

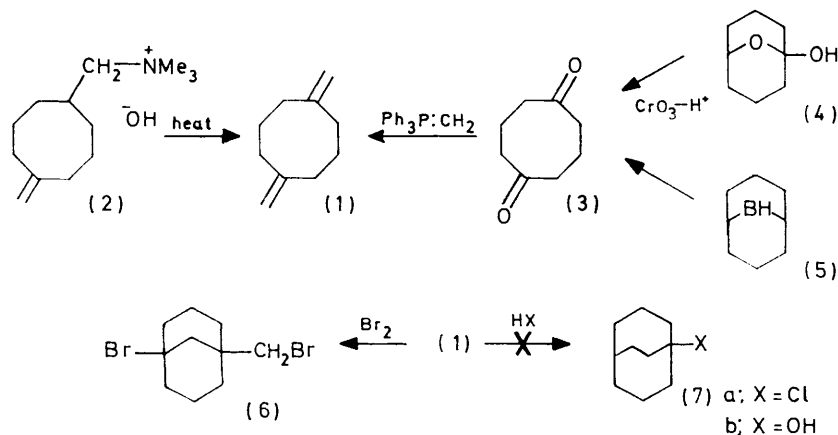
Transannular Addition to 1,5-Dimethylenecyclo-octane

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Improved preparations of cyclo-octane-1,5-dione and 1,5-dimethylenecyclo-octane are described. The diene reacts with bromine and strong acids to give 1,5-disubstituted derivatives of bicyclo[3.3.1]nonane in high yield; contrary to an earlier report, the bicyclo[3.3.2]decane skeleton is not formed in the latter case.

IN connection with other work¹ a convenient source of 1,5-dimethylenecyclo-octane (1) was required, this material previously having been available only *via* an involved synthetic sequence terminating in pyrolysis of the ammonium salt (2).² This objective was simply achieved by a Wittig reaction with cyclo-octane-1,5-dione

the hemiacetal (4)^{4,5} or 9-borabicyclo[3.3.1]nonane (5) can be converted into (3) by Jones oxidation.⁵ The borane has previously been oxidised to *cis*-cyclo-octane-1,5-diol⁶ and to the hemiacetal (4),⁷ so as the borane and the diol are now commercially available this route is generally the more suitable.



(3) which produced a diene identical with that formed by the previous method. The dione precursor was itself prepared in two ways. 5-Hydroxycyclo-octanone³ [which has recently been shown to exist preferentially as

In the earlier investigation² it was found that 1,5-dimethylenecyclo-octane (1) underwent addition reactions with certain reagents to produce bicyclic products, for example with bromine to give 1-bromo-5-bromomethylbicyclo[3.3.1]nonane (6). In apparent contrast, reaction with a mixture of hydrochloric and acetic acids followed by basic work-up gave compounds formulated

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¹ C. R. Eck, W. Parker, and C. I. F. Watt, unpublished data.

² K. H. Bagdaley, W. H. Evans, S. H. Graham, D. A. Jonas, and D. H. Jones, *Tetrahedron*, 1968, **24**, 3445.

³ (a) Badische Anilin- und Soda-Fabrik Akt-Ges., H. Moell, and O. Schlichting, *Ger. P.*, 1,029,368 (*Chem. Abs.*, 1960, **54** P10,901f); (b) Badische Anilin- und Soda-Fabrik Akt-Ges., B.P. 823,007 (*Chem. Abs.*, 1960, **54**, P8675e); (c) H. Moell and F. Urbanek, 'Festschr. Carl Wurster zum 60 Geburtstag,' 1960, 91 (*Chem. Abs.*, 1962, **56**, 9992e).

⁴ C. Ganter, and J.-F. Moser, *Helv. Chim. Acta*, 1969, **52**, 725.

