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PHOTOLYSIS OF THE TETRAHYDROPYRANYL ETHER OF 3-HYDROXY-2,2,4,4-TETRAMETHYLCYCLOBUTANONE TOSYLHYDRAZONE

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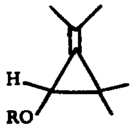
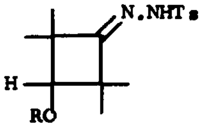
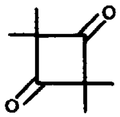
At the time of the proposal[1] (later withdrawn[2]) of structure (I) (R = $-CO\cdot CH_2\cdot CH_3$) for the cockroach sex-attractant we undertook to investigate a method of synthesis very similar to one of those envisaged by Meinwald et al.[3,4] Essentially it involved the photolysis of the sodium salt of the requisite derivative of 3-hydroxy-2,2,4,4-tetramethyl-cyclobutanone tosylhydrazone (II) in the hope that the carbene intermediate of the photolysis would undergo ring contraction[5] to (I).



(I)



(II)

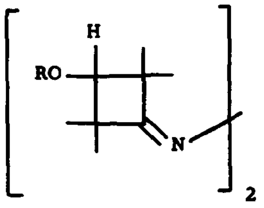


(III)

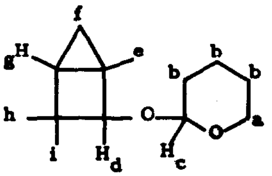
To ascertain whether or not ring contraction would occur with this system, the tetrahydropyranyl ether (II) (R = tetrahydropyranyl) was synthesized and irradiated as the sodium salt.

2,2,4,4-Tetramethylcyclobutan-1,3-dione (III), by reaction with one equivalent of tosylhydrasine[6], was converted to its monotosylhydrazone which was then reduced, conveniently as the crude product, with potassium borohydride to 3-hydroxy-2,2,4,4-tetramethylcyclobutanone tosylhydrazone (II) (R = H) (m.p. 132-3°. Found: C 58.5, H 7.1; $C_{15}H_{22}N_2O_3S$ req. C 58.0, H 7.1). The tosylhydrazone grouping was unaffected during this reduction and also seemed to be quite resistant to refluxing with lithium aluminium hydride in tetrahydrofuran.[7] Reaction of (II) (R = H) with dihydropyran in the presence of p-toluenesulphonic acid[8] followed by purification of the product on alumina gave the tetrahydropyranyl ether (II) (R = tetrahydropyranyl) (m.p. 135-6°. Found: C 61.2, H 7.7, N 7.1; $C_{20}H_{30}N_2O_4S$ req. C 60.9, H 7.7, N 7.1) in 32% overall yield from (III).

Irradiation (Hanovia medium-pressure mercury arc lamp) of the sodium salt of (II) (R = tetrahydropyranyl) (ca. 3% in diglyme) formed in situ with sodium hydride[9], in a quartz vessel purged with nitrogen provided the most clear cut results giving only two products which were easily separated by chromatography on alumina. These were the bistetrahydropyranyl ether of bis[3-hydroxy-2,2,4,4-tetramethylcyclobutyl]azine (IV) (R = tetrahydropyranyl) (homogeneous on thin layer chromatography, m.p. 108-110°. Found: C 69.8, H 10.0, N 6.5; $C_{26}H_{44}N_2O_4$ req. C 69.6, H 9.9, N 6.25; $\nu_{max.}$ 1685 cm.$^{-1}$ (CCl_4)) and the oily tetrahydropyranyl ether of 1,3,3-trimethylbicyclo[2:1:0]pentan-2-ol (V) (homogeneous on thin layer and gas chromatography). The respective yields of these compounds were 48% and 26% after chromatography.



(IV)



(V)

Acid hydrolysis of (IV) (R = tetrahydropyranyl) gave the diol (IV) (R = H) (Found: C 68.4, H 10.0, N 9.6; $C_{16}H_{28}N_2O_2$ req. C 68.5, H 10.1, N 10.0; $\nu_{max.}$ 1676 cm.$^{-1}$ (Nujol)). The NMR spectrum of the diol in $CDCl_3$ showed two singlets at τ 6.26(2H) and τ 8.31(2H) and three peaks at τ 8.68, 8.74 and 8.79(6, 12 and 6H respectively). Each of the four methyl groups on a cyclobutane ring in the diol is in a different molecular environment because of (a) the asymmetry at C-3 and (b) the asymmetry at the unsaturated nitrogen. Thus, the methyl signal in the NMR spectrum probably results from the partial superimposition of two pairs of peaks. By comparison, the methyl signal in the NMR spectrum of 3-hydroxy-2,2,4,4-tetramethylcyclobutan-2-one[+] appears as a simple pair. The lack of a sharp melting point indicates that the diol is a mixture of some of the three possible stereoisomeric forms of

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[+] The tetrahydropyranyl ether of this compound is a product of the irradiation of (II) (R = tetrahydropyranyl) in the presence of sodium methoxide.

the molecule, or that these undergo interconversion near the melting point. Mass spectral examination of the diol confirmed the molecular weight as being 280 as well as showing a strong peak at m/e 140.

