806. *Reactions of Some Pyrazole Derivatives.*

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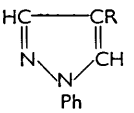
4-Formyl-1-phenylpyrazole has been converted into anils and these have been reduced to the corresponding amines. Some reactions of β-(1-phenyl-4-pyrazolyl)acrylic acid have also been investigated.

4-FORMYL-1-PHENYLPYRAZOLE [1] has been condensed with aniline [1] and the three isomeric monobromoanilines to yield the corresponding anils; [2] 2,4,6-tribromoaniline does not condense under the same conditions. The anils were reduced by sodium borohydride [3] to the corresponding amines, the toluene-*p*-sulphonyl derivatives of which were formed except by the *o*-bromo-amine. With malonic acid [4] the formylpyrazole gave the diacid (I) which in refluxing pyridine gave β-(1-phenyl-4-pyrazolyl)acrylic acid.[1] Bromination of this acid and its ethyl ester in acetic acid solution [5] gave the β-bromoacrylic acid (II) and the corresponding ester. Alkaline hydrolysis of the bromo-acid (II) gave β-oxo-β-(1-



(I) R = CH:C(CO$_2$H)$_2$
(II) R = CBr:CH·CO$_2$H
(III) R = CO·CH$_2$·CO$_2$H

phenyl-4-pyrazolyl)propionic acid (III) and 4-acetyl-1-phenylpyrazole, the latter also being obtained by decarboxylation of the former. β-(1-Phenyl-4-pyrazolyl)propionic acid has been obtained by Clemmensen reduction [6] of both the acrylic and the bromoacrylic acid. The acrylic acid reacted with hydroxylamine [7] to give a saturated β-amino-acid and underwent the Meerwein reaction [8] with diazonium salts to form the corresponding ethylenes.

EXPERIMENTAL

Anils of 4-Formyl-1-phenylpyrazole.—A mixture of the formylpyrazole (1·7 g., 0·001 mole) and *p*-bromoaniline (1·7 g. 0·001 mole) in absolute ethanol (20 c.c.) was warmed on a steam-bath for 15 min., then cooled, and the precipitate recrystallised from benzene or ligroin to give the p-*bromoanil* (2·9 g., 90%) as white needles, m. p. 168—169° (Found: C, 59·2; H, 3·7; N, 12·9; Br, 24·2. $C_{16}H_{12}N_3Br$ requires C, 58·9; H, 3·7; N, 12·9; Br, 24·5%). In the same way were obtained the m-*bromoanil* (90%) from methanol as plates, m. p. 125—126° (Found: C, 59·1; H, 3·7; N, 12·95; Br, 24·2%), and the o-*bromoanil* (80%) from methanol as needles, m. p. 101·5—102° (Found: C, 58·9; H, 3·9; N, 12·6; Br, 24·2%).

Reduction of the Anils.[3]—To a 5% (w/w) suspension of the *N*-(1-phenyl-4-pyrazolylmethylidene)aniline (1 mol.) in absolute methanol at 50° was added portionwise solid sodium borohydride (2 mol.); the vigorous reaction was allowed to subside between each addition of borohydride. When addition was complete the mixture was refluxed for 15 min., and then cooled, and an equal volume of water was added. The precipitate was collected and recrystallised from ethanol. The anil (2·0 g., 0·008 mole) yielded the *amine* (1·8 g., 90%) as plates, m. p. 70—71° (Found: C, 76·8; H, 6·1; N, 17·2. $C_{16}H_{15}N_3$ requires C, 77·1; H, 6·1; N, 16·9%). The amine yielded the *toluene*-p-*sulphonamide* as needles (from ethanol), m. p. 163—164° (Found: S, 7·75. $C_{23}H_{21}O_2N_3S$ requires S, 7·95%).

The p-*bromo-amine* (67%) was obtained as needles, m. p. 89—90° (Found: C, 58·4; H, 4·2; N, 13·0; Br, 24·1. $C_{16}H_{14}N_3Br$ requires C, 58·5; H, 4·3; N, 12·8; Br, 24·35%), yielding a *toluene*-p-*sulphonamide*, needles (from methanol), m. p. 162—162·5° (Found: S, 6·85.

