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Similarity and Differences in the Regioselectivities of Thermal and Acid-Catalyzed van Alphen–Hüttel Rearrangements in the Series of 3,3-Diphenyl-3*H*-pyrazoles Containing Electron-Withdrawing Substituents on C^4 and C^5

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Abstract—3,3-Diphenyl-3*H*-pyrazoles containing an electron-withdrawing substituent in the 5-position undergo van Alphen–Hüttel rearrangement with migration of one phenyl group to C^4 on heating in an aprotic solvent (benzene, toluene), as well as on keeping at 20°C in acetic acid in the presence of a catalytic amount of concentrated sulfuric acid. Under similar conditions, 3,3-diphenyl-3*H*-pyrazoles with a strong electron-withdrawing group (sulfo or cyano) on C^4 isomerize to 1*H*-pyrazoles via migration of one phenyl group to N^2. If a moderate electron-withdrawing substituent (alkoxycarbonyl or acetyl group) is present in the 4-position, the acid-catalyzed phenyl group migration is directed mainly to the C^4 atom, while thermal migration, toward N^2. Probable reasons for the observed similarity and differences in the regioselectivities of the thermal and acid-catalyzed van Alphen–Hüttel rearrangements have been proposed.

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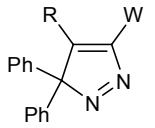
Thermal isomerization of 3,3-disubstituted 3*H*-pyrazoles to 1*H*- and/or 4*H*-pyrazole derivatives is known as van Alphen–Hüttel rearrangement [1–4]. Our previous studies [5–8] on the thermal rearrangement of 3,3-diphenyl-3*H*-pyrazoles revealed important structural factors determining its regioselectivity. In particular, it was found that the regioselectivity depends on the nature and position of substituents on the endocyclic C=C bond in the initial compound. 3*H*-Pyrazoles with an electron-withdrawing substituent on C^4 are converted mainly to *N*-phenyl-1*H*-pyrazole derivatives (1,5-sigmatropic C→N migration of the phenyl group), whereas their 5-substituted isomers preferentially give rise to the corresponding 4*H*-pyrazole derivatives via migration of one phenyl group to the C^4 carbon atom. These findings were interpreted in terms of topological equivalence of the transition state in the rearrangement and π-system of non-alternate diazabicyclo[3.1.0]hexatriene [8].

Considerable acceleration of the rearrangement was observed under acidic conditions, which made it possible to carry out it at room temperature [6, 9–11]. However, in some cases, the compositions of products obtained by thermal and acid-catalyzed rearrangement of the same 3*H*-pyrazoles were somewhat different. It may be presumed that both acid-catalyzed and thermal rearrangements involve 1,5-Ph shift but in the corresponding pyrazolium ion rather than in neutral pyrazole.[1] Increased electronegativity of the positively charged nitrogen atom should stabilize the rearrangement transition state [8], so that the reaction is accelerated, and its regioselectivity may change.

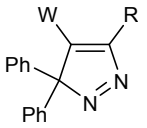
We set ourselves the task of determining and comparing the composition of rearrangement products of 3,3-diphenyl-3*H*-pyrazoles containing an electron-withdrawing substituent on C^4 or C^5 under thermolysis conditions (in an aprotic solvent, benzene or toluene) and at 20°C in a protic solvent (acetic acid) in the presence of H_2SO_4 as catalyst. For convenience in discussing the results, the substrates were divided into three

[†] Deceased.

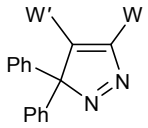
[1] 3*H*-Pyrazoles can be protonated at either nitrogen atom of the heterocycle, but protonation of one of them is generally preferential [9].



1a, **3a**, **3b**, **5a**, **5c–5e**



2a, **2b**, **4a**, **4b**, **6a–6e**



7a, **7d**, **8e**

Hereinafter: W = CO_2Me (**a**), CN (**b**), C(O)Me (**c**), SO_2Me (**d**), Ts (**e**); **1**, **2**, R = H; **3**, **4**, R = Me; **5**, **6**, R = Ph; **7**, W′ = CO_2Me; **8**, W′ = CN.

groups: (1) 3*H*-pyrazoles **1a**, **3a**, **3b**, **5a**, and **5c–5e** containing an electron-withdrawing substituent on C^5, (2) analogous 4-substituted derivatives **2a**, **2b**, **4a**, **4b**, and **6a–6e**, and (3) 3*H*-pyrazoles **7a**, **7d**, and **8e** having two electron-withdrawing substituents on C^4 and C^5.

The data on the rearrangements of **4a**, **5a**, **5d**, **5e**, **6a**, **6b**, **6d**, **6e**, **7a**, **7d**, and **8e** were taken from [6–8, 10, 11]. The rearrangement of the other 3*H*-pyrazole derivatives was either not studied previously or it was not carried out under acid catalysis. These substrates were 4(5)-monosubstituted 3*H*-pyrazoles **1a**, **2a**, and **2b**, and regioisomeric pairs of disubstituted pyrazoles **3a**/**4a**, **3b**/**4b**, and **5c**/**6c**.

3*H*-Pyrazoles **3b**, **4b**, **5c**, and **6c** were synthesized for the first time in this work. Compounds **3b** and **4b** were obtained at a ratio of 1:3.3 by reaction of but-2-ynenitrile with diphenyldiazomethane in anhydrous diethyl ether at 20°C (20 days in the dark). Isomer **4b** was isolated by flash chromatography on silica gel. We failed to isolate isomer **3b** since it underwent complete isomerization to the corresponding 4*H*-pyrazole during chromatography (see below). However, having a sample of **4b** in hands, we succeeded in distinguishing signals of **3b** in the ^1H and ^{13}C NMR spectra of the reaction mixture. The structures of regioisomers **3b** and **4b** were assigned by comparing their ^1H NMR spectra: the signal of the methyl group of **4b** appeared in a weaker field (δ 2.73 ppm) relative to that of **3b** (δ 2.31 ppm) due to deshielding effect of the azo fragment in the former (cf. [5]. The structure of 3*H*-pyrazole **4b** was additionally confirmed by ^1H–^{15}N HMBC experiment which revealed coupling of N^1 with protons of the neighboring methyl group; no such coupling could be expected for structure **3b**.

