A Simple Synthesis of 6-Phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones

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Abstract: A novel synthesis of substituted 6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones via reaction of various 2-substituted or 2,5-disubstituted 2,4-dihydro-3*H*-pyrazol-3-ones with phenylpropynoyl chloride using calcium hydroxide in refluxing 1,4-dioxane is described. N-Unsubstituted representatives were obtained by treatment of 4-methoxybenzyl-protected congeners with trifluoroacetic acid.

Key words: pyrazolones, acylations, cyclizations, fused-ring systems, PMB protecting group

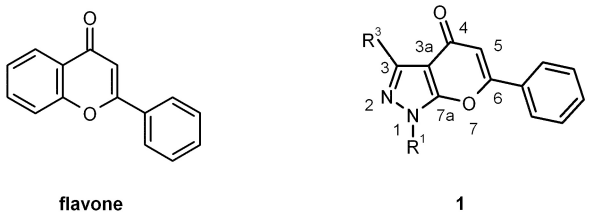
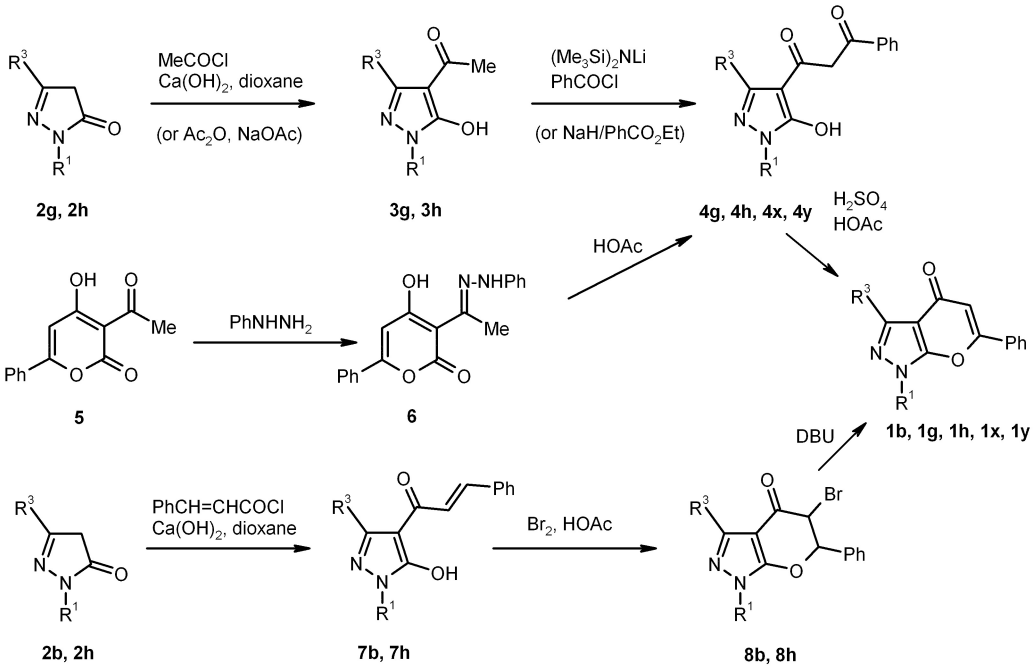


Figure 1

The 6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one moiety **1** is an interesting heterocyclic system as it represents a pyrazole analogue of flavone (2-phenyl-4*H*-chromen-4-one), the latter being the parent system for a large variety of natural products which play important roles in numerous biological processes (Figure 1).[1] Few representatives of type **1** are hitherto known (for instance **1b**,[2] **1g**,[3] **1h**,[4–7] **1x**,[7] **1y**[5]); reported pathways for their synthesis are displayed in Scheme 1. Accordingly, derivatives **1g**, **1h**, **1x**, and **1y** have been obtained by acid-catalyzed cyclization of 1,3-diketones **4**,[3–7] the latter being available either from 2-pyrazolin-5-ones **2** by acetylation and subsequent Claisen condensation[4,7] [or treatment with lithium bis(trimethylsilyl)amide/benzoyl chloride][3,6] or via ring-transformation of phenylhydrazone **6** derived from 3-acetyl-4-hydroxy-6-phenyl-2*H*-pyran-2-one (**5**).[5,6] Alternatively, reaction of 4-cinnamoyl-5-hydroxypyrazoles **7** with bromine followed by treatment of the resulting bro-



