The Attempted Synthesis of Nitrogen-containing Analogues of [10]Paracyclophane

By B. Coffin and R. F. Robbins

A [10]paracyclophane in which –NH– or –NTs– replace the 2′,9′–CH_2-groups of the " para " bridge was the anticipated product of the acyloin condensation of the appropriate bisamino-esters, but elimination and not cyclisation occurred. From the *NN*′-ditoluene-*p*-sulphonate of the ester the similar derivative of 1,4-bisaminomethylbenzene was obtained. The preparation of bisamino-esters is described.

THE [10]paracyclophane (I; $X = Y = CH_2$) can be readily dehydrogenated to give pyrene or a reduced derivative.[1] The replacement of two methylene groups in the " para " bridge by –NH– and the dehydrogenation of such nitrogen-containing analogues offers, in principle, a new route to many unknown diazapyrenes.

To investigate this possibility and also as part of a study of transannular interaction, the acyloins (I; X = NH, $Y = CH_2$) and (I; $X = CH_2$, Y = NH or NTs) were required. Necessary for the proposed acyloin condensations were, respectively, the amino-esters (II; X = NH, $Y = CH_2$) and (II; $X = CH_2$, Y = NH or NTs).

This Paper describes the preparation of two of these esters and the results of their attempted acyloin condensation. The amino-ester (II; X = NH, $Y = CH_2$)

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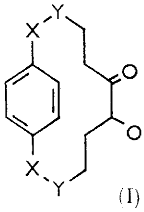
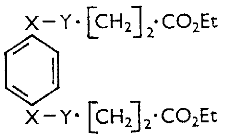
[1] D. J. Cram and H. U. Daeniker, *J. Amer. Chem. Soc.*, 1954, **76**, 2743.

could not be prepared by reacting *p*-phenylene-diamine with ethyl 4-bromobutyrate in the presence of sodium carbonate. The product was the dipyrollidone (III). There was no reaction between the *NN'*-diacetate or *NN'*-ditoluene-*p*-sulphonate of *p*-phenylenediamine and ethyl 4-bromobutyrate in methanol containing sodium methoxide. There was evidence of reaction between *p*-phenylenediamine and ethyl 3-formyl-propionate to give the dianil (IV), and treatment of the product with sodium borohydride gave an oil which may have been the required ester (II; X = NH, Y = CH_2). Unfortunately its instability precluded proper characterisation and its use in the proposed acyloin reaction.



(I)



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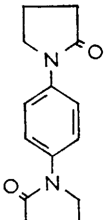

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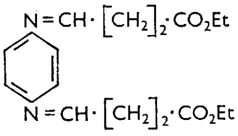

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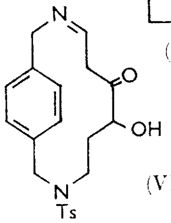
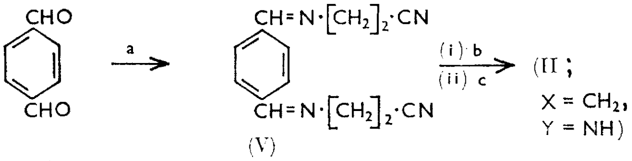


(VI)

The preparation of ethyl 3-formylpropionate is of interest. We were unable to repeat the published[2] method which involves the mild hydrolysis and decarboxylation of ethyl 2-formylsuccinate but obtained the formyl ester by reducing ethyl succinoyl chloride at −78° with lithium tri-t-butoxyaluminohydride.

The amino-ester (II; X = CH_2, Y = NH) proved easier to prepare than the previous one. Even so, attempts to condense 1,4-bisaminomethylbenzene with methyl acrylate did not give it. The apparently related condensation of benzylamine with methyl acrylate gives methyl 3-benzylaminopropionate.[3] The method finally devised for the preparation of the amino-ester depends on an initial reaction of terephthalaldehyde with 3-aminopropionitrile. Thus:

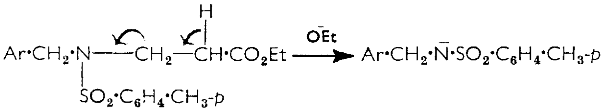


(V)