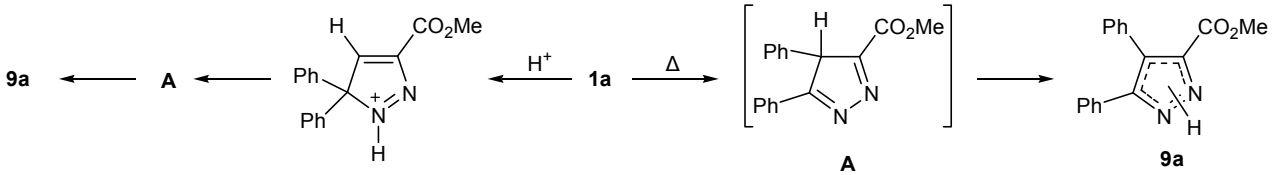
3*H*-Pyrazoles **5c** and **6c** were synthesized by reaction of 4-phenylbut-3-yn-2-one diphenyldiazomethane in diethyl ether (20°C, 6 days); compounds **5c** and **6c** were formed at a ratio of 1.3:1 and were separated by flash chromatography on silica gel. Their structure was determined on the basis of IR and ^1H and ^{13}C NMR spectra. The regioisomer structures were assigned taking into account strong difference in the chemical shifts of protons of the acetyl group (Δδ = 0.91 ppm) in the ^1H NMR spectra. The isomer with the larger chemical shift was assigned structure **5c** since the acetyl protons therein are deshielded by the azo fragment. In keeping with this assignment, the more downfield two-proton signal in the spectrum of **6c** (δ 7.92–7.95 ppm) should be assigned to *ortho* protons of the phenyl group, which suffer from strong deshielding effect of the azo fragment (cf. [6]). In the spectrum of regioisomer **5c**, signals of aromatic protons are located in the region below δ 7.36 ppm. In addition, 3*H*-pyrazoles **3b**, **4b**, **5c**, and **6c** characteristically showed in the ^{13}C NMR spectra a signal at δ_C ~110 ppm due to C^3 [6–8].

Let us consider first the results of isomerization of 3*H*-pyrazoles with an electron-withdrawing substituent on C^5. According to published data [12], the thermolysis of 3*H*-pyrazole **1a** in an aprotic solvent yields 1*H*-pyrazole **9a**. The direction of the phenyl group migration is determined by the acceptor character of the substituent[2] on C^5 [8]: 4*H*-pyrazole **A** is formed, and next follows fast proton transfer therein. The van Alphen–Hüttel rearrangement of 3*H*-pyrazole **1a** in acetic acid at 20°C in the presence of a catalytic amount of sulfuric acid occurs in the same direction. The rearrangement is favored by protonation of the initial 3*H*-pyrazole at the N^2 atom (Scheme 1). The rearrangement product, compound **9a**, was isolated in the crystalline state and was identified by the melting points and spectral parameters given in [1, 12].

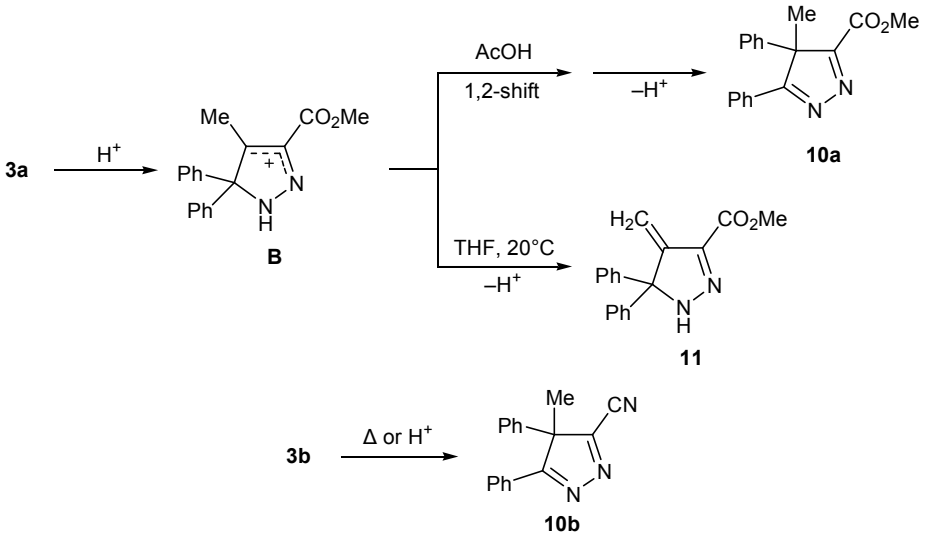
Next, let us turn to the results of rearrangements of disubstituted 3*H*-pyrazoles **3a** and **3b** containing an electron-donating methyl group in the 4-position. It is known [5] that the thermolysis of **3a** gives exclusively 4*H*-pyrazole **10a**. It was found that the same product is also obtained from **3a** in acetic acid containing a catalytic amount of H_2SO_4 at 20–60°C. Furthermore, when 3*H*-pyrazole **3a** was kept in THF in the presence of a catalytic amount of H_2SO_4 at 20°C, it isomerized to known 4-methylidene-4,5-dihydro-1*H*-pyrazole **11**

[2] The constants σ_I (σ^-) of the electron-withdrawing substituents in the 3*H*-pyrazoles considered in this work were taken from [13]: SO_2Me 0.60 (1.05), CN 0.56 (0.99), C(O)Me 0.20 (0.82), CO_2Me 0.20 (0.74), Ph 0.12 (0.08).

Scheme 1.



Scheme 2.



[14] (Scheme 2). Obviously, dihydropyrazole **11** arises from the same cationic intermediate **B** as that formed from **3a** and transformed to 4*H*-pyrazole **10a** in two stages. We can state that THF as a basic aprotic solvent favors deprotonation of **B** and that polar protic solvent (acetic acid) favors its rearrangement.

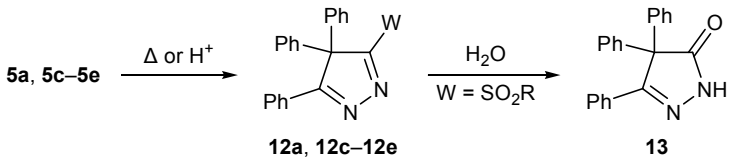
Likewise, 3*H*-pyrazole **3b** is converted to 4*H*-pyrazole **10b** which is analogous to **10a** during chromatography (see above), probably due to the presence of traces of a mineral acid in the sorbent. Quite naturally, the protonation of 3*H*-pyrazoles **3a** and **3b** involves the N^2 atom, which is facilitated by the presence of a donor methyl group on C^4.