The bicyclic product (V), which had no characteristic IR absorptions other than those due to the tetrahydropyranyl ether, showed NMR absorptions centered at τ 5.4 (multiplet, 1H,c),[*] τ 6.38 (complex absorption, 3H, a + d), τ 8.22 (multiplet partially obscured by adjacent absorptions, 1H, g), τ 8.45 (multiplet, 6H, b), τ 8.70 (doublet, 3H, h), τ 8.86 (singlet, 3H, i), τ 9.34 (singlet, 3H, e), τ 9.65 (multiplet, 2H, f).[10] Mass spectral examination revealed only a very weak parent ion at m/e 210, but more intense peaks at m/e 126 (M-84) and m/e 109 (M-101). Rearrangements accompanied by loss of a methyl group afforded strong peaks at m/e 93 and m/e 91. A comparison sample of the tetrahydropyranyl ether of n-butanol gave a weak parent ion at m/e 158 with stronger peaks at m/e 74 (M-84) and m/e 57 (M-101). Both ethers, as expected, showed intense peaks at m/e 85.

As further confirmation of the identity of (V), hydrogenolysis with PtO_2 in acetic acid[11] was shown to give 2,2,5-trimethylcyclopentanol (VI) by mass-spectral and gas-chromatographic comparison of the product on both a 15% Apiezon 'L' and a 15% polyethyleneglycol succinate column with

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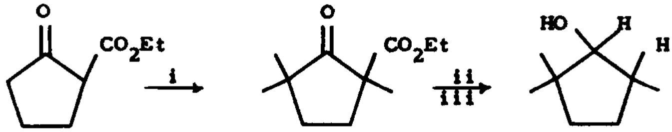
[*] Data in parentheses represent (multiplicity, equivalent number of protons, probable structural assignment of absorption).

an independently synthesised sample of (VI). This latter was prepared, albeit in rather low yield, from 2-carbethoxycyclopentanone[12] (VII) via 2,2,5-trimethylcyclopentanone.



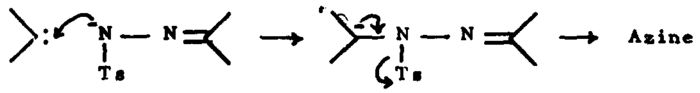
(VII) (VI)

i MeI/NaH ii TsOH/aq.AcOH iii $LiAlH_4$

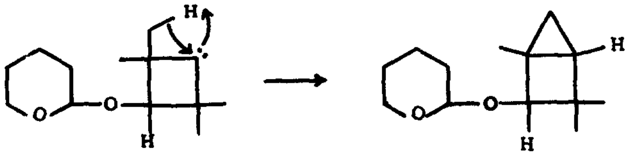
Meinwald[3] has also reported the formation of an azine in his experiments; the azine probably arises by electrophilic attack of the intermediate carbene on the tosylhydrazone sodium salt[13,14] (scheme (a)).

The bicyclopentanol (V) is the product of intramolecular hydrogen abstraction from a methyl group by the carbene (scheme (b)). The alternative process required to form the isopropylidenecyclopropane ether (I) (R = tetrahydropyranyl) (scheme (c)) does not occur in this case, whereas thermolysis of the sodium salt of the tosylhydrazone of 2,2,4,4-tetramethylcyclobutanone[3] does give some isopropylidenecyclopropane amongst other products and the sodium salt of cyclobutanone tosylhydrazone itself[5] gives isopropylidenecyclopropane as the major product. The difference in the case under consideration may be to some extent due to the inductive effect of the ether oxygen.

(a)

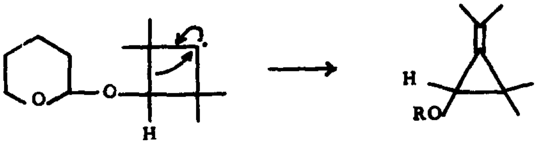


(b)



(V)

(c)



(I)

Irradiation of (II) (R = tetrahydropyranyl) in the presence of sodium methoxide instead of sodium hydride gave a more complex mixture of products which, however, did not appear to contain any (I) (R = tetrahydropyranyl) and evaluation of these materials as well as the products of irradiation of the sodium salt of the free alcohol (II) (R = H) is in progress.

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