Reagents: a, $H_2N[CH]_2CN$; b, $NaBH_4$; c, EtOH–H_2SO_4

An attempted acyloin condensation of the amino-ester (II; X = CH_2, Y = NH) in toluene at 110° gave an uncharacterisable oil. Using liquid ammonia as solvent effected no improvement. When the *NN'*-ditoluene-*p*-sulphonate (II; X = CH_2, Y = NTs) was treated with " powdered " sodium in toluene, a crystalline product was obtained. But this was not the acyloin (I; X = CH_2, Y = NTs) or one derived from it by base-catalysed elimination of toluene-*p*-sulphinic acid, *e.g.*, (VI). Analogous elimination reactions are known[4] and are especially easy when α-carbon (with respect to nitrogen) is predisposed to anion formation by an attached electron-attracting substituent. Elimination can, on occasion, precede a possible cyclisation reaction and, by forming a sterically inconvenient anil,[5] inhibit ring formation.

In our case, neither acyloin nor anil formation took place. The treatment of the *NN'*-ditoluene-*p*-sulphonate (II; X = CH_2, Y = NTs) with sodium caused an elimination of the type:



The product was the *NN'*-ditoluene-*p*-sulphonate of 1,4-bisaminomethylbenzene, as shown by a number of pieces of evidence but first suspected from its proton magnetic resonance spectrum. The line positions, coupling constants, and relative areas for the compound are as expected while the doublet methylene band ($\tau \sim 6{\cdot}05$) became a singlet of the same area on the addition of D_2O and as NH was converted into ND.

EXPERIMENTAL

Infrared spectra were determined in Nujol mulls using a Perkin-Elmer Infracord, model 237. N.m.r. spectra were kindly measured with a Varian A.60 spectrometer by Dr. G. Kirby.

The Dipyrollidone (III).—After 6 hours' boiling, a solution of *p*-phenylenediamine (2 g.) and ethyl 4-bromobutyrate[6] (8 g.) in ethanol (100 ml.) containing sodium carbonate (5 g.) was evaporated *in vacuo* to small volume. The crystallisation from ethanol of the precipitate obtained on diluting with water gave the *product* (3·7 g., 71%), m. p. 250° (Found: C, 68·8; H, 6·7; N, 11·3. $C_{14}H_{16}N_2O_2$ requires C, 68·8; H, 6·6; N, 11·5%).

Ethyl 3-Formylpropionate.—Ethyl succinoyl chloride (25 g.) in diethylene glycol dimethyl ether (50 ml.) was added to a stirred solution at −78° of lithium tri-t-butoxyaluminohydride[7] (20 g.) in the same solvent (100 ml.). After 6 hr. the mixture was poured on to ice. Extraction with ether, followed by evaporation of the dry (Na_2SO_4) extracts, gave an oil from which the product (12·3 g., 62%) was isolated by distillation, b. p. 82—84°/11 mm. (lit.,[2] 84°/12 mm.). It formed a 2,4-*dinitrophenylhydrazone* (Found: C, 46·6; H, 4·7; N, 18·1. $C_{12}H_{14}N_4O_6$ requires C, 46·5; H, 4·6; N, 18·1%), m. p. 105° (from ethanol).

The Dianil (V).—Aminopropionitrile[8] (70 g.) was added

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[2] T. Yoshioka, *J. Pharm. Soc. Japan*, 1955, **75**, 622.

[3] G. Stork and S. M. McElvain, *J. Amer. Chem. Soc.*, 1947, **69**, 971.

[4] W. Paterson and G. R. Proctor, *Proc. Chem. Soc.*, 1961, 248.

[5] W. Paterson and G. R. Proctor, *J. Chem. Soc.*, 1965, 485.

[6] A. W. D. Avison and A. L. Morrison, *J. Chem. Soc.*, 1950, 1473.

[7] H. C. Brown and R. F. McFarlin, *J. Amer. Chem. Soc.*, 1958, **80**, 5372.

[8] S. R. Buc, J. H. Ford, and E. C. Wise, *J. Amer. Chem. Soc.*, 1945, **67**, 92.

to a solution of terephthalaldehyde (64 g.) in methanol (500 ml.). The *product* (109·3 g., 92%) separated after 1 hr. at 100° and after collection and crystallisation from ethanol had m. p. 143° (Found: C, 70·5; H, 5·8; N, 23·5. $C_{14}H_{14}N_4$ requires C, 70·6; H, 5·9; N, 23·5%).