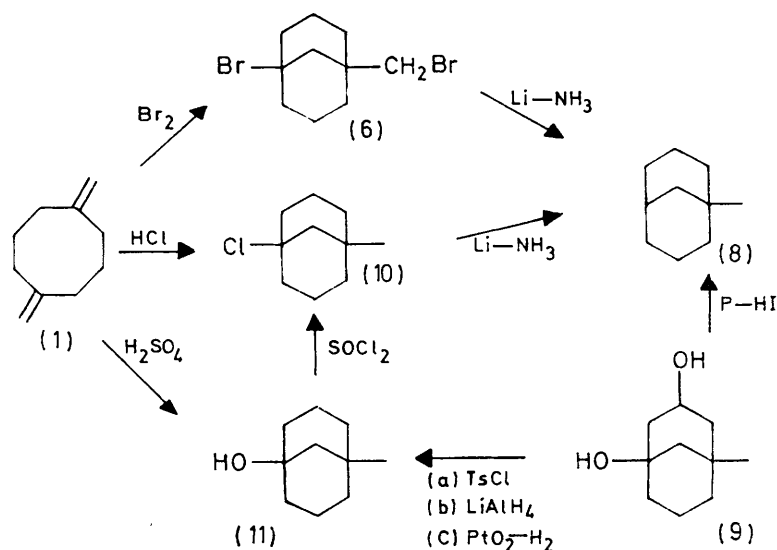
⁵ G. I. Glover, R. B. Smith, and H. Rapoport, *J. Amer. Chem. Soc.*, 1965, **87**, 2003.

⁶ E. F. Knights and H. C. Brown, *J. Amer. Chem. Soc.*, 1968, **90**, 5280.

⁷ C. B. Quinn and J. R. Wiseman, *J. Amer. Chem. Soc.*, 1973, **95**, 1342.

as 1-chlorobicyclo[3.3.2]decane (7a) and bicyclo[3.3.2]-decan-1-ol (7b). However, when these two compounds were later prepared unambiguously by bridgehead functionalisation of bicyclo[3.3.2]decane⁸ it was clear that they were different from the earlier substances.⁹ The improved availability of the diene (1) has now enabled a further study to be made of these transannular addition reactions.

Treatment of (1) with bromine gave a product whose characteristics agreed with the previously proposed structure (6). A sample was reduced with lithium-liquid ammonia to 1-methylbicyclo[3.3.1]nonane (8), thereby confirming the formation of the bicyclo[3.3.1]nonane skeleton in the addition reaction. Compound (8) was



identical with an authentic sample produced by reduction with red phosphorus-hydroiodic acid of 1-methylbicyclo[3.3.1]nonane-3,5-diol (9).¹⁰

When the diene (1) was treated with hydrochloric and acetic acids as described previously,² a chloride and an alcohol were formed whose characteristics corresponded in all respects except n.m.r. spectra with those of the compounds reported earlier. These products were identified as 1-chloro-5-methylbicyclo[3.3.1]nonane (10) and 5-methylbicyclo[3.3.1]nonan-1-ol (11).¹¹ They could be produced more efficiently by treating (1) with concentrated hydrochloric acid or 50% sulphuric acid, respectively, at room temperature (yields 83 and 88%).

The structural assignment was confirmed by two methods. First, the chloride (10) was reduced by lithium-liquid ammonia to 1-methylbicyclo[3.3.1]nonane (8), identical with the authentic sample. Secondly, both (10) and (11) were synthesised by an independent route. Conversion of 1-methylbicyclo[3.3.1]nonane-3,5-diol (9)¹⁰ into the monotosylate followed by successive reduc-

tions with lithium aluminium hydride and hydrogen (catalytic) gave 5-methylbicyclo[3.3.1]nonan-1-ol, which on treatment with thionyl chloride yielded 1-chloro-5-methylbicyclo[3.3.1]nonane. These compounds were identical with the samples formed from reactions of the diene with the two acids.

The only significant difference between the data found in the present work and those reported earlier for the two compounds was in their n.m.r. spectra. Both adducts (10) and (11) clearly showed methyl singlets at τ 9.1, a feature missing in the previous spectra, which contained signals at too high a field (up to τ 9.7) for the proposed bicyclo[3.3.2]decane structures. The range of values quoted is compatible with the original spectra being

interpreted by using the strong signal as internal reference.

Oxidative cyclisation of 5-(1-hydroxyethyl)cyclo-octanone followed by Cagliotti reduction was originally thought to provide an independent route to the bicyclic alcohol product,² but consideration of the mechanism of the acid-catalysed aldol condensation¹² makes it improbable that the product is a derivative of bicyclo[3.3.1]nonane.

These present results show that there is no disparity between the behaviour of (1) with bromine and with strong acid. In both cases transannular reaction between the intermediate cation and the remaining olefinic bond results in efficient formation of 1,5-disubstituted derivatives of bicyclo[3.3.1]nonane. Related transannular reactions in medium-sized rings are well documented,¹³ and in particular this behaviour is directly paralleled by the closures of 3,7-dimethylenecyclo[3.3.1]nonane (12)¹⁴ and 1,3,5,7-tetramethylenecyclo-octane (13)¹⁵ to derivatives of adamantane. In common with these, the

⁸ R. C. Bingham and P. v. R. Schleyer, *J. Org. Chem.*, 1971, **36**, 1198.

