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CAMPHOR ENOL AND HOMOENOL ACETATES

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Camphor enol acetate (VI-H) seemed a promising intermediate for the preparation of certain α-substituted camphor derivatives. Attempts to prepare this compound by the usual methods [(a) acetic anhydride and p-toluenesulfonic acid at 138° and at 200°, (b) acetic anhydride and sulfuric acid at 160°, (c) acetic anhydride and boron trifluoride at 138°, (d) isopropenyl acetate and sulfuric acid at 96°, and (e) acetyl chloride at 52°] gave recovered camphor and no evidence for the formation of any acetylation product.

Therefore, resort was had to the previously described preparation of camphor enol acetate by the lead tetraacetate or tetrapropionate oxidation of tricyclene (I) and camphene (III). Repetition of this reaction according to the published procedure (2) with tricyclene gave a crude product (45% yield) showing two major GLC peaks of retention times 2.90 min. (A, ~85%) and 5.40 min. (B, ~15%).† The less polar, lower-boiling component A could be separated from B in a state of 90-95% purity by fractional distillation,

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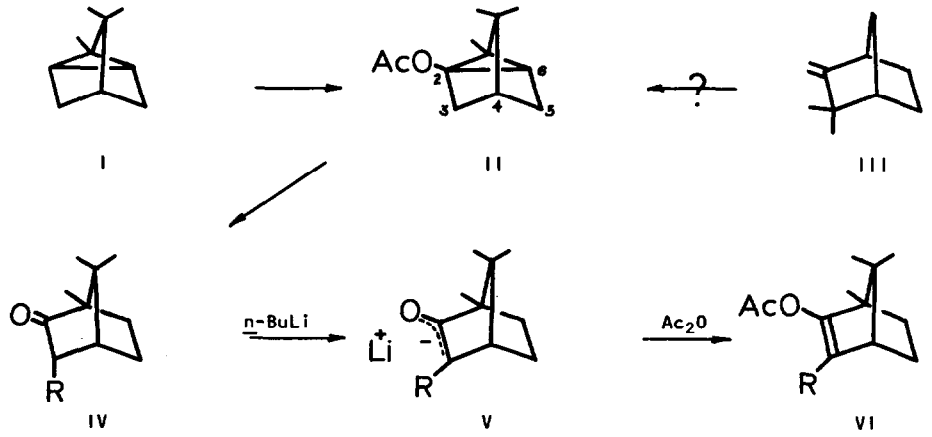
b.p. 62-64° (9.5 mm.) as described by Heya (2) or by chromatography on neutral alumina. A pure sample of A , $C_{12}H_{18}O_2$,[§§] for spectral analysis was obtained by preparative GLC on a 2-m. column of 1% butanediol succinate on siliconized Chromosorb P at 150°. Methanolic potassium hydroxide converted A into camphor (IV-H), which reaction had been used by the Japanese workers (1,2) as the basis for assignment of the enol acetate structure VI-H to their compound. However, A exhibits no vinyl hydrogen absorption in its NMR spectrum (Fig. 1a). The hydrolysis to camphor and the combined evidence of the NMR spectrum (3 quaternary methyl groups), the infrared spectrum $\nu_{max}^{CS_2}$ 3055 (Δ-H), 1750 (ester C=O), and 1225 $cm.^{-1}$ (C-O-C), and the ultraviolet spectrum (ε_{210}^{EtOH} 360) show clearly that A is not VI-H but instead the hitherto unrecognized camphor 2,6-homoenol acetate (II) which on saponification reverts mainly to camphor via the homoenol II (OH for OAc) (cf. ref. 3).[§] The ready availability of camphor 2,6-homoenol acetate from a convenient one-step synthesis should be of interest in current studies of homoenolization phenomena (3b); comment on its mode of formation is reserved until later except to note that in our hands lead tetraacetate oxidation of camphene free from I gave a crude product which contained not more than 1-2%, if any, of II.



In formulas IV, V and VI, R=H, Cℓ, or Br.

† A 2-m. column of 1% butanediol succinate on Chromosorb P at 130° was used.

