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REARRANGEMENTS OF OCTALIN TOSYLATES ADSORBED ON ALUMINA; PART 1, SYNTHESIS OF A SUBSTITUTED BICYCLO[4,4,1]UNDEC-1-ENE

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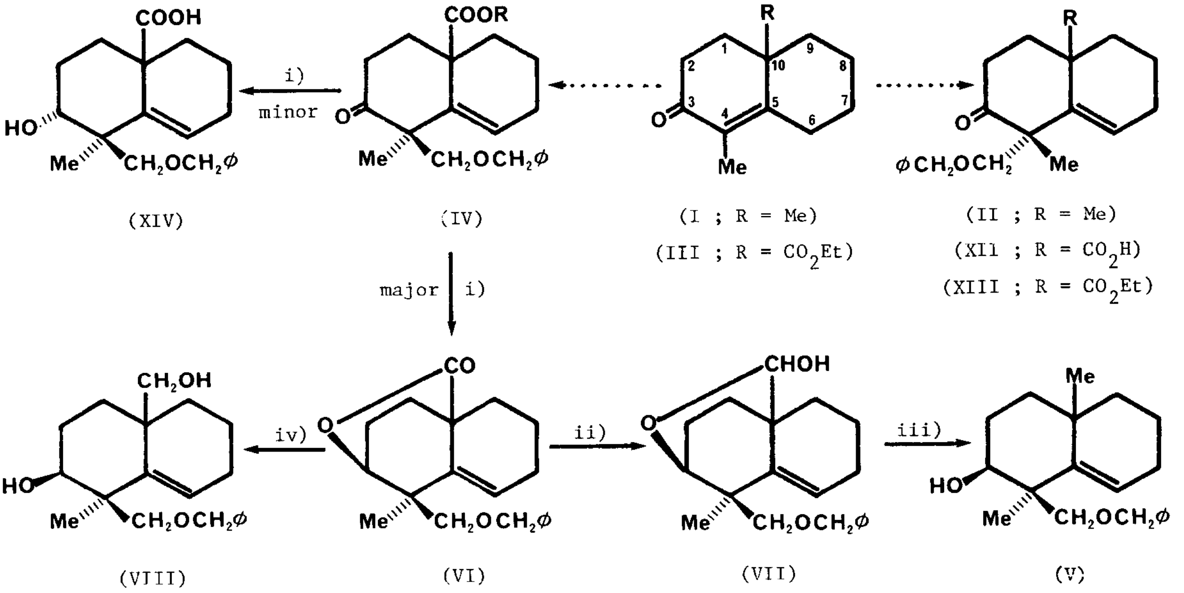
Summary: A unique homoallylic neopentyl rearrangement, observed during liquid chromatography on alumina, leads to an efficient synthesis of a substituted bicyclo[4,4,1]undec-1-ene.

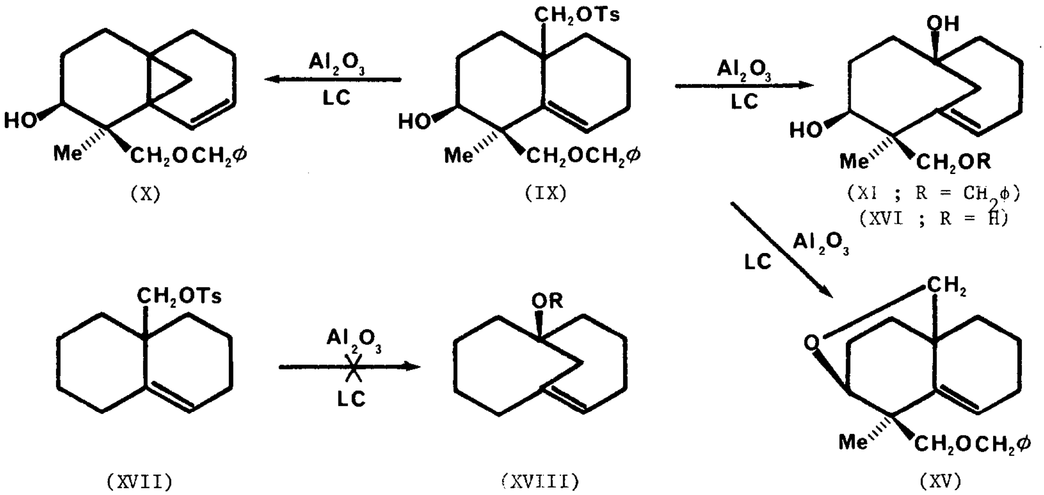
In contrast to the observed 4α-benzyloxymethylation of the octalone (I) to yield (II)[1], benzyloxymethylation of the corresponding ester (III) occurs, presumably with stereoelectronic control, predominantly at the β face to yield (IV; R = Et)[2]. Accordingly, the synthesis, in the angular methylated series, of the 4β-benzyloxymethylated alcohol (V) was accomplished efficiently[3] from the ester (IV; R = Et) *via* the lactone (VI) → lactol (VII) reductive sequence followed by Wolff-Kishner reduction, as shown in Scheme I.



