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Spiro-Fused (C2)-Azirino-(C4)-pyrazolones, a New Heterocyclic System. Synthesis, Spectroscopic Studies and X-ray Structure Analysis[1]

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Reaction of 1-substituted 4-acyl-5-hydroxy-3-methyl-1*H*-pyrazoles (**2**) with hydroxylamine gives the corresponding "oximes" **3**, which are mainly present as (*Z*)-2,4-dihydro-4-[(hydroxyamino)methylene]-3*H*-pyrazol-3-ones. Treatment of compounds **3** with trichloroacetyl isocyanate/potassium carbonate in anhydrous diethyl ether affords 7-methyl-1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-ones (**4**). The structure of compounds **4** was elucidated by means of single-crystal X-ray analysis (**4f**, **4h**) and confirmed by NMR spectroscopic investigations (^{1}H, ^{13}C).

Introduction

4-Acyl-5-hydroxy-3-methyl-1*H*-pyrazoles (tautomer to 4-acyl-1,2-dihydro-3*H*-pyrazol-3-ones) (**2**) are effective chelating and extracting reagents for many metal ions[2] and are used as starting materials for the synthesis of biologically active compounds,[3] as well as for the construction of condensed heterocyclic systems.[4,5] Moreover, these compounds are of particular interest due to their ability to exist in several tautomeric forms, such as the OH (form A), the NH (form B), the CH (form C), and the hydroxymethylene forms (D, E), with isomers A and D having the possibility to be stabilized via an intramolecular hydrogen bond (A′, D′) (Figure 1).[6] The tautomerism of such compounds in solution and in the solid state has been the subject of extensive investigations.[6−11] Recently, we presented NMR spectroscopic studies that revealed a complex behavior of such compounds in solution with the chelated OH form A′ being the main isomer in $CDCl_3$ or C_6D_6, whereas in DMSO-d_6 an equilibrium between the OH form (A) and NH form (B) is assumed.[12] In continuation of our investigations regarding the tautomerism, chemistry, and synthetic potential of pyrazolones[12−17] we here report the transformation of compounds **2** into the corresponding oximes **3**

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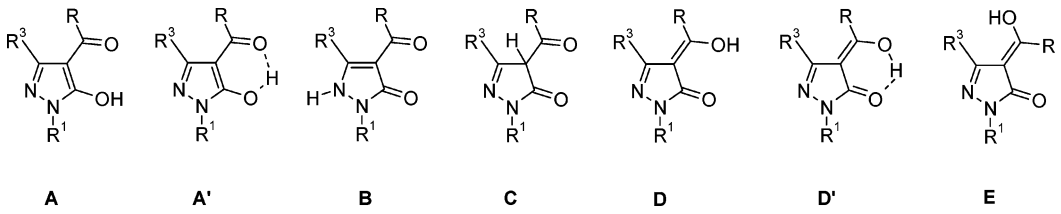
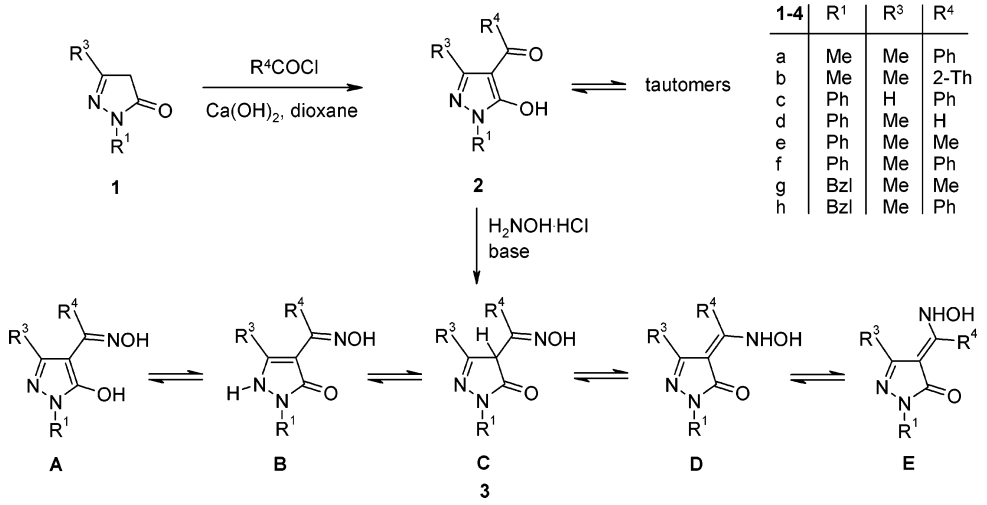


FIGURE 1. Possible tautomeric forms of 4-acyl-1,2-dihydro-3*H*-pyrazol-3-ones (**2**).

SCHEME 1. Synthesis and Possible Tautomeric Forms of Compounds 3



1-4	R^1	R^3	R^4
a	Me	Me	Ph
b	Me	Me	2-Th
c	Ph	H	Ph
d	Ph	Me	H
e	Ph	Me	Me
f	Ph	Me	Ph
g	Bzl	Me	Me
h	Bzl	Me	Ph

and subsequent reaction of the latter with trichloroacetyl isocyanate. Cyclization of compounds **3** under the influence of this mild and effective dehydrating agent[18] was considered as a possible approach to 6*H*-pyrazolo[4,3-d]-isoxazoles (**5**) (see Scheme 3), a class of compounds with reported antibacterial activity.[19]

Results and Discussion

Synthesis and Structure of Compounds 3. The acylpyrazolones **2**, easily accessible from pyrazolones **1** following the method of Jensen (heating with RCOCl/Ca-$(OH)_2$ in dioxane),[20] were transformed into the corresponding oximes **3** by treatment with hydroxylamine hydrochloride in the presence of a base (Scheme 1). Like parent pyrazolones **2**, compounds **3** can also, in principle, exist in several tautomeric forms (Scheme 1); however, the situation for **3** is more complex. In addition to tautomerism also *E*/*Z*-diastereomerism at the C=N double bond has to be considered, and moreover, intramolecular hydrogen bonding is possible in a number of tautomers. For model compound **3f** ($R^1 = R^4 = Ph$, $R^3 = Me$) we quite recently have shown by single-crystal X-ray analysis and by detailed NMR spectroscopic investigations that this species is present as (*Z*)-configurated enaminopyrazolone (form D in Scheme 1) in the solid state and in DMSO-d_6 solution.[17] From the similarity of the chemical shifts, particularly in the ^{13}C NMR spectra, and the results of NOE-difference experiments (pronounced NOEs between protons of R^3 and R^4) it is very probable that also the other investigated compounds of type **3** are mainly present in this isomeric form in DMSO-d_6 solution. However, marked line broadening for a variety of signals points to a dynamic behavior, and quick exchange with other forms cannot be excluded. Moreover, because the NMR spectra of some representatives (**3b**, **3d**, **3e**, **3g**) exhibited a (minor) second set of signals, the simultaneous existence of an additional isomeric form in DMSO-d_6 or $CDCl_3$ solution must be assumed in these cases. A C−H isomeric structure (form C) can be ruled out owing to the lack of signals due to a C(sp^3)-H fragment. It would be imaginable that the different signal sets originate from the simultaneous presence of forms D and A and/or B; however, it is well-known that interconversion between OH and NH forms is quick compared to the NMR time scale, which would rather result in only one averaged signal set, maybe accompanied by some line broadening.[21] Considering the ^{13}C chemical shifts in corresponding pairs of isomers also excludes the possibility of simple *E*/*Z*-oxime mixtures. In such a case, characteristic γ-effects would lead to highfield shifts for the γ-carbon atoms being located in a position *cis* to the oxime oxygen atom.[17,22] A possible explanation for the observed phenomenon consists of restricted rotation around the exocyclic C−N bond in isomers D (Scheme 1), which has some double character.[17] Indeed, coalescence of corresponding lines occurs in the ^1H NMR spectra of, for instance, **3b** or **3g** at elevated temperature (>100 °C). Similar effects with related enaminopyrazolones are described in the literature.[23−25] It should be mentioned