Scheme 1 Known methods for the synthesis of the title compounds **1**

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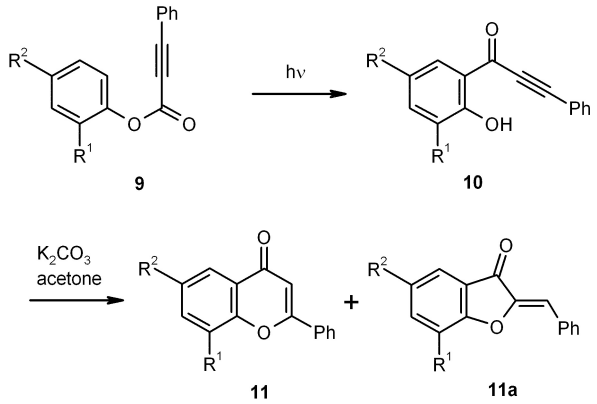
mo compounds **8** with DBU afforded **1b**[2] and **1h**,[6] respectively. However, these traditional preparations are multistep reactions characterized by poor overall yields.

In the benzene series, an interesting strategy for the synthesis of substituted flavones **11** consists of a base-catalyzed 6-*endo-dig* cyclization of *o*-phenylpropynoylphenols **10**.[8–11] Strongly dependent on the reaction conditions, the formation of 5-*exo-dig* product **11a** (aurones) is also possible.[8,11] The starting phenylpropynoyl compounds **10** are available, for instance, by photo-Fries rearrangement of aryl phenylpropynoates **9** (Scheme 2).[8,9]

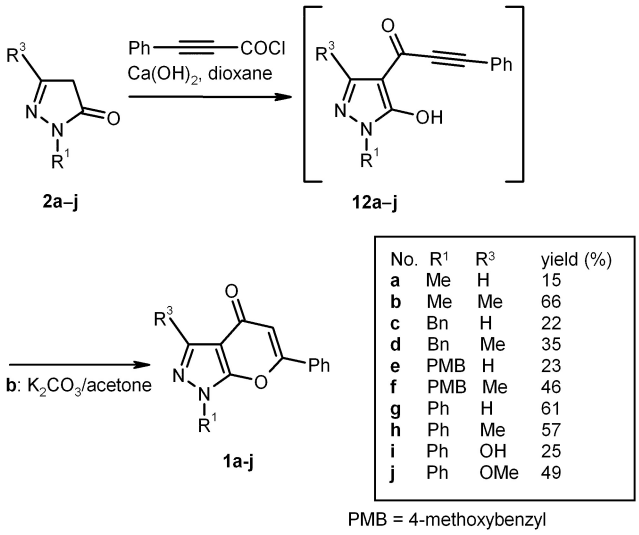


Scheme 2 Synthesis of flavones by cyclization of *ortho*-phenylpropynoylphenols

We herein, wish to report a straightforward synthesis of various 6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones **1** following a related approach. It includes acylation of pyrazolones **2** with phenylpropynoyl chloride following the general procedure described by Jensen [RCOCl, $Ca(OH)_2$, refluxing dioxane][12] in order to obtain the corresponding 4-phenylpropynoyl-substituted 5-hydroxypyrazoles of type **12**. Subsequently, the latter could be cyclized into target compounds **1** (Scheme 3).

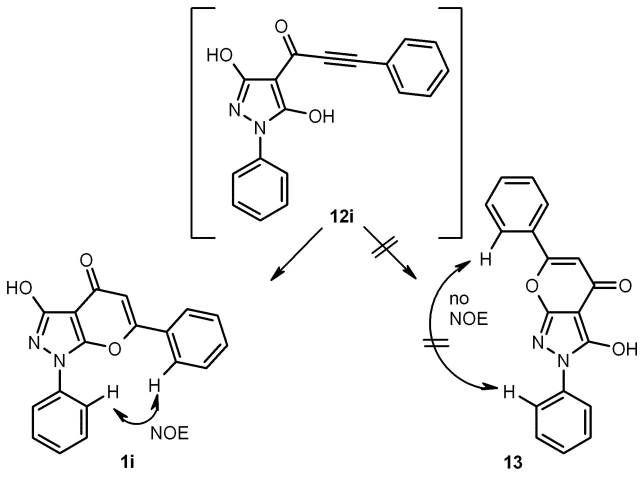
However, it turned out that even under the acylation conditions pyran ring-closure into **1** occurred. For this reason, apparent intermediates **12** were not isolated and cyclization was completed with prolonged reaction times (six hours instead of two hours for a 'normal' Jensen-acylation). After reaction of *N*-methylpyrazolone **2b** with phenylpropynoyl chloride the crude product still contained 50% of non cyclized intermediate **12b**. Nevertheless, cyclization to **1b** could be obtained smoothly, by subsequent treatment of this mixture with potassium carbonate in anhydrous acetone. Although yields are average, the presented approach leads to the desired 6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones **1** in a quick and simple reaction and thus seems to be superior and much more convenient than those hitherto used syntheses.

