*, m, NPh H-2,6), 9.22 (1*H*, br s, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8 (3-Me, ^1J = 129.0 Hz), 104.6 (pyraz C-4, ^3J(C4,3Me) = 2.7 Hz), 121.8 (NPh C-2,6), 127.1 (CPh C-5), 127.9 (CPh C-6), 129.3 (NPh C-3,5), 130.1 (CPh C-3), 130.5 (CPh C-2), 131.4 (CPh C-4), 132.3 (NPh C-4), 135.7 (NPh C-1), 137.3 (CPh C-1), 148.7 (pyraz C-3, ^2J(C3,3Me) = 6.9 Hz), 160.4 (pyraz C-5), 190.2 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −192.1 (pyraz N-1), −101.3 (pyraz N-2). IR (KBr): ν (cm^{-1}) 1625 (C=O). MS (*m/z*, %): 346/348/350 (M^+, 28/20/3), 311/313 (M^+−Cl, 100/35), 139/141 (2-chlorobenzoyl, 77/29), 111/113 (ClC_6H_4, 64/25). Anal. Calcd for

$C_{17}H_{12}Cl_2N_2O_2$: C, 58.81; H, 3.48; N, 8.07. Found: C, 58.80; H, 3.34; N, 8.01.

4.2.11. (3-Chloro-6-fluoro-1-benzothiophen-2-yl)(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)methanone (24)

Yield 53%; brownish solid; mp 199 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.13 (3*H*, s, 3-Me), 7.30 (1*H*, dt, BTh H-5, ^3J(H5,H4) = 8.9 Hz, ^3J(H5,F6) = 8.8 Hz, ^4J(H5,H7) = 2.1 Hz), 7.34 (1*H*, m, NPh H-4), 7.49 (2*H*, m, NPh H-3,5), 7.58 (1*H*, dd, BTh H-7, ^3J(H7,F6) = 8.3 Hz, ^4J(H7,H5) = 2.1 Hz), 7.87 (2*H*, m, NPh H-2,6), 7.90 (1*H*, dd, BTh H-4, ^3J(H4,H5) = 8.9 Hz, ^4J(H4,F6) = 5.0 Hz), 9.49 (1*H*, br s, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9 (3-Me, ^1J = 129.0 Hz), 105.4 (pyraz C-4, ^3J(C4,3Me) = 2.7 Hz), 109.1 (BTh C-7, ^2J(C7,F6) = 26.0 Hz), 115.5 (BTh C-5, ^2J(C5,F6) = 24.9 Hz), 120.8 (BTh C-3, ^3J(C3,H4) = .7 Hz), 121.0 (NPh C-2,6), 124.6 (BTh C-4, ^3J(C4,F6) = 9.5 Hz), 127.1 (NPh C-4), 129.2 (NPh C-3,5), 131.8 (BTh C-2, ^5J(C2,F6) = 3.8 Hz), 132.8 (BTh C-3a), 136.9 (NPh C-1), 138.9 (BTh C-7a, ^3J(C7a,F6) = 10.6 Hz), 148.5 (pyraz C-3, ^2J(C3,3Me) = 6.9 Hz), 159.9 (pyraz C-5), 162.1 (BTh C-6, ^1J(C6,F6) = 249.5 Hz), 183.6 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −189.9 (pyraz N-1), −100.2 (pyraz N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −112.2 (F-6, ddd, ^3J(F6,H5) = 8.8 Hz, ^3J(F6,H7) = 8.3 Hz, ^4J(F6,H4) = 5.0 Hz). IR (KBr): ν (cm^{-1}) 1635 (C=O). MS (*m/z*, %): 386/388 (M^+, 8/3), 351 (100), 352 (23), 200 (53), 91 (36), 67 (27), 51 (22). Anal. Calcd for $C_{19}H_{12}ClFN_2O_2S$: C, 58.99; H, 3.13; N, 7.24. Found: C, 58.81; H, 3.05; N, 7.13.

4.3. General procedure for the synthesis of anellated systems 17–19, 22 and 25

Method a. Under anhydrous conditions, to a solution of the corresponding 4-aroyl pyrazol-5-ol (**8**–**13**, **21**, **24**) (1 mmol) in anhydrous DMF (5 mL) was added NaH (60% in mineral oil; 40 mg, 1 mmol). The reaction mixture was stirred at 150 °C overnight and then the solvent was removed under reduced pressure. Water (5 mL) was added to the residue and stirring was continued for 1 h further. The precipitate formed was filtered off, washed with H_2O and petroleum ether and recrystallized from the solvent given below.

Method b. Under anhydrous conditions, to the corresponding 4-aroylpyrazol-5-ol (1 mmol) in dry acetonitrile (5 mL) was added K_2CO_3 (276 mg, 2 mmol) and the mixture was heated at reflux overnight. Then the solvent was removed under reduced pressure, H_2O (5 mL) was added and the mixture was stirred for 1 h. The precipitate was filtered off, washed with H_2O and recrystallized from the solvent given below.

4.3.1. 5-Fluoro-3-methyl-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (14a)

Yield 83% (method a); colorless solid; mp 167–169 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.67 (3*H*, s, 3-Me), 7.10 (1*H*, ddd, H-6, ^3J(H6,F5) = 10.7 Hz, ^3J(H6,H7) = 8.2 Hz, ^4J(H6,H8) = 1.1 Hz), 7.33 (1*H*, dt, H-8, ^3J(H8,H7) = 8.5 Hz, ^4J(H8,H6) = 1.1 Hz, ^5J(H8;F5) = 1.2 Hz), 7.40 (1*H*, m, NPh H-4), 7.45 (2*H*, m, NPh H-3,5), 7.62 (1*H*, d′t′, H-7, ^3J(H7,H8) = 8.5 Hz, ^3J(H7,H6) = 8.2 Hz, ^4J(H7,F5) = 5.4 Hz), 7.85 (2*H*, m, NPh H-2,6). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 (3-Me, ^1J = 129.4 Hz), 105.4 (C-3a, ^3J(C3a,3Me) = 2.7 Hz), 113.0 (C-6, ^2J(C6,F5) = 21.4 Hz), 113.6 (C8, ^4J(C8,F5) = 4.3 Hz), 113.8 (C4a, ^2J(C4a,F5) = 9.7 Hz), 121.3 (NPh C-2,6), 127.5 (NPh C-4), 129.4 (NPh C-3,5), 133.6 (C-7, ^3J(C7,F5) = 11.1 Hz), 136.9 (NPh C-1), 148.4 (C-3, ^2J(C3,3-Me) = 7.2 Hz), 152.1 (C-9a), 155.7 (C-8a, ^3J(C8a,F5) = 3.8 Hz), 162.2 (C5, ^1J(C5,F5) = 265.6 Hz), 172.1 (C-4). ^{15}N NMR (50 MHz, $CDCl_3$): δ −193.6 (N-1), −95.5 (N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −110.6 (F-5, ^3J(F5,H6) = 10.7 Hz, ^4J(F5,H7) = 5.4 Hz, ^5J(F5,H8) = 1.2 Hz). IR (KBr): ν (cm^{-1}) 1672 (C=O). MS (*m/z*, %): 295 (M^++1, 16), 294 (M^+, 100), 293 (M^+−1, 60), 91 (35), 77 (74), 51 (40). Anal. Calcd for $C_{17}H_{11}FN_2O_2 \cdot 0.8\ H_2O$: C, 66.14; H, 4.11; N, 9.07. Found: C, 66.00; H, 3.81; N, 9.00.