Reagents: i) $NaBH_4$; ii) $LiAl(OEt)_3H$; iii) Wolff-Kishner ; iv) $LiAlH_4$

Scheme I

In connection with another synthetic problem, we have investigated an alternative strategy for converting (IV) into (V), which involves the homoallylic neopentyl tosylate rearrangement of the monotosylate (IX) into the synthetically interesting vinylcyclopropane (X), by analogy with well-documented steroid[4] and octalin[5] chemistry. However, on attempting to purify the monotosylate (IX) by liquid chromatography on alumina[6], we have observed (Scheme II) what is, to our knowledge, the first example of a homoallylic neopentyl tosylate rearrangement[7] to yield a bicyclo[4,4,1]undec-1-ene, namely the diol (XI).

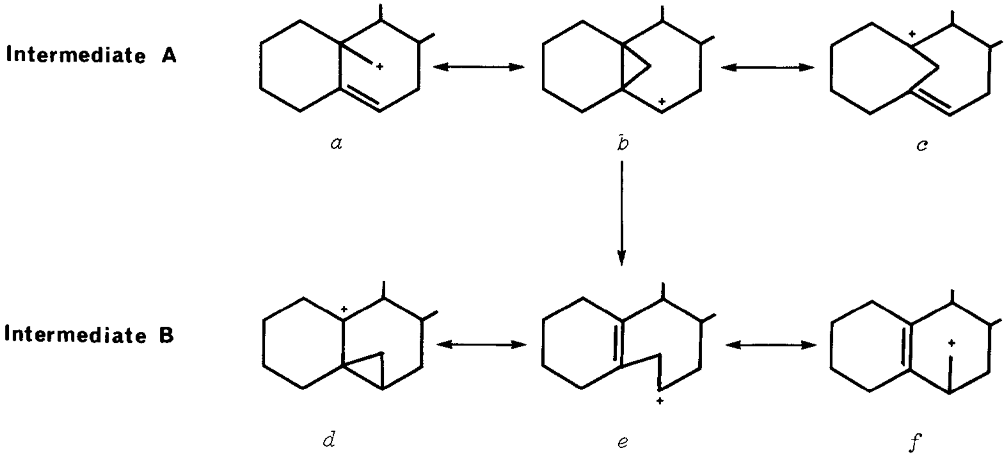


Scheme II

The keto-acids [(XII); m.p. 66°C][8] and [(IV; R = H); m.p. 103.5 - 105°C (lit.[2] m.p. 96°C] were separated by Prep LC of the mixture obtained by hydrolysing the crude esters [(XIII) + (IV; R = Et)] from benzyloxymethylating the octalone (III).[2,3] Sodium borohydride reduction of keto-acid (IV; R = H) gave the known[3] lactone (VI) and a small amount of the 3α-hydroxyacid [(XIV)[8]; m.p. 123°C; (VI):(XIV)/9:1]. Lithium aluminium hydride reduction of (VI) gave the diol (VIII), m.p. 108°C (lit.[2] m.p. 106°C), which was tosylated [TsCl (1.8 mole), anhyd. pyridine, 0°C, 22 hrs.] to produce the monotosylate (IX)[9], contaminated with some presumed ditosylate. Chromatography of this mixture on alumina [Woelm Neutral, Activity I] in benzene,[10] after adsorption for 15 hours, gave:- the ether (XV)[8], 22%,b.p. 145°C/0.02 mm Hg; the vinylcyclopropane (X)[8], 5%, b.p. 165°C/0.7 mm Hg, also characterized as the 3,5-dinitrobenzoate[8], m.p. 124°C; a small amount of starting diol (VIII); and the novel diol (XI)[8], 71%,m.p. 140°C, which was debenzylated (H_2/Pd-C) to the triol (XVI)[8], m.p. 212°C. In contrast, rearrangement of the parent tosylate (XVII) under identical conditions yields no 6-hydroxybicyclo[4,4,1]undec-1-ene (XVIII; R = H).[11] When the homoallylic neopentyl rearrangement of the monotosylate (IX) was carried out in pyridine in the dark,[5a] a poor yield of the mixture (XV):(X):(VIII):(XI)/12:20:15:5 was obtained.

The bicyclo[4,4,1]undec-1-ene structures for (XI) and (XVI) follow from mechanistic considerations and analysis of the ^1H and ^{13}C NMR spectral data,[12] the AB quartet (J = 13 Hz) and the triplet (J = 6 Hz) of the bridging methylene and olefinic protons respectively, being characteristic, apparently,[13] of the bridged bicyclic structures[14] present in (XI) and (XVI).