[1] (*a*) Finar and Godfrey, *J.*, 1954, 2294; (*b*) Finar and Lord, *J.*, 1957, 3314.
[2] Lowy and Downey, *J. Amer. Chem. Soc.*, 1921, **43**, 346.
[3] Billman and Diesing, *J. Org. Chem.*, 1957, **22**, 1068.
[4] Knoevenagel, *Ber.*, 1898, **31**, 2598; Doebner, *Ber.*, 1900, **33**, 2140.
[5] Cf. Sudborough and Thompson, *J.*, 1903, **83**, 666.
[6] Clemmensen, *Ber.*, 1914, **47**, 51.
[7] Posner, *Ber.*, 1905, **38**, 2320; Steiger, *Org. Synth.*, Coll. Vol. III, 1955, p. 91.
[8] Meerwein, *J. prakt. Chem.*, 1939, **152**, 237; Bergmann, *J. Org. Chem.*, 1944, **9**, 408.

$C_{23}H_{20}O_2N_3BrS$ requires S, 6·65%); the m-*bromo-amine* (73%) formed plates, m. p. 86·5—87·5° (Found: C, 58·8; H, 4·3; N, 13·1; Br, 24·1%), yielding a *toluene*-p-*sulphonamide*, needles (from ethanol), m. p. 156—156·5° (Found: S, 6·8%), and the o-*bromo-amine* (50%) formed needles, m. p. 65—65·5° (Found: C, 58·4; H, 4·4; N, 12·85; Br, 24·1%).

1-*Phenyl*-4-*pyrazolylmethylenemalonic Acid* (I).—A mixture of the formylpyrazole (3·4 g., 0·02 mole) and malonic acid (4·2 g., 0·04 mole) was dissolved in pyridine (16 c.c.), and piperidine (4 drops) was added; the whole was left at room temperature for 5 days. Excess of 3N-hydrochloric acid was then added, and the precipitate collected and recrystallised several times from aqueous ethanol and then methanol to give the *diacid* (3·5 g., 67%) as a creamy powder, m. p. 212·5—214° (decomp.) (Found: C, 60·75; H, 3·75; N, 10·8. $C_{13}H_{10}O_4N_2$ requires C, 60·5; H, 3·9; N, 10·85%).

Decarboxylation of 1-*Phenyl*-4-*pyrazolylmethylenemalonic Acid* (I).—The methylenemalonic acid (0·25 g.) was refluxed in pyridine (10 c.c.) for 1 hr. The solution was acidified with 3N-hydrochloric acid, and the precipitate collected and recrystallised twice from aqueous acetic acid to give the acrylic acid as needles, m. p. and mixed m. p. 187—188°.

Ethyl β-(1-*Phenyl*-4-*pyrazolyl*)*acrylate*.—A mixture of β-(1-phenyl-4-pyrazolyl)acrylic acid [1a] (15·0 g., 0·07 mole), thionyl chloride (24·8 g., 0·21 mole), and benzene (60 c.c.) was refluxed for 1·5 hr., the excess of thionyl chloride and benzene evaporated under reduced pressure, and absolute ethanol (50 c.c.) added. The mixture was refluxed for 1 hr. and then cooled. The precipitate was collected and recrystallised from ethanol, to give the *ethyl ester* (15·2 g., 89%) as needles, m. p. 113—113·5° (Found: C, 69·3; H, 5·8; N, 11·8. $C_{14}H_{14}O_2N_2$ requires C, 69·4; H, 5·8; N, 11·6%).

β-*Bromo*-β-(1-*phenyl*-4-*pyrazolyl*)*acrylic Acid* (II) *and its Ethyl Ester*.—To the acrylic acid (5·0 g., 0·023 mole) in glacial acetic acid (25 c.c.) on the steam-bath was added dropwise bromine (3·75 g., 0·046 mole) in acetic acid (10 c.c.). After 15 min. the mixture was cooled and diluted with water. The precipitate was collected and recrystallised from ethanol, to give the *bromoacrylic acid* (4·6 g., 66%), as needles, m. p. 223·5—224·5° (Found: C, 49·1; H, 2·85; N, 9·35; Br, 27·05. $C_{12}H_9O_2N_2Br$ requires C, 49·2; H, 3·1; N, 9·6; Br, 27·25%). In a similar manner was obtained the *ethyl bromoacrylate* (66%), as needles, m. p. 118—118·5° (Found: C, 52·3; H, 3·9; N, 8·4; Br, 24·9. $C_{14}H_{13}O_2N_2Br$ requires C, 52·35; H, 4·1; N, 8·7; Br, 24·9%).

