Pyrazoles VI: The Electron-Releasing Capacity of the Pyrazole Ring (1)

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UV and PMR spectral data and C=O frequencies of some methylpyrazoles containing in the 3-, 4- or 5-position, a formyl-, acetyl- or ethoxycarbonyl group are reported. These data confirm earlier conclusions that, in particular, the 4-pyrazolyl group acts as an electron releasing group. The syntheses of a number of formyl-, acetyl- and ethoxycarbonyl pyrazoles are described. In addition, some 4-dicyanovinyl- and 4-tricyanovinylpyrazoles were investigated.

Introduction.

Substituent vibrations can give information about electron donor and electron acceptor abilities of heteroaromatic rings (2). In particular, the C=O stretching vibration has been used to measure the electron releasing ability of heteroaromatic rings as compared to the benzene nucleus and to distinguish between electron releasing capacities of the different positions in the ring.

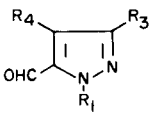
In order to investigate the electron-releasing capacity of the pyrazole ring and to examine the differences in electron-releasing capacities of the 3-, 4- and 5-positions we have synthesized a number of formyl pyrazoles. Many formyl pyrazoles are described in the literature (3), but most contain phenyl groups. For our purpose we decided to use only methyl substituted derivatives (4). For the same reason we have synthesized a number of only methyl substituted acetyl- and ethoxycarbonyl pyrazoles. Carbonyl frequencies of these compounds are compared as well as the UV and PMR spectral data (Tables 2 and 3).

TABLE 1

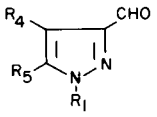
C=O Stretching Vibrations of Formyl-, Acetyl- and Ethoxycarbonyl Pyrazoles

No.	R_1	R_3	R_4	R_5	ν	ϵ	$\Delta\nu$ (a)
I	CH_3	CH_3	H	CHO	1687	333	- 14
II	CH_3	CHO	H	CH_3	1692	379	- 9
III	CH_3	H	CHO	H	1679	434	- 22
IV	CH_3	CH_3	CHO	H	1671	391	- 30
V	CH_3	H	CHO	CH_3	1674	460	- 27
VI	CH_3	CH_3	CHO	CH_3	1666	460	- 35
IX	H	CH_3	H	$COCH_3$	1681	272	- 2
X	CH_3	$COCH_3$	H	CH_3	1677	292	- 6
XI	H	H	$COCH_3$	H	1671	296	- 12
XII	CH_3	CH_3	$COCH_3$	CH_3	1657	227	- 26
XIII	CH_3	CH_3	H	$COOC_2H_5$	1719	292	+10
XIV	CH_3	$COOC_2H_5$	H	CH_3	1719	305	+10
XVII	CH_3	CH_3	$COOC_2H_5$	CH_3	1695	355	- 14
XVIII	CH_3	H	H	$COOC_2H_5$	1722	333	+13
XX	CH_3	H	$COOC_2H_5$	H	1710	344	+1

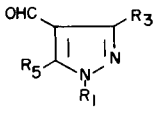
(a) $\Delta\nu$: Calculated for formylpyrazoles by subtraction from ν (C=O) of benzaldehyde (1701 cm^{-1}); for acetylpyrazoles by subtraction from the frequency of acetophenone (1683 cm^{-1}) and for the esters by subtraction from the frequency of ethyl benzoate (1709 cm^{-1}).



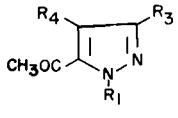
I : $R_1 = R_3 = CH_3, R_4 = H$
VII : $R_1 = R_4 = H, R_3 = CH_3$
VIII: $R_1 = R_3 = R_4 = H$



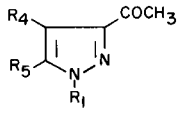
II: $R_1 = R_5 = CH_3, R_4 = H$



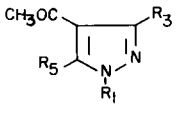
III: $R_1 = CH_3, R_3 = R_5 = H$
IV: $R_1 = R_3 = CH_3, R_5 = H$
V : $R_1 = R_5 = CH_3, R_3 = H$
VI: $R_1 = R_3 = R_5 = CH_3$



