## 719. *The Synthesis of Dibenzo[c,f][1,2]diazepin-11-one.*

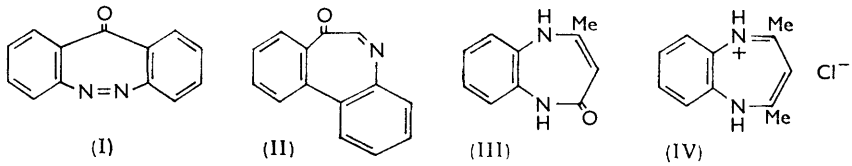
By R. B. Johns and K. R. Markham.

Dibenzo[*c*,*f*][1,2]diazepin-11-one (I) has been synthesized and the physical and chemical properties are shown to be consistent with a tropone-type ring system. In the preparation a further example of carbon–carbon bond fission by lithium aluminium hydride was encountered.

The concept of six π-electrons resonating in seven *p*-orbitals accounts for much of the chemistry of tropone and more particularly of α-tropolone.[1] The molecular-orbital description of the π-electron system of benzene has been successfully applied, with modifications, to describe the electronic structures of heterocyclic analogues, *e.g.*, pyridine and pyrrole, and there is no obvious reason why the same concept should not apply to azatropones. The most suitable example would be one in which one *p*-electron is formally contributed by the nitrogen atom to the π-electron cloud, as occurs in pyridine. This paper reports the synthesis of the dibenzodiazepinone (I) which may be considered as derived from a diazatropone. A dibenzazepin-4-one [2] (II), as well as other heterocycles, (III) [3] and (IV),[4] which are interesting in this context but approximate to the tropone system, have been reported. The cation (IV) readily undergoes ring contraction which suggests that this diazepine may not prove to be as stable as the cycloheptatrienylium cation. We have synthesized the benzodiazepinone (I) because of its relative accessibility and the enhanced stability that should result from fusion of the benzene rings, although we were aware of the limitations and modifications to the chemistry of this system which would result.

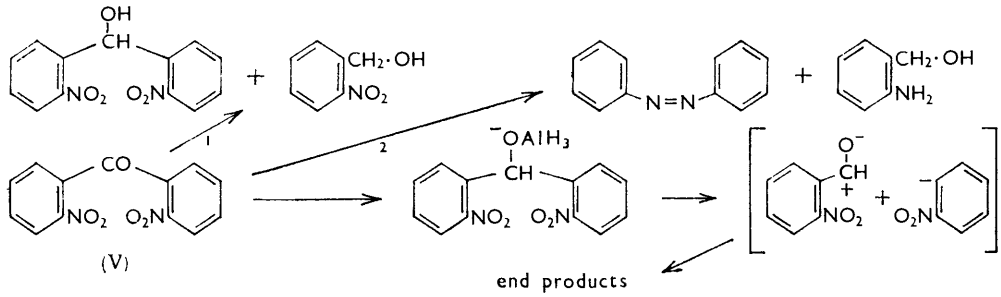
[1] Doering and Knox, *J. Amer. Chem. Soc.*, 1952, **74**, 5683.
[2] Proctor, *Chem. and Ind.*, 1960, 408; Proctor and Paterson, *Proc. Chem. Soc.*, 1961, 248.
[3] Rossi, Hunger, Kebrle, and Hoffmann, *Helv. Chim. Acta*, 1960, **43**, 1298.
[4] Barltrop, Richards, Russell, and Ryback, *J.*, 1959, 1132.

Bis-*o*-nitrophenylmethane [5] was oxidized by chromic oxide to 2,2'-dinitrobenzophenone (V) in 80% yield. Reduction of the ketone by lithium aluminium hydride did not lead to the ring formation expected by analogy with the reductive cyclization of



(I) (II) (III) (IV)

dinitrodiphenylmethane,[5] but rather to a variety of products depending on the temperature of reaction (Scheme 1). This provides a further example [6-9] of carbon–carbon bond



Scheme 1.

1, $LiAlH_4$; −35°. 2, $LiAlH_4$; 19°.

