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THE CLEMMENSEN REDUCTION OF ENOL ETHERS: CYCLOPROPYL ETHERS FROM MONO- AND DI-METHOXYCYCLOHEXA-1,4-DIENES

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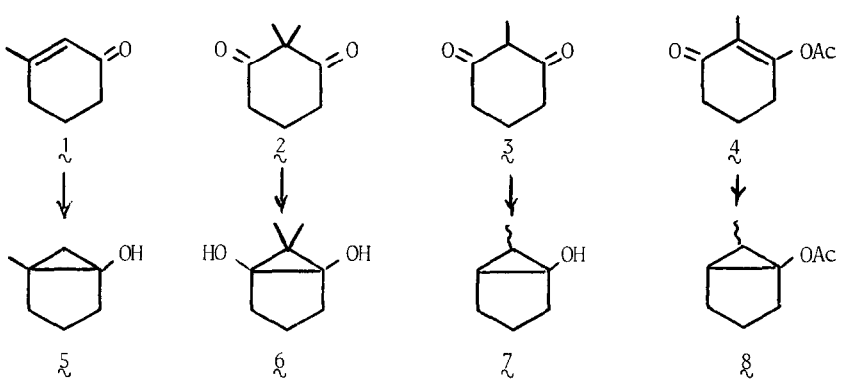
Abstract: Clemmensen reduction (zinc and hydrogen chloride in dry diethyl ether) of 1-methoxy- and 1,5-dimethoxy-cyclohexa-1,4-diene affords the cyclopropyl ethers, 1-methoxy- and 1,5-dimethoxy-bicyclo[3.1.0]hexane; in the presence of acetic anhydride, reduction of 6-acetyl-1-methoxy-6-methyl-cyclohexa-1,4-diene leads regiospecifically to 7-acetoxy-1-methoxy-6,7-dimethyl-bicyclo[4.1.0]hept-4-ene.

The Clemmensen reduction (amalgamated zinc and hydrogen chloride) of α,β-unsaturated ketones and of 1,3-diketones often leads to rearranged products. The reaction has been shown to involve intermediate cyclisation to cyclopropanols or cyclopropane-diols, and a number of these have been trapped as their acetates by carrying out the reaction in the presence of acetic anhydride.[1, 2] Some typical examples are shown in Scheme 1; whereas the α,β-

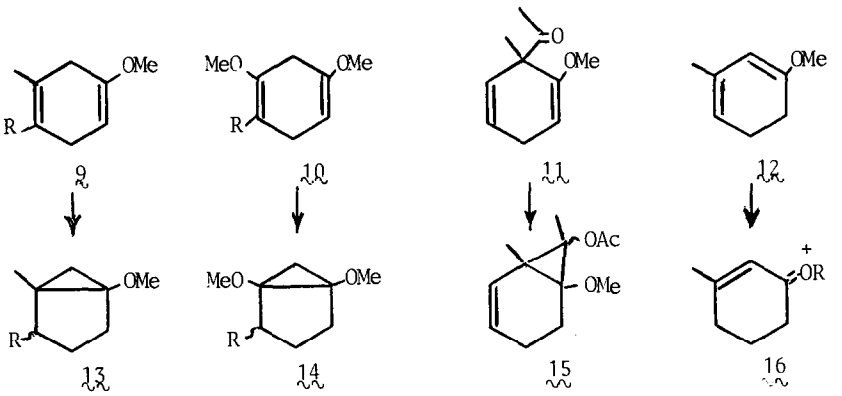


Scheme 1

enone 1 and the "non-enolisable" 2,2-disubstituted 1,3-diketone 2 undergo a 2-electron reduction to the cyclopropanol 5 and cyclopropane-diol 6, respectively, the enolisable 1,3-diketone 3 undergoes a 4-electron reduction to the cyclopropanol 7; similarly, the mono-enol acetate 4 affords the cyclopropyl acetate 8.[2d]

Here we report that the Clemmensen reduction (in dry diethyl ether at -35°C) of enol ethers formally derived from cyclohexenones and cyclohexane-1,3-diones also leads, in some cases, to cyclised products. The course of the reaction is not, however, always the one that might have been expected by analogy with the corresponding enones and 1,3-diketones.

Reduction of the enol ether 9a[3] led in 40% yield to the cyclopropyl ether 13a;[4] some 1- and 3-methylcyclohexene were also formed. Similarly, the bis-(enol ether) 10a, although formally derived from an enolisable 1,3-diketone, also underwent a 2-electron reduction to give the cyclopropyl diether 14a (40% yield).[4]



Scheme 2. R = a, H; b, Me; c, iPr.

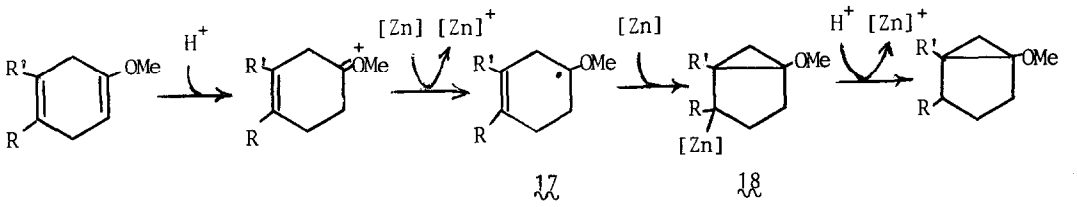
An alkyl group R on one of the double bonds in 9 and 10 disfavours cyclisation to a cyclopropyl ether. Thus, no cyclopropyl ether 13c was obtained from 9c, which gave the aromatic disproportionation product 4-isopropyl-3-methylanisole, and the cyclised diethers 14b were formed in only 15% yield from 10b and were accompanied by polymers.[4]