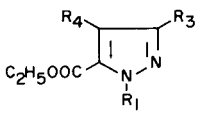
IX: $R_1 = R_4 = H, R_3 = CH_3$



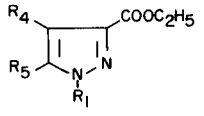
X: $R_1 = R_5 = CH_3, R_4 = H$



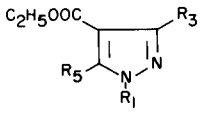
XI : $R_1 = R_3 = R_5 = H$
XII: $R_1 = R_3 = R_5 = CH_3$



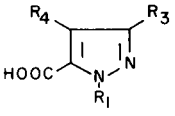
XIII: $R_1 = R_3 = CH_3, R_4 = H$
XV : $R_1 = R_4 = H, R_3 = CH_3$
XVIII: $R_1 = CH_3, R_3 = R_4 = H$



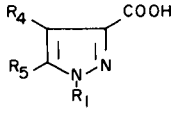
XIV: $R_1 = R_5 = CH_3, R_4 = H$
XIX: $R_1 = CH_3, R_4 = R_5 = H$



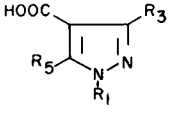
XVI : $R_1 = H, R_3 = R_5 = CH_3$
XVII: $R_1 = R_3 = R_5 = CH_3$
XX : $R_1 = CH_3, R_3 = R_5 = H$



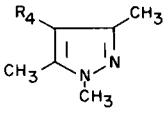
XXIII: $R_1 = CH_3, R_3 = R_4 = H$



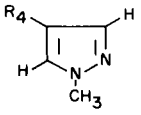
XXI: $R_2 = CH_3, R_4 = R_5 = H$



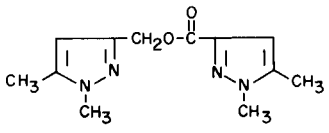
XXII: $R_1 = CH_3, R_3 = R_5 = H$



XXIV: $R_4 = CH{=}C(CN)_2$



XXV : $R_4 = CH{=}C(CN)_2$
XXVI : $R_4 = CH(CN)CH(CN)_2$
XXVII: $R_4 = C(CN){=}C(CN)_2$



XXVIII

Discussion.

According to the literature 5-formyl-1,3-dimethyl- and 3-formyl-1,5-dimethylpyrazole (I and II), can be synthesized by Rosemund reduction of the acid chlorides (8). In an attempt to use Brown and McFarlins procedure (9) for the reduction of acid chlorides, 1,5-dimethyl-3-pyrazolecarbonyl chloride was reacted with tri-*t*-butoxylithium aluminum hydride in diglyme. Due to poor solubility of the carbonyl chloride in diglyme the reaction was run several times at different temperatures varying from -45° to 0°. Only when the reaction was performed at -45° could a trace of aldehyde be detected in the reaction mixture. The only product which could be isolated in reasonable yield (27%, reaction temperature -10° to 0°) was the ester of 3-hydroxymethyl-1,5-dimethylpyrazole and 1,5-dimethyl-3-pyrazole carboxylic acid (XXVIII). Eventually we obtained I and II by oxidation of the corresponding alcohols following the procedure of Partch (10). The alcohols were obtained by lithium aluminum hydride reduction of the esters.

The formylation procedures described in part V of this series (1, see also 11) was used for the syntheses of the 4-formylpyrazoles (III, IV, V and VI). The yields of these formylations varied from 50 to 80%.

TABLE 2

UV Spectra of Formyl-, Acetyl- and Ethoxycarbonyl.Pyrazoles in Methanol (in mμ)

No.	R_1	R_3	R_4	R_5	λ max	log ε
I	CH_3	CH_3	H	CHO	247	3.80
II	CH_3	CHO	H	CH_3	243-244	3.97
III	CH_3	H	CHO	H	246	4.02
IV	CH_3	CH_3	CHO	H	248	4.07
V	CH_3	H	CHO	CH_3	250	4.11
VI	CH_3	CH_3	CHO	CH_3	252	4.12
VII	H	CH_3	H	CHO	236	3.89
IX	H	CH_3	H	$COCH_3$	234-235	3.94
X	CH_3	$COCH_3$	H	CH_3	242	3.99
XII	CH_3	CH_3	$COCH_3$	CH_3	248	4.07
XVIII	CH_3	H	H	$COOC_2H_5$	226-227	4.02
XIX	CH_3	$COOC_2H_5$	H	H	222-223	3.95
XX	CH_3	H	$COOC_2H_5$	H	224	4.04

