753. *Reactions of Some Unsaturated Pyrazole Compounds.*

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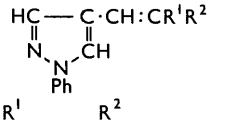
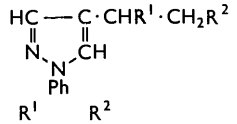
1-Phenyl-4-vinylpyrazole and its dibromide have been prepared; the latter was found to react with aqueous ethanolic potassium hydroxide in an unusual manner to form 4-acetyl-1-phenylpyrazole. Various unsaturated pyrazole compounds have been treated with *o*-nitrobenzenesulphenyl chloride and these reactions compared with those of the benzene analogues.

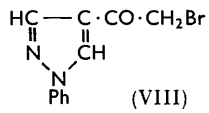
β-(1-PHENYL-4-PYRAZOLYL)ACRYLIC ACID [1] has been decarboxylated to 1-phenyl-4-vinylpyrazole (I) which, with bromine, gave 1,2-dibromo-2-(1-phenyl-4-pyrazolyl)ethane (V). Reaction of the ethane (V) with aqueous ethanolic potassium hydroxide gave 4-acetyl-1-phenylpyrazole,[2a] and hydrolysis gave 2-bromo-1-(1-phenyl-4-pyrazolyl)ethanol (VI), isolated as the hydrobromide. Attempts to isolate the ethanol (VI) itself failed, an oil being obtained. Treatment of an ethereal solution of the oil with hydrogen bromide gave the hydrobromide of (VI). The structure of the ethanol (VI) was confirmed by oxidation



	R^1	R^2
(I)	H	H
(II)	H	*o*-$NO_2 \cdot C_6H_4 \cdot S$
(III)	CO_2H	*o*-$NO_2 \cdot C_6H_4 \cdot S$
(IV)	CO_2Et	*o*-$NO_2 \cdot C_6H_4 \cdot S$



	R^1	R^2
(V)	Br	Br
(VI)	OH	Br
(VII)	Cl	*o*-$NO_2 \cdot C_6H_4 \cdot S$

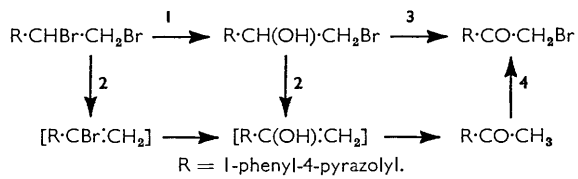


(VIII)

(IX) $Ph \cdot CHCl \cdot CH_2 \cdot S \cdot C_6H_4 \cdot NO_2$-*o*

$Ph \cdot CH{:}C(CO_2H) \cdot S \cdot C_6H_4 \cdot NO_2$-*o* (X)

with acid sodium dichromate to 4-bromoacetyl-1-phenylpyrazole (VIII) which was also prepared by bromination of 4-acetyl-1-phenylpyrazole. The following sequence of reactions is suggested:



R = 1-phenyl-4-pyrazolyl.

Reagents: 1, H_2O. 2, KOH–EtOH–H_2O. 3, $Na_2Cr_2O_7$. 4, Br_2.

It is postulated that, in the conversion of the dibromopyrazolyl-compound into 4-acetyl-1-phenylpyrazole, the reaction proceeds mainly *via* 1-bromo-1-(1-phenyl-4-pyrazolyl)ethylene and only to a small extent through 2-bromo-1-(1-phenyl-4-pyrazolyl)-ethanol (VI). When this bromohydrin was treated with aqueous ethanolic potassium

[1] Finar and Godfrey, *J.*, 1954, 2293.

[2] (*a*) Finar and Lord, *J.*, 1959, 1819; (*b*) Lord, Ph.D. Thesis, London, 1958.

hydroxide, under the same conditions, the ketone could not be isolated, although a small amount of its 2,4-dinitrophenylhydrazone was obtained.[2b] The conversion of 1-bromo-1-(1-phenyl-4-pyrazolyl)ethylene into 4-acetyl-1-phenylpyrazole is analogous to the alkaline hydrolysis of β-bromo-β-(1-phenyl-4-pyrazolyl)acrylic acid to β-oxo-β-(1-phenyl-4-pyrazolyl)propionic acid and 4-acetyl-1-phenylpyrazole.[3]