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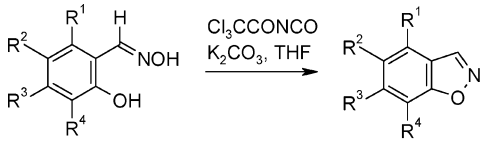
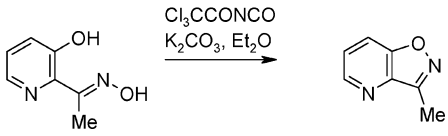
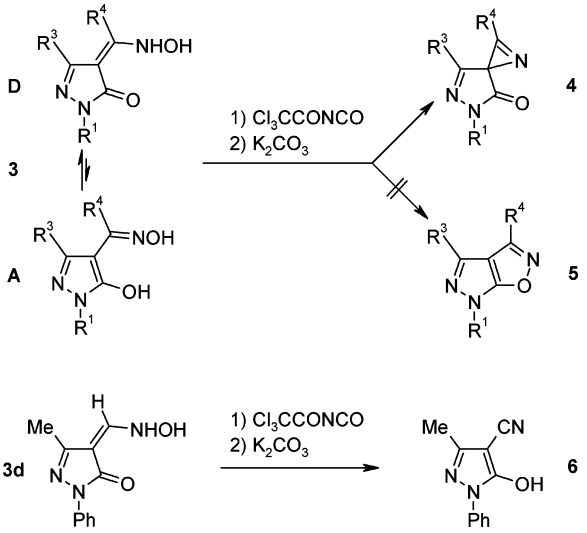
SCHEME 2. Synthesis of Condensed Isoxazoles via Trichloroacetyl Isocyanate Mediated Cyclization





SCHEME 3. Reaction of Compounds 3 with Trichloroacetyl Isocyanate



that an enaminopyrazolone structure D for **3e** and **3f** was already suggested in 1988 by Hennig and Mann;[26] however, no spectral support for these assumptions was provided. In the course of recording high-temperature spectra at ~120 °C with the aldehyde-derived compound **3d** in DMSO-d_6 solution, rapid and complete conversion into the corresponding nitrile **6** (Scheme 3) was observed.

Reaction of Compounds 3 with Trichloroacetyl Isocyanate and Other Cyclization Agents. Trichloroacetyl isocyanate has been found a mild and effective reagent in the preparation of 1,2-benzisoxazoles from salicylaldoximes or (2-hydroxyphenyl)ketoximes[18] and, particularly, for the conversion of methyl 3-hydroxy-2-pyridyl ketone oxime into 3-methylisoxazolo[4,5-*b*]pyridine (Scheme 2).[27]

Subjecting 4-acyl-derived compounds of type **3** under these reaction conditions revealed the formation of a dominating reaction product and the complete consumption of the educt. Although microanalytical data of the obtained products were in accordance with the expected 6*H*-pyrazolo[4,3-*d*]isoxazole (**5**) structures (Scheme 3), spectroscopic investigations ruled out the latter. Thus, the IR spectra of compounds **4** showed two intensive bands in the range between 1700 and 1810 cm^{-1}, and in the ^{13}C NMR spectra the occurrence of a signal due to a quarternary sp^3-hybridized carbon atom (~45 ppm) was detected, both findings being incompatible with structures **5**. Ultimately, on the basis of single-crystal X-ray analyses the obtained products could unambiguously be assigned 1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-one (**4**)

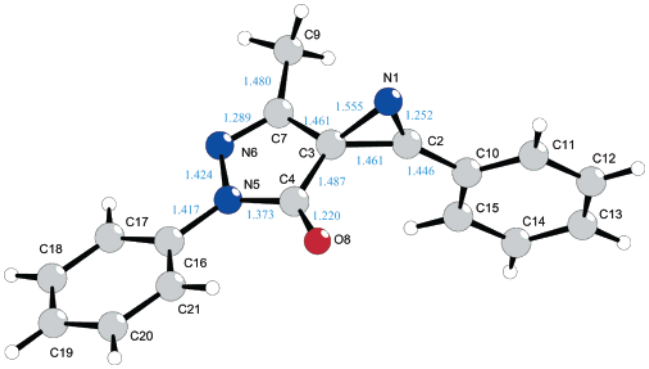


FIGURE 2. Molecular structure and selected bond lengths of 2,5-diphenyl-7-methyl-1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-one (**4f**).

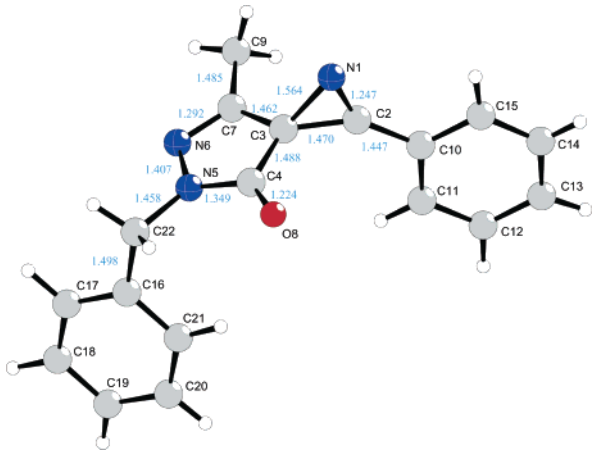


FIGURE 3. Molecular structure and selected bond lengths of 1-benzyl-7-methyl-2-phenyl-1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-one (**4h**).

structures (see below), accounting for all the spectroscopic characteristics. In Figures 2 and 3 are shown the molecular structures and some selected bond lengths for **4f** and **4h**, respectively. Spiro compounds **4** are stable at room temperature (only **4c** turned out to be labile); however, heating to temperatures over 80 °C obviously results in rapid decomposition. Further investigations regarding the reactivity and chemical properties of compounds **4** are in progress and will be reported elsewhere.

In contrast, applying the above reaction conditions to the aldehyde-derived compound **3d** did not result in the formation of the corresponding spiro compound **4d** but, expectedly, gave nitrile **6** in good yields (Scheme 3).

A possible reaction mechanism for the formation of compounds **4** is outlined in Scheme 4. It is related to the well-known Lossen reaction of O-acylated hydroxamic acids (Scheme 4, lower trace), which upon treatment with a base afford an intermediate nitrene; stabilization of the latter occurs by rearrangement to an isocyanate.[28] Compounds **3** present in the enaminopyrazolone form (form

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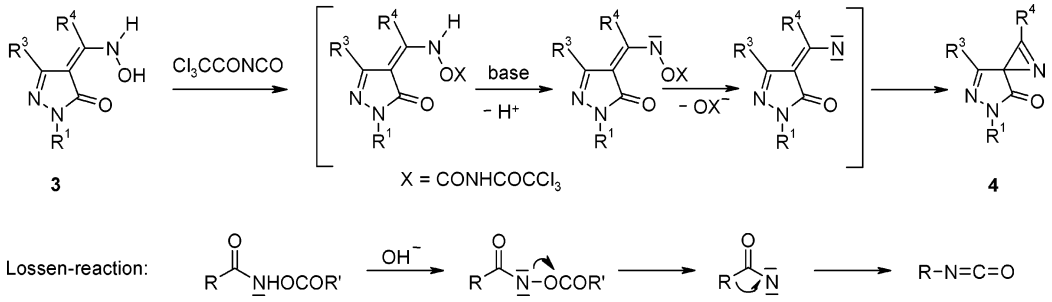
SCHEME 4. Possible Reaction Mechanism for Formation of Spiro Compounds 4



D in Scheme 1) can be seen as vinylogous hydroxamic acids, which are attacked by trichloroacetyl isocyanate at the OH function. After base-induced abstraction of the NH proton elimination of the good leaving group OX^- then leads to a nitrene, which in contrast to the Lossen reaction can stabilize not by rearrangement but by azirine ring closure to afford the spiro compounds **4**. It should be mentioned that related transient vinylnitrenes are assumed to be key intermediates in azirine ring synthesis[29,30] and are also formed within the thermally induced ring expansion of different 2-halo-2*H*-azirines into 4-haloisoxazoles.[31] An alternative but rather less probable mechanism for the conversion **3** → **4** is a Nebertype reaction;[32] however, this would require compounds **3** to be present as CH-isomers (form C in Scheme 1) that never could be detected by spectroscopic means.

