Reactions of Some αβ-Unsaturated Pyrazolyl Compounds with Bromine and with Grignard Reagents

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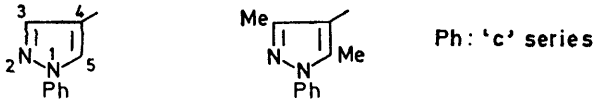
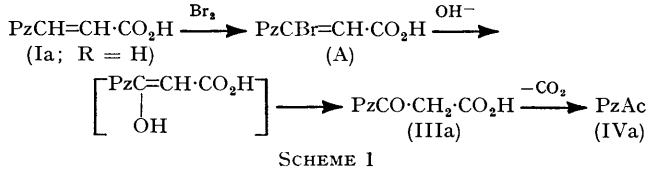
The reaction of bromine with 3-(1-phenylpyrazol-4-yl)acrylic acid and its esters has been reinvestigated, and the product has now been shown to be the α- and not the β-bromo-derivative as was believed previously. This has been established by n.m.r. spectroscopy and an elimination–addition mechanism has been suggested to explain the conversion of the α-bromoacrylic acid into the β-keto-acid by alkali. Pyrazolylpropynoic acids and pyrazolylacetylenes have been isolated and hydrated in alkaline solution to β-keto-acids and acetylpyrazoles, respectively. Reactions of Grignard reagents with pyrazolylacrylic esters and pyrazolylprop-2-en-1-ones have also been studied.

FINAR and UTTING [1] found that bromination of 3-(1-phenylpyrazol-4-yl)acrylic acid (Ia; R = H) [2] and its ethyl ester (Ia; R = Et) [1] in acetic acid solution gave a

(I) $-CH=CH\cdot CO_2R$
(II) $-CH=CBr\cdot CO_2R$
(III) $-CO\cdot CH_2\cdot CO_2H$
(IV) $-Ac$
(V) $-CH=CH_2$
(VI) $-CH=CH\cdot COR'$
(VII) $-CH=C(CO_2R)_2$
(VIII) $-CH=CBr\cdot COPh$
(IX) $-C\equiv C\cdot CO_2H$
(X) $-C\equiv CH$
(XI) $-CH=CH\cdot C(OH)R_2'$
(XII) $-CHR'\cdot CH_2\cdot COR'$
(XIII) $-CHR'\cdot CH_2\cdot CO_2R$
(XIV) $-CH(p\text{-}MeC_6H_4)\cdot CHBr\cdot CO\cdot C_6H_4Me\text{-}p$
(XV) $-CHR'\cdot CH(CO_2R)_2$
(XVI) $-CHR'\cdot CH_2\cdot CO_2H$



bromoacrylic acid and the corresponding ester. Alkaline hydrolysis of the bromo-acid gave the β-keto-acid (IIIa) and the 4-acetyl derivative (IVa).[3] The latter was also obtained by decarboxylation of the former. The sequence of reactions that was suggested is shown in Scheme 1.[1] This was based on the assumption that

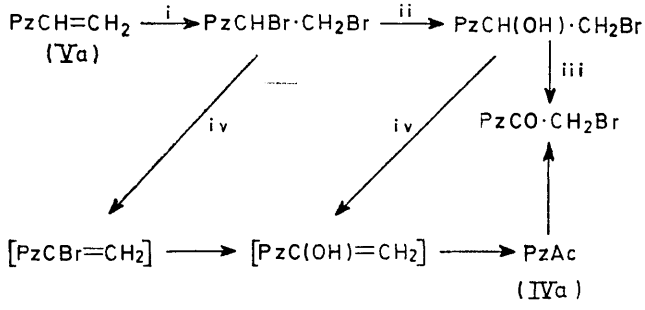


SCHEME 1

hydrolysis of the bromo-acid (A) occurred by a substitution mechanism [4] and (A) was therefore believed to be 3-bromo-3-(1-phenylpyrazol-4-yl)acrylic acid. The structure of (A) appeared to be supported [4] by the conversion of (Va) into (IVa) as shown in Scheme 2.[5]

The structure of (A) has now been reinvestigated; it has been shown that the bromo-acid is 2-bromo-3-(1-phenylpyrazol-4-yl)acrylic acid (IIa; R = H) and it is suggested that the conversion of this acid into the keto-acid (IIIa) occurs by an elimination–addition mechanism.

