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OXYMERCURATION-DEMERCURATION OF 6-METHYLENETRICYCLO[3.2.1.$0^{2,7}$]OCT-3-EN-8-ONE DERIVATIVES. AN EFFICIENT SYNTHESIS OF 2,4-CYCLOHEXADIENONE DERIVATIVES

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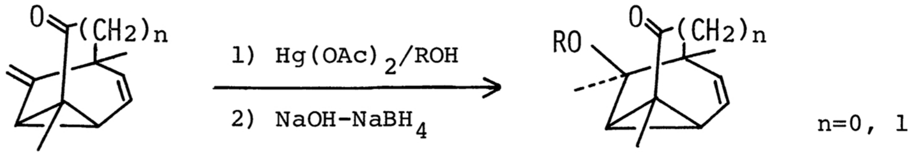
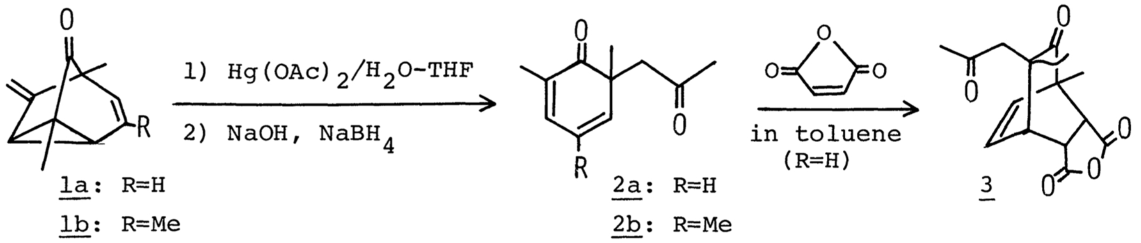
Oxymercuration-sodium borohydride reduction of 1,5-dimethyl- and 1,3,5-trimethyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-one was found to give 6-acetonyl-2,6-dimethyl- and 6-acetonyl-2,4,6-trimethyl-2,4-cyclohexadienones in good yields. The possible intermediates and the reaction mechanism were studied.

The oxymercuration-demercuration sequence in aqueous tetrahydrofuran (THF) with mercury (II) acetate is a mild, convenient method for affecting the Markownikoff hydration of olefins in very high yields.[1] In our previous work, solvomercuration-demercuration of 1,5-dimethyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-one and its related compounds was found to undergo stereospecific solvent incorporation on exo-methylene group.[2] In this paper, the hydroxymercuration-sodium borohydride reduction of 1,5-dimethyl- and 1,3,5-trimethyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-ones (1a and 1b)[3] is described to afford novel 6-acetonyl-2,6-dimethyl- and 6-acetonyl-2,4,6-trimethyl-2,4-cyclohexadienones (2a and 2b) in fairly good yields.

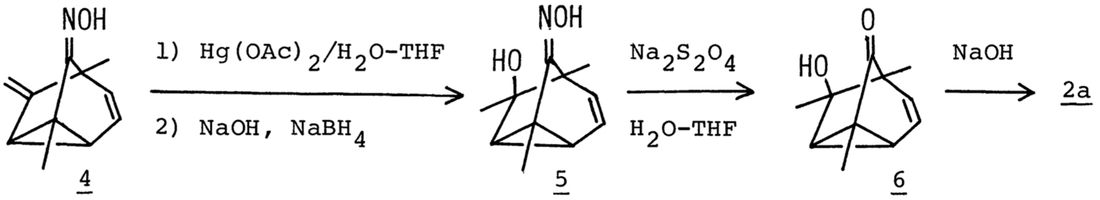


A well stirred solution of 1a in H_2O-THF (1/4) was treated with an equivalent amount of mercury (II) acetate at room temperature. After 30 min, the reaction mixture was treated with 3 mol dm^{-3} aqueous sodium hydroxide and then with sodium borohydride according to the literature procedure.[1,4] The reaction mixture was carefully filtered through celite and the filtrate was extracted with ether. The ether extract was dried, and concentrated on a rotary evaporator to give 90% yield of 2,4-cyclohexadienone derivative 2a[5]: slight yellow oil, bp 121 °C/866 Pa; IR (film) 1719, 1657, 1641 cm^{-1}; ^1H-NMR (CCl_4) δ 1.04 (3H, s), 1.85 (3H, d, J=1.2 Hz), 1.95 (3H, s), 2.53 (1H, d, J=17.4 Hz), 3.21 (1H, d, J=17.4 Hz), 5.93-6.11 (1H, m), 6.05 (1H, d, J=4.2 Hz), 6.06-6.87 (1H, m). The similar treatment of 1b afforded