It should be mentioned that attempted conversion of "oximes" **3** into 6*H*-pyrazolo[4,3-*d*]isoxazoles (**5**) by application of various standard reaction systems used for the cyclization of (2-hydroxyaryl)ketoximes or -aldoximes into anellated 1,2-oxazoles (i.e., heating in methanolic or ethanolic potassium hydroxide, heating with acetic anhydride/pyridine, treatment with thionyl chloride/pyridine in ether, etc.)[33] failed. Also isoxazole ring closure via intramolecular Mitsunobu reaction, which was recently reported to proceed smoothly in the benzene series,[34] was unsuccessful. This behavior can be explained by the obviously complete absence of a 5-hydroxypyrazole form for compounds **3** (also under the reaction conditions), which would be required for such ring closure reactions. Thus, for the synthesis of target structures **5** we recently reported an alternative route employing isoxazole ring formation with oximes derived from 4-benzoyl-5-chloropyrazoles, a strategy that circumvents the problems arising from pyrazolone tautomerism.[35]

Spectroscopic Investigations with Compounds 4. The IR spectra of spiro compounds **4** exhibit the pyrazolone C═O stretching vibration as a strong band at ~1700 cm^{-1}, whereas the C═N absorption of the strained azirine ring occurs at higher frequencies and with somewhat lower intensity. Thus, for instance, ν(C═N) was found to have 1810 cm^{-1} for **4g** (R^4 = Me), and in cases with R^4 being an aromatic system (**4a**−**c**, **4f**, **4h**) it is shifted to lower frequencies (1770−1780 cm^{-1}) as a result of conjugation effects. Comparing the ^{1}H NMR data of compounds **4** (R^3 = Me) with those of **3** reveals some upfield shift for the pyrazole-Me line, for instance, **3g** DMSO-d_6, 2.16 ppm; **4g** ($CDCl_3$), 1.78 ppm. Nevertheless, in the ^{13}C NMR spectra more significant differences are obvious; thus, in compounds **4** the pyrazole carbon atoms C-3 and C-5 receive a marked downfield shift (C-3 in **3g**, 160.6; in **4g**, 170.5; C-5 in **3g**, 145.9; in **4g**, 156.7). In the ^{1}H NMR spectrum of **4h** the two protons of the benzylic methylene group are nonequivalent as a result of the chiral center at C-3 giving rise to an AB spin system (^2J = 15.1 Hz). Unambiguous assignment of signals and spin coupling constants was achieved on the basis of standard 1D and 2D NMR techniques, together with the use of 1D-TOCSY[36] and 1D[37] and 2D long-range INEPT experiments.[38]

Conclusions

We have presented the straightforward synthesis of a variously substituted new spiro-heterocyclic system of type **4** starting from easily available 4-acylpyrazolones **2**. Key intermediates are the "oximes" **3**, which are present as enaminopyrazolone tautomers. The special structural features of compounds **3** explain their reactivity in the system trichloroacetyl isocyanate/potassium carbonate, exclusively leading to spiro compounds **4** and not to 6*H*-pyrazolo[4,3-*d*]isoxazoles **5**. The most likely mechanism for the formation of compounds **4** is related to the Lossen reaction and assumes an intermediate vinylnitrene that stabilizes upon spiro ring formation. Studies regarding the chemistry of spiro compounds **4** are currently under investigation.

Experimental Section

The numbering of atoms in the listings of NMR signals for compounds **2** is always given for the hydroxypyrazole form (**A**

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in Figure 1) and for compounds **3** in the enaminopyrazolone form (**D** in Scheme 1). With compounds **3**, not all lines of the corresponding minor isomers could be assigned unambiguously, owing to overlap with signals due to the predominating major isomer and massive line broadening, respectively. Acylpyrazolones **2a**,[39] **2b**,[40] **2c**,[41] **2d**,[42] and **2h**[43] are known compounds, which except for aldehyde **2d** were prepared according to the Jensen method[20] as described below for novel compound **2g**. Compounds **2e** and **2f** are commercially available.

5-Hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-carbaldehyde (2d).[42] ^{13}C NMR ($CDCl_3$): δ 12.3 (3-Me), 105.7 (pyrazole C-4), 120.9 (Ph C-2,6), 126.9 (Ph C-4), 129.1 (Ph C-3,5), 136.9 (Ph C-1), 149.0 (pyrazole C-3), 158.9 (pyrazole C-5), 184.4 (CO).

1-(1-Benzyl-5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)ethanone (2g). Under cooling and vigorous stirring, to a suspension of 2-benzyl-1,2-dihydro-5-methyl-3*H*-pyrazol-3-one (**1g**)[44] (1.882 g, 10 mmol) and calcium hydroxide powder (1.482 g, 20 mmol) in 20 mL of dioxane (dried over 4Å molecular sieves) was added a solution of acetyl chloride (785 mg, 10 mmol) in 5 mL of dioxane, and the mixture was then refluxed for 2 h. After cooling, 25 mL of 2 N HCl was added, and the mixture was vigorously stirred for 1 h and was then poured onto 100 mL of water. After extraction with dichloromethane the combined organic phases were washed with water, dried over anhydrous Na_2SO_4, and evaporated in vacuo. Kugelrohr distillation (250 °C, 12 mbar) afforded 1.059 g (46%) of a tan oil. ^{1}H NMR ($CDCl_3$): δ 2.36 (s, 3 H, 3-Me), 2.38 (s, 3 H, COMe), 5.05 (s, 2 H, CH_2), 7.22−7.35 (m, 5 H, Ph), 8.61 (br s, 1 H, OH). ^{13}C NMR ($CDCl_3$): δ 15.3 (3-Me, ^1J = 128.2 Hz), 27.0 (COMe, ^1J = 127.8 Hz), 49.4 (CH_2, ^1J = 139.9 Hz), 103.1 (pyrazole C-4), 127.7 (Ph C-2,6), 127.8 (Ph C-4), 128.6 (Ph C-3,5), 135.6 (Ph C-1), 146.9 (pyrazole C-3, ^2J(C-3,3-Me) = 6.8 Hz), 159.5 (pyrazole C-5), 194.8 (CO, ^2J(CO,COMe) = 5.9 Hz). IR (KBr): ν 1644 cm^{-1} (CO). MS: *m*/*z* (%) = 231 (13), 230 (M$^+$, 84), 215 (21), 153 (12), 137 (36), 126 (60), 106 (10), 92 (11), 91 (100), 84 (15), 65 (33), 43 (32). Anal. Calcd for $C_{13}H_{14}N_2O_2$ (230.27): C 67.81, H 6.13, N 12.17. Found: C 68.09, H 6.27, N 12.40.