Table 1 lists the n.m.r. spectral data of a number of pyrazolyl αβ-unsaturated carbonyl compounds. Three compounds containing the benzene ring instead of



SCHEME 2 Reagents: i, Br_2; ii, H_2O; iii, $Na_2Cr_2O_7$; iv, KOH–EtOH–H_2O

pyrazole have been included for comparison. The τ values of the 1-phenyl protons, the pyrazole 3- and 5-protons, and the pyrazole 3- and 5-methyl groups are similar to those obtained previously.[6]

Table 1 shows that the olefinic protons are in the *trans*-position (J 15·5—17·1 Hz) and that they absorb in the aromatic region τ 2·2—2·5 and in the range τ 3·5—4·0. Since the olefinic β-protons in (VIIa; R = Et) [7] and in (VIIc; R = Et) [8] absorb at the lower field, the upper field absorption must be due to the α-proton. The n.m.r. spectrum of the bromoacrylic ester (IIa; R = Et) [1] showed a multiplet at τ 2·18—2·72 due to the phenyl protons. The two singlets at τ 1·32 and 1·82 corresponded to one and two protons, respectively. Thus, the former is due to the 5-proton and the latter to both the 3-proton and the olefinic β-proton. These assignments are supported by the n.m.r. data of (IIb; R = Et) and (VIIIa),[9] in both cases integration showing the presence of only one olefinic proton. Confirmation was obtained by treatment of the bromoacrylic ester with *p*-tolylmagnesium bromide. The crystalline product was a saturated aryl ketone ($\nu_{max.}$ 1664 cm^{-1}), shown by elemental analysis and n.m.r.

[1] I. L. Finar and K. Utting, *J. Chem. Soc.*, 1959, 4015.
[2] I. L. Finar and K. E. Godfrey, *J. Chem. Soc.*, 1954, 2293.
[3] I. L. Finar and G. H. Lord, *J. Chem. Soc.*, 1959, 1819.
[4] *Cf.* (*a*) C. A. Grob and G. Cseh, *Helv. Chim. Acta*, 1964, **47**, 194; (*b*) C. A. Grob, J. Csapilla, and G. Cseh, *ibid.*, p. 1590.
[5] I. L. Finar and K. J. Saunders, *J. Chem. Soc.*, 1963, 3967.
[6] I. L. Finar and E. F. Mooney, *Spectrochim. Acta*, 1964, **20**, 1269; I. L. Finar and D. M. Rackham, *J. Chem. Soc.* (*B*), 1968, 211.
[7] I. L. Finar and K. J. Saunders, *J. Chem. Soc.*, 1965, 3862.
[8] D. S. Breslow and C. R. Hauser, *J. Amer. Chem. Soc.*, 1940, **62**, 2385.
[9] S. Z. Mahmud, M.Phil. Thesis, University of London, 1969.

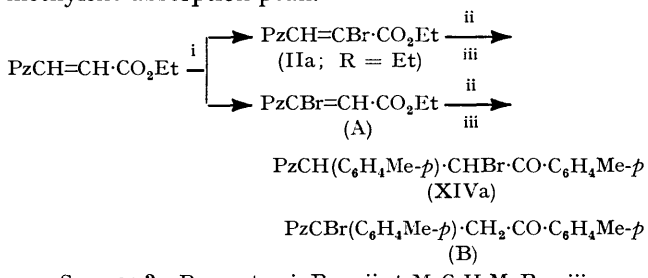
spectroscopic studies to be 2-bromo-3-(1-phenylpyrazol-4-yl)-1,3-di-*p*-tolylpropan-1-one (XIVa), τ 2·72 (s, Ph), 2·19 (s) and 2·06 (s) (pyrazole 3- and 5-protons, respectively), 7·66 (6H, 2 × CH_3·C_6H_4), and 4·39 (d) and 5·13 (d) (*J* 12·9 Hz). The presence of two adjacent methine groups is supported by the fact that the n.m.r. spectrum of ethyl 2,3-dibromo-3-phenylpropionate showed two doublets at τ 4·39 and 5·15 (*J* 12·0 Hz). Hence, the bromine atom in the bromoacrylic ester must be in the α-position; had it been in the β-position the expected product (B) would have shown a singlet methylene absorption peak.

TABLE 1

^{1}H N.m.r. spectra (τ values; solvent $CDCl_3$)

Compound	Ph	3-H	5-H	3-Me	5-Me	Olefinic H (*J*/Hz)	CO_2H	CH_3—CH_2 (*J*/Hz)	Bu^t
(Ia; R = H) *	2·59s	2·20s	1·93s			2·81d 3·81d (17·1)			
(Ia; R = Et)	2·22—2·70m	2·08s	1·91s			2·35d 3·71d (17·0)		8·69t 5·73q (7·7)	
(Ia; R = Bu^t)	2·25—2·80m	21·5s	1·99s			2·51d 3·83d (15·5)			8·50s
(Ib; R = H)	2·58s			7·56s	7·62s	2·23d 3·88d (16·3)	—1·98s		
(Ib; R = Et)	2·61s			7·60s	7·66s	2·33d 3·89d (17·1)		8·69t 5·75q (7·7)	
(Ib; R = Bu^t)	2·60s			7·60s	7·65s	2·44d 4·05d (17·0)			8·48s
(Ic; R = H) *trans*	2·55s					2·17d 3·54d (16·7)	—3·21s		
(Ic; R = Et) *trans*	2·62s					2·21d 3·51d (17·1)		8·78t 5·73q (7·7)	
(IIa; R = Et)	2·18—2·72m	1·82s	1·32s			1·82s		8·63t 5·65q (7·7)	
(IIb; R = Et)	2·40s			7·70s	7·72s	1·85s		8·80t 5·80q (7·7)	
(VIb; R′ = Ph)	2·62s			7·60s	7·62s	2·30d 2·92d (16·3)			
(VIIa; R = Et)	2·26—2·84m	2·22s	1·76s			2·32s		8·73t 5·75q (7·7)	
(VIIc; R = Et)	2·61s					2·2s		8·80t 5·73q (7·7)	
(VIIIa)	2·19—2·73m	1·84s	1·32s			1·84s			