The mechanism of homoallylic neopentyl tosylate rearrangements has been discussed widely for simple octalin rearrangements[5b] and particularly for rearrangements of 19-hydroxysteroid derivatives.[4] Tadanier[15] considers that the various observed steroidal rearrangement products can arise *via* two resonance stabilized intermediates such as A and B (Scheme III);



Scheme III

products from the former reflect kinetic control and from the latter, thermodynamic control of the rearrangement.[15] Whilst octalin and steroidal tosylates have been observed to rearrange to yield products which, formally, may be considered to arise from the classical carbenium ions *a*,*b*, and *d*-*f*, it is interesting to note that rearrangement products which may be considered to be derived from carbenium ion *c* have not been reported previously in the literature. This, together with our own observations with the unsubstituted octalin tosylate (XVII),[11] might suggest steric and/or electronic participation from the C-3 and C-4 substituents. Presently, we are synthesizing the three diols which are epimeric to (VIII) at C-3/C-4 from the corresponding 3α-hydroxyacid (XIV) and the keto-acid (XII), which we have in hand. We will be reporting on the reactivity of their monotosylate derivatives, adsorbed on alumina, in due course.

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2. F.J. McQuillin and P.L. Simpson, *J. Chem. Soc.*, 1963, 4726.
3. F.J. McQuillin and R.B. Yeats, *J. Chem. Soc.*, 1965, 4273.
4. For example, see J.J. Bonet, H. Wehrli, and K. Schaffner, *Helv. Chim. Acta*, 1962, **45**, 2615; M. Akhtar and D.H.R. Barton, *J. Amer. Chem. Soc.*, 1964, **86**, 1528; J.-L. Borgna and M. Mousseron-Canet, *Bull. Soc. Chim. Fr.*, 1970, 2210, 2218.
5. For example, see a) J.W. Rowe, A. Melera, D. Arigoni, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1957, **40**, 1; b) Y. Hikino and P. de Mayo, *Chem. Comm.*, 1965, 550; c) J.R. Williams and G.M. Sarkisian, *J. Org. Chem.*, 1980, **45**, 5088.
6. For synthetically useful reactions achieved on the surface of alumina, see G.H. Posner, S.S. Okada, K.A. Babiak, K. Miura, and R.K. Rose, *Synthesis*, 1981, 789, and references therein.
7. L.H. Knox, E. Velarde, and A.D. Cross, *J. Amer. Chem. Soc.*, 1965, **87**, 3727, have reported that 19-hydroxyandrost-4-en-3 , 17-dione rearranges into a bicyclo[4,4,1]undecenone using $Et_2N.CF_2.CHFCl$, although Δ^5-19-hydroxysteroids behave differently, see L.H. Knox, E. Velarde, S. Berger, I. Delfin, R. Grezemkovsky, and A.D. Cross, *J. Org. Chem.*, 1965, **30**, 4160. The rearrangement, on alumina, of a benzene solution of 19-tosyloxyandrosta-4,7-diene-3,17-dione has been observed to yield 6β,19-cycloandrosta-4,7-diene-3,17-dione; however, the authors report no corresponding bicyclo[4,4,1]undecenone, P.H. Bentley, M. Todd, W. McCrae, M.L. Maddox, and J.A. Edwards, *Tetrahedron*, 1972, **28**, 1411.
8. All new compounds gave satisfactory ir, nmr, ms, and elemental analyses.
9. This structure is supported spectroscopically but all attempts to isolate an analytically pure sample have failed to date.
10. The benzene was distilled but not otherwise dried; the effect of other solvents is under investigation.
11. C.S. Chan and R.B. Yeats, Rearrangements of Octalin Tosylates Adsorbed on Alumina, Part II, to be submitted for publication.
12. For example, the triol (XVI) shows: - ^1H NMR ($CDCl_3/CD_3OD$, δppm), 5.85 (t, J = 6Hz, 1H), 3.92 and 3.37 (AB, J = 11 Hz, 2H), 3.24 and 3.19 (dd, J = 3, 12 Hz, 1H), 2.59 and 2.41 (AB, J = 13 Hz, 2H) and 1.3 (s, 3H); ^{13}C NMR ($CDCl_3/CD_3OD$, δ ppm, INEPT), 140.5 ($\underline{C}$=), 128.7 ($\underline{C}H$=), 83.5 ($\underline{C}HOH$), 71.1 ($\underline{C}$-OH), 65.2 ($\underline{C}H_2OH$), 47.3 ($-\overset{|}{\underset{|}{\underline{C}}}-$), 44.9, 37.8, 34.6, 28.6, 26.5, and 24.3 (6 × $\underline{C}H_2$), and 21.0 ($\underline{C}H_3$).
13. Unpublished data, S. Thomas and R.B. Yeats. In contrast, all compounds of the octalin type show a triplet, J = 3 Hz, for the olefinic proton.
14. Similar coupling constants and chemical shifts have been reported by D.B. Ledlie, T. Swan, J. Pile, and L. Bowers, *J. Org. Chem.*, 1976, **41**, 419, for the parent hydrocarbon and the methoxy derivative (XVIII; R = Me).
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