1-(1-Benzyl-5-hydroxy-3-methyl-1*H*-pyrazol-4yl)(phenyl)methanone (2h).[43] Under cooling and vigorous stirring, to a suspension of **1g**[44] (1.882 g, 10 mmol) and calcium hydroxide powder (1.482 g, 20 mmol) in 20 mL of dioxane was added a solution of benzoyl chloride (1.406 g, 10 mmol) in 5 mL of dioxane, and the mixture was then refluxed for 2 h. After cooling, 25 mL of 2 N HCl was added, and the mixture was vigorously stirred for 1 h and was then poured onto 100 mL of water. The precipitated solid was filtered off, washed with water, and recrystallized from EtOH to afford 1.89 g (65%) of colorless needles of mp 175 °C (EtOH). ^{1}H NMR ($CDCl_3$): δ 2.00 (s, 3 H, 3-Me), 5.13 (s, 2 H, CH_2), 7.33 (m, 1 H, Bzl H-4), 7.35 (m, 4 H, Bzl H-2,3,5,6), 7.47 (m, 2 H, COPh H-3,5), 7.54 (m, 1 H, COPh H-4), 7.60 (m, 2 H, COPh H-2,6), 9.91 (br s, 1 H, OH). ^{13}C NMR ($CDCl_3$): δ 15.7 (3-Me, ^1J = 128.6 Hz), 49.7 (CH_2, ^1J = 140.1 Hz), 102.5 (pyrazole C-4, ^3J(C-4,3-Me) = 2.7 Hz), 127.7 (COPh C-2,6), 128.0 (Bzl C-2,4,6), 128.3 (COPh C-3,5), 128.7 (Bzl C-3,5), 131.6 (COPh C-4), 135.6 (Bzl C-1), 138.3 (COPh C-1), 147.2 (pyrazole C-3, ^2J(C-3,3-Me) = 6.8 Hz), 160.6 (pyrazole C-5, ^3J(C-5,NCH$_2$) = 2.5 Hz), 192.8 (CO). IR (KBr): ν 1620 cm^{-1} (CO). MS: *m*/*z* (%) = 292 (M$^+$, 41), 215 (16), 213 (10), 188 (17), 137 (16), 106 (17), 105 (44), 91 (100), 67 (27), 65 (26). Anal. Calcd for $C_{18}H_{16}N_2O_2$ (292.34): C 73.96, H 5.52, N 9.58. Found: C 74.08, H 5.75, N 9.71.

General Procedure for the Synthesis of Compounds 3. Method (a). A mixture of 4-acyl-5-hydroxypyrazole **2** (10 mmol) and hydroxylamine hydrochloride (2.78 g, 40 mmol) in ethanol (20 mL) and pyridine (3 mL) was heated to reflux for 4 h and then poured onto an excess of water (200 mL). The resulting suspension was exhaustively extracted with dichloromethane (and ethyl acetate, if necessary), and the combined organic phases were washed with water, dried over anhydrous Na_2SO_4, and evaporated in vacuo. The crude product was purified by recrystallization. **Method (b).** A mixture of 4-acyl-5-hydroxypyrazole **2** (10 mmol) and hydroxylamine hydrochloride (2.085 g, 30 mmol) in ethanol (80 mL) and water (20 mL) was stirred at room temperature for 1 h. Then NaOH pellets (1.20 g, 30 mmol) were added, and the mixture was refluxed for 2 h. After 12 h of standing at room temperature the precipitate was filtered with suction and purified by recrystallization.

(*Z*)-2,4-Dihydro-2,5-dimethyl-4-[(hydroxyamino)phenylmethylene]-3*H*-pyrazol-3-one (3a). Yield 58% (method a), colorless crystals of mp 179−181 °C (EtOH). ^{1}H NMR (DMSO-d_6): δ 1.55 (s, 3 H, 5-Me), 3.41 (s, 3 H, 2-Me), 7.39−7.53 (m, 5 H, Ph), 12.10 (br s, 2 H, OH, NH). ^{13}C NMR (DMSO-d_6): δ 14.1 (5-Me, ^1J = 127.5 Hz), 32.1 (2-Me, ^1J = 139.3 Hz), 94.3 (pyrazole C-4), 128.1 (Ph C-2,6), 128.4 (Ph C-3,5), 129.8 (Ph C-4), 133.9 (br, Ph C-1), 144.7 (pyrazole C-5, ^2J(C-5,5-Me = 6.8 Hz), 151.3 (br, C-N), 156.2 (br, pyrazole C-3). MS: *m*/*z* (%) = 231 (M$^+$, 13), 213 (45), 212 (27), 142 (28), 105 (13), 78 (10), 77 (79), 67 (15), 66 (13), 51 (48), 50 (17), 44 (11), 43 (100), 42 (70), 41 (34). Anal. Calcd for $C_{12}H_{13}N_3O_2$ (231.26): C 62.33, H 5.67, N 18.17; found: C 62.48, H 5.66, N 18.25.

(*Z*)-2,4-Dihydro-2,5-dimethyl-4-[(hydroxyamino)(2-thienyl)methylene]-3*H*-pyrazol-3-one (3b). Yield 54% (method b), colorless needles of mp 195 °C (EtOH). ^{1}H NMR (DMSO-d_6): (isomers X:Y = 1.6:1), isomer X δ 1.86 (s, 3 H, 5-Me), 3.44 (s, 3 H, 2-Me), 6.93 (dd, ^3J = 3.6 Hz, ^4J = 1.1 Hz, 1 H, Th H-3), 7.00 (dd, ^3J(H-4,H-5) = 5.0 Hz, ^3J(H-4,H-3) = 3.6 Hz, 1H, Th H-4), 7.45 (dd, ^3J = 5.0 Hz, ^4J = 1.1 Hz, 1 H, Th H-5), 10.97 and 11.90 (br s, 2 H, OH, NH); isomer Y δ 1.93 (s, 3 H, 5-Me), 3.44 (s, 3 H, 2-Me), 7.15 (dd, ^3J = 3.8 Hz, ^4J = 1.2 Hz, 1 H, Th H-3), 7.05 (dd, ^3J(H-4,H-5) = 5.1 Hz, ^3J(H-4,H-3) = 3.8 Hz, 1 H, Th H-4), 7.68 (dd, ^3J = 5.1 Hz, ^4J = 1.2 Hz, 1H, Th H-5), 10.97 and 11.90 (br s, 2 H, OH, NH). ^{13}C NMR (DMSO-d_6): isomer X δ 13.6 (5-Me, ^1J = 127.4 Hz), 32.4 (br, 2-Me, ^1J = 139.8 Hz), 93.9 (br, pyrazole C-4), 126.7 (Th C-5), 127.1 (Th C-4), 127.5 (Th C-3), 140.3 (br, Th C-2), 144.3 (pyrazole C-5), 145.2 (C-N), 152.3 (very br, pyrazole C-3); isomer Y δ 12.6 (br, 5-Me), 32.4 (br, 2-Me), 98.0 (very br, pyrazole C-4), 125.4 (Th C-4), 130.2 (Th C-5), 130.6 (Th C-3), 132.9 (Th C-2), 142.6 (C-N), 144.7 (pyrazole C-5), 152.3 (very br, pyrazole C-3). MS: *m*/*z* (%) = 237 (M$^+$, 33), 221 (18), 220 (21), 219 (100), 218 (37), 150 (16), 149 (20), 148 (51), 136 (21), 122 (13), 121 (14), 112 (11), 111 (29), 110 (21), 97 (11), 69 (23), 67 (33), 66 (24), 58 (22), 52 (11), 45 (30), 43 (51), 42 (30), 41 (11). Anal. Calcd for $C_{10}H_{11}N_3O_2S$ (237.28): C 50.62, H 4.67, N 17.71. Found: C 50.85, H 4.54, N 17.64.