Protonation of the enol ether 12 has been shown to afford the conjugated cation 16b;[5] this is the O-methyl derivative of 16a, which is the protonation product of the cyclohexenone 1, and the postulated first intermediate in the Clemmensen reduction of this enone to the cyclopropanol 5. We therefore expected that the reduction of the enol ether 12 would lead to the corresponding cyclopropyl ether 13a. This, however, is not the case; reduc-

tion of 12 led to a mixture of 1- and 3-methylcyclohexene (1:6 ratio) and m-methylanisole. These products presumably result from the disproportionation of 12, triggered by a radical intermediate[3b,c] (cf. 17), to form m-methylanisole and 3-methoxycyclohexene; reduction of the latter by zinc and hydrogen chloride is known[6] to afford very selectively 3-methylcyclohexene, the less stable olefin.

We have also carried out the reduction of compound 11,[7] an enol ether derived from a "non-enolisable" 1,3-diketone (cf. 2). The reductive cyclisation of this compound could lead to four different cyclopropane derivatives. In the event, the reaction was found to be regiospecific; reduction of 11 in the presence of acetic anhydride afforded, in 70% yield, the cyclopropane-diol ether acetates 15[8] (2 epimers, 1:1.4). The relatively high yield obtained in this case may reflect the fact that the original cyclohexadiene 11 has a quaternary carbon atom and cannot disproportionate to an aromatic compound.

Clemmensen reductions probably involve successive proton and 1-electron transfers (from the medium and from the zinc surface, respectively), and a plausible mechanism for the formation of cyclopropyl ethers from the enol ethers 9 and 10 is shown in Scheme 3. Disproportionation of these cyclohexadiene substrates (which are effective H· donors) is probably caused by an intermediate radical such as 17, the adsorption of which on the zinc surface (and hence its further reduction to give 18) is hindered when R = alkyl.



17 18

Scheme 3. [Zn] = bulk zinc; R' = Me or OMe.

The formation of the cyclopropyl ethers 13 and 14 may therefore represent the first examples of the direct conversion of 4-cyclohexenyl radical intermediates 17 into stable bicyclo[3.1.0] compounds in simple unstrained systems.[9]

Foonotes

1. E. Vedejs, Organic Reactions, 1975, 22, 401.
2. (a) E. Wenkert and E. Kariv, Chem.Comm., 1965, 570; (b) I. Elphimoff-Felkin and P. Sarda, Tetrahedron Letters, 1969, 3045; Tetrahedron, 1975, 31, 2781; (c) B.R. Davis, G.W. Rewcastle and P.D. Woodgate, J.C.S.Perkin I, 1979, 2815; (d) I. Elphimoff-Felkin and M. Urrea, Tetrahedron Letters, 1980, 525.
3. (a) A.J. Birch and G. Subba Rao, Aust.J.Chem., 1970, 23, 1641; (b) A.J. Birch and K.P. Dastur, J.C.S.Perkin I, 1973, 1650; (c) A.J. Birch and G. Subba Rao, Adv.Org.Chem., 1972, 8, 1.
4. 13a NMR: δ_{CCl_4} = 0.3 (1H), 0.45 (1H), 1.15 (3H, s), 1.75 (6H, m), 3.2 (3H, s). 14a NMR: δ_{CCl_4} = 0.65 (1H), 0.95 (1H), 1.7 (6H, m), 3.3 (6H,s). 14b (CH_3 and OCH_3 cis) 95%, trans 5%. NMR: cis δ_{CDCl_3} = 0.77 (1H), 0.91 (1H), 1.02 (3H, d), 3.35 (3H, s), 3.4 (3H, s). We thank Dr. S.G. Davies (Oxford) for the determination of this structure (J.Chem.Research(S),1982, 197) and Professor M. Perrin (Lyon) for a generous gift of 4-isopropyl-3-methylanisole.
5. N.A.J. Rogers and A. Sattar, Tetrahedron Letters, 1964, 131 and 1965, 1471.
6. I. Elphimoff-Felkin and P. Sarda, Organic Syntheses, 1977, 56, 101.
7. L.N. Mander and M. Woolias, Synthesis, 1979, 3, 185.
8. 15 (OAc and OMe cis) (42%); NMR: δ_{CDCl_3} = 1.22 (3H, s), 1.5 (3H, s), 1.9 (3H, s), 2.17 (4H, m), 3.36 (3H, s), 5.47 (2H, m); 15 (OAc and OMe trans) (58%); NMR: δ_{CDCl_3} = 1.18 (3H, s), 1.36 (3H, s), 2.03 (3H, s), 2.37 (4H, m), 3.35 (3H, s), 5.63 (2H, m). The stereochemistry of these acetates was determined by reduction ($LiAlH_4$ in ether at -10° followed by saturated boric acid at 0°) to the corresponding cyclopropane diol monoethers, both of which are unstable. The cis isomer shows an intramolecular H bond (IR, CCl_4: 3630 and 3580 cm^{-1}).
9. For closely related rearrangements see L.H. Slaugh, J.Am.Chem.Soc., 1965, 87, 1522; P.K. Freeman, F.A. Raymond, J.C. Sutton and W.R. Kindley, J.Org. Chem., 1968, 33, 1448; E.C. Friedrich and R.L. Holmstead, ibid., 1971, 36, 971.

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