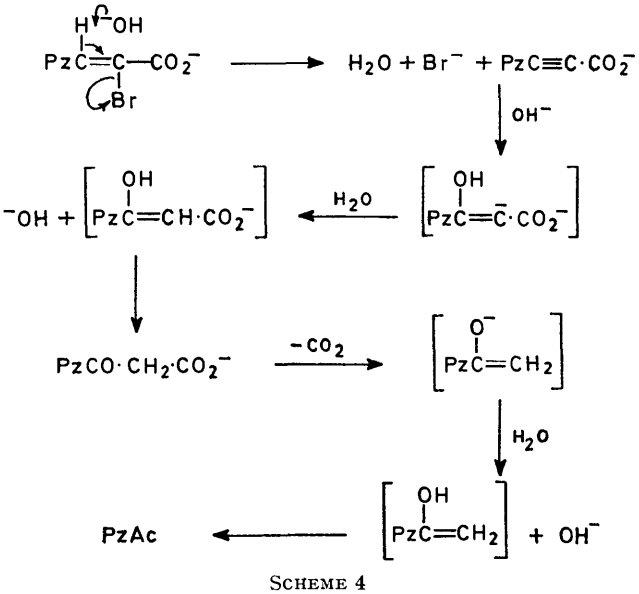
* As sodium salt in D_2O, with sodium 3-trimethylsilylpropane-1-sulphonate as internal reference.



SCHEME 3 Reagents: i, Br_2; ii, *p*-MeC_6H_4MgBr; iii, H_2SO_4–H_2O

Since it was then clear that bromination of (Ia; R = H) gives the α-bromo-derivative (IIa; R = H), it was necessary to reformulate the course of hydrolysis. Alkaline hydrolysis of (IIa; R = H) gave (IIIa),[1] and the i.r. spectrum of the crude product showed the presence of a small amount of an acetylenic compound ($\nu_{max.}$ 2212 cm^{-1}). It was therefore thought that (IIIa) might have been formed *via* an elimination–addition mechanism (Scheme 4).

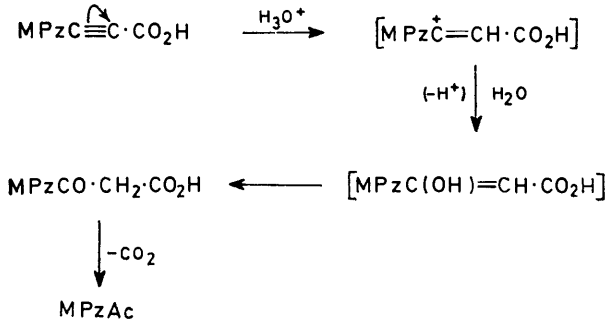
Attempts to isolate 3-(1-phenylpyrazol-4-yl)propynoic acid (IXa) from the hydrolysis products of the bromoacrylic acid (IIa; R = H) failed, but were successful when the ethyl bromo-ester (IIa; R = Et) was used. Similarly, (IIb; R = Et) gave (IXb) under the same conditions. When the acids (IXa and b) were heated with aqueous alkali, the corresponding acetyl derivatives (IVa and b) were obtained. Compound (IVb) was also obtained when the propynoic acid (IXb) was warmed with aqueous sulphuric acid. The course of this reaction may be formulated [10] as in Scheme 5.



SCHEME 4

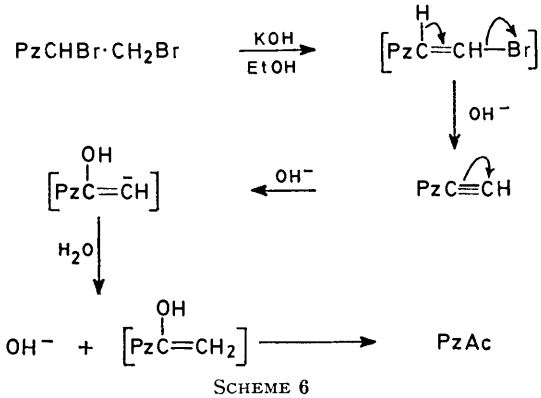
[10] *Cf.* D. S. Noyce, M. A. Matesich, M. D. Schiavelli, and P. E. Peterson, *J. Amer. Chem. Soc.*, 1965, **87**, 2295.