90% yield of 2b: slight yellow oil, bp 114 °C/399 Pa; IR (film) 1723, 1660 cm^{-1}; ^1H-NMR (CCl_4) δ 0.97 (3H, s), 1.78 (3H, broad s), 1.82 (3H, broad s), 1.90 (3H, s), 2.40 (1H, d, J=17.0 Hz), 3.06 (1H, d, J=17.0 Hz), 5.53 (1H, broad s), 6.45 (1H, broad s). On examination of a Diels-Alder reaction of 2a with maleic anhydride in refluxing toluene, the adduct (3) was obtained.[6] This fact and the spectral properties of 2a and 2b are in good agreement with the proposed structures.[7]



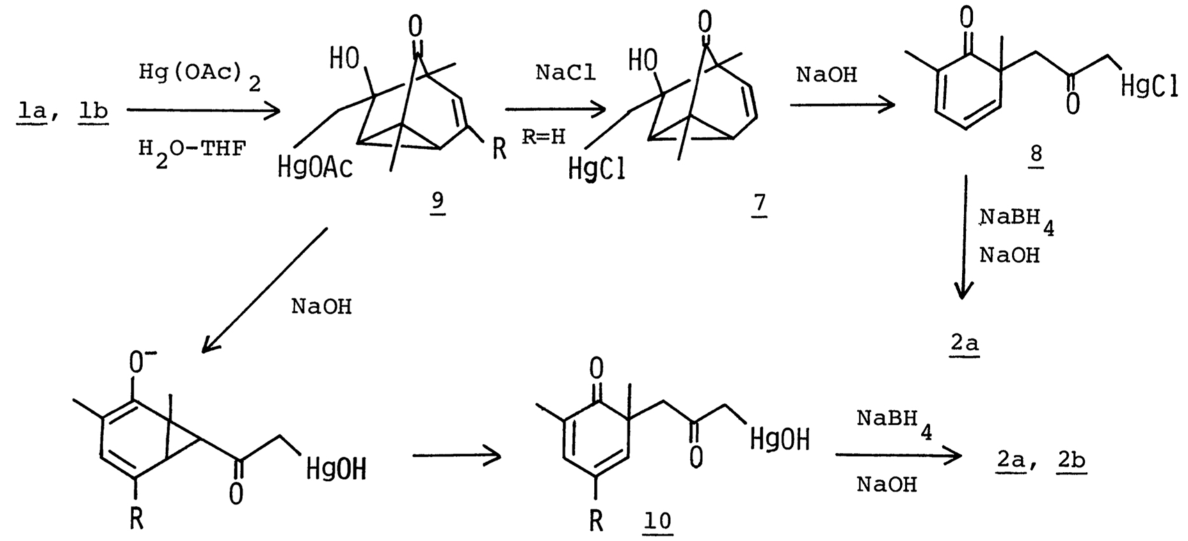
Several reactions were carried out to clarify the intermediates and the reaction pathway of the present reaction involving the skeletal rearrangement. At first, the isolation of the plausible intermediate such as 6 which is one of the anticipated products for the oxymercuration-demercuration reaction of 1a, was investigated. The hydroxymercuration-sodium borohydride reduction of oxime 4[8] in a similar manner to the case of 1a and 1b afforded 23% yield of 5[9] along with 6% of the starting material 4. The reductive hydrolysis of 5 with sodium dithionate afforded 30% of expected 6.[10] The spectral properties of 5 and 6 are in good agreement with the



proposed structures: 5, mp 159-160 °C; IR (KBr) 3500-3100, 1656, 1378, 1119 cm^{-1}; ^1H-NMR (acetone-d_6) δ 1.05 (6H, s), 1.13 (1H, d, J=3.0 Hz), 1.63 (3H, s), 1.71-1.89 (1H, m), 3.56 (1H, broad s), 5.36 (1H, dxd, J=8.4, 3.0 Hz), 5.86 (1H, dxd, J=8.4, 6.0 Hz), 9.13 (1H, broad s); 6, IR (film) 3600-3200, 1722 cm^{-1}; ^1H-NMR (CCl_4) δ 0.92 (3H, s), 1.11 (3H, s), 1.71 (3H, s), 1.82-2.00 (2H, m), 3.00 (1H, broad s), 5.23 (1H, dxd, J=8.7, 3.0 Hz), 5.82 (1H, dxd, J=8.7, 4.8 Hz). Then the treatment of 6 with 3 mol dm^{-3} sodium hydroxide in THF afforded 90% of 2,4-cyclohexadienone derivative 2a. Therefore this base induced rearrangement is ascribed to be a retro-aldol condensation assisted by the strain relief.[11]

To gain more insight into the mechanism for the formation of 2a or 2b, the following experiment was performed. The reaction of 1a with mercury (II) acetate in H_2O-THF (1/4), then with saturated aqueous sodium chloride[13] afforded 80% yield of mercury incorporated product 7: mp 150-151 °C (from CH_2Cl_2); IR (KBr) 3500-3400, 1760-1632 (very broad absorption) cm^{-1}; ^1H-NMR (acetone-d_6) δ 1.08 (3H, s), 1.20