Various 1-phenyl-4-pyrazolyl compounds with an unsaturated side-chain have been treated with *o*-nitrobenzenesulphenyl chloride [4] and the reactions compared with those of the corresponding benzene compounds. 1-Phenyl-4-vinylpyrazole and styrene behaved similarly to give the saturated chloro-*o*-nitrophenylthio-compounds (VII) and (IX), respectively, in good yields. Hydrogen chloride was easily eliminated from the pyrazole compound to give the unsaturated derivative (II), whereas the benzene analogue was relatively stable. By using Cowell and Finar's method [5] in which the reactants are melted together, ethyl β-(1-phenyl-4-pyrazolyl)acrylate [3] and *o*-nitrobenzenesulphenyl chloride gave a good yield of the unsaturated ester (IV). Ethyl cinnamate, under similar conditions, gave some bis-*o*-nitrophenyl disulphide [6] and a product which, on hydrolysis, gave a poor yield of the unsaturated acid (X). When β-(1-phenyl-4-pyrazolyl)acrylic acid and *o*-nitrobenzenesulphenyl chloride were melted the unsaturated acid (III) was obtained. With cinnamic acid, under similar conditions, the only product isolated was bis-*o*-nitrophenyl disulphide, although only 20% of the original acid could be recovered.

Experimental

Reagents.—Ether used in bromination experiments was dried over sodium. For reactions with *o*-nitrobenzenesulphenyl chloride, styrene and ethyl cinnamate were freshly distilled and dried ($CaCl_2$); solids were dried *in vacuo* (P_2O_5).

1-*Phenyl*-4-*vinylpyrazole* (I).—β-(1-Phenyl-4-pyrazolyl)acrylic acid (10·0 g., 0·047 mole) was heated at 230°/20 mm. for 3 hr. in a flask with a short take-off. The distillate, which solidified on cooling, was dissolved in ether, and the solution washed with dilute aqueous sodium carbonate and water and dried. Evaporation of the ether left the *product* (4·3 g., 54%) as an amorphous white solid, m. p. 39—40° (Found: C, 77·5; H, 5·85; N, 16·5. $C_{11}H_{10}N_2$ requires C, 77·6; H, 5·9; N, 16·5%).

1,2-*Dibromo*-2-(1-*phenyl*-4-*pyrazolyl*)*ethane* (V).—To an ice-cold solution of 1-phenyl-4-vinylpyrazole (1·7 g., 0·01 mole) in ether (20 c.c.) a freshly prepared ice-cold saturated solution of bromine in ether was added drop-wise until a pale yellow colour persisted. The ethereal solution was decanted from a small amount of sticky solid; evaporation of this solution left the *dibromide* (2·8 g., 85%) as needles, m. p. 65—65·5° (Found: Br, 48·6. $C_{11}H_{10}Br_2N_2$ requires Br, 48·4%).

Behaviour of 1,2-*Dibromo*-2-(1-*phenyl*-4-*pyrazolyl*)*ethane* (V).—(*a*) *In alkali.* The freshly prepared dibromide (0·66 g., 0·002 mole) was refluxed for 1 hr. with 0·7N-aqueous ethanolic (1 : 1) potassium hydroxide (20 c.c.). Acidification of the resulting solution gave 4-acetyl-1-phenylpyrazole (0·31 g., 83%), m. p. and mixed m. p. 127—129°.

(*b*) *In air.* The dibromide (3·3 g., 0·01 mole) was left in an open vessel in the dark for 3 days. The resulting sticky white solid was triturated with ether to give 2-*bromo*-1-(1-*phenyl*-4-*pyrazolyl*)*ethanol hydrobromide* (VI,HBr) (2·4 g., 69%), m. p. 97—99° (Found: C, 38·1; H, 3·5; Br, 45·8; N, 7·9. $C_{11}H_{12}Br_2N_2O$ requires C, 37·95; H, 3·5; Br, 45·9; N, 8·05%). When the salt was shaken with water for a few minutes and the extracted bromine then estimated by Volhard's method, 48·5% of the bromine originally present in the hydrobromide was found in the aqueous extract.

(*c*) *In water.* The freshly prepared dibromide (0·60 g., 0·0018 mole) was left under water (100 c.c.) in the dark for 2 days. The aqueous layer was then decanted from the resulting oil which was again covered with water (20 c.c.) and left for a further day. The residual oil was then washed with water (3 × 5 c.c.). The combined aqueous extracts contained 49·9% of the

[3] Finar and Utting, *J.*, 1959, 4015.
[4] Hubacher, *Org. Synth.*, Coll. Vol. II, 1943, p. 455.
[5] Cowell and Finar, *J.*, 1962, 4146.
[6] Bogert and Stull, *Org. Synth.*, Coll. Vol. I, 1941, p. 220.

bromine originally present in the dibromide. The oil was 2-bromo-1-(1-phenyl-4-pyrazolyl)-ethanol (VI), identified as the hydrobromide. After being dissolved in ether and dried (Na_2SO_4), the oil (0·24 g.) was dissolved in dry ether, and a solution of hydrogen bromide in ether added until no further turbidity was produced. The white precipitate was collected and triturated with ether to give 2-bromo-1-(1-phenyl-4-pyrazolyl)ethanol hydrobromide (0·18 g., 28%), m. p. and mixed m. p. 97—99°.