Now let us consider the rearrangements of 4-phenyl-substituted 3*H*-pyrazoles **5a** and **5c**–**5e**. It is known that phenyl group can act as both donor and acceptor. The rearrangements of **5c** both in boiling benzene and under acidic conditions at 20°C gave the same result: the only product was 4*H*-pyrazole **12c**. The structure of **12c** isolated as a crystalline solid was confirmed by spectral data. Its ^{13}C NMR spectrum characteristically displayed downfield signals at δ_C 76.8 and 182.4 ppm from C^3 and C^5, respectively, and its UV spectrum contained an absorption band with its maximum at λ 312 nm (logε 4.02) [5–8].

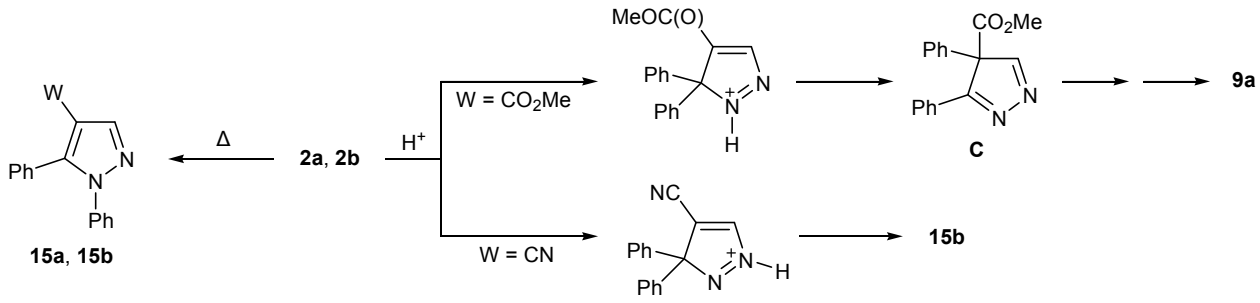
We previously [7] studied the rearrangement of sulfones **5d** and **5e** under both thermolysis conditions and acid catalysis at room temperature. Like ketone **5c**, the thermolysis of **5d** and **5e** afforded only 4*H*-pyrazoles **12d** and **12e**. The acid-catalyzed rearrangement followed the same direction, but we succeeded in isolating only 4*H*-pyrazolone **13** which is likely to be formed due to hydrolysis of **12d** and **12e** on treatment of the reaction mixture with water (Scheme 3).

According to our previous data [6], acid-catalyzed isomerization of ester **5a** at 20°C gives 4*H*-pyrazole **12a** as the only product. Under the thermolysis conditions, the rearrangement was not selective, and the

Scheme 3.



Scheme 4.



products were 4*H*-pyrazole **12a** and 1*H*-pyrazole **14** at a ratio of 5:1. We believe that high regioselectivity of the acid-catalyzed rearrangement of **5a**, as compared to the thermally induced transformation, is related to its protonation at the N^2 atom, which is favored by electron-donating effect of the phenyl group.

Let us proceed to the transformations of 3*H*-pyrazoles with an electron-withdrawing group on C^4. Consider first monosubstituted pyrazoles **2a** and **2b**. The thermal rearrangement of ester **2a** leads to the formation of 1-phenyl-1*H*-pyrazole **15a** due to effect of the substituent in the 4-position [8]. The acid-catalyzed rearrangement of **2a** takes the opposite direction, yielding 1*H*-pyrazole **9a**. In this case, the direction of 1,5-Ph shift is determined by protonation of the initial pyrazole at the N^2 atom, and relatively low acceptor power of the CO_2Me group does not prevent the protonation. The subsequent 1,5-shift of the methoxycarbonyl group (which is more labile than phenyl) in the resulting 4*H*-pyrazole **C** is followed by proton transfer to the nitrogen atom. By contrast, due to high acceptor power of the cyano group, nitrile **2b** under acid catalysis is protonated at the N^1 atom, and the only rearrangement product is 1-phenyl-1*H*-pyrazole **15b**; the same product is formed in the thermolysis of **2b** [8] (Scheme 4).

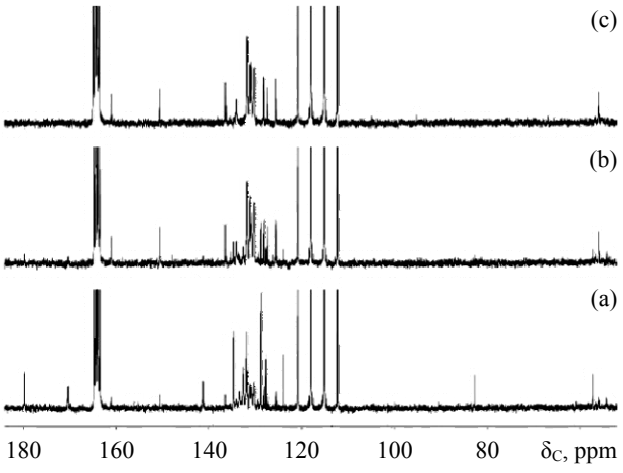


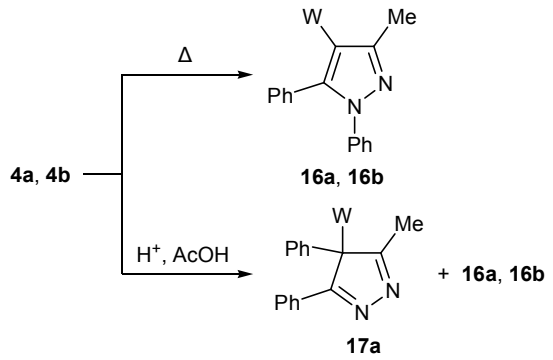
Fig. 1. ^{13}C NMR spectra of the rearrangement products of methyl 3,3-diphenyl-3*H*-pyrazole-4-carboxylate (**2a**) in trifluoroacetic acid in (a) 10 min, (b) 2 h, and (c) 24 h after dissolution.

A micro experiment was carried out with 3*H*-pyrazole **2a** directly in an NMR ampule. In 10 min after dissolution of **2a** in trifluoroacetic acid, the ^{13}C NMR spectrum of the solution displayed signals typical of 4*H*-pyrazoles like **C** (see above), specifically downfield signals of C^3 and C^5 (dimethylidenehydrazine fragment) at δ_C ~170 and 179 ppm and C^4 signal at δ_C ~83 ppm (Fig. 1). These signals disappeared with time, and approximately after 2 h, the spectrum corresponded only to final product **9a**. We failed to isolate from the mixture hypothetical 4*H*-pyrazole **C**.