(*Z*)-2,4-Dihydro-4-[(hydroxyamino)(phenyl)methylene]-2-phenyl-3*H*-pyrazol-3-one (3c). Yield 73% (method a), colorless crystals of mp 164 °C (EtOH/diisopropyl ether). ^{1}H NMR (DMSO-d_6): δ 7.22 (s, 1 H, pyrazole H-5), 7.24 (m, 1 H, 2-Ph H-4), 7.45 (m, 2 H, 2-Ph H-3,5), 7.58 (m, 2 H, C-Ph H-3,5), 7.60 (m, 1 H, C-Ph H-4), 7.62 (m, 2 H, C-Ph H-2,6), 7.92 (m, 2 H, 2-Ph H-2,6), 12.0−15.5 (br s, 2 H, OH, NH). ^{13}C NMR (DMSO-d_6): δ 96.4 (pyrazole C-4, ^2J(C-4,H-5) = 9.3 Hz), 119.6 (2-Ph C-2,6), 125.3 (2-Ph C-4), 128.8 (2-Ph C-3,5 and C-Ph C-3,5), 129.5 (C-Ph C-2,6), 130.3 (C-Ph C-1), 131.5 (C-Ph C-4), 138.7 (2-Ph C-1), 141.0 (pyrazole C-5, ^1J = 188.5 Hz), 152.8 (br, C-N), 160.2 (br, pyrazole C-3). MS: *m*/*z* (%) = 279 (M$^+$, 13), 261 (26), 260 (24), 128 (23), 91 (16), 78 (11), 77 (100), 55 (12), 53 (10), 52 (27), 51 (61), 50 (13). Anal. Calcd for

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$C_{16}H_{13}N_3O_2$ (279.30): C 68.81, H 4.69, N 15.04. Found: C 68.91, H 4.92, N 15.10.

(*Z*)-2,4-Dihydro-4-[(hydroxyamino)methylidene]-5-methyl-2-phenyl-3*H*-pyrazol-3-one (3d). Yield 88% (method b), yellowish crystals of mp 171 °C (diisopropyl ether) (lit. mp 173 °C).[42] ^{1}H NMR (DMSO-d_6): (isomers X:Y = 5:1), isomer X δ 2.15 (s, 3 H, 5-Me), 7.16 (m, 1 H, Ph H-4), 7.39 (m, 2 H, Ph H-3,5), 7.75 (s, 1 H, N-CH), 7.86 (m, 2 H, Ph H-2,6), 10.68, 12.55 and 16.25 (br s, OH, NH); isomer Y δ 2.27 (s, 3 H, 5-Me), 7.21 (m, 1 H, Ph H-4), 7.42 (m, 2 H, Ph H-3,5), 7.74 (m, 2 H, Ph H-2,6), 8.05 (s, 1 H, N-CH), 10.68, 12.55 and 16.25 (br s, OH, NH). ^{13}C NMR (DMSO-d_6): isomer X δ 12.5 (5-Me, ^1J = 128.0 Hz), 94.9 (pyrazole C-4), 119.0 (Ph C-2,6), 124.6 (Ph C-4), 128.7 (Ph C-3,5), 138.7 (Ph C-1), 139.1 (N-CH, ^1J = 174.7 Hz), 149.0 (pyrazole C-5, ^2J(C-5,5-Me) = 6.8 Hz, ^3J(C-5,N-CH) = 2.8 Hz), 161.7 (pyrazole C-3); isomer Y δ 14.2 (br, 5-Me), 120.1 (Ph C-2,6), 125.1 (Ph C-4), 128.8 (Ph C-3,5), 142.5 (N-CH, ^1J = 163.1 Hz), 146.6. (pyrazole C-5, ^2J(C-5,5-Me) = 6.8 Hz, ^3J(C-5,N-CH) = 5.2 Hz). MS: *m*/*z* (%) = 217 (M^+, 33), 199 (18), 198 (30), 132 (12), 131 (41), 103 (29), 92 (11), 91 (100), 78 (12), 77 (88), 69 (20), 68 (15), 67 (32), 66 (24), 65 (16), 64 (15), 57 (22), 55 (21), 53 (19), 52 (17), 51 (58), 50 (13), 45 (12), 43 (38), 42 (18), 41 (43).

(*Z*)-2,4-Dihydro-4-[1-(hydroxyamino)ethylidene]-5-methyl-2-phenyl-3*H*-pyrazol-3-one (3e). Yield 82% (method a), the raw product was washed with diisopropyl ether to afford colorless crystals of mp 142−144 °C (lit. mp 154−156 °C).[26] ^{1}H NMR (DMSO-d_6): (isomers X:Y = 2:1), isomer X δ 2.27 (s, 3 H, 5-Me), 2.32 (s, 3 H, Me of R[4]), 7.17 (m, 1 H, Ph H-4), 7.39 (m, 2 H, Ph H-3,5), 7.89 (m, 2 H, Ph H-2,6), 11.50 and 16.00 (br s, 2 H, OH, NH); isomer Y δ 2.29 (s, 3 H, 5-Me), 2.32 (s, 3 H, Me of R[4]), 7.14 (m, 1 H, Ph H-4), 7.39 (m, 2 H, Ph H-3,5), 7.89 (m, 2 H, Ph H-2,6), 11.50 and 16.00 (br s, 2 H, NH, OH). ^{13}C NMR (DMSO-d_6): isomer X δ 16.4 (5-Me, ^1J = 128.0 Hz), 17.3 (Me of R,[4] ^1J = 130.8 Hz), 95.5 (pyrazole C-4), 119.3 (Ph C-2,6), 124.6 (Ph C-4), 128.7 (Ph C-3,5), 138.7 (Ph C-1), 147.7 (pyrazole C-5, ^2J(C-5,5-Me) = 6.8 Hz), 152.8 (C-N), 161.3 (pyrazole C-3); isomer Y δ 12.8 (Me of R,[4] ^1J = 130.1 Hz), 15.5 (br, 5-Me, ^1J = 127.7 Hz), 96.5 (br, pyrazole C-4), 118.8 (Ph C-2,6), 124.3 (Ph C-4), 128.7 (Ph C-3,5), 138.7 (Ph C-1), 146.5 (pyrazole C-5, ^2J(C-5,5-Me) = 6.8 Hz), 157.3 (br, C-N), 160.7 (pyrazole C-3). MS: *m*/*z* (%) = 231 (M^+, 64), 215 (12), 212 (30), 199 (12), 92 (12), 91 (61), 82 (11), 81 (12), 80 (28), 78 (12), 77 (100), 69 (14), 67 (31), 66 (24), 65 (20), 64 (17), 63 (13), 54 (11), 53 (12), 52 (16), 51 (73), 50 (16), 43 (14), 42 (54), 41 (14).

