950. *Quinazolines and* 1,4-*Benzodiazepines. Part XIV.*[1] *The Nitration Products of* 7-*Substituted* 1,3-*Dihydro*-5-*phenyl*-2H-1,4-*benzodiazepin*-2-*ones.*

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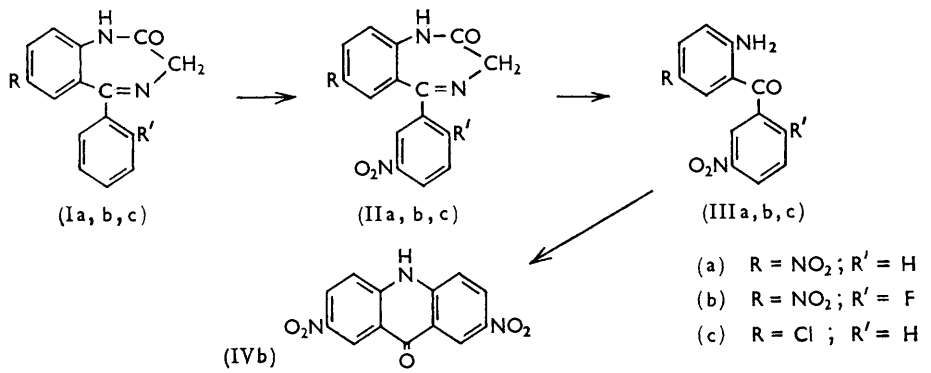
The nitration of 7-substituted 1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-ones with potassium nitrate–sulphuric acid gave exclusively the corresponding 5-*m*-nitrophenyl derivatives. Hydrolysis of these compounds gave several new aminonitrobenzophenones, the structures of which were confirmed either by direct synthesis or, in one case, by conversion into a known 9-acridone.

It has been reported [2] that the reaction of compounds related to 1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one with potassium nitrate in cold concentrated sulphuric acid gave the corresponding 7-nitro-derivatives together with traces of some unelucidated dinitro-5-phenyl-1,4-benzodiazepinones.

We have now shown that these dinitro-compounds are synthesized in excellent yields by using two equivalents of potassium nitrate in these reactions or by further nitration of the intermediate 7-nitro-derivatives. For example, compounds (Ia and b) gave the dinitro-derivatives (IIa and b).* Similarly nitration of the 7-chloro-5-phenyl-1,4-benzodiazepin-one (Ic) gave the chloronitro-compound (IIc).

Hydrolysis of the nitro-5-phenyl-1,4-benzodiazepinones (II) gave the corresponding aminonitrobenzophenones (III). The unequivocal synthesis of the new aminonitro-benzophenones (IIIa and c), and conversion [3] of the amine (IIIb) into the known acridone [4] (IVb), showed that the above nitration products were 5-*m*-nitrophenyl derivatives.



The structure of the amine (IIIa) was proved by its preparation from the known 2-chloro-3′,5-dinitrobenzophenone [5] by treatment with ammonia under pressure. The structure of the amine (IIIc) was proved by its synthesis from the known 2-amino-3′-nitro-benzophenone [6] with chlorine in acetic acid. Thus, by using as starting materials, in two synthetic approaches, compounds in which the position of one of the substituents was *a*

* Compound (IIa) was originally prepared by Keller of these laboratories, who used fuming nitric acid in a similar reaction.

[1] Part XIII, Sternbach, Saucy, Smith, Müller, and Lee, *Helv. Chim. Acta*, 1963, **46**, 1720.
[2] Sternbach, Fryer, Keller, Metlesics, Sach, and Steiger, *J. Medicin. Chem.*, 1963, **6**, 261.
[3] Fryer, Earley, and Sternbach, following Note.
[4] Bogert, Hirschfelder, and Lauffer, *Coll. Czech. Chem. Comm.*, 1930, **2**, 383; *Chem. Zentr.*, 1930, **101**, II, 1702.
[5] Loudon, Robertson, Watson, and Aiton, *J.*, 1950, 55.
[6] DeTar and Relyea, *J. Amer. Chem. Soc.*, 1954, **76**, 1680.

priori known [the nitro-group in 2-amino-3′-nitrobenzophenone and the chlorine in compound (Ic)], the position of the newly introduced substituent in both the nitration and the chlorination was established. By heating a solution of the compound (IIIb) in 2-ethoxyethanol under reflux, the dinitroacridone (IVb) was formed in an intramolecular nucleophilic exchange. Direct comparison of the infrared and ultraviolet spectra of the acridone with those of a sample prepared as reported in the literature [4] showed the two compounds to be identical (the melting points were higher than 350°).

Experimental

M. p.s were determined microscopically on a hot stage and are corrected. Infrared spectra were obtained with a Perkin-Elmer model 21 spectrophotometer and were determined for potassium bromide pellets or 3% chloroform solutions. The infrared spectra were compatible with the structures indicated. Ultraviolet spectra were determined for propan-2-ol solutions on a Carey model 14 spectrophotometer.

1,3-*Dihydro*-7-*nitro*-5-m-*nitrophenyl*-2H-1,4-*benzodiazepin*-2-*one* (IIa).—(*a*) A solution of potassium nitrate (12·15 g., 0·12 mole) in cold concentrated sulphuric acid (25 ml.) was added dropwise with stirring to a solution of 1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one [7] (11·8 g., 0·05 mole) in concentrated sulphuric acid (50 ml.) at 10°. The mixture was allowed to reach room temperature and, after 5 hours' stirring, was poured on ice (1 kg.). The solution was kept at 0° and neutralized with aqueous ammonia. The precipitate was collected and washed with warm water. Recrystallization from acetone–hexane gave the *dinitro-compound* as pale yellow prisms (9·3 g., 57%), m. p. 250—254° (Found: C, 55·3; H, 2·95; N, 16·8. $C_{15}H_{10}N_4O_5$ requires C, 55·2; H, 3·1; N, 17·2%).