Reaction of 1-*Bromo*-1-(1-*phenyl*-4-*pyrazolyl*)*ethanol with Alkali.*—The bromohydrin (0·49 g., 0·0018 mole) was refluxed for 1 hr. with 0·7N-aqueous ethanolic (1 : 1) potassium hydroxide (15 c.c.). Acidification of the resulting solution did not yield any solid material. Addition of 2,4-dinitrophenylhydrazine (0·50 g., 0·0025 mole), dissolved in concentrated sulphuric acid–ethanol (1 c.c. + 5 c.c.), gave a red precipitate (0·16 g.). Recrystallisation from acetic acid gave 4-acetyl-1-phenylpyrazole 2′,4′-dinitrophenylhydrazone (0·092 g., 14%), m. p. and mixed m. p. 259—261°. Similar treatment of 4-acetyl-1-phenylpyrazole yielded 66% of the 2,4-dinitrophenylhydrazone.

4-*Bromoacetyl*-1-*phenylpyrazole* (VIII).—To an ice-cold solution of 4-acetyl-1-phenylpyrazole (0·90 g., 0·0048 mole) in ether (150 c.c.) was added a freshly prepared ice-cold solution of bromine (0·77 g., 0·0048 mole) in ether (50 c.c.) during 0·5 hr. After a further 0·5 hr. the solution was filtered from the white precipitate and evaporated. Recrystallisation of the residue from ethanol gave 4-*bromoacetyl*-1-*phenylpyrazole* (0·25 g.) as needles, m. p. 135—136·5° (Found: C, 50·1; H, 3·6; Br, 30·0; N, 10·65. $C_{11}H_9BrN_2O$ requires C, 49·8; H, 3·4; Br, 30·1; N, 10·6%). The white precipitate was shaken with ether (50 c.c.) and water (10 c.c.), the ethereal solution dried, and the ether evaporated. Recrystallisation of the residue from ethanol gave more 4-bromoacetyl-1-phenylpyrazole (0·25 g.), m. p. 135—136·5°, the total yield being 0·5 g. (39%).

Oxidation of 2-*Bromo*-1-(1-*phenyl*-4-*pyrazolyl*)*ethanol Hydrobromide.*—A solution of the salt (3·5 g., 0·01 mole) in aqueous acetic acid (5 c.c. of acid + 2 c.c. of water) was slowly added, with stirring, to acid dichromate solution (3·0 g. of sodium dichromate, 5 c.c. of acetic acid, and 5 c.c. of water) and the mixture heated at 50° for 0·5 hr. The precipitate was washed with water and recrystallised from ethanol to give 4-bromoacetyl-1-phenylpyrazole (1·0 g., 38%), m. p. and mixed m. p. 135—136·5°.

1-*Chloro*-2-o-*nitrophenylthio*-1-(1-*phenyl*-4-*pyrazolyl*)*ethane* (VII).—A mixture of 1-phenyl-4-vinylpyrazole (1·7 g., 0·01 mole) and *o*-nitrobenzenesulphenyl chloride (1·9 g., 0·01 mole) was cautiously heated (steam-bath). When the first vigorous reaction had subsided heating was continued for 1 hr. Trituration of the resulting red mass with ether gave the *pyrazolylethane* (3·15 g., 88%), m. p. 149° (decomp.) (Found: C, 56·3; H, 3·8; Cl, 9·9; N, 11·6; S, 9·2. $C_{17}H_{14}ClN_3O_2S$ requires C, 56·7; H, 3·9; Cl, 9·85; N, 11·7; S, 8·9%).

Dehydrochlorination of 1-*Chloro*-2-o-*nitrophenylthio*-1-(1-*phenyl*-4-*pyrazolyl*)*ethane.*—A solution of the chloro-compound (1·0 g., 0·0028 mole) in acetic acid (5 c.c.) was refluxed until hydrogen chloride was no longer evolved (10 min.). Cooling gave a solid which was recrystallised from acetic acid, giving 1-o-*nitrophenylthio*-2-(1-*phenyl*-4-*pyrazolyl*)*ethylene* (II) (0·65 g., 72%) as red needles, m. p. 114—115° (Found: C, 63·2; H, 4·0; N, 13·1; S, 10·0. $C_{17}H_{13}N_3O_2S$ requires C, 63·1; H, 4·05; N, 13·0; S, 9·9%).