(*Z*)-2,4-Dihydro-4-[(hydroxyamino)phenylmethylene]-5-methyl-2-phenyl-3*H*-pyrazol-3-one (3f). Yield 76% (method a), recrystallization from ethanol afforded cream colored crystals of mp 162−170 °C (dec) (lit. mp 166 °C[45] or 168−172 °C[26]). ^{1}H NMR (DMSO-d_6): δ 1.61 (s, 3 H, 5-Me), 7.21 (m, 1 H, 2-Ph H-4), 7.44 (m, 2 H, 2-Ph H-3,5), 7.52 (m, 2 H, C-Ph H-3,5), 7.53 (m, 1 H, C-Ph H-4), 7.57 (m, 2 H, C-Ph H-2,6), 7.89 (m, 2 H, 2-Ph H-2,6), 12.90 (br s, 2 H, OH, NH). ^{13}C NMR (DMSO-d_6): δ 14.5 (5-Me, ^1J = 128.0 Hz), 96.0 (br, pyrazole C-4), 119.5 (2-Ph C-2,6), 124.9 (2-Ph C-4), 128.6 (C-Ph C-3,5), 128.8 (2-Ph C-3,5 and C-Ph C-2,6), 130.7 (C-Ph C-4), 132.1 (br, C-Ph C-1), 138.5 (2-Ph C-1), 147.5 (pyrazole C-5, ^2J(C-5,5-Me) = 7.0 Hz), 152.9 (br, C-N), 158.8 (br, pyrazole C-3). MS: *m*/*z* (%) = 293 (M^+, 7), 275 (15), 231 (27), 212 (14), 91 (56), 80 (13), 78 (11), 77 (100), 67 (22), 66 (17), 65 (16), 64 (13), 63 (10), 51 (59), 50 (13), 43 (12), 42 (34), 42 (10).

(*Z*)-2-Benzyl-2,4-Dihydro-4-[1-(hydroxyamino)ethylidene]-5-methyl-3*H*-pyrazol-3-one (3g). Yield 54% (method a), yellowish crystals of mp 133 °C (diisopropyl ether). ^{1}H NMR (DMSO-d_6): (isomers X:Y = 2:1), isomer X δ 2.16 (s, 3 H, 5-Me), 2.25 (s, 3 H, Me of R[4]), 4.86 (s, 2 H, CH_2), 7.16−7.34 (m, 3 H, Ph H-3,4,5), 7.20 (m, 2 H, Ph H-2,6), 10.61, 11.99 and 16.60 (br s, 2 H, OH, NH); isomer Y δ 2.15 (s, 3 H, 5-Me), 2.16 (s, 3 H, Me of R[4]), 4.93 (s, 2 H, CH_2), 7.16−7.34 (m, 3 H, Ph H-3,4,5), 7.18 (m, 2 H, Ph H-2,6), 10.61, 11.99 and 16.60 (br s, 2 H, OH, NH). ^{13}C NMR (DMSO-d_6): isomer X δ 16.2 (5-Me, ^1J = 127.6 Hz), 17.1 (Me of R,[4] ^1J = 130.6 Hz), 47.9 (CH_2, ^1J = 139.1 Hz), 94.0 (pyrazole C-4), 127.1 (Ph C-4), 127.4 (Ph C-2,6), 128.3 (Ph C-3,5), 137.8 (Ph C-1), 145.9 (pyrazole C-5, ^2J(C-5,5-Me) = 6.7 Hz), 151.5 (C-N), 160.6 (pyrazole C-3); isomer Y δ 12.6 (Me of R[4]), 14.5 (5-Me), 97.7 (very br, pyrazole C-4), 127.2 (Ph C-4), 127.3 (Ph C-2,6), 128.4 (Ph C-3,5), 137.6 (Ph C-1), 144.2 (pyrazole C-5, ^2J(C-5,5-Me) = 6.7 Hz), 152.5 (br, C-N). MS: *m*/*z* (%) = 245 (M^+, 12), 91 (100), 80 (11), 67 (10), 65 (29), 51 (10), 43 (17), 42 (17). Anal. Calcd for $C_{13}H_{15}N_3O_2$ (245.28): C 63.66, H 6.16, N 17.13. Found: C 63.63, H 6.13, N 17.04.

(*Z*)-2-Benzyl-2,4-Dihydro-4-[(hydroxyamino)phenylmethylene]-5-methyl-3*H*-pyrazol-3-one (3h). Yield 92% (method a), colorless needles of mp 154−156 °C (EtOH). ^{1}H NMR (DMSO-d_6): δ 1.55 (s, 3 H, 5-Me), 4.98 (s, 2 H, CH_2), 7.23 (m, 2 H, Bzl H-2,6), 7.26 (m, 1 H, Bzl H-4), 7.34 (m, 2 H, Bzl H-3,5), 7.47 (m, 2 H, =CPh H-2,6), 7.40−7.53 (m, 3 H, =CPh H-3,4,5), 12.36 (br s, 2 H, OH, NH). ^{13}C NMR (DMSO-d_6): δ 14.3 (5-Me, ^1J = 127.6 Hz), 48.3 (CH_2, ^1J = 139.0 Hz), 94.3 (pyrazole C-4), 127.2 (Bzl C-4), 127.3 (Bzl C-2,6), 128.3 (=CPh C-2,6), 128.4 (Bzl C-3,5 and =CPh C-3,5), 130.0 (=CPh C-4), 133.4 (br, =CPh C-1), 137.7 (Bzl C-1), 145.4 (pyrazole C-5, ^2J(C-5,5-Me) = 6.8 Hz), 151.6 (C-N), 157.0 (br, pyrazole C-3). MS: *m*/*z* (%) = 307 (M^+, 6), 288 (11), 212 (12), 142 (15), 91 (100), 77 (29), 65 (29), 51 (17), 42 (19). Anal. Calcd for $C_{18}H_{17}N_3O_2$ (307.36): C 70.34, H 5.58, N 13.67. Found: C 70.17, H 5.58, N 13.72.

General Procedure for the Synthesis of Spiro-Compounds 4. Under Ar and with stirring, to a solution of compound **3** (1 mmol) in 10 mL of anhydrous ether was dropwise added a solution of trichloroacetyl isocyanate (198 mg, 1.05 mmol) in 10 mL of anhydrous ether. After completion of the addition, the mixture was stirred for 30 min at room temperature, then K_2CO_3 (152 mg, 1.1 mmol) was slowly added, and the mixture was refluxed for 2 h. After evaporation of the solvent, 10 mL of water was added, the mixture was extracted with dichloromethane (3 × 10 mL), and the combined organic phases were dried over anhydrous Na_2SO_4 and evaporated in vacuo. The residue was purified by recrystallization or by chromatographic methods.

5,7-Dimethyl-2-phenyl-1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-one (4a). The crude product was purified by preparative TLC (dichloromethane/ethyl acetate 1:10) to afford a colorless oil which solidified on standing (mp 66 °C), yield 61%. ^{1}H NMR ($CDCl_3$): δ 1.80 (s, 3 H, 7-Me), 3.42 (s, 3 H, 5-Me), 7.58 (m, 2 H, Ph H-3,5), 7.69 (m, 1 H, Ph H-4), 7.81 (m, 2 H, Ph H-2,6). ^{13}C NMR ($CDCl_3$): δ 12.9 (7-Me, ^1J = 129.3 Hz), 32.2 (5-Me, ^1J = 139.8 Hz), 45.0 (C-3, ^3J(C-3,7-Me) = 3.2 Hz), 120.1 (Ph C-1), 129.6 (Ph C-3,5), 131.0 (Ph C-2,6), 135.0 (Ph C-4), 156.5 (C-7, ^2J(C-7,7-Me) = 7.6 Hz), 157.9 (C-2, ^3J(C-2, Ph H-2,6) = 5.5 Hz), 170.4 (C-4, ^3J(C-4,5-Me) = 2.2 Hz). IR (KBr): ν 1780 (C=N), 1704 (C=O) cm^{-1}. MS: *m*/*z* (%) = 213 (M^+, 55), 142 (23), 118 (16), 105 (100), 77 (31), 76 (16), 67 (90), 56 (11), 52 (11), 51 (46), 50 (22), 43 (29), 42 (10). Anal. Calcd for $C_{12}H_{11}N_3O$ (213.24): C 67.59, H 5.20, N 19.71. Found: C 67.66, H 5.34, N 19.62.

