824. *The Preparation and Properties of Some* 2 : 3-*Benzo*-1 : 4-*diazepines.*

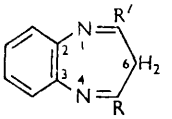
By I. L. Finar.

1 : 6-Diphenylhexane-1 : 3 : 4 : 6- and octane-2 : 4 : 5 : 7-tetraone condense with one molecule of *o*-phenylenediamine to form 2 : 3-benzo-1 : 4-diazepines. The diazepine from the former with phenylhydrazine forms 1 : 3 : 1′ : 3′-tetraphenyl-5 : 5′-dipyrazolyl, whereas that from the latter gives a pyrazolyl-diazepine. Spectroscopic evidence is presented for the double bond structure of diazepine bases.

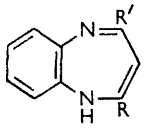
o-Phenylenediamine with 1 : 2-diketones forms quinoxalines [1] and with 1 : 3-diketones forms 2 : 3-benzo-1 : 4-diazepines.[2] With triketones that are both 1 : 2- and 1 : 3-diketones quinoxalines have been obtained: pentane-2 : 3 : 4-trione forms 2-acetyl-3-methylquinoxaline,[3] and 1 : 4-diphenylbutane-1 : 2 : 4-trione forms 2-phenacyl-3-phenylquinoxaline.[4] In the present work, two tetraketones, 1 : 6-diphenylhexane-1 : 3 : 4 : 6- and octane-2 : 4 : 5 : 7-tetraone [5] (both are 1 : 2- and 1 : 3-diketones) have been condensed with one molecule of *o*-phenylenediamine, giving the diazepines (I) and (II), respectively.

[1] Hinsberg, *Annalen*, 1887, **237**, 327; von Pechmann, *Ber.*, 1888, **21**, 1411.
[2] Thiele and Steimmig, *Ber.*, 1907, **40**, 955.
[3] Sachs and Barschall, *Ber.*, 1901, **34**, 3047; Piutti, *Gazzetta*, 1936, **66**, 276.
[4] Lutz and Stuart, *J. Amer. Chem. Soc.*, 1936, **58**, 1885.
[5] Finar, *J.*, 1955, 1205.

Other possible products are the quinoxalines derived by condensation with the 1 : 2-diketone system present in the tetraketones. The infrared spectra of compounds (I) and (II), measured in Nujol suspension and in chloroform solution, are consistent with the diazepine structure since there is no absorption between 1680 and 1700 cm.$^{-1}$ for (I) (the phenacyl group is therefore absent) or between 1700 and 1720 cm.$^{-1}$ for (II) (the acetonyl group is therefore absent). There are, however, strong bands at 1590 cm.$^{-1}$ for (I) and at 1597 and 1567 cm.$^{-1}$ for (II), both consistent with the presence of an enolised 1 : 3-diketone group.



(A)



(B)

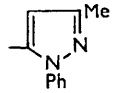
(I) ; R = CO·CH$_2$·COPh, R′ = Ph (VI); R =

(II) ; R = CO·CH$_2$·COMe, R′ = Me

(III) ; R = R′ = Me

(IV) ; R = Me, R′ = Ph R′ = Me

(V) ; R = R′ = Ph

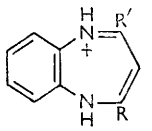


Neither diazepine (I) nor (II) reacted with a second molecule of *o*-phenylenediamine.

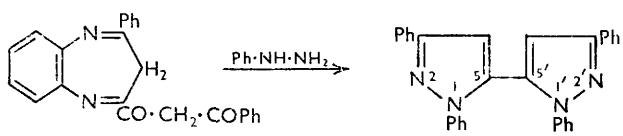
Diazepines have been comparatively little studied. Thiele and Steimmig [2] studied the benzodiazepines (III) and (IV) derived from acetylacetone and benzoylacetone and stated that an aqueous solution of the monohydrochloride of the former rapidly reacts with phenylhydrazine to form dimethylphenylpyrazole, and that of the latter to form methylphenylpyrazole. They also claim that both salts, when warmed in aqueous solution, readily decompose into benzimidazoles, and that dibenzoylmethane behaves like the other two diketones, but no details are given. Ried and Höhne [6] examined the conversion into imidazoles, and Lloyd and Marshall [7] investigated the bromination of 2 : 3-dihydro-1 : 4-diazepines.

The conversion into pyrazoles has been repeated and extended to the diazepines (I) and (II); the hydrochloride of the dimethyl-compound (III) behaved as described, but that of the methylphenyl derivative (IV) liberated the free base. This, when refluxed with phenylhydrazine in acetic acid, gave 3-methyl-1 : 5-diphenylpyrazole,[8] which was also obtained similarly from the salt itself. The diphenyl-diazepine (V), prepared by warming dibenzoylmethane with *o*-phenylenediamine in ethanol–acetic acid, gave 1 : 3 : 5-triphenylpyrazole [9] when (V) was refluxed with phenylhydrazine in acetic acid.