4.3.2. 5-Fluoro-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (14b)

Yield 64% (method a); colorless solid; mp 203–206 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.12 (1*H*, ddd, H-6, ^3J(H6,F5) = 10.7 Hz, ^3J(H6,H7) = 8.2 Hz, ^4J(H6,H8) = 1.0 Hz), 7.37 (1*H*, d′t′, H-8, ^3J(H8,H7) = 8.6 Hz, ^4J(H8,H6) = 1.0 Hz, ^5J(H8,F5) = 1.3 Hz), 7.43 (1*H*, m, NPh H-4), 7.56 (2*H*, m, NPh H-3,5), 7.65 (1*H*, d′t′, H-7, ^3J(H7,H8) = 8.6 Hz, ^3J(H7,H6) = 8.2 Hz, ^4J(H7,F5) = 5.4 Hz), 7.88 (2*H*, m, NPh H-2,6), 8.22 (1*H*, s, H-3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 107.3 (C-3a, ^2J(C3a,H3) = 10.0 Hz), 113.1 (C-6, ^2J(C6,F5) = 21.4 Hz), 113.5 (C4a, ^2J(C4a,F5) = 10.0 Hz), 113.7 (C8, ^4J(C8,F5) = 4.5 Hz), 121.4 (NPh C-2,6), 127.9 (NPh C-4), 129.5 (NPh C-3,5), 133.9 (C-7, ^3J(C7,F5) = 11.1 Hz), 136.8 (C-3, ^1J(C3,H3) = 195.0 Hz), 136.9 (NPh C-1), 152.0 (C-9a, ^3J(C9a,H3) = 4.8 Hz), 155.6 (C-8a, ^3J(C8a,F5) = 3.9 Hz), 162.2 (C5, ^1J(C5,F5) = 266.1 Hz), 171.1 (C-4). ^{15}N NMR (50 MHz, $CDCl_3$): δ −187.4 (N-1), −88.5 (N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −110.0 (F-5, ^3J(F5,H6) = 10.7 Hz, ^4J(F5,H7) = 5.4 Hz, ^5J(F5,H8) = 1.3 Hz). IR (KBr): ν (cm^{-1}) 1672 (C=O). MS (*m/z*, %): 280 (M^+, 41), 142 (31), 139 (100), 110 (20), 94 (21), 77 (94), 51 (50). Anal. Calcd for $C_{16}H_9FN_2O_2$: C, 68.57; H, 3.24; N, 10.00. Found: C, 68.29; H, 3.08; N, 9.94.

4.3.3. 5-Fluoro-1-(4-methoxybenzyl)chromeno[2,3-c]pyrazol-4(1H)-one (14c)

Yield 54% (method a); beige solid; mp 168–171 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78 (3*H*, s, OMe), 5.35 (2*H*, s, NCH_2), 6.88 (2*H*, m, Ph H-3,5), 7.08 (1*H*, ddd, H-6, ^3J(H6,F5) = 10.8 Hz, ^3J(H6,H7) = 8.2 Hz, ^4J(H6,H8) = 1.0 Hz), 7.29 (2*H*, m, Ph H-2,6), 7.31 (1*H*, d′t′, H-8, ^3J(H8,H7) = 8.5 Hz, ^4J(H8,H6) = 1.0 Hz, ^5J(H8,F5) = 1.2 Hz), 7.61 (1*H*, d′t′, H-7, ^3J(H7,H8) = 8.5 Hz, ^3J(H7,H6) = 8.2 Hz, ^4J(H7,F5) = 5.4 Hz), 8.04 (1*H*, s, H-3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 51.1 (NCH_2, ^1J = 140.9 Hz, ^3J(NCH_2,Ph H-2,6) = 4.5 Hz), 55.3 (OMe, ^1J = 144.0 Hz), 106.1 (C-3a, ^2J(C3a,H3) = 10.2 Hz), 112.8 (C-6, ^2J(C6,F5) = 21.6 Hz), 113.5 (C4a, ^2J(C4a,F5) = 9.7 Hz), 113.5 (C8, ^4J(C8,F5) = 4.3 Hz), 114.3 (Ph C-3,5), 126.8 (Ph C-1), 129.4 (Ph C-2,6), 133.7 (C-7, ^3J(C7,F5) = 11.1 Hz), 135.9 (C-3, ^1J(C3,H3) = 194.2 Hz), 152.4 (C-9a, ^3J(C9a,H3) = 5.0 Hz, ^3J(C9a,NCH_2) = 2.5 Hz), 155.5 (C-8a, ^3J(C8a,F5) = 3.8 Hz), 162.3 (C5, ^1J(C5,F5) = 265.5 Hz), 159.7 (Ph C-4), 171.1 (C-4). ^{15}N NMR (50 MHz, $CDCl_3$): δ −192.6 (N-1), −87.5 (N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −110.2 (F-5, ^3J(F5,H6) = 10.8 Hz, ^4J(F5,H7) = 5.4 Hz, ^5J(F5,H8) = 1.2 Hz). IR (KBr): ν (cm^{-1}) 1660 (C=O). MS (*m/z*, %): 324 (M^+, 23), 121 (100). Anal. Calcd for $C_{18}H_{13}FN_2O_3 \cdot 0.4\ H_2O$: C, 65.21; H, 4.20; N, 8.45. Found: C, 65.07; H, 3.93; N, 8.30.