(*b*) Potassium nitrate (6·07 g., 0·06 mole) in cold concentrated sulphuric acid (15 ml.) was added dropwise to a stirred solution of 1,3-dihydro-7-nitro-5-phenyl-2*H*-1,4-benzodiazepin-2-one [2] (14·1 g., 0·05 mole) in concentrated sulphuric acid (50 ml.) at 10°. The mixture was stirred at 10° for 4 hr. and was worked up as described above, giving the same product (11·8 g., 72·5%), m. p. 250—254°.

5-(2-*Fluoro*-5-*nitrophenyl*)-1,3-*dihydro*-7-*nitro*-2H-1,4-*benzodiazepin*-2-*one* (IIb).—5-*o*-Fluorophenyl-1,3-dihydro-7-nitro-2*H*-1,4-benzodiazepin-2-one [2] (Ib) was nitrated as in (*b*) above, to give *compound* (IIb) (81%). This crystallized from acetone as white prisms, m. p. 292—293° (decomp.) (Found: C, 52·2; H, 2·6; N, 16·2. $C_{15}H_9FN_4O_5$ requires C, 52·3; H, 2·6; N, 16·3%).

7-*Chloro*-1,3-*dihydro*-5-m-*nitrophenyl*-2H-1,4-*benzodiazepin*-2-*one* (IIc).—A solution of 7-chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one [7] (Ic) (30 g., 0·11 mole) in concentrated sulphuric acid (125 ml.) was treated with potassium nitrate (12·5 g., 0·12 mole) as in (*b*) above, to give, after recrystallization from methanol, the *product* (IIc) as colourless prisms (17 g., 53·6%), m. p. 234—238° (Found: C, 56·9; H, 3·15; N, 12·8. $C_{15}H_{10}ClN_3O_3$ requires C, 57·1; H, 3·2; N, 13·3%).

2-*Amino*-3′,5-*dinitrobenzophenone* (IIIa).—(1) A solution of the product (IIa) (3·26 g.) in ethanol (40 ml.) was heated for 15 hr. with 6N-hydrochloric acid (40 ml.), then cooled and diluted with water (300 ml.), and the product was removed by filtration. Recrystallization from methanol gave the *amine* (IIIa) as yellow needles (2·6 g., 91%), m. p. 242—243° (Found: C, 54·5; H, 3·1. $C_{13}H_9N_3O_5$ requires C, 54·4; H, 3·1%).

(2) A solution of 2-chloro-3′,5-dinitrobenzophenone [5] (5 g.) in ethanol (450 ml.) was heated in an autoclave at 150° for 24 hr. with ammonia (initial pressure 7 atm.). The mixture was concentrated to ~100 ml. and the product removed by filtration, washed with water, and recrystallized from ethanol to give the same amine (0·8 g., 17%), m. p. 240—242°.

2-*Amino*-2′-*fluoro*-5,5′-*dinitrobenzophenone* (IIIb) was obtained from compound (IIb) (5 g.) in ethanol (75 ml.) as described in method (1) and crystallized from ethanol as yellow needles (4·22 g., 96%), m. p. 228—230° (decomp.) (Found: C, 51·3; H, 2·9. $C_{13}H_8FN_3O_5$ requires C, 51·2; H, 2·6%).

2-*Amino*-5-*chloro*-3′-*nitrobenzophenone* (IIIc), orange prisms (0·1 g., 35%), m. p. 124—125° (Found: C, 56·5; H, 3·4. $C_{13}H_9ClN_2O_3$ requires C, 56·4; H, 3·3%), was similarly obtained from compound (IIc) (0·3 g.) in ethanol (10 ml.).

[7] Sternbach, Fryer, Metlesics, Reeder, Sach, Saucy, and Stempel, *J. Org. Chem.*, 1962, **27**, 3788.

Secondly, a solution of chlorine (1·2 g., 0·0169 mole) in cold (10°) acetic acid (30 ml.) was added dropwise to a stirred, cold (16°) solution of 2-amino-3′-nitrobenzophenone [6] (4·0 g., 0·0165 mole) in acetic acid (70 ml.). The mixture was stirred for 1 hr., poured on ice (500 g.), and filtered. The precipitate was dissolved in dichloromethane (100 ml.), which was washed with dilute ammonia solution and then with water. The organic phase was dried (Na_2SO_4), filtered, and evaporated. An initial recrystallization from methanol gave a dichloro-compound, yellow needles (0·4 g.), m. p. 148—151° (probably *2-amino-3,5-dichloro-3′-nitrobenzophenone*) (Found: C, 50·5; H, 2·8. $C_{13}H_8Cl_2N_2O_3$ requires C, 50·2; H, 2·6%). The methanol filtrates were evaporated and the residue recrystallized from ether–light petroleum, to give the amine (IIIc) as yellow needles (2·9 g., 61%), m. p. 105—106°. The two crystalline forms were shown to be polymorphic modifications of the same compound by their interconvertibility, and by the identity of their infrared spectra in solution.

2,7-Dinitroacridone (IVb).—A solution of the amine (IIIb) (4 g.) in 2-ethoxyethanol (50 ml.) was refluxed for 15 hr., cooled, and filtered. The product was washed with ethanol and ether and dried to give the acridone (IVb) as yellow plates (3·72 g., 97%), m. p. >350° (Found: C, 54·9; H, 2·5. Calc. for $C_{13}H_7N_3O_5$: C, 54·7; H, 2·5%).

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