The double-bond structure of the seven-membered ring is not certain. Thiele and Steimmig [2] suggested formula (A) or (B); Vaisman [10] suggested (C) for the monohydrochloride, and Lloyd and Marshall [11] believed (B) to be more likely than (A). The infrared spectrum of the diphenylbenzodiazepine (V) (dissolved in carbon tetrachloride) showed the presence of a methylene group (bands at 2901 and 2843 cm.$^{-1}$) and the absence of the NH stretching band. The diphenyl compound (V) appears to be of type (A).



(C)



When the phenacyl compound (I) was refluxed with phenylhydrazine in acetic acid 1 : 3 : 1′ : 3-tetraphenyl-5 : 5′-dipyrazolyl was obtained. This is the third isomer theoretically possible from the condensation between 1 : 6-diphenylhexane-1 : 3 : 4 : 6-tetraone

[6] Ried and Höhne, *Chem. Ber.*, 1954, **87**, 1801.
[7] Lloyd and Marshall, *J.*, 1958, 118.
[8] Knorr, *Ber.*, 1887, **20**, 1098; Drumm, *Proc. Roy. Irish Acad.*, 1931, **40**, *B*, 94.
[9] Knorr and Laubmann, *Ber.*, 1888, **21**, 1206.
[10] Vaisman, *Trudy Inst. Khim. Khar'kov Gosudarst. Univ.*, 1938, **4**, 157; 1940, **5**, 57 (*Chem. Abs.*, 1940, **34**, 5847; 1944, **38**, 750).
[11] Lloyd and Marshall, *J.*, 1956, 2597.

and phenylhydrazine; the other two, 1 : 5 : 1′ : 5′-tetraphenyl-3 : 3′- and 1 : 5 : 1′ : 3′-tetraphenyl-3 : 5′-dipyrazolyl have already been isolated.[5]

The acetoacetyl compound (II) behaved differently under the same conditions; the product was a pyrazolyldiazepine, assumed to be (VI) by analogy with the reaction between benzoylacetone and phenylhydrazine.[8,12] The infrared spectrum of this pyrazolyldiazepine (in Nujol suspension) is consistent with the presence of an *o*-disubstituted aromatic ring; it includes a characteristic strong band at 752 cm.$^{-1}$ (which is absent from the spectrum of 5 : 5′-dipyrazolyl).

Experimental

5-Benzoylacetyl-7-phenyl-2 : 3-benzo-1 : 4-diazepine (I).—1 : 6-Diphenylhexane-1 : 3 : 4 : 6-tetraone [5] [in which paper, read 30 g. of acetophenone for 15 g.] (5·88 g., 0·02 mole) was added portionwise to *o*-phenylenediamine (2·16 g., 0·02 mole) in hot acetic acid (80 c.c.), and the mixture heated on the steam-bath for 15 min. The mixture was cooled and filtered, and the red precipitate washed with acetic acid and then with water, dried at 120°, and recrystallised from chloroform, giving the *benzodiazepine* (6·1 g., 83%) as red needles, m. p. 210° (Found: C, 79·1; H, 5·1; N, 7·55. $C_{24}H_{18}O_2N_2$ requires C, 78·7; H, 4·9; N, 7·65%).

An ethanolic solution of this diazepine did not give a coloration with ferric chloride. A solution in acetic acid was yellow, and addition of hydrochloric acid produced a deep red solution.

1 : 3 : 1′ : 3′-Tetraphenyl-5 : 5′-dipyrazolyl.—The benzodiazepine (I) (12·1 g., 0·033 mole), phenylhydrazine (10·8 g., 0·1 mole), and acetic acid (80 c.c.) were refluxed for 1 hr., and set aside overnight. The precipitate was washed with acetic acid and then with water, dried at 120°, and recrystallised from methanol, giving the *dipyrazolyl* (4·3 g., 30%) as white needles, m. p. 195—195·5° (Found: C, 81·9; H, 5·2; N, 12·6. $C_{30}H_{22}N_4$ requires C, 82·2; H, 5·0; N, 12·8%).

This dipyrazolyl gives a green colour in Knorr's pyrazoline test.

4 : 4′-Dibromo-1 : 3 : 1′ : 3′-tetraphenyl-5 : 5′-dipyrazolyl.—An acetic acid solution of the dipyrazolyl was treated with excess of bromine and heated on the steam-bath for 1 hr. The mixture was set aside overnight, and the precipitate was then collected and recrystallised from glacial acetic acid, giving the *4 : 4′-dibromo-compound* as white rods, m. p. 175—176° (Found: Br, 26·8. $C_{30}H_{20}N_4Br_2$ requires Br, 26·8%).

5-Acetoacetyl-7-methyl-2 : 3-benzo-1 : 4-diazepine (II).—Octane-2 : 4 : 5 : 7-tetraone [5] (3·4 g., 0·02 mole) was added to *o*-phenylenediamine (2·16 g., 0·02 mole) in hot ethanol (30 c.c.), and the mixture heated (steam-bath) for 5 min. The mixture was cooled and filtered, and the orange precipitate recrystallised from ethanol, giving the *diazepine* (2·8 g., 58%) as orange needles, decomp. 186—188° (Found: C, 69·8; H, 5·8; N, 11·8. $C_{14}H_{14}O_2N_2$ requires C, 69·4; H, 5·8; N, 11·6%).

