The Thermolysis of 3-Azabicyclo[3,2,0]hept-6-enes

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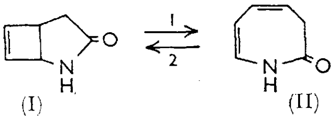
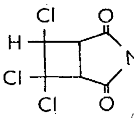
Derivatives of 3-methyl-3-azabicyclo[3,2,0]hept-6-ene-2,4-diones have been prepared by the ultraviolet irradiation of *N*-methylmaleimide and alkylacetylenes. The products were unchanged at 500°, but after reduction with lithium aluminium hydride they formed the corresponding 3-methyl-3-azabicyclo[3,2,0]hept-6-enes which at 500° rearranged smoothly to alkylbenzenes with elimination of methylamine. Addition of trichloroethylene to *N*-methylmaleimide followed by dechlorination with zinc gave 6-chloro-3-methyl-3-azabicyclo[3,2,0]hept-6-ene-2,4-dione. When this was reduced with lithium aluminium hydride and the product heated at 500°, a low yield of *N*-methylaniline was obtained.

THE photochemical addition of derivatives of maleic acid to carbon–carbon multiple bonds is now a well established reaction for the preparation of [3,2,0] oxa- and aza-bicycloheptane derivatives.[1] Cases are also known where fission of the transannular linkage can be induced by pyrolysis, and thus give rise to unsaturated cycloheptane derivatives. The possibility of using reactions of this type to prepare derivatives of azepine was suggested by interconversion of (I) and (II);[2] many other examples (*e.g.*, ref. 3) have been quoted of the formation of cyclohepta-1,3-dienes by the action of heat on the bicyclo[3,2,0]heptenes.



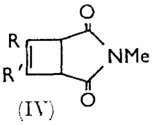
(I) (II)



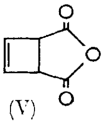
(III)

1, Heat at 500°. 2, Ultraviolet irradiation

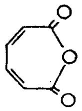
When a solution of *N*-methylmaleimide in trichloroethylene was irradiated with ultraviolet light in the presence of benzophenone as a sensitiser, 6,6,7-trichloro-3-methyl-3-azabicyclo[3,2,0]heptane-2,4-dione (III) was obtained, and this reacted with zinc to give 6-chloro-3-methyl-3-azabicyclo[3,2,0]hept-6-ene-2,4-dione (IV; R = Cl, R′ = H). Although the stereochemistry at the ring junction of the adducts (III) and (IV) was not established, it is assumed to be *cis* by analogy with related cases.[1] Unlike (I), the chloro-compound (IV) was unchanged at 500°, and it is of interest that Fonken[4] reported that 3-oxabicyclo[3,2,0]hept-6-ene-2,4-dione (V) was not converted into *cis,cis*-muconic anhydride (VI) when heated at 500°.



(IV)



(V)



(VI)

It seemed therefore that the carbonyl groupings were stabilising the bicyclic structures; accordingly, (IV) was reduced with lithium aluminium hydride, and it gave the 3-azabicyclo[3,2,0]heptene (VII; R = Cl, R′ = H) in good yield. Derivatives of this ring system have not been described previously. The adduct (IV; R = R′ = Et) was prepared by the photochemical addition of *N*-methylmaleimide to hex-3-yne, and was similarly reduced to the corresponding amine (VII; R = R′ = Et) with lithium aluminium hydride. Thermolysis of the 3-azabicyclo[3,2,0]heptene (VII; R = R′ = Et) at 520° caused a clean rearrangement to *o*-diethylbenzene, identified by gas chromatography and n.m.r. comparison with an authentic specimen, and methylamine, identified as the picrate. In the same manner, reduction of the adduct (IV; R = Bu^n, R′ = H) of *N*-methylmaleimide and hex-1-yne gave a colourless oil which was immediately pyrolysed, to give a high yield of n-butylbenzene. In contrast, however, pyrolysis of (VII; R = Cl, R′ = H) at 500° gave no detectable chlorobenzene (g.l.c.), and extensive decomposition was observed. A minor product was *N*-methylaniline (identification by g.l.c.), but the main product was an unstable oil showing ultraviolet absorption at *ca.* 300 mμ but which has not been identified.