§ The formal possibility that A is the homoenol acetate with a C_2-C_4 bond instead is excluded by the fact that methanolysis of A in methanol-O-d_1, with sodium methoxide produces camphor which has a proton at C_4 that can be seen in the NMR spectrum of the derived camphorquinone.

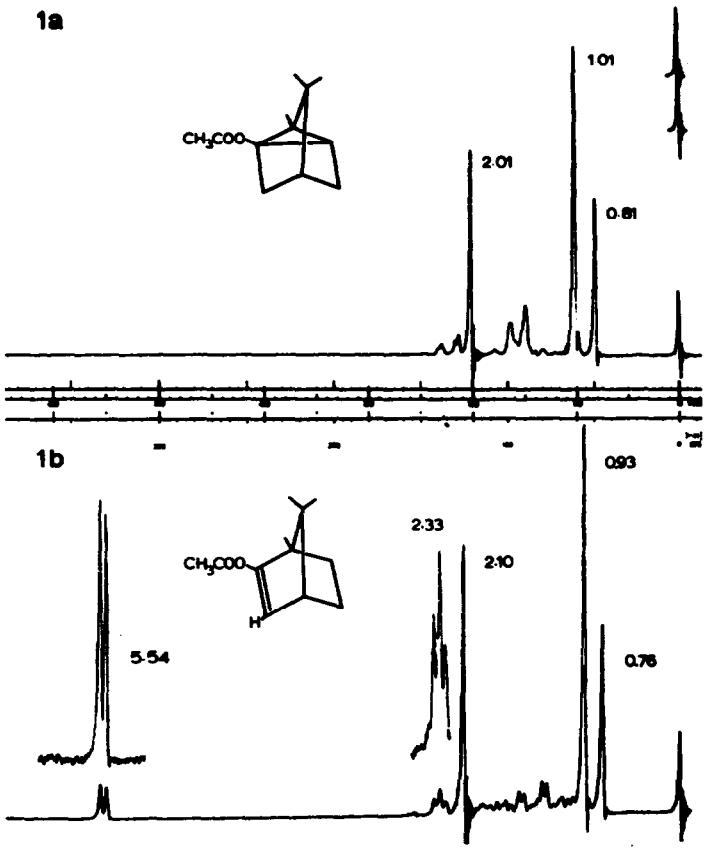


Fig. 1. NMR Spectra of Camphor Homoenol and Enol Acetates in $CDCl_3$ at 60 Mc/s.

These frustrations in achieving the original goal forced consideration of other, at first thought less promising, approaches. Although it has been reported that camphor undergoes carbonyl addition with Grignard reagents (4,5), methyllithium (5) and phenyllithium (6), there is also extensive enolization with several of these reagents. We now find that with the somewhat stronger base n-butyllithium at room temperature the relative rate of α-proton abstraction to carbonyl addition in IV-H has increased to the point of exclusion of any addition. In fact, this is the best method we have found in which to generate camphor enolate anion quantitatively. Moreover, acylation of the camphor lithium enolate V-H so formed with acetic anhydride at -50° gives only

O-acylation with no amount of C-acylation detectable in the NMR spectrum of the crude product (cf. ref. 7)[¶]. Thus, addition of a solution of 64 mmoles of n-butyllithium (Foote Mineral Co.) to 7.7 g. (50 mmoles) of (+) camphor dissolved in 200 ml. of dry tetrahydrofuran at room temperature followed by addition of 10 ml. (100 mmoles) of acetic anhydride at -50° yielded after work up and distillation 7.88 g. (81%) of a colorless liquid,[§§] b.p. 92 - 93° (8.5 mm.), $[\alpha]_D$ + 16.5° (c, 8.16 in $CHCl_3$) which gave a single peak of retention time 3.40 min. on GLC analysis[†]. The NMR spectrum (Fig. 1b) with one vinyl hydrogen at δ^{CDCl_3} 5.54 ppm. (J = 3.5 cps.) and an acetate methyl singlet at δ 2.10 ppm., the infrared spectrum [$\nu_{max}^{CS_2}$ 1765 (ester C=O), 1610 and 1630 (C=C), and ~1200 $cm.^{-1}$ (C-O-C)], and the ultraviolet spectrum [λ_{inf}^{EtOH} 215mμ (ε 3600)] establish its structure as camphor enol acetate (VI-H)[††].