α-2-o-*Nitrophenylthio*-β-(1-*phenyl*-4-*pyrazolyl*)*acrylic Acid* (III).—A mixture of β-(1-phenyl-4-pyrazolyl)acrylic acid (2·1 g., 0·01 mole) and *o*-nitrobenzenesulphenyl chloride (1·9 g., 0·01 mole) was heated at 120° for 4 hr. Trituration of the cooled mixture with ether left the *pyrazolyl-acid* (1·0 g., 28%), yellow needles, m. p. 222·5—224° (from acetic acid) (Found: C, 58·8; H, 3·7; N, 11·35; S, 8·6. $C_{18}H_{13}N_3O_4S$ requires C, 58·8; H, 3·6; N, 11·4; S, 8·7%).

Ethyl α-2-o-*nitrophenylthio*-β-(1-*phenyl*-4-*pyrazolyl*)*acrylate* (IV).—A mixture of ethyl β-(1-phenyl-4-pyrazolyl)acrylate (2·4 g., 0·01 mole) and *o*-nitrobenzenesulphenyl chloride was heated at 120° for 6 hr. Trituration of the cooled solid with ether left the *pyrazolylacrylate* (3·0 g., 77%), yellow needles, m. p. 145·5—147° (from ethanol) (Found: C, 61·1; H, 4·3; N, 10·8; S, 8·2. $C_{20}H_{17}N_3O_4S$ requires C, 60·75; H, 4·3; N, 10·6; S, 8·1%). Hydrolysis with dilute aqueous ethanolic potassium hydroxide gave the corresponding acid (III) (67%).

1-*Chloro*-1-o-*nitrophenylthio*-1-*phenylethane* (IX).—A mixture of styrene (2·3 g., 0·022 mole) and *o*-nitrobenzenesulphenyl chloride (3·8 g., 0·02 mole) was left overnight at room temperature. The resulting brown oil was triturated with light petroleum (b. p. 40—60°), and the solid so obtained recrystallised from light petroleum (b. p. 40—60°)–ether (2 : 1), giving the *phenylethane* (4·7 g., 80%) as an amorphous yellow solid, m. p. 49—53°. After 2 weeks *in vacuo* over

paraffin wax, it had m. p. 55·5—57·5° (Found: C, 57·6; H, 4·1; Cl, 12·3; N, 4·6; S, 11·0. $C_{14}H_{12}ClNO_2S$ requires C, 57·2; H, 4·1; Cl, 12·1; N, 4·8; S, 10·9%).

2-o-*Nitrophenylthiocinnamic Acid* (X).—A mixture of ethyl cinnamate (1·8 g., 0·01 mole) and *o*-nitrobenzenesulphenyl chloride (1·9 g., 0·01 mole) was heated at 120° for 6 hr. The resulting brown sludge was warmed with ethanol (10 c.c.), giving a yellow precipitate of bis-*o*-nitrophenyl disulphide (0·3 g.), m. p. and mixed m. p. 195—197°, which was filtered off. The filtrate was mixed with 5N-sodium hydroxide (10 c.c.) and heated (steam-bath) for 1 hr. The solution was then diluted with water (50 c.c.), the solvent partially evaporated, and the solution cooled and filtered. The filtrate was carefully acidified with dilute hydrochloric acid. At first a brown oil separated out, but as acidification proceeded a buff solid was precipitated; recrystallisation from aqueous ethanol (charcoal) and then benzene gave the *thiocinnamic acid* (0·6 g., 19%) as yellow needles, m. p. 184—186° (Found: C, 59·6; H, 3·8; N, 4·7; S, 10·6. $C_{15}H_{11}NO_4S$ requires C, 59·8; H, 3·7; N, 4·65; S, 10·6%).

Reaction between Cinnamic Acid and o-*Nitrobenzenesulphenyl Chloride.*—A mixture of cinnamic acid (1·5 g., 0·01 mole) and *o*-nitrobenzenesulphenyl chloride (1·9 g., 0·01 mole) was heated at 120° for 6 hr.; hydrogen chloride was evolved. Trituration of the cooled mixture with ether gave a yellow precipitate (1·0 g.), which after recrystallisation from acetic acid gave bis-*o*-nitrophenyl disulphide (0·8 g.), m. p. and mixed m. p. 195—197°. Only unchanged cinnamic acid (0·3 g., 20%) could be isolated from the ethereal solution.

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