Consider the rearrangements of 5-methyl-3*H*-pyrazoles **4a** and **4b**. Like monosubstituted analog **2a**, 3*H*-pyrazole **4a** in boiling benzene was converted exclusively to 1-phenyl-1*H*-pyrazole **16a** [8], but its acid-catalyzed rearrangement in acetic acid containing H_2SO_4 afforded a mixture of 1*H*- and 4*H*-pyrazoles **16a** and **17a**. The fraction of **16a** in the product mixture increased with rise in temperature, and equimolar amounts of the **16a** and **17a** were obtained at 60°C. Presumably, the rearrangement simultaneously involves both protonated and unprotonated forms of **3a**. 3*H*-Pyrazole **4b**, like its monosubstituted analog **2b**, was converted to 1-phenyl-1*H*-pyrazole **16b** as the only product under both thermolysis and acid-catalyzed conditions (Scheme 5).

4*H*-Pyrazole **17a** was isolated in the pure state, and its structure was confirmed by IR, ^1H and ^{13}C NMR, and UV spectra. In particular, the ^{13}C NMR spectrum of **17a** showed downfield signals at δ_C 173.3 and 175.7 ppm due to carbon atoms of the C=N–N=C fragment, and its UV spectrum displayed an absorption maximum at λ 286 nm (logε 3.96). The structure of 1*H*-pyrazole **16b** was determined on the basis of its IR and ^1H and ^{13}C NMR spectra with account taken of the corresponding data for compound **16a**.

Scheme 5.



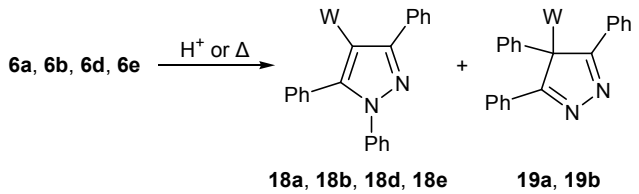
Let us discuss the behavior of 3,3,5-triphenyl-3*H*-pyrazoles **6a**–**6c**. Ester **6a** was converted to a mixture of 1*H*-pyrazole **18a** and 4*H*-pyrazole **19a** at a ratio of 7.5:2 on heating in benzene at 135°C. The acid-catalyzed transformation of **6a** at 20°C produced exclusively 4*H*-pyrazole **19a** [6]. It should be noted that, according to the data of [10], a mixture of the same products **18a** and **19a** at a ratio of 1:1.25 was formed when pyrazole **5a** was heated at 85°C in acetic acid containing a catalytic amount of sulfuric acid. Change of the product composition can also be attributed to concurrent isomerization of protonated and neutral forms of **5a**.

Nitrile **6b** in boiling toluene gave rise to a mixture of 1*H*-pyrazole **18b** and 4*H*-pyrazole **19b** at a ratio of 10:1 [11]. There are no data on its acid-catalyzed transformations at room temperature, whereas heating of **6b** in acetic acid at 100°C in the presence of H_2SO_4 [11] led to the formation of a mixture of the same products, but pyrazole **18b** was the major one (ratio **18b**:**19b** ~2:1).

Sulfonyl-substituted 3*H*-pyrazoles **6d** and **6e** rearranged to 1*H*-pyrazoles **18d** and **18e**, respectively, both on keeping in acetic acid containing H_2SO_4 at 20°C and on heating in boiling toluene [7].

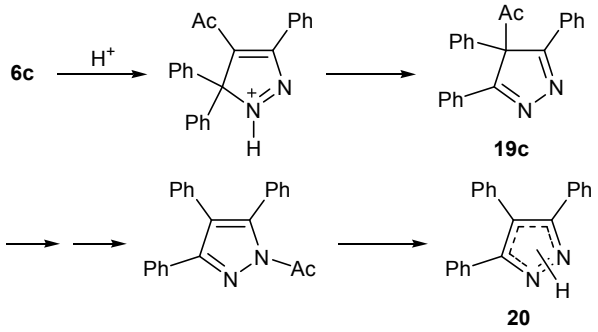
The lower regioselectivity of the transformations of 3*H*-pyrazoles **6a** and **6b** in comparison to **2a**, **2b**, **4a**, and **4b** is likely to be related to the competitive effect of the weak acceptor substituent (phenyl group) in the 5-position. The fact that 4*H*-pyrazole **19a** is formed as the only product in the acid-catalyzed rearrangement of **6a** at 20°C provides an additional support to our conclusion that the 4-methoxycarbonyl group does not prevent protonation of 3*H*-pyrazole at the N^2 atom. Compounds **6b**, **6d**, and **6e** are protonated mainly at N^1, which favors formation of 1-phenyl-1*H*-pyrazoles **18** (Scheme 6).

Scheme 6.



The behavior of acetylpyrazole **6c** seems to be quite specific. Both thermolysis of **6c** and its acid-catalyzed rearrangement at 20°C afforded 1*H*-pyrazole **20** containing no acetyl group (Scheme 7). The result of acid-catalyzed rearrangement may be acceptably explained taking into account fairly similar acceptor powers of the acetyl and methoxycarbonyl groups. This is the reason why ketone **6c**, like ester **6a**, is protonated at the N^2 atom, which leads to the formation of 4*H*-pyrazole **19c**. However, due to assumingly higher sigmatropic mobility of acetyl group (in comparison to methoxycarbonyl), compound **19c** undergoes double 1,5-sigmatropic shifts with the formation of 1-acetyl-1*H*-pyrazole which is then deacetylated to give NH-pyrazole **20** (Scheme 7).

Scheme 7.



Our assumption on the high mobility of the acetyl group is based on the fact that an analog of **19c**, 4*H*-pyrazole **19a** is also transformed to 1*H*-pyrazole **20**, but only at elevated temperature (185°C) [6].

The results of thermal transformations of ketone **6c** are more difficult to explain. The van Alphen–Hüttel rearrangement of this compound could be expected not to be strictly regioselective, as is also typical of its analog, ester **6a**. It seemed that the major rearrangement product would be 1-phenyl-1*H*-pyrazole **18c** (analog of **18a**) and that 4*H*-pyrazole **19c** (precursor to **20**) would be the minor one. It remains unclear why the thermolysis products of 3*H*-pyrazole **6c** contain no compound **18c** corresponding to migration of the phenyl group to the nitrogen atom.

Finally, let us consider the rearrangements of 3*H*-pyrazoles **7a**, **7d**, and **8e** with two electron-withdrawing substituents in positions *4* and *5*. The 4- and 5-substituents in diester **7a** are identical. As shown in [8], electron-withdrawing substituents on C^4 and C^5 oppositely affect the regioselectivity of the rearrangement; therefore, the results of studying the behavior of compound **7a** are especially important. The acid-catalyzed rearrangement of **7a** at room temperature gives exclusively 4*H*-pyrazole **21** [8, 15]. This is quite explainable in terms of the conclusions drawn above for compounds **2a** and **4a**, according to which the CO_2Me group, being a moderate acceptor, does not prevent protonation of the initial 3*H*-pyrazole at N^2, thus determining the direction of phenyl group migration. However, it turned out that the thermolysis of **7a** in boiling benzene [8] gives the same product, 4*H*-pyrazole **21**. These findings suggest that under pure thermolysis conditions, the effect of the ester group on C^5 is stronger than the effect of the same substituent on C^4.