4.3.4. 6-Fluoro-3-methyl-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (15a)

Yield 80% (method a); colorless solid; mp 163–169 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.69 (3*H*, s, 3-Me), 7.40 (3*H*, m, H-7 and Ph H-4), 7.52 (1*H*, dd, H-8, ^3J(H8,H7) = 5.0 Hz, ^4J(H8,F6) = 4.1 Hz), 7.55 (2*H*, m, Ph H-3,5), 7.86 (2*H*, m, Ph H-2,6), 7.99 (1*H*, dd, H-5, ^3J(H5,F6) = 8.3 Hz, ^4J(H5,H7) = 3.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 (3-Me, ^1J = 129.3 Hz), 104.6 (C-3a, ^3J(C3a,3Me) = 2.7 Hz), 112.2 (C-5, ^2J(C5,F6) = 24.2 Hz), 119.4 (C-8, ^3J(C8,F6) = 7.8 Hz), 121.4 (Ph C-2,6), 121.4 (C-7, ^2J(C7,F6) = 25.4 Hz), 124.9 (C-4a, ^3J(C4a,F6) = 6.8 Hz), 127.5 (Ph C-4), 129.4 (Ph C-3,5), 136.9 (Ph C-1), 148.1 (C-3, ^2J(C3,3-Me) = 7.1 Hz), 150.5 (C8a, ^4J(C8a,F6) = 2.1 Hz), 153.1 (C-9a), 159.6 (C-6, ^1J(C6,F6) = 246.6 Hz), 172.5 (C-4, ^4J(C4,F6) = 1.9 Hz). ^{15}N NMR (50 MHz, $CDCl_3$): δ −193.0 (N-1), −94.8 (N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −115.4 (F-6, ^3J(F6,H5) = 8.3 Hz, ^3J(F6,H7) = 7.3 Hz, ^4J(F6,H8) = 4.1 Hz). IR (KBr): ν (cm^{-1}) 1662 (C=O). MS (*m/z*, %): 295 (M^++1, 16), 294 (M^+, 100), 293 (M^+−1, 77), 91 (20), 77 (57), 51 (30). Anal. Calcd for $C_{17}H_{11}FN_2O_2$: C, 69.38; H, 3.77; N, 9.52. Found: C, 69.48; H, 3.85; N, 9.32.

*4.3.5. 7-Fluoro-3-methyl-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (**16a**)*

Yield 90% (method a); colorless solid; mp 165–169 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.69 (3*H*, s, 3-Me), 7.17 (1*H*, ddd, H-6, ^3J(H6,H5) = 8.8 Hz, ^3J(H6,F7) = 7.9 Hz, ^4J(H6,H8) = 2.4 Hz), 7.23 (1*H*, dd, H-8, ^3J(H8,F7) = 8.9 Hz, ^4J(H8,H6) = 2.4 Hz), 7.40 (1*H*, m, Ph H-4), 7.55 (2*H*, m, Ph H-3,5), 7.85 (2*H*, m, Ph H-2,6), 8.36 (1*H*, dd, H-5, ^3J(H5,H6) = 8.8 Hz, ^4J(H5,F7) = 6.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 (3-Me, ^1J = 129.3 Hz), 104.8 (C-8, ^1J(C8,H8) = 167.0 Hz, ^2J(C8,F7) = 26.2 Hz, ^3J(C8,H6) = 4.1 Hz, ^4J(C8,H5) = 1.4 Hz), 104.9 (C-3a, ^3J(C3a,3Me) = 2.7 Hz), 113.6 (C-6, ^1J(C6,H6) = 167.5 Hz, ^2J(C6,F7) = 22.1 Hz, ^3J(C6,H8) = 4.3 Hz), 120.2 (C-4a, ^4J(C4a,F7) = 2.7 Hz), 121.4 (Ph C-2,6), 127.6 (Ph C-4), 129.1 (C-5, ^1J(C5,H5) = 167.7 Hz, ^3J(C5,F7) = 10.6 Hz), 129.5 (Ph C-3,5), 136.9 (Ph C-1), 148.2 (C-3, ^2J(C3,3-Me) = 7.2 Hz), 153.0 (C-9a), 155.5 (C-8a, ^2J(C8a,H8) = 5.0 Hz, ^3J(C8a,F7) = 13.0 Hz, ^3J(C8a,H5) = 10.7 Hz, ^4J(C8a,H6) = 1.6 Hz), 165.6 (C-7, ^1J(C7,F7) = 255.3 Hz), 172.6 (C-4). ^{15}N NMR (50 MHz, $CDCl_3$): δ −192.8 (N-1), −95.4 (N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −102.8 (F-7, ^3J(F7,H6) = 7.9 Hz, ^3J(F7,H8) = 8.9 Hz, ^4J(F7,H5) = 6.3 Hz). IR (KBr): ν (cm^{-1}) 1660 (C=O). MS (*m/z*, %): 295 (M^++1, 18), 294 (M^+, 100), 293 (M^+−1, 79), 91 (19), 77 (55), 51 (29). Anal. Calcd for $C_{17}H_{11}FN_2O_2$: C, 69.38; H, 3.77; N, 9.52. Found: C, 69.44; H, 3.89; N, 9.45.

*4.3.6. 8-Fluoro-3-methyl-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (**17a**)*

Yield 64% (method a); colorless solid; mp 165–170 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.69 (3*H*, s, 3-Me), 7.37 (3*H*, m, Ph H-4 and H-6, ^3J(H6,H5) = 8.1 Hz, ^3J(H6,H7) = 8.1 Hz, ^4J(H6,F8) = 4.5 Hz), 7.48 (1*H*, ddd, H-7, ^3J(H7,H6) = 8.1 Hz, ^3J(H7,F8) = 10.2 Hz, ^4J(H7,H5) = 1.5 Hz), 7.54 (2*H*, m, Ph H-3,5), 7.92 (2*H*, m, Ph H-2,6), 8.09 (1*H*, d′t′, H-5, ^3J(H5,H6) = 8.1 Hz, ^4J(H5,H7) = 1.5 Hz, ^5J(H5,F8) = 1.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 (3-Me, ^1J = 129.3 Hz), 105.0 (C-3a, ^3J(C3a,3Me) = 2.7 Hz), 119.9 (C-7, ^1J(C7,H7) = 165.2 Hz, ^2J(C7,F8) = 16.8 Hz, ^2J(C7,H6) = 0.9 Hz, ^3J(C7,H5) = 9.5 Hz), 120.7 (Ph C-2,6), 121.7 (C-5, ^1J(C5,H5) = 167.5 Hz, ^2J(C5,H6) = 1.3 Hz, ^3J(C5,H7) = 8.5 Hz, ^4J(C5,F8) = 3.8 Hz), 124.8 (C-6, ^1J(C6,H6) = 166.3 Hz, ^2J(C6,H5) = 1.1 Hz, ^2J(C6,H7) = 1.7 Hz, ^3J(C6,F8) = 6.5 Hz), 125.5 (C-4a, ^3J(C4a,H6) = 8.7, ^3J(C4a,F8) = 0.6 Hz), 127.4 (Ph C-4), 129.5 (Ph C-3,5), 136.9 (Ph C-1), 143.0 (C8a, ^2J(C8a,F8) = 11.8 Hz, ^3J(C8a,H5) = 7.5 Hz, ^3J(C8a,H7) = 9.6 Hz, ^4J(C8a,H6) = 1.7 Hz), 148.2 (C-3, ^2J(C3,3-Me) = 7.2 Hz), 150.9 (C-8, ^1J(C8,F8) = 252.7 Hz), 152.2 (C-9a, ^4J(C9a,F8) = 1,1 Hz), 172.5 (C-4, ^3J(C4,H5) = 3.7 Hz, ^4J(C4,F8) = 2.6 Hz). ^{15}N NMR (50 MHz, $CDCl_3$): δ −192.3 (N-1), −95.4 (N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −133.6 (F-8, ^3J(F8,H7) = 10.2 Hz, ^4J(F8,H6) = 4.5 Hz, ^5J(F8,H5) = 1.3 Hz). IR (KBr): ν (cm^{-1}) 1667 (C=O). MS (*m/z*, %): 295 (M^++1, 18), 294 (M^+, 100), 293 (M^+−1, 80), 91 (37), 77 (94), 51 (60). Anal. Calcd for $C_{17}H_{11}FN_2O_2{\cdot}0.1\,H_2O$: C, 68.96; H, 3.81; N, 9.46. Found: C, 68.99; H, 3.59; N, 9.36.