It seems probable that the first step in these pyrolytic reactions is an isomerisation to the dihydroazepines (VIII). This reaction, which must be a disrotatory process, is not a favoured concerted process according to the Woodward–Hoffmann rules[5] and occurs only slowly at a high temperature. It is possible on the basis of the observed ultraviolet absorption that the unstable product derived from (IV; R = Cl, R′ = H) is the isomeric dihydroazepine (IX). The *N*-methylaniline could arise from the dehydrochlorination of either of these dihydroazepines, giving *N*-methylazepine, which is known[6] to be unstable to heat. Other examples of the formation of *N*-substituted anilines by rearrangement of *N*-substituted *H*-azepines have been described.[6,7] The precise mechanism for the formation of the alkylbenzenes has not been established, but it is relevant that the

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[1] D. Bryce-Smith and J. E. Lodge, *J. Chem. Soc.*, 1962, 2675; P. de Mayo, R. W. Yip, and S. T. Reid, *Proc. Chem. Soc.*, 1963, 54; G. O. Schenck *et al.*, *Chem. Ber.*, 1962, **95**, 1642; 1963, **96**, 498; R. Robson, P. W. Grubb, and J. A. Barltrop, *J. Chem. Soc.*, 1964, 2153; F. Korte *et al.*, *Chem. Ber.*, 1965, **98**, 764, 3672; 1966, **99**, 1299; *Angew. Chem., Internat. Edn.*, 1965, **4**, 429; *Tetrahedron Letters*, 1966, 2033; G. Koltzenburg, P. G. Fuss, and J. Leitich, *ibid.*, p. 3409.

[2] E. Vogel, R. Erb, G. Lenz, and A. A. Bothner-by, *Annalen*, 1965, **682**, 1.

[3] W. G. Dauben and R. L. Cargill, *Tetrahedron*, 1961, **12**, 186; O. L. Chapman, D. J. Pasto, G. W. Borden, and A. A. Criswold, *J. Amer. Chem. Soc.*, 1962, **84**, 1220.

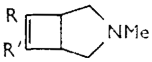
[4] G. J. Fonken, *Chem. and Ind.*, 1961, 1575.

[5] R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, 1965, **87**, 395.

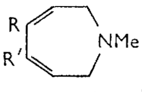
[6] K. Hafner and C. Konig, *Angew. Chem., Internat. Edn.*, 1963, **2**, 96.

[7] K. Hafner *et al.*, *Angew. Chem., Internat. Edn.*, 1964, **3**, 165; *Tetrahedron Letters*, 1964, 1733; M. Appl and R. Huisgen, *Chem. Ber.*, 1958, **91**, 12.

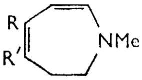
hydrogenolysis of the *N*-methylazepine (X) in methanolic solution causes the formation of dimethyl 2,3-dimethylterephthalate and methylamine.[8] Moreover, when *N*-ethoxycarbonylazepine was heated it yielded phenylurethane.[9]



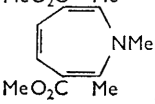
(VII)



(VIII)



(IX)



(X)

EXPERIMENTAL

Ultraviolet spectra were determined on ethanolic solutions with a Unicam SP 700 instrument, and infrared spectra (only main max. quoted) were measured with a Unicam SP 100 instrument (carbon tetrachloride solutions). N.m.r. spectra were measured on a Perkin-Elmer R 10 spectrometer operating at 60 Mc./sec. Melting points were taken on a Kofler block. Irradiations were carried out with a Hanovia 400 w medium pressure lamp with a Pyrex filter and water-cooling. The solution to be irradiated was placed about 2 cm. from the light source. The Perkin-Elmer 800 gas chromatograph was used with a 15 ft. × 1/8 in. column with a packing of silicone oil, DC 710 (5—8%) on Chromosorb W (80—100 mesh) treated with 5% methanolic sodium hydroxide. Pyrolyses of the 3-azabicyclo[3,2,0]hept-6-ene derivatives were conducted in a nitrogen atmosphere in a tube (45 × 2 cm.) packed with calcium oxide pellets (0·4 cm. diam.). The sample was injected with a hypodermic needle through a rubber cap, and it passed through a preheater (18 × 2 cm.) at 350° before it reached the furnace.