TABLE 3

PMR Spectra: Chemical Shifts (in p.p.m.) of Formyl-, Acetyl- and Ethoxycarbonyl Pyrazoles (in Deuteriochloroform)

No.	Compound				Chemical shifts (δ)			
	R_1	R_3	R_4	R_5	R_1	R_3	R_4	R_5
I	CH_3	CH_3	H	CHO	4.00	2.21	6.57	9.69
II	CH_3	CHO	H	CH_3	3.82	9.79	6.44	2.26
III	CH_3	H	CHO	H	3.91	7.80	8.70	7.87
IV	CH_3	CH_3	CHO	H	3.86	2.42	9.81	7.87
V	CH_3	H	CHO	CH_3	3.77	7.47	9.78	2.50
VI	CH_3	CH_3	CHO	CH_3	3.63	2.29-2.41	9.75	2.29-2.41
IX	H	CH_3	H	$COCH_3$	–	2.51	6.46	2.30
X	CH_3	$COCH_3$	H	CH_3	3.80	2.50	6.45	2.28
XII	CH_3	CH_3	$COCH_3$	CH_3	3.72	2.40-2.43	2.49	2.40-2.43
XVI	H	CH_3	$COOC_2H_5$	CH_3	12.33	2.45	1.39 t 4.25 q	2.45
XVII	CH_3	CH_3	$COOC_2H_5$	CH_3	3.65	2.36-2.45	1.33 t 4.21 q	2.36-2.45
XVIII	CH_3	H	H	$COOC_2H_5$	4.12	7.47 d	6.75 d	1.34 t 4.40 q
XIX	CH_3	$COOC_2H_5$	H	H	3.95	1.38 t 4.37 q	6.70 d	7.40 d
XX	CH_3	H	$COOC_2H_5$	H	3.90	7.76-7.84	1.36 t 4.16 q	7.76-7.84

3(5)-Acetyl-5(3)-methylpyrazole (IX), 3-acetyl-1,5-dimethylpyrazole (X) and 4-acetylpyrazole (XI) were synthesized from the corresponding carboxylic acids and methyllithium (12). The syntheses of the first two compounds were carried out once in ether and once in a mixture of tetrahydrofuran and ether as the reaction medium. The reactions were followed by hydrolysis of small samples in excess water and analysis by TLC on

silica gel (chloroform/methyl= 9/1; the spots were identified under UV light and by 2,4-dinitrophenylhydrazine). When no more increase of ketone could be observed the reaction mixtures were worked-up. In tetrahydrofuran/ether solution the reaction times were only a fraction of those in pure ether and twice as much product was obtained. The acetylpyrazoles were isolated by continuous extraction of the alkaline solution obtained after hydrolysis of the reaction mixture with ether for twenty hours. The extracted solution checked for the presence of acetylpyrazole contained only the lithium salts of the pyrazolecarboxylic acid. No appreciable formation of the dimethylcarbinol was detected (< 2%).

Acetylation of 1,3,5-trimethylpyrazole gave 4-acetyl-1,3,5-trimethylpyrazole (XII) (13).

The ethyl esters (XIII, XIV, XV, XVI and XVII) of 1,3-dimethyl-5-, 1,5-dimethyl-3-, 3(5)-methyl-5(3-, 3,5-dimethyl-4- and 1,3,5-trimethyl-4-pyrazole carboxylic acids were prepared by standard condensation reactions (8, 14, 15). The ethyl esters (XVIII, XIX and XX) of 1-methyl-5-, 1-methyl-3- and 1-methyl-4-pyrazole carboxylic acid were obtained by esterification of the acids, which in turn were obtained by oxidation of the appropriate dimethylpyrazoles. Contrary to other pyrazolecarboxylic acids, 1-methyl-3-pyrazolecarboxylic acid (XXI) could not be isolated in the usual way by acidification of the alkaline filtrate of the permanganate oxidation mixture.

The 4-(2,2-dicyanovinyl)pyrazoles (XXIV and XXV) were obtained from the condensation reaction of VI and III with malononitrile. Addition of hydrogen cyanide to XXV gave 4-(1,2,2-tricyanoethyl)-1-methylpyrazole (XXVI) which in turn was oxidized with bromine to give 4-(1,2,2-tricyanovinyl)-1-methylpyrazole (XXVII).