Reaction of pyrazolone **2i** with phenylpropynoyl chloride represents a special case: the intermediate 3,5-dihydroxy-4-phenylpropynoylpyrazole (**12i**) can either cyclize into the 3-hydroxy-1,6-diphenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (**1i**) or – upon attack of 3-OH on the alkyne triple



Scheme 3 Novel one-pot synthesis of 6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones

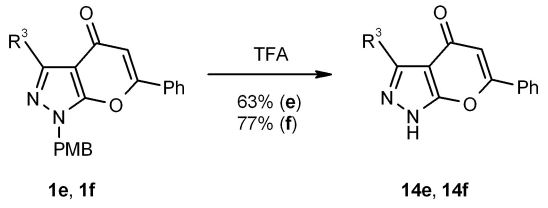
bond – into the isomeric 3-hydroxy-2,6-diphenylpyrano[2,3-*c*]pyrazol-4(2*H*)-one (**13**; Scheme 4). Isomers **1i** and **13** are difficult to discriminate on the basis of their spectroscopic properties. However, NOE-difference experiments and NOESY spectra unambiguously revealed the structure of **1i** as the isolated reaction product. Accordingly, a clear NOE on the signal of NPh-H-2,6 protons upon irradiation of the CPh-H-2,6 transition (and, reversely, on the signal of CPh-H-2,6 upon disturbing the NPh-H-2,6 transition) provides proof of the spatial proximity of the two phenyl rings and thus the 4(1*H*)-one structure (Scheme 4). In contrast, the corresponding phenyl protons in **13** are too far apart for an NOE to be detected.



Scheme 4

Recently, we presented the application of the 4-methoxybenzyl (PMB) protecting group in the synthesis of N-unsubstituted 4-acylpyrazolones.[13] This protecting group resists the conditions of primary pyrazolone ring synthesis

as well as those of 4-acylation under the 'Jensen' conditions and, moreover, it can be conveniently removed by the action of trifluoroacetic acid. Similarly, i.e. by treatment of 1-PMB-substituted compounds **1e** and **1f** with trifluoroacetic acid, the N-unsubstituted bicyclic target compounds **14e** and **14f** were easily available (Scheme 5). Compound **14e** represents the 'parent' pyrazole analogue of flavone.



Scheme 5

Detailed NMR spectroscopic investigations in DMSO-d_6 solution revealed **14e** to be involved in prototropic tautomerism resulting in an equilibrium between the 1*H*-form **A** and 2*H*-form **B** (Figure 2). This mainly follows from the magnitude of the geminal spin-coupling constant ^2J(C-3a,H-3). Corresponding coupling constants have been shown to be sensitive probes for discrimination between forms having an 'intact' lone-pair at N-2 and those characterized by an N2-H (N2-R) substructure.[14] In the case of **14e** this coupling (^2J = 8.6 Hz) is significantly reduced compared to ^2J(C-3a,H-3) in the corresponding N-1 substituted 3-H congeners **1a**, **1c**, **1e**, and **1g** (10.1–10.5 Hz). This situation closely resembles that of pyrazole, where – due to fast prototropic exchange – the observed geminal ^{13}C,^{1}H coupling (^2J = 9.9 Hz, in $CDCl_3$) represents a mean value between the larger ^2J(C-4,H-3) coupling and the smaller ^2J(C-4,H-5) one,[15,16] whereas in 'fixed' 1-phenylpyrazole the pyrazole C-4 atom is involved in two different geminal couplings [^2J(C-4,H-3) = 10.3 Hz, ^2J(C-4,H-5) = 8.1 Hz] (Figure 2).[17]

Moreover, an NOE on the signal of H-3 upon irradiation of the NH transition additionally hints at a contribution of the 2*H*-form **B** to the structure of **14e** (Figure 2).