When heated to their m.p.s the acids (IXa and b) underwent decarboxylation to give the corresponding pyrazolylacetylenes (Xa and b). These, on heating with aqueous alkali, gave, respectively, the acetyl



SCHEME 5

derivatives (IVa and b). The acetylene (Xb) also gave (IVb) when warmed with aqueous sulphuric acid. It is therefore probable that the dehydrobromination step with ethanolic potassium hydroxide gives the acetylene derivative, which is then converted into the acetyl derivative (Scheme 6).

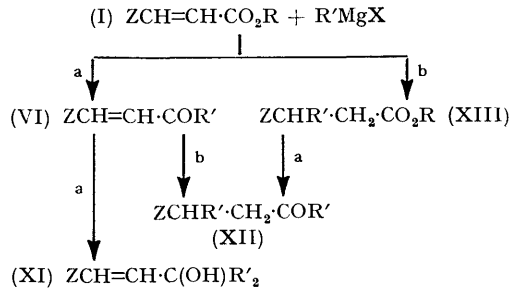


SCHEME 6

Hydration of acetylenic compounds by the acid-catalysed reaction in the presence of a mercury salt is a well-known process. The purely acid-catalysed reaction is less common.[10] Hydration of pyrazole acetylenic compounds in aqueous alkali appears to be the first example of this type of reaction, and is particularly interesting in that dehydrohalogenation of 1,2-dihalides in alkaline media is a standard method of preparing acetylenes.

The reaction between the pyrazolylacrylic esters and Grignard reagents has also been investigated. The possible courses this reaction may take are shown in Scheme 7.[11] There appears to be no definite rule for predicting the nature of the product from a knowledge of Z, R, and R′, but in the presence of a copper(I) halide as catalyst, the predominant product is usually (XIII). Table 2 lists the reactions carried out, together with the products.

The diester (XVa; R = Et, R′ = Me) on hydrolysis, acidification, and heating of the resulting dicarboxylic acid (XVa; R = H, R′ = Me), gave the acid (XVIa; R′ = Me). Similarly, the diester (XVa; R = Et, R′ = Ph) gave the acid (XVIa; R′ = Ph).



SCHEME 7 a, 1,2-addition; b, 1,4-addition

According to Scheme 7, compound (XII) could be produced *via* either (VI) or (XIII). Kohler and Heritage,[12] who examined the reaction between methyl cinnamate (Ic; R = Me) and phenylmagnesium bromide, obtained (XIIIc; R = Me, R′ = Ph) as the major

TABLE 2

Reaction between Grignard reagents and esters or propenones

Compound; R	R′ in R′MgX	Substrate: Grignard ratio	Product * (% yield)
(Ia); Et	Me	1 : 2	(XIa) [a] (40)
(Ia); Et	Me	1 : 5	(XIa) [a] (57·5)
(Ia); Et	Ph	1 : 2	(XIIa) (35)
(Ia); Et	Ph	1 : 1·2 [b]	(XIIIa) (80)
(Ia); Bu^t	Ph	1 : 1·2	(XIIIa) (83)
(Ia); Et	*o*-tolyl	1 : 2	(XIIa) (49); (XIIIa) (35·3)
(Ia); Et	Pz	1 : 2	S.m. (94·5)
(Ia); Et	Pz	1 : 2 [b]	S.m. (97·5)
(Ia); Et	MPz	1 : 2	(XIIa) (63)
(Ia); Et	MPz	1 : 2 [c]	(XIIa) (32·8)
(Ib); Et	Me	1 : 5	(XIb) (80·5)
(Ib); Et	*o*-tolyl	1 : 2·1	S.m. (49) [d]; (XIIIb) (8·1) [d]
(VIa) [e]	Ph	1 : 2	S.m. (86)
(VIa) [e]	Ph	1 : 1 [b]	S.m. (80)
(VIa) [e]	Ph	1 : 5 [c]	(XIIa) (56·3)
(VIa) [e]	MPz	1 : 1	S.m. (89)
(VIb) [e]	Me	1 : 1·2	(XIIb) [f] (57·5)
(VIb) [e]	Me	1 : 5	(XIIb) [f] (87·4)
(VIIa); Et	Me	1 : 3	(XVa) (86)
(VIIa); Et	Ph	1 : 3	(XVa) (75·5)
(XIIIa); Et	Ph	1 : 1·2	(XIIa) (25)

[a] See ref. 4. In the presence of: [b] CuCl; [c] CuBr. [d] Estimated as acid. [e] R′ = Ph. [f] CHR′ = CHMe.

* S.m. = starting material.

product and (XIIc; R′ = Ph) as the minor product, and assumed that the latter was formed *via* (VIc; R′ = Ph). We have found that (XIIa; R′ = Ph) is formed *via* (XIIIa; R = Et, R′ = Ph), since (VIa; R′ = Ph) did not react with phenylmagnesium bromide in the absence of copper(I) bromide as catalyst (see Table 2).