A comparison of C=O frequencies (see Table 1) shows that with the exception of the ethoxycarbonyl pyrazoles (XIII, XIV, XVIII and XX) these frequencies are 2 to 35 cm^{-1} lower then their corresponding parent benzene compound indicating that in general the pyrazole ring donates electrons more readily then the phenyl ring. The 4-position appears to have the highest electron releasing capacity: $\Delta\nu$ -12 to -35 cm^{-1}. This confirms our earlier conclusions concerning the interaction found for example in 4-nitroso- and 4-nitropyrazoles (16, 17) as observed from their acidities and UV spectral data. No difference is found between the 3- and 5-position: $\Delta\nu$ -2 to -14 cm^{-1} for the formyl and acetyl pyrazoles.

Methyl groups depress the C=O frequency, especially in the case of the 4-carbonyl group. As was expected, the lowest frequencies are found in the 1,3,5-trimethyl-4-carbonyl compounds due to the inductive effect of the three methyl groups. This is in concurrence with our conclusions that in these 5-membered heteroaromatic rings, steric hindrance of conjugation by ortho methyl groups is absent or less then in benzene (17).

The fact that the 4-position has the highest electron releasing capacity is in agreement with chemical data which shows that electrophilic substitution (3) in the pyrazole nucleus takes place preferentially in the 4-position. Recently, molecular orbital calculations by Finar (18) and by Lynch (19) revealed that the π-electron density is also highest in the 4-position.

Several workers have concluded from their UV spectral studies on pyrazoles (20, 21, 22) that a methyl group in any position has a bathochromic effect. This is also shown in the case of our formyl- and acetylpyrazoles, the longest wavelengths belonging to the 1,3,5-trimethyl derivatives (see Table 2).

We were curious to know if this electron releasing effect of a 4-pyrazolyl group would result in colored products when the aldehyde group is replaced by a 2,2-dicyanovinyl or a 1,2,2-tricyanovinyl group as happens in the case of *p-N,N*-dimethylaminobenzaldehyde (23). However, 4-(2,2-dicyanovinyl)-1-methylpyrazole (XXV) is a colorless compound (λ max 317 mμ) and 4-(1,2,2-tricyanovinyl)-1-methylpyrazole (XXVII) is pale yellow (λ max 354 mμ). The C=C stretching vibration of the latter compound has a much lower frequency then the dicyano derivative (1550 and 1590 cm^{-1}), a difference which parallels the shift to longer wavelength in the ultraviolet, showing an increase in conjugation in going from the dicyanovinyl to the tricyanovinyl pyrazole. The C≡N frequencies do not show a similar difference, but it is known that C=C frequencies are more susceptible to conjugation (24). There is a close parallel between the positions of the C=C stretching vibration and the position of the first electron transition in the ultraviolet for neutral cyanovinyl compounds (24). These shifts are interpreted in light of increasing extent of conjugation, as for example in the case of 1,2,2-tricyanovinylbenzene which absorbs at much longer wavelength than 2,3-dicyano-4,4-dimethyl-2-pentenenitrile (λ max 343 and 250 mμ) (24).

From C^{13} magnetic resonance data (19) and PMR spectra (25, 26, 27), it has been concluded that the electron density in the pyrazole ring is highest in the 4-position. In a previous paper (27) it was noted from PMR data that in the course of electron donation in 4-substituted pyrazoles a positive charge is developed at N-1. The same may be concluded from the PMR data presented here. The N-methyl resonance peak of the three 1,3,5-trimethyl-4-substituted pyrazoles appear to be at lower magnetic field then any of the others, indicating a larger electron shift towards the 4-carbonyl group resulting in a higher positive charge density at N-1 (see Table 3) as compared to other pyrazoles.

Summary.

The data presented here constitute further evidence for the conclusion that in substituted pyrazoles the pyrazole ring and in particular the 4-pyrazolyl group acts as an electron releasing group.

EXPERIMENTAL

All melting points are uncorrected. The purity of all compounds was checked by thin layer chromatography. Elemental analyses were performed in the Micro Analytic Department of the University of Amsterdam, Amsterdam, The Netherlands.

5-Formyl-1,3-dimethylpyrazole (I).

This compound had b.p. 82-86°/18 mm.; lit., 80-83°/12 mm (8).

3-Formyl-1,5-dimethylpyrazole (II).

This compound had m.p. 56° lit., 56° (8).

4-Formyl-1-methylpyrazole (III).

This compound had b.p. 106-108°/20 mm.; lit., 119-121°/25 mm. (11). In our hands this compound appeared to be a solid, m.p. 30°.