5,7-Dimethyl-2-(2-thienyl)-1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-one (4b). The crude product was purified by preparative TLC (dichloromethane/ethyl acetate 1:1) to afford yellowish-orange crystals of mp 93 °C, yield 54%. ^{1}H NMR ($CDCl_3$): δ 1.82 (s, 3 H, 7-Me), 3.42 (s, 3 H, 5-Me), 7.28 (dd, ^2J(H-4,H-5) = 5.0 Hz, ^2J(H-4,H-3) = 3.8 Hz, 1 H, Th H-4), 7.67 (dd, ^3J(H-3,H-4) = 3.8 Hz, ^4J(H-3,H-5) = 1.2 Hz, 1 H, Th H-3), 7.97 (dd, ^3J(H-5,H-4) = 5.0 Hz, ^4J(H-5,H-3) = 1.2 Hz, 1 H, Th H-5). ^{13}C NMR ($CDCl_3$): δ 12.9 (7-Me, ^1J = 129.3 Hz), 32.2 (5-Me, ^1J = 139.8 Hz), 45.6 (C-3, ^3J(C-3,7-Me) = 3.2 Hz), 121.7 (Th C-2, ^2J(C-2,H-3) = 5.9 Hz, ^3J(C-2,H-4) = 10.9 Hz, ^3J(C-2,H-5) = 6.5 Hz), 128.9 (Th C-4, ^1J = 172.4 Hz, ^2J(C-4,H-3) = 4.8 Hz, ^2J(C-4,H-5) = 3.9 Hz), 137.1 (Th C-3, ^1J = 171.6 Hz, ^2J(C-3,H-4) = 5.9 Hz, ^3J(C-3,H-5) = 9.5 Hz), 137.4 (Th C-5, ^1J = 187.8 Hz, ^2J(C-5,H-4) = 7.5 Hz, ^3J(C-5,H-3) = 11.0 Hz), 151.1

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(C-2, ^3J(C-2,Th H-3) = 3.5 Hz, ^4J(C-2,Th H-5) = 2.2 Hz), 156.4 (C-7, ^2J(C-7,7-Me) = 7.6 Hz), 170.0 (C-4, ^3J(C-4,5-Me) = 2.2 Hz). IR (KBr): ν 1770 (C=N), 1698 (C=O) cm^{-1}. MS: *m*/*z* (%) = 219 (M$^+$, 58), 148 (24), 124 (10), 111 (100), 69 (19), 67 (66), 57 (10), 45 (11), 44 (32), 43 (17). HRMS calcd for $C_{10}H_9N_3OS$, 219.0466; found 219.0472 ± 0.0011.

2,5-Diphenyl-1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-one (4c). The crude product was purified by preparative TLC (dichloromethane/ethyl acetate 10:1) to afford an unstable orange oil, yield 38%. ^{1}H NMR ($CDCl_3$): δ 7.24 (m, 1 H, 5-Ph H-4), 7.45 (m, 2 H, 5-Ph H-3,5), 7.46 (s, 1 H, H-7), 7.62 (m, 2 H, 2-Ph H-3,5), 7.70 (m, 1 H, 2-Ph H-4), 7.88 (m, 2 H, 2-Ph H-2,6), 7.98 (m, 2 H, 5-Ph H-2,6). ^{13}C NMR ($CDCl_3$): δ 45.2 (C-3), 118.6 (5-Ph C-2,6), 120.0 (2-Ph C-1), 125.5 (5-Ph C-4), 129.0 (5-Ph C-3,5), 129.7 (2-Ph C-3,5), 131.3 (2-Ph C-2,6), 135.3 (2-Ph C-4), 149.0 (C-7), 157.4 (C-2).

2,7-Dimethyl-5-phenyl-1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-one (4e). The crude product was purified by preparative TLC (dichloromethane/ethyl acetate 1:10) to afford a yellowish oil, yield 50%. ^{1}H NMR ($CDCl_3$): δ 1.90 (s, 3 H, 7-Me), 2.66 (s, 3 H, 2-Me), 7.18 (m, 1 H, Ph H-4), 7.39 (m, 2 H, Ph H-3,5), 7.90 (m, 2 H, Ph H-2,6). ^{13}C NMR ($CDCl_3$): δ 12.4 (2-Me, ^1J = 134.2 Hz), 13.1 (7-Me, ^1J = 129.9 Hz), 45.4 (C-3), 118.5 (Ph C-2,6), 125.1 (Ph C-4), 128.8 (Ph C-3,5), 138.5 (Ph C-1), 157.5 (C-7, ^2J(C-7,7-Me) = 7.5 Hz), 158.6 (C-2, ^2J(C-2,2-Me) = 8.8 Hz), 169.3 (C-4). MS: *m*/*z* (%) = 213 (M$^+$, 14), 67 (11), 44 (100), 43 (15). HRMS calcd for $C_{12}H_{11}N_3O$, 213.0902; found 213.0909 ± 0.0011.

2,5-Diphenyl-7-methyl-1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-one (4f). The crude product was crystallized from diethyl ether/light petroleum to afford colorless crystals of mp 125−127 °C, yield 59%. ^{1}H NMR ($CDCl_3$): δ 1.94 (s, 3 H, 7-Me), 7.20 (m, 1 H, 5-Ph H-4), 7.43 (m, 2 H, 5-Ph H-3,5), 7.62 (m, 2 H, 2-Ph H-3,5), 7.72 (m, 1 H, 2-Ph H-4), 7.87 (m, 2 H, 2-Ph H-2,6), 8.00 (m, 2 H, 5-Ph H-2,6). ^{13}C NMR ($CDCl_3$): δ 13.1 (7-Me, ^1J = 129.5 Hz), 46.1 (C-3, ^3J(C-3,7-Me) = 3.3 Hz), 118.4 (5-Ph C-2,6), 119.9 (2-Ph C-1), 125.0 (5-Ph C-4), 128.8 (5-Ph C-3,5), 129.8 (2-Ph C-3,5), 131.1 (2-Ph C-2,6), 135.2 (2-Ph C-4), 138.7 (5-Ph C-1), 157.6 (C-7, ^2J(C-7,7-Me) = 7.5 Hz), 157.6 (C-2), 168.9 (C-4). IR (KBr): ν 1778 (C=N), 1704 (C=O) cm^{-1}. MS: *m*/*z* (%) = 275 (M$^+$, 7), 105 (100), 91 (13), 77 (88), 69 (16), 67 (75), 64 (11), 63 (10), 51 (46). Anal. Calcd for $C_{17}H_{13}N_3O$ (275.31): C 74.17, H 4.76, N 15.26. Found: C 74.11, H 4.83, N 15.17.

5-Benzyl-2,7-dimethyl-1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-one (4g). The crude product was purified by preparative TLC (dichloromethane/ethyl acetate 1:4) to afford a tan oil, yield 39%. ^{1}H NMR ($CDCl_3$): δ 1.78 (s, 3 H, 7-Me), 2.62 (s, 3 H, 2-Me), 4.89 (s, 2 H, CH_2), 7.25−7.35 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$): δ 12.6 (2-Me, ^1J = 133.9 Hz), 13.1 (7-Me, ^1J = 129.2 Hz), 44.5 (C-3), 48.8 (CH_2, ^1J = 139.0 Hz), 127.7 (Ph C-4), 128.2 (Ph C-2,6), 128.6 (Ph C-3,5), 136.4 (Ph C-1), 156.7 (C-7, ^2J(C-7,7-Me) = 7.6 Hz), 158.9 (C-2, ^2J(C-2,2-Me) = 8.8 Hz), 170.5 (C-4, ^3J(C-4,CH_2) = 2.3 Hz). IR (KBr): ν 1810 (C=N), 1704 (C=O) cm^{-1}. MS: *m*/*z* (%) = 227 (M$^+$, 52), 149 (16), 123 (22), 91 (100), 80 (46), 67 (30), 65 (20), 57 (13), 43 (22). HRMS calcd for $C_{13}H_{13}N_3O$, 227.1059; found: 227.1062 ± 0.0014.