Now it becomes clear why the acid-catalyzed rearrangement ($AcOH/H_2SO_4$, 20°C) of sulfone **7d** in which the CO_2Me substituent is linked to C^4 yields 4*H*-pyrazole **22**. The formation of the latter is determined by protonation of the N^2 atom in **7d**. The hydrolysis of **22** during the isolation procedure gives 1*H*-pyrazol-5(4*H*)-one **23**. 4*H*-Pyrazole **22** was obtained by thermolysis of **7d** in benzene [8]; it was isolated and characterized, and its facile hydrolysis was proved. In this case, the direction of the thermal rearrangement is determined by the electron-withdrawing substituent on C^5 whose effect is stronger than the effect of the SO_2Me group on C^4 (Scheme 8).

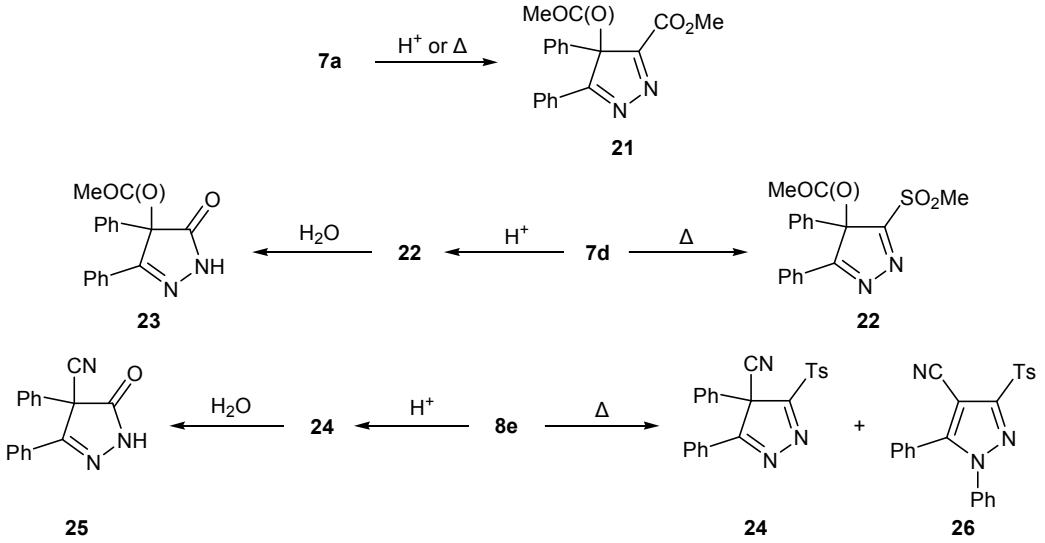
Compound **8e** containing strong electron-withdrawing substituents in positions *4* and *5*, cyano and sulfonyl groups, respectively, was converted to 4*H*-pyrazole **24** and then to pyrazolone **25** under acid catalysis conditions. This may be explained by the preferential protonation of N^1 in the initial compound. On the other hand, the thermal rearrangement of **8e** was not so selective, and a mixture of 1-phenyl-1*H*-pyrazole **26** and 4*H*-pyrazole **24** was formed at a ratio of 3 : 1 [8].

The IR spectra of **23** and **25** showed a strong carbonyl stretching band at ~1730 cm^{-1} and NH stretching band at ~3220 cm^{-1} [16]. In the ^1H NMR spectra of these compounds, the NH proton resonated as a broadened singlet at δ ~9.17 ppm.

Thus, the van Alphen–Hüttel rearrangement of seven 3,3-diphenyl-3*H*-pyrazoles with an electron-withdrawing substituent in the 5-position is strictly regioselective under both thermolysis conditions and acid catalysis at room temperature, and it involves migration of one phenyl group to C^4. The direction of the thermal rearrangement is determined by the known effect of the electron-withdrawing substituent [8], whereas the same direction of the acid-catalyzed rearrangement is additionally favored by protonation of the initial pyrazole at the N^2 atom to produce more stable intermediate cation.

Substantial differences in the course of the van Alphen–Hüttel rearrangement were observed for nine 3,3-diphenyl-3*H*-pyrazoles containing an electron-withdrawing substituent on C^4, depending on the reaction conditions. In almost all cases, except for ketone **6c**, the thermal rearrangement involved 1,5-Ph shift to

Scheme 8.



N^2, in keeping with the previously established pattern [8]. Change of the regioselectivity in going to the acid-catalyzed rearrangement is related to the effect of the 4-substituent on the site of protonation of the initial 3*H*-pyrazole. Strong electron-withdrawing groups hamper protonation of N^2, which reduces the regioselectivity or sometimes changes it completely in comparison to the purely thermal conditions.

The results of studying the rearrangement of three 3,3-diphenyl-3*H*-pyrazoles having two electron-withdrawing substituents in positions *4* and *5* showed that the direction of phenyl group migration is determined by the relative acceptor power of those substituents.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded from solutions in $CDCl_3$ on a Jeol ECX-400 spectrometer at 400 and 100 MHz, respectively. The IR spectra were measured in KBr on an InfraLYuM FT-02 spectrometer with Fourier transform. The UV spectra were recorded on a Shimadzu UV-2600 spectrophotometer and were processed using UV Probe 2.4. The elemental analyses were obtained on a Vario Micro CHNS analyzer. Analytical thin-layer chromatography was performed on Sorbfil plates using light petroleum ether–acetone (4:1) as eluent; spots were visualized by treatment with iodine vapor. The products were isolated by flash chromatography on Merck 60 silica gel (for TLC) using *tert*-butyl methyl ether–petroleum ether (1:4) as eluent. The melting points were measured in sealed glass capillaries with a Mettler Toledo MP-50 melting point analyzer (Switzerland).

3*H*-Pyrazoles **2a**, **2b**, **7d**, **8e** [12] **3a**, and **4a** [5] were synthesized according to known procedures.

