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THE REACTION OF ISODRIN WITH AZIDES: THE PREPARATION OF SOME NEW DERIVATIVES OF THE BIRDCAGE HYDROCARBON

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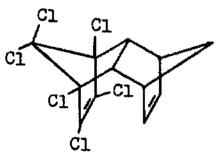
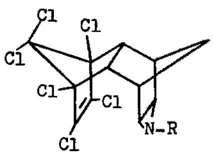
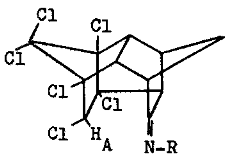
We have been interested in the reactions of isodrin (I) with azides as an approach to the synthesis of 4-amino-1,8,9,10,11,11-hexachlorohexacyclo[6.2.1.1^{3,6}.0^{2,7}.0^{4,10}.0^{5,9}]dodecane (IVb), an amino derivative of the chlorinated birdcage hydrocarbon (1,2). We have found that the reaction of *p*-toluenesulfonyl azide with I gives the aziridine derivative IIa, no intermediate dihydrotriazole being observed. In contrast, *tert*-butyl azidoformate behaves like phenyl azide (3) and gives Vc as the initial product. These observations are in agreement with recent studies of the reactions of related azides with norbornene (4,5,6). Both IIa and Vc undergo a series of transformations, related to those of the epoxide of I (endrin) (3,7,8), leading to the desired caged amine IVb.



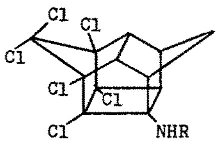
I



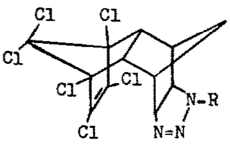
IIa,b,c



IIIa,b,c



IVa,b



Vc

a R = $-SO_2$⌬CH_3
b R = H
c R = $-COOC(CH_3)_3$

A mixture of I and p-toluenesulfonyl azide in boiling carbon tetrachloride evolved nitrogen and gave a 48% yield of IIa (m.p. 240-241.5° dec.; chlorinated C=C stretching at 6.22μ);* no reaction was apparent at room temperature. In hot trifluoroacetic acid IIa was converted in 83% yield to the half-cage ketimine IIIa (m.p. 194-195°; C=N stretching at 6.07μ). When IIIa was heated in fused ammonium acetate at ca. 140°, it was transformed almost quantitatively into the closed cage derivative IVa (m.p. 267-268°; N-H stretching at 2.98μ, aromatic C=C stretching at 6.25μ). Removal of the p-toluenesulfonyl group from IVa with sulfuric acid at 110° yielded 89% of the amine IVb (chars without melting; N-H stretching doublet at 2.90μ, N-H bending at 6.20μ). An alternative route to IVb involved hydrolysis of IIIa with refluxing hydrochloric and acetic acids to give a 94% yield of the hydrochloride of the ketimine IIIb (chars without melting; C=N stretching at 5.85μ), which was converted to IVb in 46% yield in fused ammonium acetate; partial acetylation of the amino group occurred during the latter reaction.

When I was heated on the steam-bath with tert-butyl azidoformate in a little benzene, there was no apparent evolution of nitrogen. The oily product, which was substantially free of both starting materials (only a trace of I on thin layer chromatography and only weak azide bands at 4.60 and 4.70μ), was presumably the crude dihydrotriazole Vc (broad C=O stretching at 5.75μ, chlorinated C=C stretching at 6.24μ). When chromatography on neutral alumina was attempted, Vc decomposed with vigorous gas evolution. Elution of the column with benzene-chloroform gave the crude aziridine IIc (broad C=O stretching at 5.9μ, chlorinated

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* All new crystalline compounds gave satisfactory elemental analyses. IR spectra were taken in Nujol mull for solids and in neat film for liquids.

C=C stretching at 6.24μ) as an oil, which with hydrogen chloride in acetone-ether gave the crystalline hydrochloride of IIb (m.p. 235° dec.; chlorinated C=C stretching at 6.25μ, N-H bending at 6.35μ). The over-all yield of IIb from I was 23%. Treatment of IIb with p-toluenesulfonyl chloride in pyridine gave IIa in 85% yield. Formic acid at room temperature converted crude IIc in 20% yield (based on I) to the half-cage ketimine IIIc (m.p. 172-174° dec.; C=O and C=N stretching at 5.78 and 5.90μ), which with trifluoroacetic acid gave IIIb, isolated as its hydrochloride in 60% yield.

P.m.r. spectra (Varian A-60; in $CDCl_3$ with TMS as internal standard) of the half-cage ketimines IIIa-c showed a clear one-proton signal for the isolated hydrogen H_A. In IIIb (as free base) and in the corresponding half-cage ketone (3), this signal was a sharp spike (δ = 5.50 in IIIb and 5.08 in the ketone). In the butyloxycarbonyl ketimine IIIc, it was slightly broadened (δ = 5.37), and in the p-toluenesulfonyl ketimine IIIa it appeared as two unequal spikes (centered at δ = 4.9) separated by 0.08 p.p.m. We believe that the two peaks in IIIa arise from the two isomers differing in stereochemistry about the C=N bond (9). The spectrum of IIIa was also remarkable in showing two broad humps (centered at δ = 4.5), together equivalent to one proton, 1.2 p.p.m. downfield from the main cage methine proton signal. The latter corresponded to only four protons and we surmise that in each of the isomers of IIIa one of the cage methine protons is unexpectedly deshielded by the p-toluenesulfonyl group. This anomaly was not noted in the other p-toluenesulfonyl derivatives IIa and IVa. P.m.r. spectra of these and all the remaining purified compounds reported were readily interpreted in terms of the proposed structures.

References

1. S. Winstein, Experientia, Supplementum II, 137 (1955).
2. R. E. Lidov and H. Bluestone, U.S. Patent 2,714,617 (1955).
3. S. B. Soloway, A. M. Damiana, J. W. Sims, H. Bluestone and R. E. Lidov, J. Amer. Chem. Soc., **82**, 5377 (1960).
4. J. E. Franz, C. Osuch and M. W. Dietrich, J. Org. Chem., **29**, 2922 (1964).
5. L. H. Zalkow, A. C. Oehlschlager, G. A. Cabat and R. L. Hale, Chem. and Ind., 1556 (1964).
6. P. Scheiner, J. Org. Chem., **30**, 7 (1965).
7. C. W. Bird, R. C. Cookson and E. Crundwell, J. Chem. Soc., 4809 (1961).
8. P. Carter, R. Howe and S. Winstein, J. Amer. Chem. Soc., **87**, 914 (1965).
9. R. W. Layer, Chem. Reviews, **63**, 489 (1963).