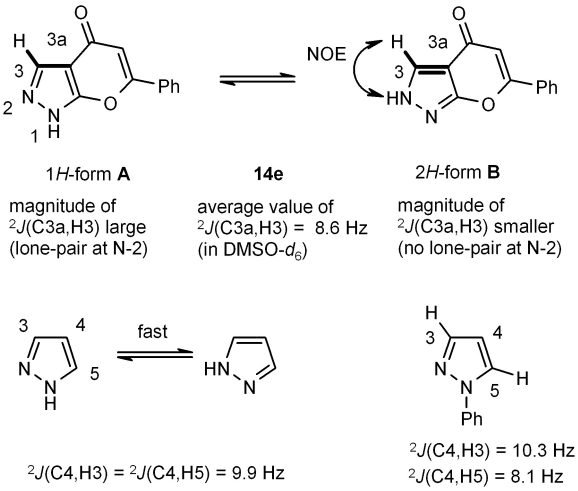


Figure 2 Prototropic tautomerism in pyrazole and in **14e**

Detailed NMR analyses for all prepared compounds were undertaken, considering also characteristic ^{13}C,^{1}H spin-coupling constants as well as ^{15}N NMR chemical shifts. Owing to their low solubility in $CDCl_3$, the spectra of compounds **1i**, **14e**, and **14f** were recorded in DMSO-d_6 solutions. The data obtained show a high degree of consistency and are summarized in Table 1 (^{1}H NMR), Table 2 (^{13}C NMR chemical shifts), Table 3 (^{13}C,^{1}H coupling constants), and Table 4 (^{15}N NMR chemical shifts).

Table 1 ^{1}H NMR Data of Compounds **1a–j** and **14e**,**f**

Compd	Solvent	H of R^1	H of R^3	H-5	H of 6-Ph
1a	$CDCl_3$	4.00 (Me)	7.96 (H-3)	6.66	7.81 (2,6), 7.53 (3,4,5)
1b	$CDCl_3$	3.90 (Me)	2.55 (Me)	6.59	7.79 (2,6), 7.51 (3,4,5)
1c	$CDCl_3$	7.38 (Ph-2,3,4,5,6), 5.48 (NCH_2)	8.02 (H-3)	6.65	7.71 (2,6), 7.51 (3,4,5)
1d	$CDCl_3$	7.36 (Ph-2,3,4,5,6), 5.39 (NCH_2)	2.58 (Me)	6.59	7.69 (2,6), 7.50 (3,4,5)
1e	$CDCl_3$	7.33 (Ph-2,6), 6.90 (Ph-3,5), 5.41 (NCH_2), 3.79 (OMe)	7.99 (H-3)	6.64	7.73 (2,6), 7.53 (3,4,5)
1f	$CDCl_3$	7.31 (Ph-2,6), 6.89 (Ph-3,5), 5.32 (NCH_2), 3.78 (OMe)	2.57 (Me)	6.59	7.71 (2,6), 7.51 (3,4,5)
1g	$CDCl_3$	7.89 (Ph-2,6), 7.59 (Ph-3,5), 7.45 (Ph-4)	8.18 (H-3)	6.77	7.82 (2,6), 7.53 (3,4,5)
1h	$CDCl_3$	7.86 (Ph-2,6), 7.56 (Ph-3,5), 7.40 (Ph-4)	2.66 (Me)	6.77	7.80 (2,6), 7.53 (3,4,5)
1i	DMSO-d_6	7.83 (Ph-2,6), 7.60 (Ph-3,5), 7.39 (Ph-4)	11.53 (OH)	6.83	7.94 (2,6), 7.57 (3,4,5)
1j	$CDCl_3$	7.85 (Ph-2,6), 7.55 (Ph-3,5), 7.36 (Ph-4)	4.13 (OMe)	6.70	7.78 (2,6), 7.53 (3,4,5)
14e	DMSO-d_6	13.80 (NH)	8.45 (H-3)	6.75	7.99 (2,6), 7.56 (3,4,5)
14f	DMSO-d_6	13.40 (NH)	2.53 (Me)	6.66	7.95 (2,6), 7.53 (3,4,5)

Table 2 ^{13}C NMR Chemical Shifts of Compounds **1a–j** and **14e**,**f** (Solvents as in Table 1)