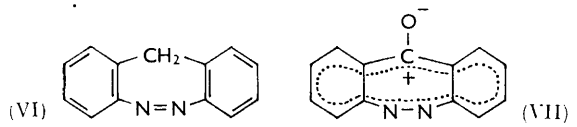
fission by lithium aluminium hydride. The two reactions differ essentially in the temperature of reaction and probably proceed by the same mechanistic path. The isolation of partially reduced material suggests that cleavage follows reduction. In reported examples the hydrocarbon is formed from a carbanion which can be stabilized by electron-withdrawing substituents as in our case, or by a structure facilitating electron delocalization as, for example, in 9-benzoylanthracene.[8] The intermediates in Scheme 1 follow from Lansbury's suggested mechanism [9] for carbon–carbon cleavage and which he has shown is facilitated by the presence of a co-ordinating agent to complex with the aluminium hydride. In our reaction the formation of amine would provide a suitable complexing agent and account for the development of colour during reaction; the nitro-group would stabilize the carbanion so that cleavage can occur by a reverse aldol condensation. It is possible that reductive cleavage could be general for similarly substituted acyclic compounds.

More vigorous methods of reducing the benzophenone (V), such as zinc in methanolic potassium hydroxide, resulted in nucleophilic displacement of a nitro-group to yield 2-methoxy-2'-nitrobenzophenone. With alkaline glucose solution, however, the dibenzodiazepinone (I) was obtained directly. The yield in the cyclization step was 80%. Alternative approaches directed towards substituting the methylene group in (VI), initially as bis-4-aminophenylmethane, were unsuccessful.

Freundler [10] reported a compound, m. p. 76°, to which he ascribed structure (VI), as being obtained by the cyclization of 2-phenylazobenzyl alcohol. We have repeated the preparation of VI by Theilacker and Korndörfer's method [5] and obtained their product, as yellow needles, m. p. 110°, which is reported by them and by Allinger and Yongdale [11] to

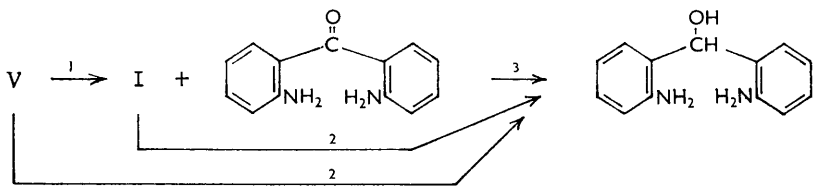
[5] Theilacker and Korndörfer, *Tetrahedron Letters*, 1959, No. 18, 5.
[6] Reynaud, *Bull. Soc. chim. France*, 1951, 612.
[7] Dornow and Fust, *Chem. Ber.*, 1957, **90**, 1774.
[8] Rona and Feldman, *J.*, 1958, 1737.
[9] Lansbury, *Chem. and Ind.*, 1960, 151.
[10] Freundler, *Compt. rend.*, 1903, **136**, 1136; 1904, **138**, 1276.
[11] Allinger and Yongdale, *Tetrahedron Letters*, 1959, No. 9, 10.

give the corresponding hydrazo-derivative. Our azo-compound was soluble in dilute acid, contrary to the report by Freundler who also stated that chromic acid oxidation of his supposed compound (VI) gave the dibenzodiazepinone (I). No physical data were given. There seems no reason to doubt the structures assigned by recent workers,[5,11] and we suggest that Freundler's assignment of structure was mistaken.




Dibenzo[*c*,*f*][1,2]diazepin-11-one (I) crystallized as orange needles, m. p. 198°, and could be sublimed. The analytical data together with the lack of N–H absorption in the infrared region, and formation of bis-*o*-aminophenylmethanol (Scheme 2) on reduction permit the assignment of structure (I). The classical formulation (I) can be considered resonant with (VII) and it is of interest to assess the extent to which formulation (VII) represents the electron distribution in the unreacting molecule. (I) may be considered as representing the interaction of two opposing groups within the molecule whilst (VII) represents the polarization expected if indeed (I) were a diazatropone.

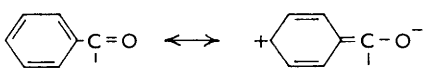
2,3:5,6-Dibenzotropone [12a] and tropone [12b] form 2,4-dinitrophenylhydrazones but (I) was recovered unchanged from both mild and vigorous condensation reactions with 2,4-dinitrophenylhydrazine. Benzophenone when treated similarly readily formed a derivative. Compound (I) is stable in alkaline and acid solution. Alkaline reduction




*Scheme* 2.