EXPERIMENTAL

I.r. spectra were recorded on Perkin-Elmer 137 NaCl, 157 NaCl, and KBr Prism Infracord spectrometers for liquid

[11] M. S. Kharasch and O. Reinmuth, 'Grignard Reactions of Nonmetallic Substances,' Constable and Co., London, 1954, pp. 196, 563.

[12] E. P. Kohler and G. Heritage, *Amer. Chem. J.*, 1905, **33**, 21.

films or Nujol mulls. ^{1}H N.m.r. spectra were recorded for solutions in deuteriochloroform on a Perkin-Elmer 60 MHz R10 spectrometer, with tetramethylsilane as standard.

3-Pyrazol-4-ylacrylic Esters.[2]—A mixture of 3-(3,5-dimethyl-1-phenylpyrazol-4-yl)acrylic acid [13] (Ib; R = H) (24·2 g, 0·1 mol), thionyl chloride (35·7 g, 0·3 mol), and benzene (100 ml) was heated on a steam-bath for 1·5 h. Benzene and excess of thionyl chloride were evaporated off under reduced pressure, absolute ethanol (70 g, 1·5 mol) was added, and the mixture was heated on a steam-bath for 1·5 h and then set aside to cool. The precipitate was recrystallised from aqueous ethanol to give the *ethyl acrylic ester* (Ib; R = Et) (80%), m.p. 61—62° (Found: C, 71·3; H, 6·8; N, 10·4. $C_{16}H_{18}N_2O_2$ requires C, 71·1; H, 6·7; N, 10·4%) (see Table 1).

t-Butyl esters (Ia and b; R = Bu^t). These were prepared by adding dropwise the corresponding acid chloride (0·04 mol) in benzene (100 ml) to a heated solution of t-butyl alcohol (0·048 mol) and *NN*-dimethylaniline (0·048 mol) in ether (100 ml). The mixture was heated for 5 h, then cooled; water (100 ml) was added and the product was stirred until all the precipitated dimethylaniline hydrochloride had dissolved. The ether layer was washed successively with 10% sulphuric acid (5 × 25 ml), saturated aqueous sodium hydrogen carbonate (15 ml), and water, and then dried (Na_2SO_4) and evaporated. The residue was recrystallised from aqueous ethanol to give the *t-butyl acrylic ester* (Ia; R = Bu^t) (69·5%), m.p. 131·5—132° (Found: C, 70·9; H, 6·8; N, 10·2. $C_{16}H_{18}N_2O_2$ requires C, 71·1; H, 6·7; N, 10·4%) (see Table 1); or (Ib; R = Bu^t) (65%), m.p. 81—82° (Found: C, 72·4; H, 7·5; N, 9·1. $C_{18}H_{22}N_2O_2$ requires C, 72·5; H, 7·4; N, 9·4%) (see Table 1).

Bromination of Pyrazolyl Acids and their Ethyl Esters.[1]—To a solution of ethyl 3-(3,5-dimethyl-1-phenylpyrazol-4-yl)acrylate (Ib; R = Et) (13·5 g, 0·05 mol) in glacial acetic acid (50 ml) heated on a steam-bath was added dropwise a solution of bromine (8 g, 0·05 mol) in glacial acetic acid (30 ml). The mixture was heated for a further 15 min, then cooled; water (800 ml) was added, and the oil was extracted with ether (3 × 50 ml). The combined ethereal extracts were washed with aqueous N-sodium thiosulphate (20 ml) and water (3 × 20 ml), dried (Na_2SO_4), and evaporated to give the *bromo-ester* (IIb; R = Et) (5·3%) as an oil. This was repeatedly precipitated from acetone–light petroleum (b.p. 40—60°) (Found: C, 54·9; H, 4·9; N, 8·1. $C_{16}H_{17}BrN_2O_2$ requires C, 55·0; H, 4·9; N, 8·1%) (see Table 1).

Alkaline Hydrolysis of 2-Bromoacrylic Acids and their Esters.[1]—A solution of 2-bromo-3-(3,5-dimethyl-1-phenylpyrazol-4-yl)acrylic acid (IIb; R = H) (1·8 g, 0·0056 mol) in aqueous 2N-sodium hydroxide (30 ml) was heated under reflux for 1 h. Water (100 ml) was added and the mixture was extracted with ether (5 × 60 ml); the combined extracts were washed with water, dried (Na_2SO_4), and evaporated. The residue was recrystallised from acetone–light petroleum (b.p. 40—60°) to give *4-acetyl-3,5-dimethyl-1-phenylpyrazole* (IVb) (66%), m.p. 62—62·5° (Found: C, 72·7; H, 6·7; N, 13·2. $C_{13}H_{14}N_2O$ requires C, 73·0; H, 6·5; N, 13·1%); $\nu_{max.}$ 1639 cm^{-1} (CO); τ 2·58 (s, Ph), 7·48 (s, 3-Me), 7·51 (s, 5-Me), and 7·53 (s, 4-Ac), identical with material synthesised independently by oxidation with acid dichromate of 1-(3,5-dimethyl-1-phenylpyrazol-4-yl)ethanol, formed by reaction between 3,5-dimethyl-1-phenylpyrazole-4-carbaldehyde and methylmagnesium iodide (*cf.* ref. 3).