Reaction of but-2-ynenitrile with diphenyldiazomethane. A solution of 1 g (5 mmol) of diphenyldiazomethane [17] in 10 mL of anhydrous diethyl ether was added to a solution of 0.33 g (5 mmol) of but-2-ynenitrile [18] in 20 mL of anhydrous diethyl ether. The mixture was kept for 20 days at 20°C with protection from light. Evaporation of the solvent left a mixture of 3*H*-pyrazoles **3b** and **4b** at a ratio of 1:3.3. Pure compound **4b** was isolated by flash chromatography on silica gel. Isomer **3b** was not isolated since it was converted to 4*H*-pyrazole **10b** during chromatographic separation.

4-Methyl-3,3-diphenyl-3*H*-pyrazole-5-carbonitrile (3b). The ^{1}H and ^{13}C NMR spectra were obtained by subtracting signals of **4b** from the spectra of the reaction mixture. ^{1}H NMR spectrum, δ, ppm: 2.31 (3H, CH_3), 7.08 d (2H, J = 7.8 Hz), 7.30–7.48 m (8H). ^{13}C NMR spectrum, δ_C, ppm: 12.9 (CH_3), 108.9 (C^3), 112.2 (CN), 127.9 (4C) and 129.35 (4C, C^m, C^o), 134.2 (2C, C^i), 170.0 (C^5); presumably, the C^p signal (2C) was overlapped by the stronger signal at δ_C 129.35 ppm, and the C^4 signal was difficult to identify because of its low intensity.

5-Methyl-3,3-diphenyl-3*H*-pyrazole-4-carbonitrile (4b). Yield 0.93 g (70%), bright yellow crystals, mp 105–106°C. IR spectrum, ν, cm^{-1}: 2220 w, 1636 w, 1628 w, 1490 m, 1457 m, 1447 m, 989 m, 775 m, 760 m, 697 v.s, 659 m. ^{1}H NMR spectrum, δ, ppm: 2.73 s (3H, CH_3), 7.30–7.33 m (4H, H_{arom}), 7.36–7.39 m (6H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.6 (CH_3), 108.8 (C^3), 113.8 (CN), 123.3 (C^4), 127.6 (4C) and 129.20 (4C, C^m, C^o), 129.24 (2C, C^p), 135.0 (2C, C^i), 162.9 (C^5). Found, %: C 78.78; H 5.10; N 16.07. $C_{17}H_{13}N_3$. Calculated, %: C 78.74; H 5.05; N 16.20.

4-Methyl-3,4-diphenyl-4*H*-pyrazole-5-carbonitrile (10b). Yield 0.28 g (21%), colorless crystals, mp 94–95°C. IR spectrum, ν, cm^{-1}: 2234 w, 1509 s, 1497 m, 1489 m, 1439 m, 1385 w, 1011 w, 776 m, 695 v.s, 625 w. ^{1}H NMR spectrum, δ, ppm: 1.90 s (3H, CH_3), 7.15–7.18 m (2H, H_{arom}), 7.35–7.44 m (5H, H_{arom}), 7.50 t (1H, H_{arom}, J = 7.4 Hz), 7.75 d (2H, H_{arom}, J = 7.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.6 (CH_3), 69.5 (C^4), 111.3 (CN), 125.9 (2C, CH_{arom}), 127.6 (C_{arom}), 129.2 (2C, CH_{arom}), 129.46 (2C, CH_{arom}), 129.67 (CH_{arom}), 130.2 (2C, CH_{arom}), 131.2 (C_{arom}), 133.0 (CH_{arom}), 160.2 (C^5), 180.1 (C^3). Found, %: C 78.71; H 5.16; N 16.11. $C_{17}H_{13}N_3$. Calculated, %: C 78.74; H 5.05; N 16.20.

3-Methyl-1,5-diphenyl-1*H*-pyrazole-4-carbonitrile (16b). A solution of 0.1 g (0.4 mmol) of 3*H*-pyrazole **4b** in 6 mL of anhydrous toluene was refluxed for 3 h. The solvent was removed on a rotary evaporator, and the residue was recrystallized from light petroleum ether. Yield 85 mg (85%), colorless crystals, mp 189–190°C. IR spectrum, ν, cm^{-1}: 2222 v.s, 1593 w, 1536 w, 1505 s, 1451 m, 1428 w, 779 s, 768 m, 706 s, 695 m. ^{1}H NMR spectrum, δ, ppm: 2.50 s (3H, CH_3), 7.22–7.25 m (2H, H_{arom}), 7.29–7.41 m (8H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 12.8 (CH_3), 93.9 (C^4), 114.5 (CN), 125.3 (2C, CH_{arom}), 127.2 (C_{arom}), 128.6 (CH_{arom}), 129.05 (2C, CH_{arom}), 129.11 (2C, CH_{arom}), 129.30 (2C, CH_{arom}), 130.1 (CH_{arom}), 138.8 (C_{arom}), 148.0 (C^3), 152.8 (C^5). Found, %: C 78.81; H 4.98; N 16.34. $C_{17}H_{13}N_3$. Calculated, %: C 78.74; H 5.05; N 16.20.

Acid-catalyzed rearrangement of 3*H*-pyrazole (4b). A solution of 0.1 g (0.4 mmol) of compound **4b** in 10 mL of acetic acid containing 2–3 drops of concentrated sulfuric acid was kept for 8 h at 20°C. The mixture was diluted with 10 mL of water and extracted with diethyl ether (3×10 mL). The combined extracts were washed with a 5% solution of $NaHCO_3$ and water, dried over $MgSO_4$ for 20 h, and evaporated on a rotary evaporator. The residue was analyzed by ^{1}H NMR. Recrystallization of the product gave 77 mg (77%) of 1*H*-pyrazole **16b**.

Reaction of 4-phenylbut-3-yn-2-one with diphenyldiazomethane. A solution of 1.85 g (9.5 mmol) of diphenyldiazomethane in 10 mL of anhydrous diethyl ether was added to a solution of 1.25 g (8.7 mmol) of 4-phenylbut-3-yn-2-one [19] in 50 mL of anhydrous diethyl ether. The mixture was left to stand for 6 days at 20°C with protection from light (until red–violet color of the initial diazo compound disappeared). According to the ^{1}H, NMR data, isomeric 3*H*-pyrazoles **5c** and **6c** were formed at a ratio of 1.3:1. The pure products were isolated by flash chromatography.