⁹ Ref. 8; footnote 12.

¹⁰ P. Rabe, *Ber.*, 1904, **37**, 1671.

¹¹ S. H. Graham and D. A. Jonas, *J. Chem. Soc. (C)*, 1969, 188.

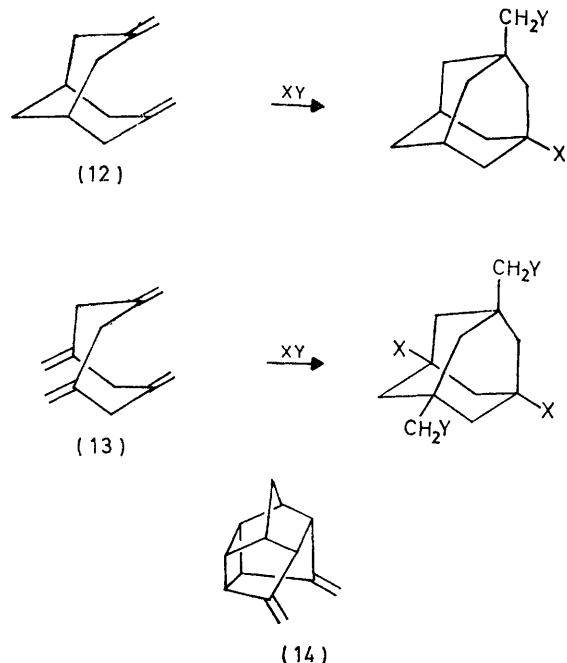
¹² A. T. Nielson and W. J. Houlihan, *Org. Reactions*, 1968, **16**, 1.

¹³ A. C. Cope, M. M. Martin, and M. A. McKerverve, *Quart. Rev.*, 1966, **20**, 119.

¹⁴ H. Stetter and J. Gärtner, *Chem. Ber.*, 1966, **99**, 925.

¹⁵ F. N. Stepanov, V. D. Sukhoverkhov, V. F. Baklan, and A. G. Yurchenko, *J. Org. Chem. (U.S.S.R.)*, 1970, **6**, 887.

transannular addition to (1) is of synthetic utility, and the thermodynamically favoured ring skeleton is formed.



In comparing 1,5-dimethylenecyclo-octane and these other 1,5-dienes it is worth clarifying literature reports on a further feature of their chemical reactivity. It has been reported that (13) undergoes transannular 1,7-addition of tetracyanoethylene (TCNE) to give a [4.3.3]-propellane derivative,¹⁶ but that in contrast the diene (1) failed to undergo a similar process.² This latter observation has been confirmed in the present study, for although a red complex is readily formed no crystalline adduct was produced under the conditions reported for reaction of (13). This apparent anomaly is explicable by the work of Stepanov *et al.*,¹⁵ who have found that samples of (13) prepared by fragmentation of 1,3-dibromo-5,7-bisbromomethyladamantane likewise do not react with TCNE. It has been suggested that the allene tetramer originally assigned^{16,17} structure (13) is probably an isomer containing a conjugated diene system; either the 1,2,4,6-¹⁷ or the 1,3,4,6-tetramethylenecyclo-octane.¹⁵

This failure of non-conjugated 1,5-dimethylenes such as (1) and (13) to undergo the thermal symmetry-allowed [$\pi 2_s + \pi 2_s + \pi 2_s$] reaction¹⁸ with TCNE is furthermore shared by the cage diene (14), for which interaction between the olefinic groups has been demonstrated by photoelectron spectroscopy.¹⁹ The possibility of related interactions between the non-conjugated π -electron systems of (1) is under investigation.

EXPERIMENTAL

¹H N.m.r. spectra were recorded for solutions in carbon tetrachloride at 60 MHz with a Perkin-Elmer R10 instru-

¹⁶ J. K. Williams and R. E. Benson, *J. Amer. Chem. Soc.*, 1962, **84**, 1257.

¹⁷ R. E. Benson and R. V. Lindsey, jun., *J. Amer. Chem. Soc.*, 1959, **81**, 4247; see footnote 2.

ment (tetramethylsilane as internal standard). Analytical g.l.c. was carried out on a Perkin-Elmer F11 instrument (6 ft \times $\frac{1}{8}$ in column of 5% FFAP on Chromosorb G and N₂ at 10 lb in⁻²). For preparative g.l.c. an Autoprep A-700 instrument (12 ft \times $\frac{3}{8}$ in 10% Carbowax column) was used.