The ethyl ester (IIa; R = Et) (0·0156 mol) and aqueous 2N-sodium hydroxide (100 ml) were heated under reflux for 1 h; after cooling, the mixture was extracted with ether (4 × 50 ml). The combined extracts were washed with water, dried (Na_2SO_4), and evaporated to give unchanged ester (4—12%). The mother liquor was acidified; the precipitate was collected and recrystallised from aqueous ethanol to give 3-(*1-phenylpyrazol-4-yl*)*propynoic acid* (IXa) (81·6%), m.p. (decomp.) 151·5—152·5° (Found: C, 68·0; H, 3·9; N, 13·5. $C_{12}H_8N_2O_2$ requires C, 68·0; H, 3·8; N, 13·2%); $\nu_{max.}$ 2212 cm^{-1} (C≡C); τ 0·97 (s, 5-H), 1·89 (s, 3-H), and 2·02—2·62 (m, Ph). Similarly, the ethyl ester (IIb; R = Et or Bu^t) gave 3-(*3,5-dimethyl-1-phenylpyrazol-4-yl*)*propynoic acid* (IXb) (44—53% from acetone–light petroleum), m.p. (decomp.) 136—137° (Found: C, 69·9; H, 5·2; N, 11·7. $C_{14}H_{12}N_2O_2$ requires C, 70·0; H, 5·0; N, 11·65%); $\nu_{max.}$ 2212 cm^{-1} (C≡C); τ 2·59 (s, Ph), 7·57 (s, 3-Me), and 7·63 (s, 5-Me).

Decarboxylation of Acrylic and Propynoic Acids.[4]—3-(3,5-Dimethyl-1-phenylpyrazol-4-yl)acrylic acid (Ib; R = H) (2·5 g, 0·0135 mol) was heated *in vacuo* at 195° and 0·7 mmHg to give *3,5-dimethyl-1-phenyl-4-vinylpyrazole* (72%) (Found: C, 78·4; H, 7·1; N, 14·5. $C_{13}H_{14}N_2$ requires C, 78·7; H, 7·1; N, 14·2%).

The propynoic acid (IXa) (1·2 g, 0·0058 mol) was heated in a sublimation apparatus at 150° and 15 mmHg. The white sublimate of *1-phenylpyrazol-4-ylacetylene* (Xa) (0·6 g, 63%) had m.p. 69—70° (Found: C, 78·8; H, 4·9; N, 16·6. $C_{11}H_8N_2$ requires C, 78·55; H, 4·8; N, 16·65%); $\nu_{max.}$ 3257 and 2105 cm^{-1} (monosubstituted acetylene); τ 1·61 (s, 5-H), 1·95 (s, 3-H), 2·19—2·75 (m, Ph), and 7·53 (s, ≡CH).

The acid (IXb), on similar treatment, gave an oil which was dissolved in ether; the solution was extracted with alkali, washed, dried, and evaporated to give *3,5-dimethyl-1-phenylpyrazol-4-ylacetylene* (Xb) (30%), b.p. 145° at 0·3 mmHg (Found: C, 79·3; H, 6·2; N, 14·5. $C_{13}H_{12}N_2$ requires C, 79·6; H, 6·2; N, 14·3%); $\nu_{max.}$ 3247 and 2092 cm^{-1} (monosubstituted acetylene); τ 2·58 (s, Ph), 7·55 (s, ≡CH), 7·58 (s, 3-Me), and 7·63 (s, 5-Me).

Hydration of the Acetylenic Compounds.—3-(1-Phenylpyrazol-4-yl)propynoic acid (IXa) (0·01 mol) and aqueous 2N-sodium hydroxide (30 ml) were heated under reflux for 1 h. The precipitate was collected, washed with water, and recrystallised from acetone–light petroleum (b.p. 40—60°) to give 4-acetyl-1-phenylpyrazole [1] (IVa) (71·5%), m.p. 127—128°. Acidification of the mother liquor gave unchanged propynoic acid (28%). Similar treatment of 3-(3,5-dimethyl-1-phenylpyrazol-4-yl)propynoic acid (IXb) gave 4-acetyl-3,5-dimethyl-1-phenylpyrazole (IVb) (60%) and unchanged acid (33·3%). In the same way, the pyrazol-4-ylacetylenes (Xa and b) gave, respectively (IVa) (36%) and (IVb) (51%).

Compound (IXb) (0·6 g, 0·0025 mol) and 1 : 1 water–sulphuric acid (25 ml) were heated at 60° for 10 min. The mixture was cooled and extracted with chloroform (3 × 25 ml); the extracts were combined, washed with water, dried, and evaporated to give the acetylpyrazole (IVb) (56%).