N-*Methylmaleimide*.—Maleic anhydride (100 g.) was dissolved in the minimum quantity of dry benzene, and anhydrous methylamine was passed through the solution. The precipitate was separated from the benzene frequently, dried, and distilled rapidly *in vacuo* in small batches (*ca.* 25 g.). The distillate solidified and was further purified either by recrystallisation from ether or sublimation at 80°/15 mm., to give *N*-methylmaleimide (*ca.* 50 g., 44%), m. p. 90—92° (lit.,[10] 90—92°).

6,6,7-*Trichloro*-3-*methyl*-3-*azabicyclo*[3,2,0]*heptane*-2,4-*dione*.—*N*-Methylmaleimide (6 g.) and benzophenone (3 g.) were dissolved in oxygen-free trichloroethylene (250 ml.) and irradiated at 20° for 36 hr., with stirring. The reaction mixture was filtered to remove any polymers, and the filtrate evaporated *in vacuo*, to give a brown residue. The addition of ether (50 ml.) caused the *product* to be precipitated, and this was separated and washed with ether. Cooling of the ether solution to 0° for several hours gave more of the product. Crystallisation of the combined solids from chloroform gave prisms (4 g., 31%), m. p. 168—170° (Found: C, 34·7; H, 2·6; N, 5·55. $C_7H_6Cl_3NO_2$ requires C, 34·6; H, 2·5; N, 5·75%), $\nu_{max.}$ (KBr) 1703, 1766, 1779 cm.$^{-1}$. N.m.r. spectrum ($CHCl_3$) showed resonances at τ 6·93 (s; *N*-methyl) and an AMX system for the cyclobutane protons at 6·52, [q; C-1 proton, (X)]; 5·93, [q; C-5 proton; (M)], and 5·24 [q; C-7 proton (A)] with J_{AM} = 1·5, J_{MX} = 7·5, and J_{AX} = 5·0 c./sec.

6-*Chloro*-3-*methyl*-3-*azabicyclo*[3,2,0]*hept*-6-*ene*-2,4-*dione*.—(*a*) The foregoing trichloro-derivative (1 g.) and powdered zinc (1 g.) were heated under reflux in 1,2-dimethoxyethane (20 ml.) for 6 hr. The inorganic residue was separated and washed with more solvent, the washings being combined with the filtrate. Removal of the solvent from the filtrate *in vacuo* gave an oil that crystallised on standing. Sublimation at 50°/0·1 mm. on to a probe at −25° gave the microcrystalline *product* (0·57 g., 80%), m. p. 81·5—82·5° (Found: C, 48·6; H, 3·8; Cl, 20·5; N, 8·1. $C_7H_6ClNO_2$ requires C, 49·0; H, 3·5; Cl, 20·7; N, 8·15%), $\lambda_{max.}$ 203, 242 mμ (ε 14,300, 671), λ_{infl} 216 mμ (ε 216), $\nu_{max.}$ (KBr) 1767, 1732, 1707, 1700, 1694, 1634, 1605, 1584 cm.$^{-1}$. N.m.r. spectrum (acetone) showed resonances at 7·15 (s; *N*-methyl) and an AMX system for the cyclobutene protons at τ 6·22 (q; C-1 proton, X); 5·96 (d; C-5 proton, M), and 3·59 (d; C-7 proton, A) with J_{AM} = 0, J_{MX} = 3, and J_{AX} = 1·25 c./sec.

(*b*) The trichloro-derivative (500 mg.; above) was slowly sublimed at 180°/0·1 mm. through zinc dust in a glass tube. The sublimate crystallised to a colourless solid (250 mg., 71%), m. p. 80—81°, identical with the material obtained from the preceding reaction.