1-(3,3,4-Triphenyl-3*H*-pyrazol-5-yl)ethanone (5c). Yield 0.96 g (33%), yellow oily material. IR spectrum, ν, cm^{-1}: 1694 s, 1597 m, 1586 m, 1566 m, 1509 m, 1489 s, 1462 m, 1443 s, 1416 m, 1358 m, 1312 m, 1181 m, 1115 m, 1076 m, 1053 m, 1026 m, 1003 m, 953 m, 918 m, 775 m, 752 s, 698 v.s, 583 m, 567 m, 517 m. ^{1}H NMR spectrum, δ, ppm: 2.81 s (3H, CH_3), 7.07–7.09 m (2H, H_{arom}), 7.15–7.18 m (4H, H_{arom}), 7.27–7.36 m (9H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 30.8 (CH_3), 109.5 (C^3), 128.2 (2C, C_{arom}), 128.7 (4C, C_{arom}), 128.9 (6C, C_{arom}), 129.4 (2C, C_{arom}), 130.4 (2C, C_{arom}), 130.7 (C_{arom}), 133.5 (C_{arom}), 149.5 (C^4), 162.3 (C^5), 194.4 (C=O). Found, %: C 81.58; H 5.42; N 8.36. $C_{23}H_{18}N_2O$. Calculated, %: C 81.63; H 5.36; N 8.28.

1-(3,3,5-Triphenyl-3*H*-pyrazol-4-yl)ethanone (6c). Yield 1.35 g (46%), yellow crystals, mp 86–87°C. IR spectrum, ν, cm^{-1}: 1694 s, 1686 v.s, 1489 m, 1354 m, 1304 w, 1181 w, 1115 w, 772 m, 756 m, 721 m, 694 s. ^{1}H NMR spectrum, δ, ppm: 1.90 s (3H, Me), 7.30–7.34 m (4H, H_{arom}), 7.34–7.37 m (6H, H_{arom}), 7.52–7.56 m (3H, H_{arom}), 7.92–7.95 (2H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 31.8 (Me), 111.0 (C^3), 128.6 (4C, C_{arom}), 128.8 (6C, C_{arom}), 129.1 (2C, C_{arom}), 129.4 (2C, C_{arom}), 130.0 (C_{arom}), 130.7 (C_{arom}), 135.2 (C_{arom}), 147.6 (C^4), 154.8 (C^5), 200.1 (C=O). Found, %: C 81.55; H 5.44; N 8.32. $C_{23}H_{18}N_2O$. Calculated, %: C 81.63; H 5.36; N 8.28.

Acid-catalyzed rearrangement of 3*H*-pyrazoles 5c and 6c (*general procedure*). A solution of 0.6 mmol of 3*H*-pyrazole **5c** or **6c** in 10 mL of acetic acid containing 2–3 drops of concentrated sulfuric acid was kept at 20°C for 24 h (**5c**) or 1 h (**6c**). The mixture was diluted with 10 mL of water and extracted with diethyl ether (3×10 mL). The combined extracts were washed with a 5% solution of $NaHCO_3$ and water, dried over $MgSO_4$ for 20 h, and evaporated on a rotary evaporator, and the residue was analyzed by ^{1}H NMR. From compound **5c** we obtained 4*H*-pyrazole **12c**, and from **6c**, 3,4,5-triphenyl-1*H*-pyrazole (**20**, yield 58%); the physical constants and spectral characteristics of **20** coincided with those given in [7].

1-(4,4,5-Triphenyl-4*H*-pyrazol-4-yl)ethanone (12c). Yield 187 mg (94%), light yellow crystals, mp 175–176°C. IR spectrum, ν, cm^{-1}: 1694 v.s, 1509 m, 1489 s, 1439 m, 1358 m, 1316 m, 1111 m, 779 m, 764 m, 710 m, 698 v.s, 583 m. UV spectrum (MeOH): λ_{max} 312 nm (logε 4.02). ^{1}H NMR spectrum, δ, ppm: 2.58 s (3H, CH_3), 7.25–7.31 m (11H, H_{arom}), 7.36–7.41 m (2H, H_{arom}), 7.80–7.84 m (2H, $2H_{arom}$). ^{13}C NMR spectrum, δ_C, ppm: 28.1 (CH_3), 76.8 (C^4), 128.56 (2C, C_{arom}), 128.60 (2C, C_{arom}), 128.63 (4C, C_{arom}), 129.1 (4C, C_{arom}), 129.9 (2C, C_{arom}), 132.1 (C_{arom}), 133.3 (2C, C_{arom}), 175.9 (C^5), 182.1 (C^3), 193.3 (C=O). Found, %: C 81.68; H 5.34; N 8.31. $C_{23}H_{18}N_2O$. Calculated, %: C 81.63; H 5.36; N 8.28.

Thermal rearrangement of 3*H*-pyrazoles 5c and 6c (*general procedure*). A solution of 0.6 mmol of 3*H*-pyrazole **5c** or **6c** in 10 mL of anhydrous benzene was refluxed for 3–4 h. The solvent was removed on a rotary evaporator, and the residue was analyzed by NMR. From compound **5c** we obtained 4*H*-pyrazole **12c** (yield 85%), and from **6c**, 76% of **20**.

Acid-catalyzed isomerization of 3*H*-pyrazoles 2a, 2b, 3a, and 4a (*general procedure*). A solution of 1 mmol of 3*H*-pyrazole **2a**, **2b**, **3a**, or **4a** in 20 mL of acetic acid containing a catalytic amount of sulfuric acid was kept at 20°C for 2 h (**2b**, **3a**), 4 h (**4a**), or 24 h (**2a**). The mixture was diluted with 20 mL of water and extracted with diethyl ether (3×20 mL). The extract was washed with a 5% aqueous solution of $NaHCO_3$ and with water (2×10 mL) and dried over $MgSO_4$. The solvent was removed on a rotary evaporator, and the residue was analyzed by ^{1}H NMR. From 3*H*-pyrazoles **2a** and **2b** we obtained compounds **9a** and **15b** which were isolated in the pure state in 80 and 92% yield, respectively. From compound **3a** we obtained 4*H*-pyrazole **10a** as the only product, and the rearrangement of **4a** afforded a mixture of 4*H*- and 1*H*-pyrazoles **16a**

and **17a** at a ratio of 1 : 1.25. By silica gel column chromatography we isolated 115 mg (39%) of **16a** and 148 mg (51%) of **17a**. The physical constants and spectral characteristics of **9a**, **15b**, and **16a** coincided with those reported in [8].