Reaction between Esters or Propenones and Grignard Reagents.—To a solution of the pyrazolyl Grignard reagent [14] was added the ester or propenone; when a catalyst was used, this (1 mol %) was added to the Grignard reagent before the addition of the second component. In a typical

[13] I. L. Finar and M. Manning, *J. Chem. Soc.*, 1961, 2733.
[14] R. J. Brooklyn and I. L. Finar, *J. Chem. Soc.* (*C*), 1968, 466; 1969, 1515.

reaction, to a solution of 3,5-dimethyl-1-phenylpyrazol-4-ylmagnesium bromide (0·05 mol) in ether (140 ml) and benzene (100 ml) was added dropwise over 1·5 h a solution of ethyl 3-(1-phenylpyrazol-4-yl)acrylate (Ia; R = Et) (0·025 mol) in benzene (90 ml). The mixture was heated for 3·5 h, cooled, and hydrolysed with crushed ice (100 g) and aqueous 25% ammonium chloride (25 ml). The benzene–ether solution was separated and the aqueous layer extracted with ether (3 × 50 ml). The benzene–ether solution and the ethereal extracts were combined, washed with water (3 × 50 ml), dried (Na_2SO_4), and evaporated to give an oil which, on recrystallisation from acetone–light petroleum (b.p. 40—60°) gave 1,3-*bis*-(3,5-*dimethyl*-1-*phenylpyrazol*-4-*yl*)-3-(1-*phenylpyrazol*-4-*yl*)*propan*-1-*one* (XIIa; R′ = MPz), m.p. 150—151° (Found: C, 75·4; H, 6·0; N, 15·3. $C_{34}H_{32}N_6O$ requires C, 75·6; H, 5·9; N, 15·6%); $\nu_{max.}$ 1645 cm^{-1} (CO); τ 2·26 (s, 5-H), 2·42 (s, 3-H), 2·60 (s, Ph), 5·15 (t, CH), 6·41 (d, CH_2), 7·43 and 7·56 (s, 3-Me and 5-Me, respectively, in pyrazole ring attached to C-3), and 7·0 (s, 3-Me and 5-Me in pyrazole ring attached to C-1).

The results of these Grignard reactions are given in Table 2.

4-(3,5-*Dimethyl*-1-*phenylpyrazol*-4-*yl*)-2-*methylbut*-3-*en*-2-*ol* (XIb; R′ = Me) had m.p. 136—137° (Found: C, 75·2; H, 7·8; N, 10·7. $C_{16}H_{20}N_2O$ requires C, 75·0; H, 7·8; N, 10·9%); $\nu_{max.}$ 3300 (OH), 1377, and 1153 cm^{-1} (tert.-C–OH); τ 2·62 (s, Ph), 3·53 and 4·05 (doublets, olefinic protons, *J* 17·1 Hz), 5·0 (s, OH), 7·66 (s, 3-Me), 7·76 (s, 5-Me), and 8·65 (s, CMe_2).

3-(1-*Phenylpyrazol*-4-*yl*)-1,3-*di*-o-*tolylpropan*-1-*one* (XIIa; R′ = *o*-tolyl) had b.p. 120° at 0·1 mmHg (Found: C, 82·2; H, 6·2; N, 7·1. $C_{26}H_{24}N_2O$ requires C, 82·1; H, 6·3; N, 7·4%); $\nu_{max.}$ 1695 cm^{-1} (CO); τ 2·41 and 2·61 (s, 5-H and 3-H, respectively, in pyrazole ring), 2·68 (s, 1-Ph), 5·19 (t, CH), 7·10 (d, CH_2), and 7·70 and 7·76 (s, MeC_6H_4).

3-(3,5-*Dimethyl*-1-*phenylpyrazol*-4-*yl*)-1-*phenylbutan*-1-*one* (XIIb; COR′ = COPh, CHR′ = Me) had b.p. 125° at 0·5 mmHg (Found: C, 79·0; H, 7·0; N, 8·7. $C_{21}H_{22}N_2O$ requires C, 79·2; H, 6·9; N, 8·8%); $\nu_{max.}$ 1675 cm^{-1} (CO); τ 2·74 (s, Ph), 7·75 and 7·80 (s, 3-Me and 5-Me, respectively, in pyrazole ring), and 8·72 (d, CH*Me*).