1-Benzyl-7-methyl-2-phenyl-1,5,6-triazaspiro[2.4]hepta-1,6-dien-4-one (4h). The crude product was crystallized from diethyl ether/light petroleum to afford colorless crystals of mp 104 °C, yield 64%. ^{1}H NMR ($CDCl_3$): δ 1.80 (s, 3 H, 7-Me), 4.95 and 4.99 (AB-system, J = 15.1 Hz, 2 H, CH_2), 7.33 (m, 1 H, Bzl H-4), 7.37 (m, 2 H, Bzl H-3,5), 7.39 (m, 2 H, Bzl H-2,6), 7.61 (m, 2 H, 2-Ph H-3,5), 7.71 (m, 1 H, 2-Ph H-4), 7.83 (m, 2 H, 2-Ph H-2,6). ^{13}C NMR ($CDCl_3$): δ 13.1 (7-Me, ^1J = 129.3 Hz), 45.2 (C-3, ^3J(C-3,7-Me) = 3.2 Hz), 48.9 (CH_2, ^1J = 139.0 Hz), 120.2 (2-Ph C-1), 127.7 (Bzl C-4), 128.2 (Bzl C-2,6), 128.7 (Bzl C-3,5), 129.7 (2-Ph C-3,5), 131.1 (2-Ph C-2,6), 135.1 (2-Ph C-4), 136.6 (Bzl C-1), 156.9 (C-7, ^2J(C-7,7-Me) = 7.6 Hz), 158.0 (C-2, ^3J(C-2,2-Ph H-2,6) = 5.3 Hz), 170.3 (C-4, ^3J(C-4, NCH_2) = 2.3 Hz). IR (KBr): ν 1780 (C=N), 1698 (C=O) cm^{-1}. MS: *m*/*z* (%) = 289 (M$^+$, 20), 142 (28), 105 (26), 91 (100), 77 (26), 67 (21), 65 (30), 51 (27), 42 (10), 41 (18). Anal. Calcd for $C_{18}H_{15}N_3O$ (289.34): C 74.72, H 5.23, N 14.52. Found: C 74.84, H 5.07, N 14.28.

TABLE 1. Crystal Data and Selected Experimental Details from Crystal Structures of Compounds 4f and 4h

	4f	4h
crystallized from	diethyl ether/ light petroleum	ethanol
formula	$C_{17}H_{13}N_3O$	$C_{18}H_{15}N_3O$
formula weight (g/mol)	275.30	289.33
crystal system	triclinic	orthorhombic
space group	*P*-1	$P2_12_12_1$
unit cell dimensions		
a (Å)	8.1150(3)	4.8250(2)
b (Å)	9.3000(4)	10.7660(4)
c (Å)	9.6950(4)	29.5020(11)
α (deg)	74.074(2)	90
β (deg)	85.712(3)	90
γ (deg)	85.968(3)	90
volume (Å^3)	700.68(5)	1532.51(10)
Z	2	4
D_c (Mg m^{-3})	1.305	1.254
absorb μ (mm^{-1})	0.084	0.080
F(000)	288	608
crystal size (mm^3)	0.48 × 0.48 × 0.42	0.5 × 0.13 × 0.13
crystal habit	pseudotrigonal pyramid	square base column
crystal color	colorless	colorless
temperature (K)	200(2)	200(2)
radiation used (λ, Å)	Mo Kα, 0.71073	Mo Kα, 0.71073
index ranges	h (0,11)	h (−6,6)
	k (−13,13)	k (−13,13)
	l (−13,13)	l (−36,36)
unique reflections	4110	3038
reflections [$I > 2\sigma(I)$]	2782	2499
refinement method	full-matrix/F^2	full-matrix/F^2
data/restraints/parameter	4110/0/243	3038/0/260
goodness-of-fit on F^2	1.038	1.063
R1 [$I > 2\sigma$(I)]	0.0437	0.0404
R1 (all data)	0.0755	0.0567
wR2 (all data)	0.1008	0.0832
final $\Delta\rho_{max}/\Delta\rho_{min}$ (e Å^{-3})	0.19/−0.16	0.11/−0.11
diffractometer	Nonius Kappa-CCD	Nonius Kappa-CCD

Reaction of 3d with Trichloroacetyl Isocyanate. Formation of 3-Methyl-5-hydroxy-1-phenyl-1*H*-pyrazole-4-carbonitrile (6). The reaction of oxime **3d** with trichloroacetyl isocyante was carried out as described in the general procedure for the synthesis of spiro-compounds **4**. Recrystallization of the raw product from ethanol afforded the nitrile **6** as yellow crystals of mp 214 °C (lit. mp 217−218 °C),[46] yield 55%. Microanalytical and spectroscopic data (^{1}H NMR, ^{13}C NMR, IR, MS) are in full agreement with those given in the literature.[46]

X-ray Analysis. Crystals suitable for X-ray investigation were prepared by slow evaporation of solutions of the respective compounds. Crystals were grown from ether/light petroleum in the case of **4f**, from ethanol in the case of **4h**.

Crystallographic data of **4f** and **4h** are summarized in Table 1. Intensity data for all structures were obtained on a Nonius Kappa instrument with CCD detector at 200 K with a crystal to detector distance of 35 mm. Compounds **4f** and **4h** were solved by direct methods, using the programs SIR92[47] and refined with SHELXL97.[48] The geometrical analysis were

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(47) SIR92: Program for Crystal Structure Solution. Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A. *J. Appl. Crystallogr.* **1993**, *26*, 343−350.

(48) SHELX97: Programs for Crystal Structure Analysis (Release 97−2). Sheldrick, G. M. Institut für Anorganische Chemie der Universität: Tammanstrasse 4, D-37077 Göttingen, Germany, 1998.

calculated with programs implemented in PLATON,[49] and structure drawings were prepared using Diamond 2.1.a.[50] For the coordination of the programs WINGX v.1.63.01[51] was used. The CIF files have been deposited with the Cambridge Crystallographic Data Center (203036 (**4h**) and 203037 (**4f**)).

(49) PLATON: (a) Van der Sluis, P.; Spek, A. L. *Acta Cryst., Sect. A* **1990**, *A46*, 194−201. (b) Spek, A. L. *PLATON: A Multipurpose Crystallographic Tool*; Utrecht University: Utrecht, The Netherlands, 1988.

(50) *DIAMOND 2.1a: Visual Crystal Structure Information System*; Brandenburg, K. Universität Bonn: Bonn, Germany, 1999.

(51) WINGX v1.63.01: System of Windows Programs for the Solution, Refinement and Analysis of Single-Crystal X-ray Diffraction Data. Farrugia, L. J. *J. Appl. Crystallogr.* **1999**, *32*, 837−838.

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Supporting Information Available: ^{1}H NMR spectra of **2g**, **3a**, **3b**, **4a**, **4b**, **4f**, **4h**, **6**; ^{13}C NMR spectra of **2g**, **3a**, **3b**, **4a**, **4b**, **4e**, **4f**, **4g**, **4h**, **6**; HMQC of **3b**; selective long-range INEPT of **4b**; IR of **4a**, **4b**, **4f**, **4h**, **6**; and X-ray data of **4f** and **4h**. This material is available free of charge via the Internet at http://pubs.acs.org.

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