4-Formyl-1,3-dimethylpyrazole (IV).

This compound had b.p. 129-131°/18 mm, m.p. 47° (from petroleum ether 40-60°).

Anal. Calcd. for $C_6H_8N_2O$: C, 58.05; H, 6.50; N, 22.57. Found: C, 58.34; H, 6.74; N, 22.52.

4-Formyl-1,5-dimethylpyrazole (V).

This compound had b.p. 129°/18 mm, m.p. 58° (after sublimation).

Anal. Calcd. for $C_6H_8N_2O$: C, 58.05; H, 6.50; N, 22.57. Found: C, 58.45; H, 6.53; N, 22.31.

4-Formyl-1,3,5-trimethylpyrazole (VI). See Part V (1).

3-(5)-Formyl-5(3)-methylpyrazole (VII).

This compound was crystallized from ethanol, m.p. 184°, lit., 185-187°; after sublimation, m.p. 188°, lit., 190° (6).

3(5)-Formylpyrazole (VIII).

This compound was crystallized from ethanol, m.p. 143°, lit., 146-147° (7).

3(5)-Acetyl-5(3)-methylpyrazole (IX).

The acid (0.03 mole) corresponding to IX was reacted once in 50 ml. of ether and once in 50 ml. of tetrahydrofuran with 50 ml. of a 2 molar solution of methyllithium in ether (Fluka). The reaction run in ether was worked up after 40 hours giving a yield of 0.9 g., 24%. In tetrahydrofuran/ether solution the reaction was complete in 2 hours; the yield was 1.85 g., 49%. Crystallization from ethyl acetate gave colorless crystals, m.p. 92°; after sublimation, m.p. 97°. Calcd. mol. wt. for $C_6H_8N_2O$: 124.0637. Found: mol. wt., 124.0636.

Semicarbazone from ethanol/water had m.p. 229°.

3-Acetyl-1,5-dimethylpyrazole (X).

The acid (0.03 mole) corresponding to X either in 50 ml. of ether or in 50 ml. of tetrahydrofuran was reacted with 30 ml. of a 2 molar solution of methyllithium in ether (Fluka). The reaction carried out in ether required 20 hours; the yield was 1.4 g., 34%. In tetrahydrofuran/ether the reaction was complete in 2 hours; the yield was 2.55 g., 61%. Crystallization from ethyl acetate gave a colorless product, m.p. 47°; after sublimation, m.p. 56°.

Anal. Calcd. for $C_7H_{10}N_2O$: C, 60.85; H, 7.30; N, 20.38. Found: C, 61.28; H, 7.46; N, 20.20.

4-Acetylpyrazole (XI).

4-Pyrazolecarboxylic acid (0.03 mole) dissolved in 70 ml. of tetrahydrofuran was reacted with 50 ml. of a 2 molar solution of methyllithium in ether in the same manner as described above for the syntheses of the 3(5) acetylpyrazoles. After purification by column chromatography (25) and crystallization from benzene, 0.11 g. were obtained, m.p. 111°.

Anal. Calcd. for $C_5H_6N_2O$: C, 54.54; H, 5.49; N, 25.44. Found: C, 54.40; H, 5.68; N, 25.28.

4-Acetyl-1,3,5-trimethylpyrazole (XII).

Acetic anhydride (10 g.) was added to a mixture of 11 g. of the trimethylpyrazole, 30 g. of aluminum chloride and 40 ml. of carbon disulfide. The reaction mixture was refluxed for one hour. After working up and crystallization from a mixture of ether and petroleum ether (40-60°), 4.2 g., (28%) were obtained, m.p. 68°, lit., 69-70° (13).

Ethyl 1,3-Dimethyl-5-pyrazolecarboxylate (XIII).

This compound had b.p. 66-72°/1 mm.; 109°/20 mm.; lit., b.p. 89°/10 mm. (31).

Ethyl 1,5-Dimethyl-3-pyrazolecarboxylate (XIV).

This compound had b.p. 108-110°/1 mm., m.p. 40°; lit., b.p. 154°/10 mm., m.p. 40-42° (31).

Ethyl 3(5)-Methyl-5(3)-pyrazolecarboxylate (XV).

This compound had m.p. 81-82°; lit., m.p. 82-83° (15).

Ethyl 3,5-Dimethyl-4-pyrazolecarboxylate (XVI).

This compound had m.p. 94°; lit., m.p. 96° (8).