Compd	C-3	C-3a	C-4	C-5	C-6	C-7a	C of 6-Ph				C of R^1	C of R^3
							C-1	C-2,6	C-3,5	C-4		
1a	134.3	107.4	174.8	109.4	160.0	153.9	130.7	126.0	129.2	131.5	34.3 (Me)	–
1b	145.4	105.5	175.6	109.6	159.7	154.1	130.9	125.9	129.1	131.1	33.8 (Me)	13.8 (Me)
1c	134.6	107.8	174.8	109.5	160.1	153.8	130.8	126.0	129.1	131.5	52.1 (NCH_2), Ph: 134.7 (1), 129.0 (3,5), 128.6 (4), 127.9 (2,6)	–
1d	145.8	105.9	175.6	109.7	159.8	154.0	130.9	125.9	129.1	131.3	51.7 (NCH_2), Ph: 135.0 (1), 129.0 (3,5), 128.4 (4), 127.8 (2,6)	13.9 (Me)
1e	134.5	107.7	174.8	109.4	160.0	153.6	130.8	126.0	129.1	131.5	55.3 (OMe), 51.7 (NCH_2), Ph: 159.8 (4), 129.4 (2,6), 126.7 (1), 114.4 (3,5)	–
1f	145.7	105.9	175.6	109.7	159.7	153.8	131.0	125.9	129.1	131.3	55.3 (OMe), 51.2 (NCH_2), Ph: 159.6 (4), 129.3 (2,6), 127.1 (1), 114.3 (3,5)	13.9 (Me)
1g	135.7	108.9	174.8	109.8	160.5	153.1	130.7	126.1	129.3	131.7	Ph: 137.0 (1), 129.6 (3,5), 127.9 (4), 121.3 (2,6)	–
1h	147.0	107.0	175.6	109.9	160.4	153.3	130.8	126.0	129.2	131.5	Ph: 137.0 (1), 129.5 (3,5), 127.5 (4), 121.1 (2,6)	13.9 (Me)
1i	151.8	96.4	173.2	109.3	159.3	156.1	130.4	126.0	129.2	131.4	Ph: 136.6 (1), 129.6 (3,5), 126.7 (4), 120.6 (2,6)	–
1j	157.8	97.1	174.0	110.0	160.1	152.5	130.7	125.9	129.3	131.5	Ph: 137.1 (1), 129.5 (3,5), 126.9 (4), 120.6 (2,6)	56.2 (OMe)
14e	127.1	107.1	175.9	107.2	161.2	161.6	131.3	126.3	129.2	131.5	–	–
14f	138.6	104.6	176.7	107.1	161.0	161.6	131.3	126.1	129.0	131.3	–	10.9 (Me)

In conclusion, we have presented a simple and straightforward one-pot synthesis for the title compounds which is advantageous compared to the hitherto used methods. Moreover, detailed NMR data material concerning 6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones was provided.

Table 3 Selected ^{13}C,^{1}H Spin-Coupling Constants (Hz) of **1a–j** and **14e**,**f** (Solvents as in Table 1)

Compd	^1J(C-3,H-3) ^1J(3-Me)	^4J(C-3,H-5)	^2J(C-3a,H-3) ^3J(C-3a,3-Me)	^3J(C-3a,H-5)	^2J(C-4,H-5)	^1J(C-5,H-5)	Other Couplings
1a	194.3	1.4	10.1	4.1	2.0	165.5	^1J(NMe) = 141.6
1b	129.0	1.5	2.8	4.2	2.1	164.9	^1J(NMe) = 141.3, ^2J(C-3,3-Me) = 7.1, ^3J(C-7a,NMe) = 2.3
1c	194.5	1.3	10.5	4.3	2.0	165.4	^1J(NCH_2) = 141.2
1d	129.0	1.5	2.6	4.1	2.1	165.0	^1J(NCH_2) = 140.5, ^2J(C3,3-Me) = 7.1, ^3J(C-7a,NCH_2) = 2.6
1e	194.1	1.5	10.1	4.3	2.1	165.4	^1J(NCH_2) = 140.8, ^3J(C-7a,NCH_2) = 2.5, ^3J(C-7a,H-3) = 5.2, ^1J(OMe) = 143.9

Table 3 Selected $^{13}C,^{1}H$ Spin-Coupling Constants (Hz) of **1a–j** and **14e**,**f** (Solvents as in Table 1) (continued)

Compd	^{1}J(C-3,H-3) ^{1}J(3-Me)	^{4}J(C-3,H-5)	^{2}J(C-3a,H-3) ^{3}J(C-3a,3-Me)	^{3}J(C-3a,H-5)	^{2}J(C-4,H-5)	^{1}J(C-5,H-5)	Other Couplings
1f	128.9	1.5	2.8	4.2	2.1	165.0	$^{1}J(NCH_2)$ = 140.5, ^{2}J(C-3,3-Me) = 7.1, ^{3}J(C-7a,NCH_2) = 2.5, ^{1}J(OMe) = 144.0
1g	194.9	1.5	10.3	4.4	2.1	165.8	^{3}J(C-7a,H-3) = 5.0
1h	129.2	1.4	2.8	4.0	2.0	165.6	^{2}J(C-3,3-Me) = 7.1
1i	–	<0.5	–	4.0	1.9	166.7	
1j	–	1.4	–	4.3	2.0	166.1	^{1}J(OMe) = 146.9, ^{3}J(C-3,OMe) = 4.0, ^{3}J(C-6,H-5) = 7.4, ^{3}J(Ph-C1,H-5) = 2.6
14e	194.5		8.6	4.5	1.8	165.5	^{3}J(C-7a,H-3) = 8.5, ^{2}J(C-6,H-5) = 6.6, ^{3}J(Ph-C1,H-5) = 2.9
14f	130.1		2.9	4.5	1.8	165.4	^{2}J(C-3,3-Me) = 7.1, ^{2}J(C-6,H-5) = 6.7, ^{3}J(Ph-C1,H-5) = 2.9