*4.3.7. 5,8-Difluoro-3-methyl-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (**18a**)*

Yield 87% (method a); colorless solid; mp 155–157 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.67 (3*H*, s, 3-Me), 7.06 (1*H*, ddd, H-6, ^3J(H6,F5) = 10.2 Hz, ^3J(H6,H7) = 9.1 Hz, ^4J(H6,F8) = 3.7 Hz), 7.39 (1*H*, m, Ph H-4), 7.45 (1*H*, ddd, H-7, ^3J(H7,H6) = 9.1 Hz, ^3J(H7,F8) = 9.5 Hz, ^4J(H7,F5) = 4.3 Hz), 7.54 (2*H*, m, Ph H-3,5), 7.90 (2*H*, m, Ph H-2,6). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 (3-Me, ^1J = 129.5 Hz), 105.4 (C-3a, ^3J(C3a,3Me) = 2.8 Hz), 112.1 (C-6, ^1J(C6,H6) = 168.2 Hz, ^2J(C6,F5) = 23.9 Hz, ^2J(C6,H7) = 0.8 Hz, ^3J(C6,F8) = 6.1 Hz), 114.9 (C-4a, ^2J(C4a,F5) = 11.3 Hz, ^3J(C4a,F8) = 1.2 Hz, ^3J(C4a,H6) = 5.3 Hz), 119.8 (C-7, ^1J(C7,H7) = 167.1 Hz, ^2J(C7,F8) = 19.0 Hz, ^3J(C7,F5) = 10.3 Hz), 120.7 (Ph C-2,6), 127.5 (Ph C-4), 129.5 (Ph C-3,5), 136.8 (Ph C-1), 143.7 (C8a, ^2J(C8a,F8) = 13.0 Hz, ^3J(C8a,F5) = 4.3 Hz, ^3J(C8a,H7) = 8.6 Hz, ^4J(C8a,H6) = 1.6 Hz), 147.2 (C-8, ^1J(C8,F8) = 249.4 Hz, ^2J(C8,H7) = 5.9 Hz, ^3J(C8,H6) = 11.2 Hz, ^4J(C8,F5) = 4.3 Hz), 148.4 (C-3, ^2J(C3,3-Me) = 7.2 Hz), 151.5 (C-9a), 157.3 (C-5, ^1J(C5,F5) = 262.4 Hz, ^2J(C5,H6) = 5.3 Hz, ^3J(C5,H7) = 11.8 Hz, ^4J(C5,F8) = 3.1 Hz), 171.2 (C-4). ^{15}N NMR (50 MHz, $CDCl_3$): δ −192.7 (N-1), −94.9 (N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −136.7 (F-8, ^3J(F8,H7) = 9.5 Hz, ^4J(F8,H6) = 3.7 Hz, ^5J(F8,F5) = 17.7 Hz), −115.9 (F-5, ^3J(F5,H6) = 10.2 Hz, ^4J(F5,H7) = 4.3 Hz, ^5J(F5,F8) = 17.7 Hz). IR (KBr): ν (cm^{-1}) 1679 (C=O). MS (*m/z*, %): 313 (M^++1, 12), 312 (M^+, 68), 311 (M^+−1, 41), 155 (37), 91 (40), 77 (100), 51 (54). Anal. Calcd for $C_{17}H_{10}F_2N_2O_2$: C, 65.39; H, 3.23; N, 8.97. Found: C, 65.01; H, 3.27; N, 8.92.

*4.3.8. Cyclization of **13a***

*4.3.8.1. 5,7-Difluoro-3-methyl-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (**19a**).* Yield 81% (method b); colorless solid; mp 178–180 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.66 (3*H*, s, 3-Me), 6.88 (1*H*, ddd, H-6, ^3J(H6,F5) = 10.8 Hz, ^3J(H6,F7) = 8.7 Hz, ^4J(H6,H8) = 2.4 Hz), 7.07 (1*H*. ddd, H-8, ^3J(H8,F7) = 8.7 Hz, ^4J(H8,F6) = 2.4 Hz, ^5J(H8,F5) = 1.8 Hz), 7.41 (1*H*, m, Ph H-4), 7.54 (2*H*, m, Ph H-3,5), 7.81 (2*H*, m, Ph H-2,6). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 (3-Me, ^1J = 129.4 Hz), 105.3 (C-3a, ^3J(C3a,3Me) = 2.7 Hz), 101.4 (C-8, ^1J(C8,H8) = 169.3 Hz, ^2J(C8,F7) = 25.9 Hz, ^3J(C8,H6) = 4.4 Hz, ^4J(C8,F5) = 4.5 Hz), 102.4 (C-6, ^1J(C6,H6) = 169.3 Hz, ^2J(C6,F5) = 25.3 Hz, ^2J(C6,F7) = 25.3 Hz, ^3J(C6,H8) = 4.4 Hz), 110.9 (C-4a, ^2J(C4a,F5) = 9.9 Hz, ^3J(C4a,H6) = 4.4 Hz, ^3J(C4a,H8) = 4.4 Hz, ^4J(C4a,H7) = 3.7 Hz), 121.4 (Ph C-2,6), 127.7 (Ph C-4), 129.5 (Ph C-3,5), 136.7 (Ph C-1), 148.4 (C-3, ^2J(C3,3-Me) = 7.2 Hz), 152.0 (C-9a), 156.5 (C8a, ^2J(C8a,H8) = 5.1 Hz, ^3J(C8a,F5) = 6.1 Hz, ^3J(C8a,F7) = 15.4 Hz), 163.1 (C-5, ^1J(C5,F5) = 267.9 Hz, ^2J(C5,H6) = 6.2 Hz, ^3J(C5,F7) = 14.8 Hz), 164.6 (C-7, ^1J(C7,F7) = 255.7 Hz, ^2J(C7,H6) = 6.0 Hz, ^2J(C7,H8) = 6.0 Hz, ^3J(C7,F5) = 15.1 Hz), 171.3 (C-4). ^{15}N NMR (50 MHz, $CDCl_3$): δ −193.2 (N-1), −95.1 (N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −105.1 (F-5, ^3J(F5,H6) = 10.8 Hz, ^4J(F5,F7) = 12.1 Hz, ^5J(F5,H8) = 1.8 Hz), −100.1 (F-7, ^3J(F7,H6) = 8.7 Hz, ^3J(F7,H8) = 8.7 Hz, ^4J(F7,F5) = 12.1 Hz). IR (KBr): ν (cm^{-1}) 1679 (C=O). MS (*m/z*, %): 313 (M^++1, 20), 312 (M^+, 100), 311 (M^+−1, 68), 156 (15), 91 (19), 77 (31), 51 (15). Anal. Calcd for $C_{17}H_{10}F_2N_2O_2$: C, 65.39; H, 3.23; N, 8.97. Found: C, 65.11; H, 2.90; N, 8.89.