Ethyl 1,3,5-Trimethyl-4-pyrazolecarboxylate (XVII).

This compound had m.p. after sublimation, 40-41°; lit., m.p. 37° (8).

Ethyl 1-Methyl-5-pyrazolecarboxylate (XVIII).

This compound had b.p. 95°/18 mm.

Anal. Calcd. for $C_7H_{10}N_2O_2$: C, 54.53; H, 6.54; N, 18.17. Found: C, 54.79; H, 6.58; N, 17.84.

Ethyl 1-Methyl-3-pyrazolecarboxylate (XIX).

This compound had b.p. 140-143°/13 mm.; m.p. 9-11°.

Anal. Calcd. for $C_7H_{10}N_2O_2$: C, 54.53; H, 6.54; N, 18.17. Found: C, 54.37; H, 6.64; N, 17.94.

Ethyl 1-Methyl-4-pyrazolecarboxylate (XX).

This compound had b.p. 120°/13 mm.

Anal. Calcd. for $C_7H_{10}N_2O_2$: C, 54.53; H, 6.54; N, 18.17. Found: C, 54.46; H, 6.55; N, 17.88.

1,5-Dimethyl-3-pyrazolylmethyl 1,5-Dimethyl-3-pyrazolecarboxylate (XXVIII).

1,5-Dimethyl-3-pyrazolecarbonyl chloride (19.3 g.) was reacted at -10° with tri-*t*-butoxylithium aluminum hydride in diblyme according to the general procedure of Brown and McFarlin (22). Working-up of the reaction mixture and crystallization from ligroin afforded 4.1 g. of colorless crystals (27%), m.p. 84°; infrared ν (C=O) 1723, (C-O-C) 1200 cm^{-1}. The PMR spectrum consisted only of singlets, δ 2.22 and 2.26, each 3 protons for the

two methyl groups in the 5-positions, 3.74 and 3.80 each 3 protons for the two *N*-methyl groups, 5.30 two protons for the methylene group, 6.12 and 6.35 for the two 4-protons. Acidification of the alkaline hydrolysate afforded 1,5-dimethyl-3-pyrazolecarboxylic acid. On comparison with original samples both this acid and 3-hydroxymethyl-1,5-dimethylpyrazole were identified by TLC (silica gel Gf 254 Merck, chloroform/methanol= 1/1).

Anal. Calcd. for $C_{12}H_{16}N_4O_2$: C, 58.05; H, 6.50; N, 22.57. Found: C, 57.87; H, 6.77; N, 22.50.

1-Methyl-3-pyrazolecarboxylic Acid (XXI).

A stream of dry hydrogen chloride gas was passed through a suspension of 1.15 g. of potassium 1-methyl-3-pyrazolecarboxylate (obtained from the permanganate oxidation of 1,3-dimethylpyrazole) in 30 ml. of chloroform. The temperature rose to 45°. Potassium chloride was filtered from the hot reaction mixture; the acid (0.4 g.) crystallized from the filtrate on cooling, m.p. 146°.

Anal. Calcd. for $C_5H_6N_2O_2$: C, 47.62; H, 4.80; O, 25.37; N, 22.22. Found: C, 47.12; H, 5.32; O, 25.20; N, 22.38.

1-Methyl-4-pyrazolecarboxylic Acid (XXII).

This compound had m.p. 205-206°; lit., m.p. 205-206° (11).

1-Methyl-5-pyrazolecarboxylic Acid (XXIII).

This compound had m.p. 219-220°; lit., m.p. 222° (28).

4-(2,2-Dicyanovinyl)-1-methylpyrazole (XXV).

The condensation of 1-methyl-4-formylpyrazole and malononitrile in ethanol solution in the presence of a catalytic amount of piperidine was performed according to the procedure for the synthesis of *p*-(2,2-dicyanovinyl)-*N*,*N*-dimethylaminobenzene (23, 29). Crystallization from a 1:1 ethanol-water mixture gave a colorless product, yield 94%, m.p. 137°; UV λ (methanol) 317 mμ (log ε, 3.34); infrared ν (C=C) 1590, (C≡N) 2215 cm^{-1} (chloroform). The PMR spectrum (acetone) showed a singlet at δ 4.05 (3 protons) for the methyl group, a singlet at 8.21 (2 protons) for the 3- and 5-protons and a singlet at 8.44 (1 proton) for the ethylene proton.