(3H, s), 2.21 (3H, s), 2.89 (2H, broad s), 4.51 (1H, s), 5.51 (1H, dxd, J=8.7, 2.7 Hz), 6.06 (1H, dxd, J=8.7, 4.8 Hz). IR spectrum shows the presence of a hydroxy group. The chemical shifts and coupling patterns of ^{1}H-NMR spectrum show the presence of the tricyclic skeleton. The treatment of 7 with 3 mol dm^{-3} sodium hydroxide in THF as in the case of 6 afforded 90% of 2,4-cyclohexadienone derivative 8: mp 180-181 °C (from CH_2Cl_2); IR (KBr) 1650-1560 (very broad absorption), 1325, 1171, 1031 cm^{-1}. The ^{1}H-NMR of 8 exhibited signals of two methyl groups at δ 1.14 (s), 2.02 (d, J=1.2 Hz), and an AB doublet at δ 2.62 (J=17.4 Hz), 3.36 (J=17.4 Hz), and a very broad signal of two methylene protons at the mercurial moiety in the range of δ 3.60-2.14 in addition to two signals of vinyl protons in the ranges of δ 6.32-5.85 (2H) and δ 6.99-6.69 (1H). These spectral properties might suggest the structure of 8 which has the 2,4-cyclohexadienone ring. Actually the sodium borohydride reduction of 8 in THF-aq NaOH (3 mol dm^{-3}) afforded 2a in 95% yield.



Consequently the reaction pathway of oxymercuration-demercuration reaction affording 2a and 2b is well explained as illustrated in the above scheme. Initially the hydroxy group incorporating ketone 9 is formed by oxymercuration of 1a and 1b. Then the base induced retro-aldol condensation of 9 occurs to give 10. Subsequent sodium borohydride reduction of 10 affords 2,4-cyclohexadienones.[14]

Since 1a and 1b are easily prepared by thermal rearrangement of 2,6-dimethylphenyl and 2,4,6-trimethylphenyl propargyl ether,[3] the present reaction is a very convenient method for the preparation of 2,4-cyclohexadienones, which have a functionalized substituent at 6-position and might have synthetic utilities.

Acknowledgement. Financial support by Science and Engineering Research Laboratory of Waseda University is gratefully acknowledged.

References and Notes

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2) M. Nitta, A. Omata, and H. Sugiyama, submitted.
3) J. Zsindely and H. Schmid, Helv. Chim. Acta, 51, 1510 (1968).
4) H. C. Brown and P. J. Geoghegen, Jr., J. Am. Chem. Soc., 89, 1522 (1967).
5) Elemental analyses are satisfactory for all new compounds.
6) Mp 121-122 °C; IR (KBr) 1862, 1780, 1720, 1237 cm^{-1}; ^{1}H-NMR (CDCl$_3$) δ 1.23 (3H, s), 1.48 (3H, s), 2.03 (3H, s), 2.30 (1H, d, J=17.4 Hz), 2.72 (1H, d, J=17.4 Hz), 2.97 (1H, d, J=8.4 Hz), 3.60 (1H, dxd, J=8.4, 4.0 Hz), 3.95 (1H, m), 5.80 1H, dxd, J=8.0, 1.0 Hz), 6.34 (1H, dxd, J=8.0, 7.8 Hz). The orientation of the acetonyl group is not determined.
7) K. Alder, F. H. Floch, and H. Lessenick, Chem. Ber., 90, 1709 (1957); H. Hart and R. M. Lange, J. Org. Chem., 31 1776 (1966); H. Hart and P. M. Collins, J. Chem. Soc., C, 895 (1967); H. Heimgartner, J. Zsindely, and H. Schmid, Helv. Chim. Acta, 55, 113 (1972).
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9) The evidence of orientations of hydroxy group of 5 as well as 6 and 7 are not given here but the exo orientation should be favored on the basis of analogy with the case of methoxymercuration of 1 and related compounds (ref. 2).
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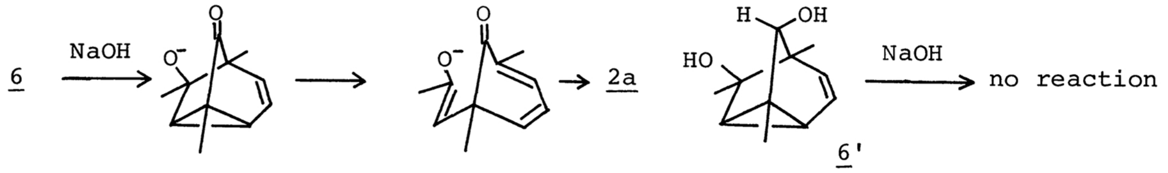
11) Another plausible mechanism may be an anionic oxy-Cope rearrangement12) presented below. However, the treatment of 6'2) with similar manner did not undergo the ring opening reaction, therefore the carbonyl group must be indispensable for this reaction. Thus the oxy-Cope rearrangement was discarded.



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