In the same manner the liquid enol acetates of 3-chlorocamphor (IV-Cℓ) and 3-bromocamphor (IV-Br) were prepared. The 3-chloro-2-bornenyl acetate (VI-Cℓ)[§§] had b.p. 108 - 110° (8.8 mm.), $[\alpha]_D$ + 41.6° (c, 10.40 in $CHCl_3$), δ^{CDCl_3} 0.77, 0.93, 1.04, and 2.16 ppm. (methyl singlets), while 3-bromo-2-bornenyl acetate (VI-Br)[§§] had b.p. 114 - 116° (10.5 mm.), $[\alpha]_D$ + 37.6° (c, 8.00 in $CHCl_3$), δ^{CDCl_3} 0.77, 0.95, 1.03, and 2.15 ppm. (methyl singlets). In the case of 3-bromocamphor debromination competed with proton removal in the reaction with n-butyllithium, and the mixture of enol acetates formed on addition of acetic anhydride was separated by distillation to give 40% of VI-H and 54% of VI-Br.

The availability of camphor enol acetate provided the opportunity to determine why it was not produced by the usual procedures. When VI-H was heated with acetic anhydride, sodium acetate and one equivalent of acetic acid at 150° for 4 hours and worked up without aqueous contact, it was found to have been transformed entirely into camphor.

[¶] A small amount (<5%) of recovered camphor was obtained, presumably from protonation of the enolate anion by traces of acid in the anhydride. The enol acetate was easily separated by chromatography on alumina.

[§§] Satisfactory analyses have been obtained for this compound.

[††] Camphor enol acetate was probably obtained by Malmgren (8) as one of the products from the reaction of bromocamphor (IV-Br) with magnesium followed by acetic anhydride, but the colorless liquid obtained was not characterized by this worker.

Likewise, when VI-H was heated at 120° for 10 hours with anhydrous acetone and a trace of p-toluenesulfonic acid, it was changed into camphor and (presumably) isopropenyl acetate. Treatment of VI-H with hydrogen chloride in acetyl chloride or in carbon tetrachloride at room temperature gave camphor and acetyl chloride. Therefore, in the reversible acylation reactions mentioned earlier, camphor enol acetate is thermodynamically less stable than camphor, and VI-H should even be a powerful reagent for enol acylation. The difference between camphor and other simple ketones is presumably associated with the increased angle and torsional strain involved in introducing a double bond into the bicyclo[2.2.1] system (9), as well as the steric repulsion of the acetate and bridgehead methyl groups of VI-H.

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REFERENCES

1. (a) Y. Matsubara, Nippon Kagaku Zasshi, 78, 726 (1957); Chem. Abstr. 53:22056e. (b) S. Wakabayashi, Nippon Kagaku Zasshi, 80, 289 (1959); Chem. Abstr. 55:4566h.

2. Y. Heya, Nippon Kagaku Zasshi, 80, 1163 (1959); Chem. Abstr. 55:4571c.

3. (a) A. Nickon, J. L. Lambert, R. O. Williams and N. H. Werstiuk, J. Am. Chem. Soc. 88, 3354 (1966). (b) J. L. Lambert and A. Nickon, Abstr. of 153rd Amer. Chem. Soc. Meeting (1967), paper O-11.

4. P. Mälkönen, Ann. Acad. Scient. Fennicae, Ser. A. II Chemica, 128, 22 (1964).

5. M. L. Capmau, W. Chodkiewicz and P. Cadiot, Tetrahedron Letters, 1619 (1965).

6. M. Lipp and D. Bernstein, Naturwissenschaften, 42, 578 (1955).

7. (a) H. House and V. Kramar, J. Org. Chem. 28, 3362 (1963). (b) W. M. Muir, P. D. Ritchie and D. J. Lyman, J. Org. Chem. 31, 3790 (1966).

8. S. M. Malmgren, Ber. 36, 2641 (1907).

9. P. R. Schleyer, J. Am. Chem. Soc. 89, 701 (1967).