Anal. Calcd. for $C_8H_6N_4$: C, 60.75; H, 3.82; H, 35.43. Found: C, 60.61; H, 4.00; N, 35.43.

4-(2,2-Dicyanovinyl)-1,3,5-trimethylpyrazole (XXIV).

The same procedure was followed as for the synthesis of XXV. Crystallization gave colorless crystals, yield 59%, m.p. 107°; UV λ (methanol) 331 mμ (log ε, 4.33); λ (heptane) 332 mμ (log ε 4.30); ν (C=C) 1597 (C≡N) 2252 cm^{-1} (potassium bromide disc).

Anal. Calcd. for $C_{10}H_{10}N_4$: C, 64.50; H, 5.41; N, 30.09. Found: C, 64.40; H, 5.50; N, 30.42.

4-(1,2,2-Tricyanoethyl)-1-methylpyrazole (XXVI).

Addition of hydrogen cyanide to the double bond of the 2,2-dicyanovinyl compound performed conform with the general procedure of McKusick c.s. (23) afforded colorless crystals after crystallization from methanol, 37%, m.p. 135-136° dec.; infrared ν (C≡N) 2275 cm^{-1} (potassium bromide discs). The PMR spectrum measured in acetone showed a singlet at δ 3.90 (3 protons), a singlet at 5.60 (2 protons) and two one proton singlets at 7.66 and 7.93; in trifluoroacetic acid the resonance absorption at 5.60 was resolved in two doublets of the two adjacent protons in the tricyanoethyl group.

Anal. Calcd. for $C_9H_7N_5$: C, 58.37; H, 3.81; N, 37.82. Found: C, 58.52; H, 3.83; N, 37.73.

4-(1,2,2-Tricyanovinyl)-1-methylpyrazole (XXVII).

The tricyanoethyl derivative was oxidized with bromine in pyridine solution according to the procedure of Sheppart, Rosetta and Henderson for the oxidation of the corresponding benzene compound (30). Crystallization gave pale yellow crystals, yield 62%, m.p. 143°; UV λ (methanol) 354 mμ (log ε, 4.28); infrared ν (C=C) 1550, (C≡N) 2220 cm^{-1} (chloroform).

Anal. Calcd. for $C_9H_5N_5$: C, 59.01; H, 2.75; N, 38.24. Found: C, 59.13; H, 2.92; N, 38.03.

Measurements.

The IR spectra of the carbonyl compounds were measured for 0.2 *M* solutions in alcohol-free chloroform in a 0.1 mm, compensated cell using a Beckmann IR-10 spectrophotometer. The chloroform was treated with calcium chloride for two days and distilled just before use discarding the first ten percent of the distillate. The spectra were calibrated with polystyrene at 1601 cm^{-1}. The IR spectra determined in potassium bromide discs (Experimental) were taken with a Perkin Elmer 137 IR instrument.

The UV spectra of the carbonyl compounds were taken at room temperature using a ZEISS PMQ II spectrophotometer. The UV spectra of the cyano compounds (Experimental) were determined with a Perkin Elmer 137 UV spectrophotometer.

PMR spectra were obtained on a Varian A-60 instrument. Chemical shifts are given in δ relative to tetramethylsilane as internal standard. Unless stated otherwise the spectra were determined in deuteriochloroform solutions.

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(4) Contrary to *N*-methyl substituted formylpyrazoles 3(5)-formyl-5(3)-methylpyrazole (VII) and 3(5)formylpyrazole (VIII) are high melting compounds (5,6,7) which are less soluble in water and in the most common organic solvents than *N*-methylsubstituted formylpyrazoles. In our hands IR spectra taken in potassium bromide discs or in Nujol mull did not show a strong absorption band which can be assigned to a C=O stretching vibration. A preliminary mass spectral investigation indicated the presence of dimers. Spectra obtained with a MS 902 instrument (ionizing voltage 70 eV, temperature 60°) contained peaks of twice the molecular weights: Calcd. for 3(5)-formylpyrazole: mol. wt., 96.0324 ($C_4H_4N_2O$); mol. wt., dimer, 192.0647 ($C_8H_8N_4O_2$). Found: C, 96.0318 and 192.0646. Calcd. for 3(5)-formyl-5(3)-methylpyrazole: mol. wt., 110.0482 ($C_5H_6N_2O$); mol. wt., dimer, 220.0960 ($C_{10}H_{12}N_4O_2$). Found: 110.0484 and 220.0957.

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