Table 4 ^{15}N NMR Chemical Shifts of **1a–j**

Compd	Solvent	N-1	N-2	Compd	Solvent	N-1	N-2
1a	$CDCl_3$	–205.1	–85.9	**1f**	$CDCl_3$	–198.5	–93.4
1b	$CDCl_3$	–211.9	–92.9	**1g**	$CDCl_3$	–186.4	–88.0
1c	$CDCl_3$	–193.5	–86.5	**1h**	$CDCl_3$	–192.5	–94.7
1d	$CDCl_3$	–200.2	–93.2	**1i**	DMSO-d_6	–211.3	not found
1e	$CDCl_3$	–191.7	–86.7	**1j**	$CDCl_3$	–210.1	not found

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). IR spectra were recorded on a Perkin-Elmer FTIR 1605 spectrophotometer. ^{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) at 28 °C. The center 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 DMSO-d_6), δ = 77.0 ppm (^{13}C in $CDCl_3$), and δ = 39.5 ppm (^{13}C in DMSO-d_6). ^{15}N NMR spectra were obtained on a Bruker Avance 500 instrument with a 'directly' detecting broadband observe probe and were referenced against external nitromethane (coaxial capillary). Full and unambiguous assignment for all NMR signals was achieved by combined application of standard NMR techniques such as fully ^{1}H-coupled ^{13}C NMR (gated decoupling), APT, 1D-TOCSY, NOE-difference, NOESY, HMQC, gs-HSQC, gs-HMBC, and selective long-range INEPT in a 1D and a 2D version.[16] The following commercially non available pyrazolones were prepared according to the literature: **2a**,[18] **2b**,[19] **2c**,[3] **2d**,[20] **2e**,[13] **2g**,[21] **2i**,[22] **2j**.[23] Yields of products **1** were not optimized.

3-Phenylprop-2-ynoyl Chloride[24]

Under anhyd conditions, to a soln of phenylpropiolic acid (10.0 g, 68.4 mmol) in CH_2Cl_2 (260 mL) was added $SOCl_2$ (24.4 g, 205 mmol) and the resulting mixture was stirred at 40 °C for 16 h. Then the solvent and excess $SOCl_2$ were removed under reduced pressure and the oily residue was subjected to vacuum distillation to afford 9.0 g (80%) of a colorless oil.

Bp 76–78 °C/1.3 mbar.

^{1}H NMR ($CDCl_3$): δ = 7.64 (m, 2 H, Ph-2,6), 7.56 (m, 1 H, Ph-4), 7.43 (m, 2 H, Ph-3,5).

^{13}C NMR ($CDCl_3$): δ = 149.5 (C=O), 133.7 (Ph-2,6), 132.2 (Ph-4), 128.9 (Ph-3,5), 118.0 (Ph-1), 94.1 (Ph*C*≡), 84.1 (≡*C*CO).

2-(4-Methoxybenzyl)-5-methyl-2,4-dihydro-3*H*-pyrazol-3-one (2f)[25]

Under cooling with an ice bath, 4-methoxybenzylhydrazine (1.52 g, 10 mmol) (prepared according to literature procedures[13]) was added slowly to ethyl acetoacetate (1.30 g, 10 mmol). After stirring for 30 min at 0 °C, the mixture was suction filtered and the remaining solid was washed with cold Et_2O (3 mL) to afford 1.64 g (75%) of a colorless powder.

Mp 128–130 °C.

^{1}H NMR ($CDCl_3$): δ = 7.27 (m, 2 H, Ph-2,6), 6.85 (m, 2 H, Ph-3,5), 4.72 (s, 2 H, NCH_2), 3.78 (s, 3 H, OMe), 3.18 (s, 2 H, pyrazole H-4), 2.05 (s, 3 H, 5-Me).

^{13}C NMR ($CDCl_3$): δ = 171.9 [pyrazole C-3, ^{2}J(C-3,H-4) = 5.1 Hz, ^{3}J(C-3,NCH_2) = 2.1 Hz], 159.1 (Ph-4), 155.6 [pyrazole C-5, ^{2}J(C-5,5-Me) = 7.6 Hz), ^{2}J(C-5,H-4) = 5.2 Hz], 129.6 (Ph-2,6), 128.8 (Ph-1), 114.0 (Ph-3,5), 55.2 (OMe, ^{1}J = 143.7 Hz), 47.2 (NCH_2, ^{1}J = 138.9 Hz), 41.6 [pyrazole C-4, ^{1}J = 133.0 Hz, ^{3}J(C-4,5-Me) = 2.9 Hz], 17.0 (5-Me, ^{1}J = 128.9 Hz).