*4.3.8.2. 5-(Dimethylamino)-7-fluoro-3-methyl-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (**19y**).* Cyclization of **13a** with NaH/DMF (method a) gave 90% of a 2:1 mixture of **19a** and **19y** which was separated by column chromatography (silica gel, eluent: light petroleum–ethyl acetate, 2:1).

Compound **19y**: colorless solid, mp 184–186 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.66 (3*H*, s, 3-Me), 2.97 (6*H*, s, NMe_2), 6.58 (1*H*, dd, H-6, ^3J(H6,F7) = 11.8 Hz, ^4J(H6,H8) = 2.5 Hz), 6.65 (1*H*, dd, H-8, ^3J(H8,F7) = 8.7 Hz, ^4J(H8,H6) = 2.5 Hz), 7.36 (1*H*, m, Ph H-4), 7.52 (2*H*, m, Ph H-3,5), 7.83 (2*H*, m, Ph H-2,6). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 (3-Me, ^1J = 129.1 Hz), 44.7 (NMe_2, ^1J = 136.8 Hz, $^3J(\underline{C}H_3,\underline{C}H_3)$ = 4.1 Hz), 105.4 (C-3a, ^3J(C3a,3Me) = 2.7 Hz), 95.9 (C-8, ^2J(C8,F7) = 26.8 Hz), 100.6 (C-6, ^2J(C6,F7) = 23.3 Hz), 110.9 (C-4a, ^4J(C4a,F7) = 2.7 Hz), 120.9 (Ph C-2,6), 127.1 (Ph C-4), 129.4 (Ph C-3,5), 137.1 (Ph C-1), 148.1 (C-3, ^2J(C3,3-Me) = 7.1 Hz), 151.7 (C-9a), 156.2 (C-5, ^3J(C5,F7) = 12.4 Hz), 159.2 (C8a, ^3J(C8a,F7) = 16.4 Hz), 165.0 (C-7, ^1J(C7,F7) = 251.2 Hz), 172.6 (C-4). MS (*m/z*, %): 337 (M^+, 33), 91 (21), 77 (100), 69 (30), 51 (61). HRMS (ESI): Calcd for $C_{19}H_{17}FN_3O_2$ (MH^+) 338.1305. Found: 338.1312.

*4.3.9. 1-(4-Fluorophenyl)-3-methylchromeno[2,3-c]pyrazol-4(1H)-one (**22d**)*

Yield 45% (method a); colorless solid; mp 182–184 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.69 (3*H*, s, 3-Me), 7.24 (2*H*, m, Ph H-3,5), 7.45 (1*H*, m, H-6), 7.51 (1*H*, m, H-8), 7.70 (1*H*, m, H-7), 7.85 (2*H*, m, Ph

H-2,6), 8.35 (1*H*, m, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 (3-Me, ^1J = 129.3 Hz), 104.9 (C-3a, ^3J(C3a,3Me) = 2.7 Hz), 116.3 (Ph C-3,5, ^2J(C3,F4) = 23.0 Hz), 117.6 (C-8), 123.2 (Ph C-2,6, ^3J(C2,F4) = 8.5 Hz), 123.4 (C-4a), 125.3 (C-6), 126.9 (C-5), 133.2 (Ph C-1, ^4J(C1,F4) = 2.8 Hz), 133.8 (C-7), 148.3 (C-3, ^2J(C3,3-Me) = 7.1 Hz), 152.9 (C-9a), 154.4 (C-8a), 161.4 (Ph F-4, ^1J(C4,F4) = 247.9 Hz), 173.5 (C-4, ^3J(C4,H5) = 4.0 Hz, ^4J(C4,H8) = 1.5 Hz). ^{15}N NMR (50 MHz, $CDCl_3$): δ −195.1 (N-1), −96.0 (N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −113.7 (Ph F-4). IR (KBr): ν (cm^{-1}) 1672 (C=O). MS (*m/z*, %): 294 (M^+, 40), 293 (M^+−1, 23), 120 (27), 109 (31), 95 (99), 74 (97), 69 (100). Anal. Calcd for $C_{17}H_{11}FN_2O_2{\cdot}0.2\,H_2O$: C, 68.54; H, 3.86; N, 9.40. Found: C, 68.61; H, 3.57; N, 9.39.