Cyclo-octane-1,5-dione (3).⁵—This was prepared by Jones oxidation below 10° of 9-oxabicyclo[3.3.1]nonan-1-ol (4)^{3,4} (83% yield) or of 9-borabicyclo[3.3.1]nonane (5).⁶

1,5-Dimethylenecyclo-octane (1).—(a) Methyltriphenylphosphonium bromide (26.8 g, 0.075 mol) was stirred in dry dioxan (100 ml) under nitrogen, then *n*-butyl-lithium solution (0.075 mol) was injected through a septum cap and stirring was continued for 2 h. Cyclo-octane-1,5-dione (4.2 g, 0.03 mol) was added, then the mixture was refluxed for 40 h, cooled, and thoroughly extracted with water and ether. The combined ethereal extracts were dried (MgSO₄) and the bulk of the ether and dioxan were distilled off at atmospheric pressure. The last few ml of solution were eluted with petroleum through a short column of basic alumina to remove the remaining triphenylphosphine oxide. Distillation was continued to give a fore-run of solvents, then 1,5-dimethylenecyclo-octane (1) (1.74 g, 42%), b.p. 172–175° at 1 atm. G.l.c. (FFAP; 90°) showed one peak, *t*_R 13.8 min (Found: C, 88.4; H, 11.8. Calc. for C₁₀H₁₆: C, 88.2; H, 11.8%); *n*_D²⁵ 1.4819 (lit.,² 1.4819); *v*_{max.} (film) 3073, 2980, 2930, 2860, 1639, 1467, 1445, 885, and 875 cm⁻¹; τ 5.27 (4H, s), 7.6–7.95 (8H, m), and 7.95–8.4 (4H, m). The diene polymerises to a transparent solid if left in air for a long period.

(b) A Hofmann elimination reaction of the ammonium salt (2)² produced a sample of (1) identical with the above (i.r. and n.m.r. spectroscopy and co-injection g.l.c.).

1-Bromo-5-bromomethylbicyclo[3.3.1]nonane (6).—The diene (1) was treated with bromine in carbon tetrachloride as previously described,² and the product distilled to give compound (6), b.p. 105–106° at 0.3 mmHg. G.l.c. (FFAP; 211°) showed one peak, *t*_R 32.8 min; *n*_D²⁵ 1.5624 (lit.,² 1.5622); *v*_{max.} (film) 3000, 2950, 2860, 1488, 1453, 1240, and 777 cm⁻¹; τ 6.8 (2H, s) and 7.5–8.5 (14H, m).

1-Methylbicyclo[3.3.1]nonane (8).—(a) 1-Methylbicyclo[3.3.1]nonane-3,5-diol (9) was reduced by the red phosphorus-hydroiodic acid method of Rabe¹⁰ to give 1-methylbicyclo[3.3.1]nonane (8), as a liquid. G.l.c. showed one peak, *t*_R 8.8 min (FFAP; 90°); *v*_{max.} (CCl₄) 2990, 2925, 2850, 1484, 1456, and 965 cm⁻¹; τ 7.9–8.8 (15H, m) and 9.2 (3H, s).

(b) 1-Bromo-5-bromomethylbicyclo[3.3.1]nonane (0.25 g) in *t*-butyl alcohol (1 ml) was added dropwise with stirring to solution of lithium (0.35 g) in liquid ammonia (30 ml) over 1 h. After stirring for 2 h methanol was added till the blue colour was discharged. After evaporation of the ammonia, the mixture was extracted with water and ether. The combined ethereal extracts were washed with 5*N*-hydrochloric acid and sodium hydrogen carbonate solution, then dried (K₂CO₃). Ether was distilled off carefully, then the residue was purified by preparative g.l.c. (Carbowax; 120°) to give 1-methylbicyclo[3.3.1]nonane (8).

(c) 1-Chloro-5-methylbicyclo[3.3.1]nonane (10) was reduced as described under (b). The samples of (8) prepared by routes (b) and (c) were identical (i.r. and n.m.r. spectra and co-injection g.l.c.) with that produced by route (a).

5-Methylbicyclo[3.3.1]nonan-1-ol (11).—(a) 1,5-Dimethyl-¹⁸ R. B. Woodward and R. Hoffmann, *Angew. Chem. Internat. Edn.*, 1969, **8**, 824.