An ethanolic solution of this diazepine did not give an immediate colour with ferric chloride; the solution, however, slowly became red. The acetic acid solution was deep red, and the colour deepened on the addition of hydrochloric acid.

5-Methyl-7-(3-methyl-1-phenyl-5-pyrazolyl)-2 : 3-benzo-1 : 4-diazepine (VI).—The benzodiazepine (II) (2·42 g., 0·01 mole), phenylhydrazine (2·7 g., 0·025 mole), and acetic acid (30 c.c.) were refluxed for 1 hr. and then set aside overnight. The precipitate was collected, dissolved in hot acetic acid (charcoal), and filtered. The filtrate was cooled, diluted with water, and the precipitate recrystallised from methanol, giving the *pyrazolyldiazepine* (1·3 g., 41%) as yellow-orange leaflets, m. p. 166—167° (Found: C, 76·2; H, 5·68; N, 18·2. $C_{20}H_{18}N_4$ requires C, 76·4; H, 5·73; N, 17·8%).

A better yield was obtained when the two reagents were heated in a mixture of ethanol (30 c.c.) and acetic acid (10 c.c.) on the steam-bath for 1 hr. The mixture was cooled and the precipitate washed with ethanol (1·8 g., 57%).

An acetic acid solution of this diazepine was yellow, and the addition of hydrochloric acid produced a dark red colour.

3 : 5-Dimethyl-1-phenylpyrazole.—Phenylhydrazine (10·8 g., 0·1 mole) and a solution of 5 : 7-dimethyl-2 : 3-benzo-1 : 4-diazepinium chloride dihydrate [2] (9·78 g., 0·04 mole) in water (400 c.c.) were shaken vigorously. The mixture was extracted with ether, and the extract washed with aqueous sodium carbonate and then with water, dried (Na_2SO_4), and evaporated. The residual orange oil was distilled at 269—270° to give the dimethylphenylpyrazole as an

[12] Finar and Simmonds, *J.*, 1958, 200.

oil (5·6 g., 82%). This formed a picrate, m. p. and mixed m. p. with an authentic specimen 103—103·5° (McConnan [13] gives b. p. 270°, and m. p. of picrate 103°; von Auwers and Broche [14] give m. p. of picrate 100—101°).

3-*Methyl*-1 : 5-*diphenylpyrazole*.—Phenylhydrazine (8·64 g.; 0·08 mole), 5-methyl-7-phenyl-2 : 3-benzo-1 : 4-diazepinium chloride trihydrate [2] (13 g., 0·04 mole), and glacial acetic acid (150 c.c.) were refluxed for 1 hr. The solution was cooled and poured into a large excess of water, and the mixture extracted with ether. The ethereal solution was washed; the residue slowly solidified to the methyldiphenylpyrazole (6·4 g., 68·3%), m. p. 63°. This formed a picrate, m. p. and mixed m. p. with an authentic specimen 126—127° (Knorr [8] gives m. p. 63°; von Auwers and Stuhlmann [15] give m. p. of picrate 125—126°, and Drumm [8] gives m. p. 124°).

When an aqueous suspension of the diazepinium chloride trihydrate was shaken with an excess of phenylhydrazine, a yellow precipitate formed immediately. This, when refluxed with phenylhydrazine in acetic acid also gave the methyldiphenylpyrazole.

5 : 7-*Diphenyl*-2 : 3-*benzo*-1 : 4-*diazepine* (V).—Dibenzoylmethane (11·2 g., 0·05 mole) and *o*-phenylenediamine (5·4 g., 0·05 mole) in a mixture of ethanol (50 c.c.) and acetic acid (18 c.c.) were heated (steam-bath) for 3 hr. The mixture was cooled, and the precipitate recrystallised from ethanol, giving the *diazepine* (7·3 g., 49·3%) as fine white needles, m. p. 140—141° (Found: C, 84·8; H, 5·2; N, 9·8. $C_{21}H_{16}N_2$ requires C, 85·1; H, 5·4; N, 9·5%).

The solution of the diazepine in acetic acid or dilute hydrochloric acid was violet.

1 : 3 : 5-*Triphenylpyrazole*.—A mixture of the diazepine (V) (5·92 g., 0·02 mole) and phenylhydrazine (3·24 g., 0·03 mole) in acetic acid (30 c.c.) was refluxed for 1 hr., water (300 c.c.) added to the cooled solution, and the precipitate recrystallised from ethanol, giving the triphenylpyrazole (5·2 g., 87·8%), m. p. and mixed m. p. with authentic material 138° (Knorr and Laubmann [9] give m. p. 136·5—137·5°).

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[13] McConnan, *Ber.*, 1904, **37**, 3525.
[14] von Auwers and Broche, *Ber.*, 1922, **55**, 3910.
[15] von Auwers and Stuhlmann, *Ber.*, 1926, **59**, 1052.