4.3.10. 1-(4-Chlorophenyl)-3-methylchromeno[2,3-c]pyrazol-4(1H)-one (22e)

Yield 77% (method b) or 33% (method a); colorless solid; mp 202–205 °C (EtOH–H_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.69 (3*H*, s, 3-Me), 7.46 (1*H*, m, H-6), 7.51 (2*H*, m, Ph H-3,5), 7.52 (1*H*, m, H-8), 7.71 (1*H*, m, H-7), 7.86 (2*H*, m, Ph H-2,6), 8.36 (1*H*, m, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 (3-Me, ^1J = 129.3 Hz), 105.1 (C-3a, ^3J(C3a,3Me) = 2.7 Hz), 117.6 (C-8), 122.2 (Ph C-2,6), 123.4 (C-4a), 125.4 (C-6), 126.9 (C-5), 129.6 (Ph C-3,5), 132.9 (Ph C-4), 133.9 (C-7), 135.6 (Ph C-1), 148.5 (C-3, ^2J(C3,3-Me) = 7.1 Hz), 153.0 (C-9a), 154.5 (C-8a), 173.5 (C-4). ^{15}N NMR (50 MHz, $CDCl_3$): δ −194.9 (N-1), −96.8 (N-2). IR (KBr): ν (cm^{-1}) 1670 (C=O). MS (*m/z*, %): 310/312 (M^+, 3/1), 243 (17), 141 (27), 69 (99), 43 (100). Anal. Calcd for $C_{17}H_{11}ClN_2O_2{\cdot}0.4\,H_2O$: C, 64.22; H, 3.74; N, 8.81. Found: C, 64.29; H, 3.38; N, 8.85.

4.3.11. 7-Fluoro-3-methyl-1-phenyl[1]benzothieno[2′,3′:5,6]pyrano[2,3-c]pyrazol-4(1H)-one (25)

Yield 97% (method a); yellowish solid; mp 228–231 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.69 (3*H*, s, 3-Me), 7.28 (1*H*, ddd, H-8, ^3J(H8,F7) = 8.6 Hz, ^3J(H8,H9) = 8.9 Hz, ^4J(H8,H6) = 2.2 Hz), 7.44 (1*H*, m, Ph H-4), 7.57 (1*H*, dd, H-6, ^3J(H6,F7) = 8.6 Hz, ^4J(H6,H8) = 2.2 Hz), 7.59 (2*H*, m, Ph H-3,5), 7.91 (2*H*, m, Ph H-2,6), 8.00 (1*H*, dd, H-9, ^3J(H9,H8) = 8.9 Hz, ^4J(H9,F7) = 5.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 (3-Me, ^1J = 129.4 Hz), 106.3 (C-3a, ^3J(C3a,3Me) = 2.7 Hz), 110.3 (C-6, ^2J(C6,F7) = 25.8 Hz), 114.9 (C-8, ^2J(C8,F7) = 25.0 Hz), 121.2 (Ph C-2,6), 123.1 (C-9, ^3J(C9,F7) = 9.7 Hz), 123.7 (C4a, ^5J(C4a,F7) = 3.3 Hz), 124.9 (C-9a, ^4J(C9a,F7) = 1.6 Hz), 127.7 (Ph C-4), 129.6 (Ph C-3,5), 137.0 (Ph C-1), 140.8 (C-5a, ^3J(C5a,F7) = 10.5 Hz), 147.3 (C-3, ^2J(C3,3-Me) = 7.2 Hz), 149.3 (C-9b, ^3J(C9b,H9) = 3.3 Hz), 153.3 (C-10a), 162.8 (C-7, ^1J(C7,F7) = 251.8 Hz), 170.3 (C-4). ^{15}N NMR (50 MHz, $CDCl_3$): δ −192.9 (N-1), −93.4 (N-2). ^{19}F NMR (470 MHz, $CDCl_3$): δ −109.3 (F-7, ^3J(F7,H6) = 8.6 Hz, ^3J(F7,H8) = 8.6 Hz, ^4J(F7,H9) = 5.0 Hz). IR (KBr): ν (cm^{-1}) 1664 (C=O). MS (*m/z*, %): 351(M^++17), 350 (M^+, 76), 349 (M^+−1, 30), 155 (22), 138 (25), 94 (26), 77 (100), 51 (44). Anal. Calcd for $C_{19}H_{11}FN_2O_2S$: C, 65.13; H, 3.16; N, 8.00. Found: C, 65.12; H, 3.22; N, 7.92.

4.4. Reaction of pyrazolone 1a with 2,6-dichlorobenzoyl chloride

Pyrazolone **1a** (1.74 g, 10 mmol), $Ca(OH)_2$ (1.48 g, 20 mmol) and 2,6-dichlorobenzoyl chloride (2.09 g, 10 mmol) were reacted as described in the general procedure for the synthesis of **8**–**13**, **21**, **24**. After addition of 2 N HCl (40 mL) and H_2O (100 mL) the mixture was exhaustively extracted with ethyl acetate. The combined organic phases were washed with H_2O, dried (Na_2SO_4) and evaporated under reduced pressure. The residue was subjected to column chromatography (silica gel, ethyl acetate) to afford 2.25 g (65%) of **26** as a brownish solid with mp 105–107 °C and 278 mg (8%) of **27** as a brownish solid with mp 175–183 °C.

4.4.1. 3-Methyl-1-phenyl-1H-pyrazol-5-yl 2,6-dichlorobenzoate (26)

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.37 (3*H*, s, 3-Me), 6.34 (1*H*, s, pyraz H-4), 7.29 (1*H*, m, NPh H-4), 7.33 (3*H*, m, CPh H-3,4,5), 7.40 (2*H*, m, NPh H-3,5), 7.58 (2*H*, m, NPh H-2,6). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4 (3-Me, ^1J = 127.8 Hz), 95.7 (pyraz C-4, ^1J(C4,H4) = 181.7 Hz, ^3J(C4,3Me) = 3.5 Hz), 123.6 (NPh C-2,6), 127.3 (NPh C-4), 128.0 (CPh C-3,5), 128.9 (NPh C-3,5), 131.5 (CPh C-1), 131.8 (CPh C-4), 132.1 (CPh C-2,6), 137.6 (NPh C-1), 143.6 (pyraz C-5, ^2J(C5,H4) = 4.6 Hz), 148.9 (pyraz C-3, ^2J(C3,3Me) = 6.7 Hz, ^2J(C3,H4) = 4.0 Hz), 160.0 (C=O). ^{15}N NMR (50 MHz, $CDCl_3$): δ −183.1 (pyraz N-1), −95.1 (pyraz N-2). IR (KBr): ν (cm^{-1}) 1775 (C=O). MS (*m/z*, %): 346/348/350 (M^+, 2.7/1.9/0.3), 173/175/177 (2,6-dichlorobenzoyl, 100/73/11), 77 (39). Anal. Calcd for $C_{17}H_{12}Cl_2N_2O_2$: C, 58.81; H, 3.48; N, 8.07. Found: C, 58.72; H, 3.36; N, 8.07.