^{15}N NMR ($CDCl_3$): δ = –55.7 (N-1), –192.4 (N-2).

6-Phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones 1; General Procedure

A solution of phenylpropynoyl chloride (823 mg, 5 mmol) in anhyd 1,4-dioxane (3 mL) was added dropwise to a mixture of the appropriate pyrazolone **2** (5 mmol), $Ca(OH)_2$ (741 mg, 10 mmol), and anhyd 1,4-dioxane (10 mL). The resulting mixture was heated at reflux for 6 h. After cooling to r.t., the mixture was treated with 2 N HCl (20 mL) and then stirred for 1 h before it was poured onto H_2O (50 mL). After 30 min, the mixture was suction filtered, the remaining solid was repeatedly washed with H_2O, and purified as outlined below. It should be mentioned that the crude products in most cases were accompanied by small amounts of highly colored by-products.

1-Methyl-6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (1a)

The crude product (416 mg) was subjected to flash chromatography (silica gel, EtOAc) and subsequently recrystallized (EtOH–H_2O) to afford 166 mg (15%) of a brownish solid.

Mp 165 °C.

IR (KBr): 1643 cm^{-1} (C=O).

MS: *m*/*z* (%) = 227 (M^+ + 1, 10), 226 (M^+, 57), 124 (100), 102 (21), 53 (16), 43 (15).

Anal. Calcd for $C_{13}H_{10}N_2O_2$ (226.23): C, 69.02; H, 4.46; N, 12.38. Found: C, 68.77; H, 4.66; N, 12.16.

1,3-Dimethyl-6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (1b)

The crude product (793 mg) consisted of a 1:1 mixture of **1b** and **12b**.

To the crude product was added K_2CO_3 (235 mg, 1.7 mmol) and anhyd acetone (60 mL) and the suspension was refluxed for 3.5 h with stirring. After filtration, the filtrate was evaporated under reduced pressure to afford 789 mg (66%) of **1b** as a yellowish powder (pure according to NMR analysis).

In another run the crude product was recrystallized (EtOH–H_2O) affording 204 mg (17%) of **1b** as yellow crystals.

Mp 197 °C (Lit.[2] 197–198 °C).

1-Benzyl-6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (1c)

Recrystallization (EtOH–H_2O) afforded 333 mg (22%) of brownish crystals.

Mp 178–179 °C.

IR (KBr): 1634 cm^{-1} (C=O).

MS: *m*/*z* (%) = 303 (M^+ + 1, 13), 302 (M^+, 77), 172 (54), 144 (52), 91 (100), 65 (31).

Anal. Calcd for $C_{19}H_{14}N_2O_2$ (302.30): C, 75.48; H, 4.67; N, 9.27. Found: C, 75.20; H, 4.58; N, 9.26.

1-Benzyl-3-methyl-6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (1d)

Recrystallization (EtOH–H_2O) afforded 554 mg (35%) of brownish crystals.

Mp 189–190 °C.

IR (KBr): 1653 cm^{-1} (C=O).

MS: *m*/*z* (%) = 317 (M^+ + 1, 19), 316 (M^+, 81), 225 (37), 186 (22), 158 (27), 91 (100), 67 (23), 65 (25).

Anal. Calcd for $C_{20}H_{16}N_2O_2$ (316.35): C, 75.93; H, 5.10; N, 8.85. Found: C, 75.73; H, 5.15; N, 8.78.

1-(4-Methoxybenzyl)-6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (1e)

Recrystallization (EtOH) afforded 376 mg (23%) of pink crystals.

Mp 220 °C.

IR (KBr): 1639 cm^{-1} (C=O)

MS: *m*/*z* (%) = 332 (M^+, 4), 240 (43), 138 (100), 70 (20), 69 (25), 67 (19), 43 (20).

Anal. Calcd for $C_{20}H_{16}N_2O_3$ (332.35): C, 72.28; H, 4.85; N, 8.43. Found: C, 72.00; H, 4.88; N, 8.38.

1-(4-Methoxybenzyl)-3-methyl-6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (1f)

Recrystallization (EtOH–H_2O) afforded 800 mg (46%) of pale pink crystals.

Mp 188 °C.

IR (KBr): 1647 cm^{-1} (C=O).

MS: *m*/*z* (%) = 346 (M^+, 26), 121 (100).