1. Glucose reduction. 2. $H_2$–Ni. 3. Zn–MeOH–KOH.

using zinc metal in methanolic ammonia at 60° emphasized the relatively greater stability of compound (I) to chemical reduction. Solutions of azo- and azoxy-benzene became colourless within 10 minutes and yielded hydrazobenzene, yet solutions of the dibenzodiazepine (VI) and the 4,4′-diamino-derivative became colourless within 15 minutes, reoxidation occurring during working up to give back starting material. In contrast, the reduction of a solution of the dibenzodiazepinone (I) caused no change in colour during 30 minutes and yielded unchanged material. These results are in keeping with a tropane formulation of (I). The ultraviolet spectrum of compound (I) is similar to a combination of partial chromophores for benzophenone and *cis*-azobenzene and resembles that of 2,3:6,7-dibenzotropone only in that the short wavelength maximum represents the transition (X).[13] The long-wavelength maximum is associated with the diazo-bond,




(X)

because in acid solution it undergoes a hypsochromic shift and intensification. This can be qualitatively used to indicate the ease of protonation of the nitrogen atoms. Compound (VI) shows marked intensification of this maximum in 0·1N-mineral acid (even in

[12] (*a*) Amiel and Ginsberg, *Tetrahedron*, 1957, **1**, 21; (*b*) Nozoe, *Proc. Japan Acad.*, 1952, **28**, 477.
[13] Braude and Nachod, "Determination of Organic Structures by Physical Methods," Academic Press, New York, 1955, p. 152.

TABLE.

Spectral and polarographic properties.

| Compound | Solvent | $\lambda_{max.}$ (ε) (mμ) | | | | Solvent | $\nu_{CO}$ (cm.$^{-1}$) | $E_{\frac{1}{2}}$ (v) −N=N− | $E_{\frac{1}{2}}$ (v) C=O |
|---|---|---|---|---|---|---|---|---|---|
| (I) ..... | EtOH–$H_2O$ | 246(4·34) | 261(4·36) | 335(3·91) | 435(2·6) | KCl disc | 1660 | −0·27 | −1·22 |
| | 2·8N-HCl | 243(4·28) | 268(4·34) | 346sh (3·73) | 406(4·0) | $CCl_4$ | 1675 | | |
| | 4·73N-HCl | 243(4·24) | 271(4·32) | | 406(4·16) | $CHCl_3$ | 1667 | | |
| (VI) ..... | EtOH–$H_2O$ | 245(3·77) | | 324(3·85) | 412(2·83) | | | −0·41 | |
| | 2·84N-HCl | | 290(3·6) | 338sh (3·74) | 402(4·08) | | | | |
| *cis*-Azobenzene ... | $C_6H_{14}$ | | | 313(4·3) | 448(2·63) | | | −0·46 | |
| Benzophenone... | EtOH | 252(4·3) | | 330(2·2) | | KCl disc | 1665 | | −1·38 |
| | | | | | | $CHCl_3$ | 1658 [1] | | |
| 2,3:6,7-Dibenzotropone ... | EtOH | 254(4·54) | 308(4·14) | 352(3·55) [2] | | $CHCl_3$ | 1660 [3] | | |
| 2-Aminobenzophenone | | | | | | KCl disc | 1629 | | −1·45 [5] |
| 2,2′-Dinitrobenzophenone | | 251(3·74) | | 340sh (2·8) | | KCl disc | 1690 | | |
| 3,4-Dimethoxybenzophenone | | | | | | Nujol | 1645 [4] | | |
| † 4′,5′-Dimethoxy-2,3:6,7-dibenzotropone | | | | | | KCl disc | 1618 | | −1·32 |
| | | | | | | $CCl_4$ | 1629 | | |
| † 4,5-Dihydro-4′,5′-dimethoxy-2,3:6,7-dibenzotropone | | | | | | KCl disc | 1631 | | −1·39 |
| | | | | | | $CCl_4$ | 1644 | | |

sh = Shoulder. [1] Bellamy and Williams, *Trans. Faraday Soc.*, 1959, **55**, 14. [2, 3] Cf. Refs. 15 and 16. [4] Lozach and Guillouzo, *Bull. Soc. chim. France*, 1957, 1221. [5] Methyl Red used as maximum repressor. † Generously supplied by Prof. J. N. Chatterjea, Patna University, India.