6-*Chloro*-3-*methyl*-3-*azabicyclo*[3,2,0]*hept*-6-*ene*.—The monochlorocyclobutene derivative (400 mg.; above) was extracted (Soxhlet) into a solution of lithium aluminium hydride (400 mg.) in dry ether (40 ml.) during 2 hr. A saturated aqueous solution of potassium sodium tartrate (20 ml.) was added, and the organic material extracted into ether (5 × 25 ml.). The ether extract was dried over magnesium sulphate, and the ether carefully removed at 15° *in vacuo*. The resulting oil was distilled 150° (bath)/60 mm., to yield a colourless liquid (170 mg., 50%), $\nu_{max.}$ 1588 cm.$^{-1}$. N.m.r. spectrum ($CDCl_3$) showed resonances at 8—8·4 (multiplet; C-1 and C-5 protons); 7·6 (s; *N*-methyl); 6·4—7·2 (complex; C-2 and C-4 protons), and 4·16 τ (s; C-7 proton); *picrate*, m. p. 157—158° (Found: C, 41·6; H, 3·4; Cl, 9·75; N, 14·6. $C_{13}H_{13}ClN_4O_7$ requires C, 41·8; H, 3·5; Cl, 9·5; N, 15·0%). The product, on standing in air, slowly deposited a brown solid.

6,7-*Diethyl*-3-*methyl*-3-*azabicyclo*[3,2,0]*hept*-6-*ene*-2,4-*dione*.—Hex-3-yne (20 g.), *N*-methylmaleimide (13·5 g.), and benzophenone (5·5 g.) were dissolved in dioxan (oxygen- and peroxide-free; 200 ml.) and irradiated for 36 hr. while nitrogen was passed through the solution. The dioxan was removed *in vacuo* and the residue fractionated. The *product* distilled at 100°/4 mm. as a thick oil (15 g., 43%) (Found: C, 68·0; H, 7·85; N, 7·55. $C_{11}H_{15}NO_2$ requires C, 68·4; H, 7·95; N, 7·25%), $\nu_{max.}$ (film) 1770, 1710 cm.$^{-1}$. N.m.r. spectrum ($CDCl_3$) showed resonances at τ 8·91 (t; J = 8 c./sec., *C*-methyls); 7·80 (q; J = 8 c./sec., methylene protons) 7·12 (s; *N*-methyl), and 6·53 (s; bridge protons).

6,7-*Diethyl*-3-*methyl*-3-*azabicyclo*[3,2,0]*hept*-6-*ene*.—The foregoing bicycloheptenedione (2 ml.) dissolved in dry ether (10 ml.) was added slowly to lithium aluminium hydride (2 g.) in refluxing ether (50 ml.), and heating continued for 3 hr. A saturated aqueous solution of potassium sodium tartrate (50 ml.) was added, and the organic material extracted into ether (5 × 25 ml.). The extract was dried over magnesium sulphate, and the ether removed at room temperature *in vacuo*. The *liquid* was distilled at 100°/30 mm. (*ca.* 1·2 g., 70%) (Found: C, 80·0; H, 11·5; N, 8·55.

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[8] R. F. Childs, R. Grigg, and A. W. Johnson, *J. Chem. Soc.* (*C*), 1967, 201,

[9] W. Lwowski, T. J. Maricich, and T. W. Mattingly, *J. Amer. Chem. Soc.*, 1963, **85**, 1202.

[10] E. Giustiniani, *Gazetta*, 1892, **22**, 169.

$C_{11}H_{19}N$ requires C, 79·9; H, 11·7; N, 8·45%), ν (film) no absorption between 1500 and 1800 cm.$^{-1}$. The n.m.r. spectrum showed resonances at τ 9·0 (t; J = 8 c./sec., *C*-methyl): 7·97 (q; J = 8 c./sec., methylene protons of ethyl groups), and 7·74 (s; *N*-methyl). The C-1 and C-5 protons occurred as a multiplet at 8·34 and the C-2 and C-4 protons as a multiplet centred at τ 7·15.