Hydrolysis of β-*Bromo*-β-(1-*phenyl*-4-*pyrazolyl*)*acrylic Acid* (II).—The bromo-acid (5·0 g., 0·017 mole) and 2N-sodium hydroxide (200 c.c.) were refluxed for 1 hr., and then cooled; sufficient water was added to dissolve the precipitate. The mixture was extracted with ether (5 × 100 c.c.), and the extracts were dried (Na_2SO_4) and evaporated to dryness. After recrystallising from ethanol the solid (1·0 g.) had m. p. 127·5—128·5°, and was identified by m. p. and mixed m. p. as 4-acetyl-1-phenylpyrazole.[1b] Acidification of the alkaline solution gave a cream-coloured precipitate which when recrystallised from ethanol yielded β-*oxo*-β-(1-*phenyl*-4-*pyrazolyl*)*propionic acid* (III) as needles (2 g.), m. p. 154—155° (decomp.) (Found: equiv., 229·7. $C_{12}H_{10}O_3N_2$ requires equiv., 230·2). Refluxing this compound with dilute hydrochloric acid gave carbon dioxide and 4-acetyl-1-phenylpyrazole.

Reduction of (1-*Phenyl*-4-*pyrazolyl*)*acrylic Acid*.—Freshly prepared amalgamated zinc (20 g.) and the acrylic acid (5·0 g., 0·023 mole) were refluxed for 2·5 hr. with 5N-hydrochloric acid (30 c.c.), more acid (25 c.c.) being added during this period. After cooling, the solution was extracted with ether (5 × 50 c.c.). The ethereal solution was dried (Na_2SO_4) and evaporated, and the residual oil taken up in carbon tetrachloride from which β-(1-*phenyl*-4-*pyrazolyl*)-*propionic acid* crystallised as plates (3·5 g., 70%), m. p. 77—77·5° (Found: C, 66·4; H, 5·7; N, 12·8. $C_{12}H_{12}O_2N_2$ requires C, 66·65; H, 5·6; N, 13·0%).

β-*Amino*-β-(1-*phenyl*-4-*pyrazolyl*)*propionic Acid*.—Sodium (2·3 g., 0·1 g.-atom) was dissolved in absolute ethanol (80 c.c.), and hydroxylamine hydrochloride (6·95 g., 0·1 mole) in hot water (5 c.c.) was added followed by cooling. The precipitated sodium chloride was filtered off and washed with absolute ethanol (10 c.c.), and the main filtrate and washings were combined and added to β-1(-phenyl-4-pyrazolyl)acrylic acid (10·7 g., 0·05 mole). This mixture was refluxed for 9 hr.; dissolution was complete after 2·5 hr. and solid began to separate after 4 hr. The precipitate was collected and washed with ethanol (15 c.c.), ice-water (5 c.c.), and finally ethanol (15 c.c.), yielding the *amino-acid* (1·67 g., 14·5%), m. p. 234—235° (decomp.) (Found: C, 61·9; H, 5·65; N, 18·1. $C_{12}H_{13}O_2N_3$ requires C, 62·3; H, 5·6; N, 18·2%).

1-p-*Bromophenyl*-2-(1-*phenyl*-4-*pyrazolyl*)*ethylene*.—To *p*-bromoaniline (3·44 g., 0·02 mole) in concentrated hydrochloric acid (5 c.c.) and water (15 c.c.) at 3° was added sodium nitrite

(1·38 g., 0·02 mole) in water (4 c.c.) at 3°. This solution was added to a suspension of β-(1-phenyl-4-pyrazolyl)acrylic acid (4·3 g., 0·02 mole) and anhydrous sodium acetate (4·0 g., 0·02 mole) in acetone (100 c.c.), cooled to 8°, with stirring. Cupric chloride (0·9 g.) in water (3 c.c.) was then added and the mixture was stirred for 2 hr. at room temperature, then left for one day. The acetone and water were distilled off and the residual solid was extracted with dilute ammonia solution. The remaining solid was recrystallised from aqueous acetic acid and then benzene–light petroleum (b. p. 40—60°), to yield 1-p-*bromophenyl*-2-(1-*phenyl*-4-*pyrazolyl*)*ethylene* (3·5 g., 21%) as pale cream needles, m. p. 177—178° (Found: C, 63·1; H, 3·9; N, 8·5; Br, 24·3. $C_{17}H_{13}N_2Br$ requires C, 62·8; H, 4·0; N, 8·6; Br, 24·6%). In a similar manner was obtained 1-p-*methoxyphenyl*-2-(1-*phenyl*-4-*pyrazolyl*)*ethylene* (0·4 g., 7·2%) as plates (from ethanol), m. p. 150—151° (Found: C, 78·1; H, 6·0; N, 10·2. $C_{18}H_{16}ON_2$ requires C, 78·3; H, 5·8; N, 10·2%).

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