4.4.2. 1-(2,6-Dichlorobenzoyl)-5-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (27)

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.71 (3*H*, s, 5-Me), 5.65 (1*H*, s, pyraz H-4), 6.90 (2*H*, m, NPh H-2,6), 7.04 (2*H*, m, COPh H-3,5), 7.07 (1*H*, m, COPh H-4), 7.13 (1*H*, m, NPh H-4), 7.14 (2*H*, m, NPh H-3,5). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.3 (5-Me, ^1J = 131.5 Hz, ^3J(5Me,H4) = 2.2 Hz), 103.3 (pyraz C-4, ^1J(C4,H4) = 182.8 Hz, ^3J(C4,5Me) = 4.5 Hz), 124.3 (NPh C-2,6), 127.6 (NPh C-4), 127.8 (COPh C-3,5), 128.8 (NPh C-3,5), 131.6 (COPh C-4), 133.0 (COPh C-2,6), 133.3 (COPh C-1), 137.4 (NPh C-1), 156.3 (pyraz C-5, ^2J(C5,5Me) = 6.8 Hz, ^2J(C5,H4) = 8.1 Hz), 163.2 (N1-CO), 168.0 (pyraz C-3, ^2J(C3,H4) = 4.9 Hz). ^{15}N NMR (50 MHz, $CDCl_3$): δ −211.5 (pyraz N-2), −190.7 (pyraz N-1). IR (KBr): ν (cm^{-1}) 1691 (C=O). MS (*m/z*, %): 346/348/350 (M^+, 2.1/1.4/0.3), 173/175/177 (2,6-dichlorobenzoyl, 100/71/11), 145 (16), 77 (36). Anal. Calcd for $C_{17}H_{12}Cl_2N_2O_2$: C, 58.81; H, 3.48; N, 8.07. Found: C, 58.83; H, 3.52; N, 8.09.

4.5. 5-Fluorochromeno[2,3-c]pyrazol-4(1H)-one (14x)

Under anhydrous conditions, a solution of the PMB-substituted tricycle **14c** (324 mg, 1 mmol) and trifluoroacetic acid (TFA, 5 mL) was stirred overnight at 70 °C. After removal of excess TFA under reduced pressure, the residue was dried over solid KOH for 1 h. Then 5 mL of ice-cold diethyl ether–acetone (2:1) was added and the resulting suspension was filtered off and washed with cold diethyl ether to give 81 mg (79%) of the N-unsubstituted compound **14x** as colorless solid, mp >295 °C (dec.).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18 (1*H*, ddd, H-6, ^3J(H6,F5) = 11.5 Hz, ^3J(H6,H7) = 8.3 Hz, ^4J(H6,H8) = 1.1 Hz), 7.45 (1*H*, d′t′, H-8, ^3J(H8,H7) = 8.5 Hz, ^4J(H8,H6) = 1.1 Hz, ^5J(H8;F5) = 0.9 Hz), 7.75 (1*H*, d′t′, H-7, ^3J(H7,H8) = 8.5 Hz, ^3J(H7,H6) = 8.3 Hz, ^4J(H7,F5) = 5.8 Hz), 8.58 (1*H*, s, H-3), 13.78 (1*H*, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 106.0 (C-3a, ^2J(C3a,H3) = 8.3 Hz), 111.4 (C-6, ^1J(C6,H6) = 167.0 Hz, ^2J(C6,F5) = 21.2 Hz, ^3J(C6,H8) = 8.1 Hz), 112.1 (C4a, ^2J(C4a,F5) = 9.8 Hz), 114.2 (C8, ^4J(C8,F5) = 4.0 Hz), 129.0 (C-3, broad), 134.8 (C-7, ^1J(C7,H7) = 165.5 Hz, ^3J(C7,F5) = 11.5 Hz), 156.5 (C-8a, ^3J(C8a,F5) = 3.9 Hz), 160.2 (C-9a, broad), 161.2 (C5, ^1J(C5,F5) = 261.9 Hz), 172.4 (C-4). ^{19}F NMR (470 MHz, $CDCl_3$): δ −112.2 (F-5, ^3J(F5,H6) = 11.5 Hz, ^4J(F5,H7) = 5.8 Hz, ^5J(F5,H8) = 0.9 Hz). IR (KBr): ν (cm^{-1}) 1652 (C=O), 3169 (NH). MS (*m/z*, %): 205 (M^++1, 12), 204 (M^+, 100), 121 (29), 94 (21), 53 (24). HRMS (EI): Calcd for $C_{10}H_5FN_2O_2$ (M^+): 204.0335. Found: 204.0341.

4.6. Reaction of 14a and 14b with methylhydrazine—formation of tetracycles 28a and 28b

A mixture of **14a** (294 mg, 1 mmol) or **14b** (280 mg, 1 mmol) and methylhydrazine (46 mg, 1 mmol) in 1,4-dioxane (8 mL) was stirred at reflux overnight. After removal of the solvent under reduced pressure, the residue was digested with H_2O. The remaining solid was filtered off, washed with H_2O and recrystallized from EtOH.

*4.6.1. 2,9-Dimethyl-7-phenyl-2,7-dihydropyrazolo[4′,3′:5,6]pyrano[4,3,2-cd]indazole (**28a**)*

Yield 195 mg (65%) of a beige solid; mp 168–170 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.55 (3*H*, s, 9-Me), 3.85 (3*H*, s, 2-Me), 6.44 (1*H*, d, H-5, ^3J(H5,H4) = 7.6 Hz), 6.69 (1*H*, d, H-3, ^3J(H3,H4) = 8.2 Hz), 7.16 (1*H*, dd, H-4, ^3J(H4,H3) = 8.2 Hz, ^3J(H4,H5) = 7.6 Hz), 7.31 (1*H*, m, NPh H-4), 7.47 (2*H*, m, NPh H-3,5), 7.80 (2*H*, m, NPh H-2,6). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 (9-Me, ^1J = 128.4 Hz), 35.5 (2-Me, ^1J = 139.1 Hz), 98.1 (C-9a, ^3J(C9a,9Me) = 3.4 Hz), 100.5 (C-5), 102.6 (C-3), 115.5 (C-9c), 121.3 (NPh C-2,6), 126.7 (NPh C-4), 129.0 (NPh C-3,5), 129.8 (C-4), 136.6 (C-9b), 137.7 (NPh C-1), 141.0 (C-2a), 143.5 (C-9, ^2J(C9,9Me) = 6.9 Hz), 148.9 (C-5a, ^2J(C5a,H5) = 4.0 Hz, ^3J(C5a,H4) = 11.9 Hz, ^4J(C5a,H3) = 1.7 Hz), 150.0 (C-6a). ^{15}N NMR (50 MHz, $CDCl_3$): δ −213.2 (N-2), −189.4 (N-7), −103.5 (N-8), −91.5 (N-1). MS (*m/z*, %): 302 (M^+, 55), 158 (21), 77 (100), 51 (39). Anal. Calcd for $C_{18}H_{14}N_4O{\cdot}0.2\ H_2O$: C, 70.67; H, 4.74; N, 18.31. Found: C, 70.77; H, 4.44; N, 18.26.