6-*n-Butyl*-3-*methyl*-3-*azabicyclo*[3,2,0]*hept*-6-*ene*-2,4-*dione*.—Hex-1-yne (20 ml.), *N*-methylmaleimide (11 g.), and benzophenone (2 g.) were dissolved in tetrahydrofuran (oxygen- and peroxide-free; 250 ml.) and irradiated for 48 hr. After removal of the solvent, the residual oil was distilled, and the fraction, b. p. 100—120°/0·2 mm., collected This was chromatographed on silica, benzophenone being eluted with benzene, and the *product* (6 g., 31%) with ether (Found: C, 68·3; H, 8·0. $C_{11}H_{15}NO_2$ requires C, 68·35; H, 7·8%), ν (film) 1771, 1705, 1698infl. cm.$^{-1}$. The n.m.r. spectrum ($CDCl_3$) showed max. at τ 9·08 (t; *C*-methyl), 8·5 (multiplet; $CH_2{\cdot}CH_2$), 7·8 (multiplet; $=C{\cdot}CH_2$), 7·02 (s; *N*-methyl), 6·28 (multiplet; C-1 and C-5 protons), and 3·83 (multiplet, C-7 proton).

Thermal Rearrangement of 6,7-*Diethyl*-3-*methyl*-3-*azabicyclo*[3,2,0]*hept*-6-*ene*.—The bicycloheptene (above) was slowly dropped (*ca.* 1 ml./30 min.) into the apparatus with the furnace at 520°. The products were collected by passing the gas stream through a trap filled with glass beads at 0° and then through a further trap cooled in liquid air. The fraction collected at 0° was dissolved in ether and extracted with dilute hydrochloric acid, sodium hydrogen carbonate solution, and water, and the remaining ether solution dried over magnesium sulphate. Removal of the ether *in vacuo* gave an oil that was distilled at 100° (bath)/20 mm., to give a compound that was identical with *o*-diethylbenzene (identical retention times on silicone oil and Carbowax g.l.c. columns of authentic and rearranged material, and superimposable n.m.r. spectra). The yield of *o*-diethylbenzene varied with fluctuations in the experimental conditions but was of the order of 80% of the crude material obtained in the trap at 0°.

The condensate in the liquid-air trap was slowly allowed to warm to room temperature, and the gases produced were bubbled through a saturated solution of picric acid in ethyl acetate. The precipitate formed was filtered off, washed, and crystallised from dry ethanol, to give methylamine picrate, m. p. and mixed m. p. 205—208°.

Thermal Rearrangement of 6-*n-Butyl*-3-*methyl*-3-*azabicyclo*-[3,2,0]*hept*-6-*ene*.— 6-n-Butyl-3-methyl-3-azabicyclo[3,2,0]-hept-6-ene-2,4-dione (IV; R = Bu^n, R′ = H) (above; 2 ml.) was reduced with lithium aluminium hydride as for the diethyl analogue (above). Distillation of the product at 160—170° (bath)/100 mm. gave a colourless oil (*ca.* 1 g.), ν (film) 1631 cm.$^{-1}$. The n.m.r. spectrum ($CDCl_3$) showed max. at τ about 9·08, 8·6, and 8·0 (multiplets of butyl group), 7·59 (s; *N*-methyl), 7·0 (multiplet; $N{-}CH_2$ groups), and 4·22 (broad s; olefinic proton).

This product was dropped (1 ml./hr.) into the furnace heated to 480°, and the products were collected at −60°. These consisted largely of n-butylbenzene (*ca.* 70%) identified by direct comparison with an authentic specimen on a silicone oil g.l.c. column; also, the infrared spectrum of the product was identical with that of an authentic specimen.

Thermal Rearrangement of 6-*Chloro*-3-*methyl*-3-*azabicyclo*-[3,2,0]*hept*-6-*ene*.—The chlorobicycloheptene (above) was dropped (1 ml./hr.) into the apparatus (furnace 500°), and the products were collected in a "dry-ice"–acetone trap. G.l.c. showed no chlorobenzene to be present, but about 5% of *N*-methylaniline (identical retention times of this and authentic material on silicone oil and Carbowax columns). The major product was partially purified by distillation at 80° (bath)/30 mm., but polymerisation prevented isolation. The ultraviolet absorption of the crude product showed max. at 305 mμ.

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