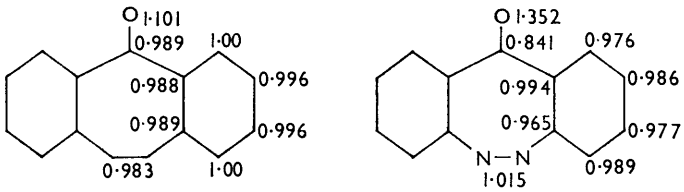
0·038N-acid an increase is apparent) whilst compound (I) shows negligible change until the acid concentration reaches 0·2N. This behaviour can be interpreted in terms of either structure (I) or (VII).

The ultraviolet spectrum of compound (I) is a modification of that for the carbocyclic series as a result of the introduction of two-hetero-atoms. Similarly, the infrared spectrum reflects the changed electron distribution (Table). Electron-donating substituents in benzophenone shift the carbonyl maximum to lower wave numbers, the reverse occurring with electron-withdrawing substituents. In the dibenzodiazepinone (I), if $\nu_{CO}$ were largely dependent upon the electron-withdrawing effect of the azo-group [14] we would expect a movement to higher wave numbers compared with that of benzophenone, whilst any significant contribution by (VII) would lower the maximum. Experimentally, spectra of both solid and solutions show little change as a result of the balance between these effects. The more complete the conjugation with the carbonyl group the lower the carbonyl maximum [15] [cf. dihydro-3,4-dimethoxybenzotropone and the corresponding tropone (Table)]. 2,3:6,7-Dibenzotropone [16] does not fall into the general pattern and it has been suggested that the high value for $\nu_{CO}$ is due to a lack of planarity [16,17] of the molecule which decreases conjugation. The ultraviolet spectrum of the dibenzodiazepinone (I) suggests negligible loss of planarity in forming the cyclic system, and, if this is correct, and as polarographic reductions indicate that the carbonyl and the azo-groups are not independent of one another, the fact that the position of the carbonyl maximum in (I) is not higher can be interpreted as due to a contribution by formulation (VII).

A more useful assessment of the importance of structures (I) and (VII) would be a determination of the relative π-electron densities on the carbonyl and azo-groups. Polarographic reduction provides the relevant data. The carbonyl and azo-groups can both be reduced under comparable conditions and the value of the half-wave potential has been

[14] Pullman and Baudet, *Compt. rend.*, 1954, **238**, 2529.
[15] Gotz, Heilbronner, Katritzky, and Jones, *Helv. Chim. Acta*, 1961, **44**, 387.
[16] Bergmann and Ginsberg, *Bull. Res. Council Israel*, 1951, **1** (No. 3), 120; *Chem. Abs.*, 1953, **47**, 3845.
[17] Bergmann, Fischer, Ginsburg, Hirschberg, Lavie, Mayot, Pullman, and Pullman, *Bull. Soc. chim. France*, 1951, 684.

correlated with the degree of conjugation of the carbonyl group,[15] and the electronegativities of substituents [18] as well as the electron density on the atoms to be reduced.[19] The currently accepted mechanism of reduction of the carbonyl group, whereby addition of the electron occurs initially at the carbon atom of the carbonyl group,[20] suggests that the lower the electron density at position 1 in the dibenzodiazepinone (I), the more readily will reduction occur, *i.e.*, the more positive the half-wave reduction potential will be. The Table shows the trend and indicates that this carbon atom is markedly reduced in electron density. One position to which the electrons could be withdrawn is the azo-group. The same line of argument [19] being followed, however, the value for $E_{\frac{1}{2}}$ for the azo-group is not consistent with an increased π-electron density in this region. The excess of electronic charge cannot be delocalized between both position 11 and the azo-group without affecting one of these groups. There remains the oxygen atom to accommodate this movement of electrons, *i.e.*, if (VII) is important the polarization of the molecule




(Rel. energy parameter for N = 0·25; O = 0·6. Rel. energ. param. for C=O bond = 1·3.)

would lower the π-electron density on both the azo-group and the ring system generally, leading to values for $E_{\frac{1}{2}}$ of the order shown. A simple molecular orbital calculation of the π-electron density distribution for compound (I) and the isoconjugate hydrocarbon [17] illustrates that polarization occurs in the direction indicated by the polarographic reductions. The Table shows that there is no direct correlation between $\nu_{CO}$ and $E_{\frac{1}{2}}$ in the series [15,19] and accords with the idea that no one factor is determining the position of the carbonyl maximum in the infrared spectrum.