*4.6.2. 2-Methyl-7-phenyl-2,7-dihydropyrazolo[4′,3′:5,6]pyrano[4,3,2-cd]indazole (**28b**)*

Yield 230 mg (80%) of a yellowish solid, mp 156-158 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.98 (3*H*, s, 2-Me), 6.60 (1*H*, d, H-5, ^3J(H5,H4) = 7.7 Hz), 6.86 (1*H*, d, H-3, ^3J(H3,H4) = 8.2 Hz), 7.31 (1*H*, dd, H-4, ^3J(H4,H3) = 8.2 Hz, ^3J(H4,H5) = 7.7 Hz), 7.39 (1*H*, m, NPh H-4), 7.54 (2*H*, m, NPh H-3,5), 7.87 (2*H*, m, NPh H-2,6), 7.96 (1*H*, s, H-9). ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.8 (2-Me, ^1J = 139.2 Hz), 98.9 (C-9a, ^2J(C9a,H9) = 10.6 Hz), 100.9 (C-5, ^1J(C5,H5) = 164.8 Hz, ^2J(C5,H4) = 1.7 Hz, ^3J(C5,H3) = 7.5 Hz), 103.1 (C-3, ^1J(C3,H3) = 165.5 Hz, ^2J(C3,H4) = 1.2 Hz, ^3J(C3,H5) = 7.4 Hz), 115.8 (C-9c, ^3J(C9c,H3) = 5.5 Hz, ^3J(C9c,H5) = 5.5 Hz, ^4J(C9c,H4) = 1.0 Hz), 121.9 (NPh C-2,6), 127.4 (NPh C-4), 129.3 (NPh C-3,5), 130.3 (C-4, ^1J(C4,H4) = 158.9 Hz, ^2J(C4,H3) = 1.2 Hz, ^2J(C4,H5) = 1.2 Hz), 133.8 (C-9, ^1J(C9,H9) = 191.4 Hz), 136.1 (C-9b), 137.8 (NPh C-1), 141.5 (C-2a), 149.1 (C-5a), 150.3 (C-6a). ^{15}N NMR (50 MHz, $CDCl_3$): δ −213.0 (N-2), −184.3 (N-7), −97.9 (N-8), −90.7 (N-1). MS (*m/z*, %): 289 (M^++1, 18), 288 (M^+, 100), 157 (29), 77 (47), 51 (33). Anal. Calcd for $C_{17}H_{12}N_4O$: C, 70.82; H, 4.20; N, 19.43. Found: C, 70.65; H, 3.98; N, 19.15.

*4.7. Reaction of **14a** with hydrazine hydrate: formation of 5-hydrazino-3-methyl-1-phenylchromeno[2,3-c]pyrazol-4(1H)-one (**29**)*

A mixture of **14a** (589 mg, 2 mmol) and hydrazine hydrate (100 mg, 2 mmol) in EtOH (20 mL) was stirred at reflux overnight. After removal of the solvent under reduced pressure, the residue was digested with H_2O, filtered off, washed with EtOH and recrystallized from CH_2Cl_2 to afford 372 mg (65%) of fine yellow fibers, mp 221–222 °C (CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.65 (3*H*, s, 3-Me), 4.01 (2*H*, s, NH_2), 6.66 (1*H*, dd, H-8, ^3J(H8,H7) = 8.0 Hz, ^4J(H8,H6) = 0.9 Hz), 7.16 (1*H*, dd, H-6, ^3J(H6,H7) = 8.5 Hz, ^4J(H6,H8) = 0.9 Hz), 7.37 (1*H*, m, NPh H-4), 7.45 (1*H*, m, H-7, ^3J(H7,H6) = 8.5 Hz, ^3J(H7,H8) = 8.0 Hz), 7.53 (2*H*, m, NPh H-3,5), 7.87 (2*H*, m, NPh H-2,6), 10.15 (1*H*, s, NH). ^{1}H NMR (500 MHz, $(CD_3)_2SO$): δ 2.50 (3*H*, s, 3-Me), 4.46 (2*H*, s, NH_2), 6.65 (1*H*, dd, H-8, ^3J(H8,H7) = 8.1 Hz, ^4J(H8,H6) = 1.0 Hz), 7.11 (1*H*, dd, H-6, ^3J(H6,H7) = 8.6 Hz, ^4J(H6,H8) = 1.0 Hz), 7.41 (1*H*, m, NPh H-4), 7.46 (1*H*, m, H-7, ^3J(H7,H6) = 8.6 Hz, ^3J(H7,H8) = 8.1 Hz), 7.58 (2*H*, m, NPh H-3,5), 7.86 (2*H*, m, NPh H-2,6), 9.91 (1*H*, s, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.1 (3-Me, ^1J = 129.1 Hz), 103.5 (C-8), 104.6 (C-3a, ^3J(C3a,3Me) = 2.7 Hz), 105.8 (C-6), 106.4 (C-4a), 121.0 (NPh C-2,6), 127.1 (NPh C-4), 129.4 (NPh C-3,5), 134.5 (C-7), 137.1 (NPh C-1), 147.8 (C-3, ^2J(C3,3-Me) = 7.2 Hz), 152.4 (C-9a), 154.9 (C-5), 156.7 (C-8a), 178.1 (C-4). ^{13}C NMR (125 MHz, $(CD_3)_2SO$): δ 13.8 (3-Me), 102.2 (C-8), 103.9 (C-3a), 105.0 (C-4a), 106.1 (C-6), 120.8 (NPh C-2,6), 127.3 (NPh C-4), 129.6 (NPh C-3,5), 134.6 (C-7), 136.7 (NPh C-1), 146.5 (C-3), 152.0 (C-9a), 154.9 (C-5), 156.3 (C-8a), 177.0 (C-4). ^{15}N NMR (50 MHz, $CDCl_3$): δ −324.4 (NH_2), −288.7 (NH), −193.6 (N-1), −97.9 (N-2). ^{15}N NMR (50 MHz, $(CD_3)_2SO$): δ −321.3 (NH_2), −285.0 (NH), −193.6 (N-1), −95.9 (N-2). IR (KBr): ν (cm^{-1}) 1631 (C=O). MS (*m/z*, %): 307 (M^++1, 24), 306 (M^+, 100), 289 (42), 275 (22), 91 (24), 77 (84), 69 (38), 51 (45). Anal. Calcd for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.61; N, 18.29. Found: C, 66.69; H, 4.38; N, 18.18.

Acknowledgement

The authors thank Mr. Ralf Dumler for experimental contributions.

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