Reduction of the Dianil (V).—The anil (24 g.) was dissolved in methanol (150 ml.) and sodium borohydride (8 g.) in methanol (50 ml.) was added. After stirring for 6 hr. at 70° the solvent was removed *in vacuo* to yield a gum. Water (100 ml.) was added and the mixture extracted with ether. Evaporation of the dry (Na_2SO_4) extracts gave an oil which, on distillation (158°/0·2 mm.), yielded the *amino-nitrile* (20·7 g., 88%) (Found: C, 69·1; H, 7·3; N, 22·7. $C_{14}H_{18}N_4$ requires C, 69·4; H, 7·5; N, 23·1%). It formed a *picrate* (Found: C, 33·1; H, 4·2; N, 24·1. $C_{26}H_{24}N_{10}O_7$ requires C, 33·3; H, 4·1; N, 23·9%), m. p. 199° (from ethanol), and a toluene-*p*-sulphonate (Found: C, 61·5; H, 5·5; N, 9·9; S, 11·3. $C_{23}H_{30}N_4O_4S_2$ requires C, 61·1; H, 5·5; N, 10·2; S, 11·6%), m. p. 186° (from ethanol).

The Amino-ester (II; X = CH_2, Y = NH).—To a solution at 0° of the foregoing amino-nitrile (10 g.) in ethanol (50 ml.) was added one, also at 0°, of concentrated sulphuric acid (50 ml.) in ethanol (50 ml.). After 6 hr. at 100° the addition of ether (500 ml.) gave a precipitate. This was collected, water (50 ml.) was added, and then sodium hydroxide to give pH 9. The extraction of this solution with ether and the evaporation of the dry (Na_2SO_4) extracts gave the amino-ester (10·7 g., 77%). It decomposed on attempted vacuum distillation but formed a *picrate* (Found: C, 45·8; H, 4·5; N, 11·1. $C_{30}H_{34}N_8O_{18}$ requires C, 45·3; H, 4·3; N, 11·2%) which crystallised from ethanol, with m. p. 174°, and a *toluene*-p-*sulphonate* (Found: C, 59·6; H, 6·1; N, 4·4; S, 10·1. $C_{32}H_{40}N_2S_2O_8$ requires C, 59·6; H, 6·3; N, 4·3; S, 9·9%), m. p. 137° (from methanol).

Attempted Acyloin Condensation.—A solution of the foregoing ditoluene-*p*-sulphonate (4 g.) in dry toluene (150 ml.) was slowly (4 hr.) added to a rapidly stirred suspension of sodium (1·5 g.) in toluene (500 ml.) at 110° under pure, dry nitrogen. After a further 8 hours' stirring at 110° the excess of sodium was carefully decomposed with acetic acid and the mixture was evaporated to dryness. The residue was washed with a little water and recrystallised from dioxan to give 1,4-*di*(*toluene*-p-*sulphonamidomethyl*)*benzene* (2·58 g., 86%) (Found: C, 57·9; H, 4·9; N, 6·3; S, 14·9%; *M*, 420. $C_{20}H_{20}N_2O_4S_2$ requires C, 57·7; H, 4·8; N, 6·7; S, 15·4%; *M*, 416·4), m. p. 215°; $\nu_{max.}$ 3280 (NH stretch), 1340 (S=O antisymmetric stretch), 1150 (S=O symmetric stretch), and 890 cm.$^{-1}$. N.m.r., τ 2·2—2·8, multiplet (12 aromatic protons); 6·0, doublet becoming singlet of similar area on addition of D_2O (4 protons) ($-CH_2-NH$); and 7·7 singlet (6 protons) (CH_3). (τ values relate to a solution in dimethyl sulphoxide. This showed the aromatic protons clearly. A pyridine solution was also used and allowed correlation of peak areas. Tetramethylsilane was used as an internal standard.)

Similar m. p., mixed m. p., and infrared-spectral data were obtained from the disulphonamide obtained from a diamine prepared by reducing terephthalaldehyde dioxime with lithium aluminium hydride.

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