## Experimental

*2,2′-Dinitrobenzophenone.*—Bis-*o*-nitrophenylmethane (0·9 g.), chromic oxide (2·35 g.), water (2·3 ml.), and glacial acetic acid (7 ml.) were refluxed for 6 hr. When cooled, the mixture was stirred into water (100 ml.). The product (0·8 g.) crystallized from acetic acid as needles, m. p. 188° (lit.,[21] m. p. 188°) (Found: C, 57·8; H, 3·1. Calc. for $C_{13}H_8N_2O_5$: C, 57·4; H, 3·0%), $\lambda_{max.}$ (in ethanol) 251 and 340 mμ (log ε) 3·74 and 2·79, $\nu_{CO}$ (KCl) 1689m.

*Reduction of 2,2′-Dinitrobenzophenone.*—(*a*) Lithium aluminium hydride (0·4 g.) in dry tetrahydrofuran (25 ml.) was added dropwise to 2,2′-dinitrobenzophenone (0·5 g.) in tetrahydrofuran (25 ml.), and the mixture was left for 1 hr. at 19°. It was refluxed for 30 min., cooled, and hydrolysed with water. Tetrahydrofuran was removed by distillation at reduced pressure, and the resultant orange solution was extracted with ether. The dried extract was then chromatographed over silica. Elution with benzene yielded azobenzene (0·13 g.), m. p. and mixed m. p. 63° (its infrared spectrum was identical with that of an authentic sample); 2% ethanolic benzene yielded fractions not containing amine, and 4% ethanolic benzene yielded 2-aminobenzyl alcohol (0·09 g.) which, after sublimation at 40°/$10^{-3}$ mm. and crystallization from cyclohexane–ether, had m. p. and mixed m. p. 84°. (The infrared spectra were also identical.)

(*b*) To a stirred solution of the ketone (0·5 g.) in tetrahydrofuran (50 ml.) at −35°, a solution of lithium aluminium hydride (0·25 g.) in tetrahydrofuran (50 ml.) was added dropwise during 15 min. The solution was allowed to warm to room temperature, water added, and the solution neutralized with dilute sulphuric acid, and stored overnight. After acidification, the

[18] Shikata and Tachi, *J. Chem. Soc. Japan*, 1932, **53**, 834.
[19] Zahradnik and Bocek, *Coll. Czech. Chem. Comm.*, 1961, **26**, 1733.
[20] Pasternak, *Helv. Chim. Acta*, 1948, **31**, 753.
[21] Staedel, *Ber.*, 1890, **23**, 2578.

solution was filtered, concentrated under vacuum, and extracted with ether. The dried extract was chromatographed on silica, benzene being used as eluate. The yellow first fraction yielded unchanged ketone (0·08 g.), m. p. 188°. Solid from the second pale yellow fraction was sublimed at 35°/$10^{-3}$ mm., and the sublimate crystallized from cyclohexane–ether, forming white needles (0·1 g.), m. p. 74° (m. p., mixed m. p., and infrared spectrum were identical with those of an authentic sample of 2-nitrobenzyl alcohol). Further sublimation of the residue at 110°/$10^{-3}$ mm. gave *bis*-o-*nitrophenylmethanol* which crystallized from cyclohexane–ether as needles (0·12 g.), m. p. 126° (Found: C, 56·8; H, 3·7. $C_{13}H_{10}N_2O_5$ requires C, 56·9; H, 3·7%). The infrared spectrum (KCl disc) was similar to that of 2-nitrobenzyl alcohol and had $\nu_{max.}$ 3580m, 1512vs, 1343vs, and 1031m cm.$^{-1}$.