Ethyl 3-*phenyl*-3-(1-*phenylpyrazol*-4-*yl*)*propionate* (XIIIa; R = Et, R′ = Ph) (from aqueous ethanol) had m.p. 93·5—94° (Found: C, 74·6; H, 6·2; N, 8·9. $C_{20}H_{20}N_2O_2$ requires C, 75·0; H, 6·25; N, 8·75%); $\nu_{max.}$ 1724 (CO) and 1175 cm^{-1} (C–O–C in esters); τ 2·43 and 2·64 (s, 5-H and 3-H, respectively, in pyrazole ring), 2·82 (s, Ph), 5·58 (t, CH), 7·15 (d, CH·CH_2), 6·06 (q, CH_2Me), and 8·93 (t, *Me*CH_2). The corresponding *t-butyl propionate* (XIIIa; R = Bu^t, R′ = Ph) had b.p. 117° at 0·5 mmHg (Found: C, 76·0; H, 6·7; N, 8·0. $C_{22}H_{24}N_2O_2$ requires C, 75·9; H, 6·9; N, 8·05%); the corresponding *ethyl* 3-o-*tolylpropionate* (XIIIa; R = Et, R′ = *o*-tolyl) had b.p. 112° at 0·3 mmHg (Found: C, 75·5; H, 6·5; N, 8·4. $C_{21}H_{22}N_2O_2$ requires C, 75·4; H, 6·6; N, 8·4%).

2-*Bromo*-3-(1-*phenylpyrazol*-4-*yl*)-1,3-*di*-p-*tolylpropan*-1-*one* (XIVa) (70%) had m.p. 173—174° (Found: C, 67·8; H, 5·05; N, 6·0. $C_{26}H_{23}BrN_2O$ requires C, 68·0; H, 5·0; N, 6·1%).

Diethyl 2-(1-*phenylpyrazol*-4-*yl*)*propane*-1,1-*dicarboxylate* (XVa; R = Et, R′ = Me) had b.p. 120° at 0·5 mmHg (Found: C, 65·7; H, 6·8; N, 8·5. $C_{18}H_{22}N_2O_4$ requires C, 65·4; H, 6·7; N, 8·4%); $\nu_{max.}$ 1718 (CO) and 1174 cm^{-1} (C–O–C in esters); τ 2·24 and 2·41 (s, 5-H and 3-H in the pyrazole ring), 2·73 (s, Ph), and 5·72—6·48 and 8·69—9·31 (m, MeCH·CH and Et).

Diethyl 2-*phenyl*-2-(1-*phenylpyrazol*-4-*yl*)*ethane*-1,1-*dicarboxylate* (XVa; R = Et, R′ = Ph) had m.p. 79—80° [from light petroleum (b.p. 60—80°)] (Found: C, 69·9; H, 6·2; N, 6·9. $C_{23}H_{24}N_2O_4$ requires C, 70·2; H, 6·4; N, 7·1%); $\nu_{max.}$ 1733 (CO) and 1139 cm^{-1} (C–O–C in an ester); τ 2·23 and 2·41 (s, 5-H and 3-H in the pyrazole ring), 2·73 (s, Ph), 5·18 (d, CH·CH), 5·74—6·25 (m, Et and CH·CH), and 8·98 (dt, Et).

Hydrolysis of Esters.—This was carried out by heating the ester with ethanolic potassium hydroxide; the solution was cooled, acidified, and extracted with ether.

3-*Phenyl*-3-(1-*phenylpyrazol*-4-*yl*)*propionic acid* (XIIIa; R = H, R′ = Ph) had m.p. 127·5—128° (from ether) (Found: C, 73·7; H, 5·5; N, 9·4. $C_{18}H_{16}N_2O_2$ requires C, 74·0; H, 5·5; N, 9·6%); τ 0·66 (s, OH), 2·40 and 2·47 (s, 5-H and 3-H in the pyrazole ring), 2·79 (s, Ph), 5·50 (t, CH), and 7·03 (d, CH_2).

3-(3,5-*Dimethyl*-1-*phenylpyrazol*-4-*yl*)-3-o-*tolylpropionic acid* (XIIIb; R = H, R′ = *o*-tolyl) had m.p. 144—145° [from acetone–light petroleum (b.p. 40—60°)] (Found: C, 75·6; H, 6·9; N, 8·5. $C_{21}H_{22}N_2O_2$ requires C, 75·5; H, 6·6; N, 8·4%); τ 2·70 (s, Ph), 7·65 and 7·81 (s, 3-Me and 5-Me in the pyrazole ring), and 7·95 (s, MeC_6H_4).

2-(1-*Phenylpyrazol*-4-*yl*)*propane*-1,1-*dicarboxylic acid* (XVa; R = H, R′ = Me) had m.p. (decomp.) 158° [from acetone–light petroleum (b.p. 40—60°)] (Found: C, 61·4; H, 5·3; N, 10·0. $C_{14}H_{14}N_2O_4$ requires C, 61·3; H, 5·1; N, 10·2%).

2-*Phenyl*-2-(1-*phenylpyrazol*-4-*yl*)*ethane*-1,1-*dicarboxylic acid* (XVa; R = H, R′ = Ph) had m.p. 76—77° (decomp.) [from acetone–light petroleum (b.p. 40—60°)] (Found: C, 68·2; H, 5·0; N, 8·6. $C_{19}H_{16}N_2O_4$ requires C, 67·9; H, 4·8; N, 8·3%).

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