Methyl 4-methyl-4,5-diphenyl-4*H*-pyrazole-3-carboxylate (10a). Yield 80%, mp 104–105°C [5]. ^{1}H NMR spectrum, δ, ppm: 1.94 s (3H, CH_3), 3.81 s (3H, OCH_3), 7.13–7.16 m (2H, H_{arom}), 7.28–737 m (5H, H_{arom}), 7.43 t (1H, H_{arom}, J = 7.5 Hz), 7.71 d (2H, H_{arom}, J = 7.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 19.2 (CH_3), 52.8 (OCH_3), 67.3 (C^4), 126.0 (2C, C_{arom}), 128.4 w (C_{arom}), 128.6 (C_{arom}), 128.9 (2C, C_{arom}), 129.1 (2C, C_{arom}), 129.6 (2C, C_{arom}), 132.2 (C_{arom}), 133.0 w (C_{arom}), 160.3 (C^5), 172.4 (C=O), 182.2 (C^3). Found, %: C 73.91; H 5.50; N 9.51. $C_{18}H_{16}N_2O_2$. Calculated, %: C 73.95; H 5.52; N 9.58.

Methyl 3-methyl-4,5-diphenyl-4*H*-pyrazole-4-carboxylate (17a). mp 107–108°C. UV spectrum (MeOH): λ_{max} 286 nm (log ε 3.96). IR spectrum, ν, cm^{-1}: 3066 w, 2956 w, 1754 v.s., 1500 m, 1447 m, 1436 m, 1378 s, 1228 s. ^{1}H NMR spectrum, δ, ppm: 2.08 s (3H, Me), 3.75 s (3H, OMe), 7.31–7.89 m (10H). ^{13}C NMR spectrum, δ_C, ppm: 13.5 (Me), 53.7 (OMe), 79.2 (C^4), 111.7 (C_{arom}), 127.3 (2C, C_{arom}), 128.4 (2C, C_{arom}), 128.9 (2C, C_{arom}), 129.0 (C_{arom}), 129.6 (2C, C_{arom}), 130.2 w (C_{arom}), 131.5 (C_{arom}), 131.8 w (C_{arom}), 166.4 (C=O), 173.3 (C^3), 175.7 (C^5). Found, %: C 74.31; H 5.58; N 9.52. $C_{18}H_{16}N_2O_2$. Calculated, %: C 73.95; H 5.52; N 9.58.

Methyl 4-methylidene-5,5-diphenyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate (11). A solution of 1 g (3.4 mmol) of 3*H*-pyrazole **3a** in 10 mL of anhydrous THF containing 2 drops of concentrated sulfuric acid was kept for 10 h at 20°C. The mixture was diluted with 10 mL of water, and the product was isolated by extraction with diethyl ether as described above. Yield 0.32 g (32%), colorless crystals, mp 154°C [14]. IR spectrum, ν, cm^{-1}: 3400 br.m (NH), 3068 w, 3030 w, 2955 m, 1718 v.s, 1525 m, 1450 s, 1400 m, 1240 s, 1100 s. ^{1}H NMR spectrum, δ, ppm: 3.91 s (3H, OMe), 5.07 s and 6.39 s (1H each, $=CH_2$), 7.02 br.s (1H, NH), 7.22–7.30 m (4H, H_{arom}), 7.33–7.43 m (6H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 52.0 (OMe), 79.3 (C^3), 112.9 ($=CH_2$), 127.5 (4C, C_{arom}), 127.9 (2C, C_{arom}), 128.8 (4C, C_{arom}), 136.8 w (C^4), 143.7 (C_{arom}), 146.7 (C^5), 162.6 (C=O). Found, %: C 74.13; H 5.57; N 9.60. $C_{18}H_{16}N_2O_2$. Calculated, %: C 73.95; H 5.52; N 9.58.

Compound **11** was also formed in a small amount from 3*H*-pyrazole **3a** during silica gel column chromatography. Heating of 0.3 g (1 mmol) of **11** in 15 mL of anhydrous THF containing H_2SO_4 at 65°C for 5 min gave 0.22 g (74%) of **10a**.

Acid-catalyzed rearrangement of 3*H*-pyrazoles 7d and 8e (*general procedure*). A solution of 1 mmol of 3*H*-pyrazole **7d** or **8e** in 20 mL of acetic acid containing a catalytic amount of concentrated sulfuric acid was kept for 24 h at 20°C. The mixture was diluted with 30 mL of water, and the precipitate was filtered off, washed on a filter with 10 mL of a 5% aqueous solution of $NaHCO_3$ and with water until neutral washings, and dried in air. Pyrazolones **23** and **25** were isolated by crystallization.

Methyl 5-oxo-3,4-diphenyl-4,5-dihydro-1*H*-pyrazole-4-carboxylate (23). Yield 180 mg (90%), colorless crystals, mp 125–126°C. IR spectrum, ν, cm^{-1}: 3214 w, 1752 s, 1732 v.s, 1694 s, 1235 m, 1208 m, 1007 w, 779 w, 691 m. ^{1}H NMR spectrum, δ, ppm: 3.74 s (3H, OMe), 7.31–7.42 m (8H, H_{arom}), 7.71 d (2H, H_{arom}, J = 7.4 Hz), 9.78 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 53.9 (OMe), 66.2 (C^4), 126.8 (2C, C_{arom}), 128.7 (2C, C_{arom}), 128.9 (5C, C_{arom}), 130.1 w (C_{arom}), 130.7 (C_{arom}), 132.3 w (C_{arom}), 156.5 (C^5), 166.7 (C=O), 173.9 (C^3). Found, %: C 69.30; H 4.87; N 9.50. $C_{17}H_{14}N_2O_3$. Calculated, %: C 69.38; H 4.79; N 9.52.

5-Oxo-3,4-diphenyl-4,5-dihydro-1*H*-pyrazole-4-carbonitrile (25). Yield 148 mg (74%), light brown crystals, mp 161–162°C. IR spectrum, ν, cm^{-1}: 3210 m, 3113 m, 2245 w (CN), 1736 v.s, 1728 v.s, 1566 m, 1555 m, 1497 m, 1447 m, 1269 m, 768 m, 752 m, 721 m, 687 m, 644 m. ^{1}H NMR spectrum, δ, ppm: 7.34 t (2H, H_{arom}, J = 7.4 Hz), 7.43 t (1H, H_{arom}, J = 6.8 Hz), 7.45 br.s (5H, H_{arom}), 7.69 d (2H, H_{arom}, J = 7.8 Hz), 9.17 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 53.2 (C^4), 113.6 (CN), 126.1 (2C, C_{arom}), 126.8 (2C, C_{arom}), 128.1 w (C_{arom}), 129.2 (2C, C_{arom}), 129.8 w (C_{arom}), 130.1 (C_{arom}), 130.3 (2C, C_{arom}), 131.6 (C_{arom}), 154.7 (C^3), 170.0 (C=O). Found, %: C 75.48; H 4.29; N 16.32. $C_{16}H_{11}N_3O$. Calculated, %: C 73.55; H 4.24; N 16.08.

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