(*c*) 2,2′-Dinitrobenzophenone (0·25 g.), 15% methanolic potassium hydroxide (25 ml.), and zinc dust (0·3 g.) were refluxed for 3 hr. Zinc oxide was filtered off and the orange filtrate evaporated to about 3 ml. Water (10 ml.) was added, and the solution was extracted with benzene. On evaporation, the extract produced crystals (0·13 g.), m. p. 130°. These were sublimed at 100°/$10^{-3}$ mm. and then crystallized from ether yielding 2-*methoxy*-2′-*nitrobenzophenone*, m. p. 132° (Found: C, 65·6; H, 4·1; N, 5·6; OMe, 12·2. $C_{14}H_{11}NO_4$ requires C, 65·4; H, 4·3; N, 5·5; OMe, 12·1%), $\nu_{max.}$ (KCl disc) 1660s, 1515s, 1344s, and 1250s cm.$^{-1}$.

*Dibenzo[c,f][1,2]diazepin-11-one* (I).—Powdered glucose (0·8 g.) was added during 30 min. to a rapidly stirred solution of 2,2′-dinitrobenzophenone (0·6 g.) in methanol (5 ml.) and 40% sodium hydroxide (5 ml.) maintained at 60°. The deep red solution was set aside at 60° for a further 20 min. after which the orange precipitate was filtered off. The filtrate was diluted with water, and more solid was precipitated. The total yield was 0·4 g. (82%). The solid was sublimed at 120°/$10^{-3}$ mm. or crystallized from ethanol or ether–light petroleum to give orange needles of the *diazepinone* (I), m. p. 197° (Found: C, 74·9; H, 3·9; N, 13·2. $C_{13}H_8N_2O$ requires C, 75·0; H, 3·9; N, 13·5%); $\nu_{max.}$ (KCl disc) 1660vs, 1695s, 1563m, 1495s, 1435m, 1316vs, and 1235m cm.$^{-1}$.

When the diazepinone (0·01 g.) in ethanol (3 ml.) was treated with 2,4-dinitrophenylhydrazine in concentrated sulphuric acid and ethanol at room temperature and the mixture was set aside for 7 hr. no precipitation occurred and the unchanged tropone was recovered quantitatively. The same result was obtained by heating the mixture for 3 hr. at 50° and by refluxing for 3 hr. In the last case the tropone was recovered by elution from a kieselguhr–bentonite column.

*Bis*-o-*aminophenylmethanol*.—2,2′-Dinitrobenzophenone (0·085 g.) in ethanol was hydrogenated at room temperature and atmospheric pressure by using Raney nickel W.4 (0·25 g.) as catalyst, to give a quantitative yield of *bis*-o-*aminophenylmethanol* which was sublimed at 140°/$10^{-3}$ mm. and recrystallized, m. p. 178° (from ethanol) (Found: C, 72·3; H, 6·6. $C_{13}H_{14}N_2O$ requires C, 72·9; H, 6·6%); $\nu_{max.}$ (KCl disc) 3450s, 3333s, 3260s, 1642s, and 1629s cm.$^{-1}$ closely resembling those for 2-aminobenzyl alcohol.

*Catalytic Reduction of* (I).—Compound (I) (0·035 g.) was hydrogenated as described for the preceding reaction. After 1 hr., 2·8 moles of hydrogen having been absorbed, the hydrogenation was stopped and the product worked up in the usual way to give *bis*-o-*aminophenylmethanol* crystals (0·03 g.), m. p. and mixed m. p. 178°.

*Polarographic Reductions*.—By using a pen-recording Cambridge polarograph, with an H-type cell, reduction potentials were measured relative to a standard calomel electrode. An aqueous solution of " AnalaR " potassium chloride (1·0M) was used as the base electrolyte, and the buffer solution was prepared from 1M-citric acid and 0·2M-sodium dihydrogen phosphate to give a pH of 7·07; 0·002M-standard solutions were made up in purified ethanol. The final cell solution consisted of a 1 : 5 : 5 mixture of base electrolyte solution, buffer, and standard solution respectively, and the resultant pH was 8·08. The cell was kept at 25° and freed from oxygen by bubbling oxygen-free nitrogen through it for 20 min., and over the surface of the solution during reduction. Where a maximum suppressor was found necessary, 2 drops of a Methyl Red solution (0·1 g. in 250 ml.) were added just before reduction. The half-wave potentials found are given in the Table.

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