¹⁹ K. Shen and N. A. Kuebler, *Tetrahedron Letters*, 1973, 2145.

enecyclo-octane (1) was treated with concentrated hydrochloric and glacial acetic acids as previously described,² giving 1-chloro-5-methylbicyclo[3.3.1]nonane (10) and 5-methylbicyclo[3.3.1]nonan-1-ol (11) with g.l.c. (FFAP; 167°) retention times of 7.8 and 12.3 min, respectively. (Any unhydrolysed acetate appeared as a bump on the trailing edge of the alcohol peak). The alcohol (11) had m.p. 72–74° (sublimes >60°; lit.,² 64–65°); ν_{\max} (CCl₄) 3605, 3350, 2995, 2915, 2845, 1488, 1455, 1138, 1063, 1013, and 787 cm⁻¹; τ 7.6 (1H, s, exchanged with D₂O), 8.0–8.9 (14H, m), and 9.1 (3H, s) (lit.,² complex absorption between 8.8 and 9.7).

(b) Tosyl chloride (3.10 g, 0.016 mol) was added at 0° to a solution of 1-methylbicyclo[3.3.1]nonane-3,5-diol (9)¹⁰ (2.72 g, 0.016 mol) in dry pyridine (7 ml) and the mixture was kept at 0° for 38 h before work-up with water and ether. The combined ethereal layers were washed with CuSO₄ solution to remove pyridine, and dried (K₂CO₃). Evaporation gave the 3-tosylate as a viscous oil, ν_{\max} (film) 3380, 3020, 2930, 1597, 1450, 1348, 1173, and 1037 cm⁻¹. The crude hydroxy-tosylate was reduced in the usual manner with lithium aluminium hydride (1.33 g, 0.035 mol) in anhydrous ether (50 ml), with refluxing for 24 h. I.r., n.m.r., and g.l.c. data indicated that a *ca.* 1:1 mixture of the two possible unsaturated alcohols was produced. This mixture in methanol (25 ml) containing Adams catalyst (10 mg) and 60% perchloric acid (4 drops) was stirred under hydrogen at 1 atm till hydrogenation was complete (i.r. and g.l.c.). Filtration through Celite followed by evaporation gave a viscous oil which was purified by column chromatography on basic alumina to give 5-methylbicyclo[3.3.1]nonan-1-ol (11) (1.81 g, 73.6% from the diol) (Found: C, 78.1; H, 11.9. C₁₀H₁₈O requires C, 77.9; H, 11.8%).

(c) Sulphuric acid (50%; 1 ml) was added with stirring to 1,5-dimethylenecyclo-octane (0.10 g). The mixture was

stirred for 2 days at room temperature, then worked up with ether and water. The combined ethereal extracts were washed with aqueous sodium hydrogen carbonate, dried (MgSO₄), and evaporated, and the product was purified as (b) to give (11) (0.10 g, 88%). The three samples of (11) were identical (i.r. and n.m.r. spectroscopy and co-injection g.l.c.).

1-Chloro-5-methylbicyclo[3.3.1]nonane (10).—The chloride was obtained from the reaction of (1) with hydrochloric and acetic acids as described above (Found: C, 69.3; H, 9.9. C₁₀H₁₇Cl requires C, 69.6; H, 9.9%); n_D^{22} 1.4902 (lit.,² 1.4892); ν_{\max} (film) 2995, 2920, 2845, 1487, 1455, 921, and 793 cm⁻¹; τ 7.6–8.9 (14H, m) and 9.1 (3H, s) (lit.,² complex absorption between 8.5 and 9.75).

(b) Thionyl chloride (1.5 ml) was added with stirring to 5-methylbicyclo[3.3.1]nonan-1-ol (11) (0.25 g) synthesised by route (b). When the initial reaction had subsided, the mixture was refluxed for 2 h then cooled. Chips of ice were added cautiously, then the product was extracted with ether, washed (NaHCO₃), and dried (MgSO₄). Evaporation gave (10) (0.23 g); n_D^{22} 1.4902.⁴

(c) 1,5-Dimethylenecyclo-octane (1) (0.41 g, 0.003 mol) was stirred at room temperature and concentrated hydrochloric acid (0.5 ml) was added dropwise. The mixture was stirred for 4 days, then work-up as in (b) gave compound (10) (0.43 g, 83%). The three samples of (10) were identical (i.r. and n.m.r. spectroscopy and co-injection g.l.c.).

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