Anal. Calcd for $C_{21}H_{18}N_2O_3$ (346.38): C, 72.82; H, 5.24; N, 8.09. Found: C, 72.55; H, 5.05; N, 8.36.

1,6-Diphenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (1g)

Recrystallization (EtOH) afforded 878 mg (61%) of beige crystals.

Mp 189 °C (Lit.[3] 190 °C).

3-Methyl-1,6-diphenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (1h)

Recrystallization (EtOH–H_2O) afforded 854 mg (57%) of tan-colored crystals.

Mp 208–209 °C (Lit.[4] 210–211 °C, Lit.[5] 209–210 °C).

MS: *m*/*z* (%) = 303 (M^+ + 1, 11), 302 (M^+, 52), 201 (15), 200 (100), 132 (27), 91 (43), 77 (13), 51 (11), 43 (15).

3-Hydroxy-1,6-diphenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (1i)

Recrystallization (EtOH–H_2O) afforded 377 mg (25%) of beige crystals.

Mp 241–244 °C.

IR (KBr): 3400–2400 (OH), 1666, 1647 cm^{-1} (C=O).

MS: *m*/*z* (%) = 304 (M^+, 0.5), 240 (26), 226 (49), 138 (50), 124 (100), 102 (22).

Anal. Calcd for $C_{18}H_{12}N_2O_3$ (304.30): C, 71.05; H, 3.97; N, 9.21. Found: C, 70.80; H, 3.98; N, 9.06.

3-Methoxy-1,6-diphenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (1j)

Recrystallization (EtOH) afforded 778 mg (49%) of beige crystals.

Mp 208–209 °C.

IR (KBr): 1661 cm^{-1} (C=O).

MS: *m*/*z* (%) = 319 (M^+ + 1, 15), 318 (M^+, 57), 317 (45), 290 (29), 289 (100), 217 (18), 216 (98), 187 (18), 133 (22), 105 (36), 102 (28), 91 (29), 83 (33), 77 (83), 51 (34).

Anal. Calcd for $C_{19}H_{14}N_2O_3$ (318.33)·0.2 H_2O: C, 70.89; H, 4.51; N, 8.70. Found: C, 70.72; H, 4.56; N, 8.74.

Compounds 14e and 14f; General Procedure

To the PMB-protected 6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (**1e** or **1f**, 1 mmol) was added TFA (2.85 g, 25 mmol) and the mixture was stirred at 70–75 °C for 24 h. After removal of excess TFA under reduced pressure, the residue was washed with cold acetone to afford a nearly colorless powder.

6-Phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (14e)

Yield: 133 mg (63%); mp 309–310 °C.

IR (KBr): 3125, 3070 (NH), 1630 cm^{-1} (C=O).

MS: *m*/*z* (%) = 213 (M^+ + 1, 15), 212 (M^+, 69), 121 (28), 110 (67), 97 (22), 83 (20), 81 (26), 69 (52), 57 (48), 55 (53), 53 (21), 45 (22), 44 (34), 43 (100).

Anal. Calcd for $C_{12}H_8N_2O_2$ (212.21)·0.2H_2O: C, 66.79; H, 3.92; N, 12.98. Found: C, 66.67; H, 3.98; N, 12.61.

3-Methyl-6-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (14f)
Yield: 174 mg (77%); mp 314–315 °C.

IR (KBr): 3152 (NH), 1643 cm^{-1} (C=O).

MS: *m*/*z* (%) = 227 (M^+ + 1, 24), 226 (M^+, 100), 124 (80), 102 (15), 67 (35).

Anal. Calcd for $C_{13}H_{10}N_2O_2$ (226.23): C, 69.02; H, 4.46; N, 12.38. Found: C, 68.76; H, 4.72; N, 12.11.

1-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-3-phenylprop-2-yn-1-one (12b)
From the mixture **1b/12b** the following NMR data for **12b** were unambiguously extracted:

^{1}H NMR ($CDCl_3$): δ = 9.25 (br s, 1 H, OH), 7.61 (m, 2 H, Ph-2,6), 7.48 (m, 1 H, Ph-4), 7.41 (m, 2 H, Ph-3,5), 3.60 (s, 3 H, NMe), 2.54 (s, 3 H, 3-Me).

^{13}C NMR ($CDCl_3$): δ = 172.1 (C=O), 159.2 (pyrazole C-5), 147.8 (pyrazole C-3), 132.7 (Ph-2,6), 130.8 (Ph-4), 128.7 (Ph-3,5), 119.9 (Ph-1), 104.6 (pyrazole C-4), 94.7 (Ph*C*≡), 86.5 (≡*C*CO), 32.5 (NMe), 14.1 (3-Me).

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