Efficient Synthesis of 2-Hydroxycyclobutanone Derivatives; Application to the Synthesis of 1,4-Diketones and Cyclopentenones

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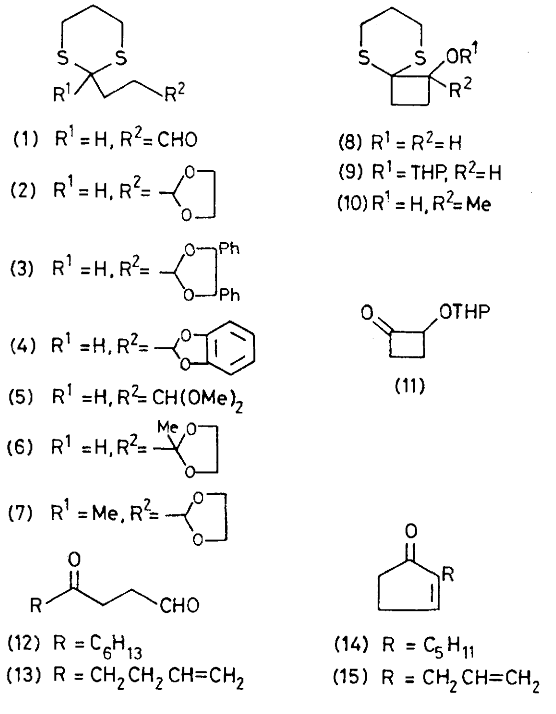
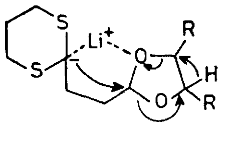
Summary Treatment of 4,4-(trimethylenedithio)butanal *meso*-1,2-diphenylethylene acetal (**3**) with butyl-lithium gave a high yield of 2,2-(trimethylenedithio)cyclobutanol (**8**), which was transformed into 2-tetrahydropyran-2-yloxycyclobutanone (**11**), a potential intermediate for the synthesis of 1,4-diketones and cyclopentenones.

Considerable effort has recently been devoted to the synthesis of cyclobutanones which are not readily accessible by non-photochemical means.[1] We now describe an efficient synthesis of derivatives of 2-hydroxycyclobutanones, which are potential intermediates for the preparation of 1,4-diketones and cyclopentenones leading to the synthesis of several important natural products.[2]

Treatment of the ethylene acetal[3] (**2**) of the aldehyde (**1**) with butyl-lithium (2 and 1 equiv., respectively) in tetrahydrofuran (THF) at -25 to -20 °C for 4 h and then at -15 °C for 20 h effected intramolecular cyclization to give the alcohol (**8**) in 80 and 57% yields [recovered (**2**), 6 and 20%], respectively. Likewise, the ethylene acetal (**6**)[3] afforded the corresponding alcohol (**10**) in 60% yield [recovered (**6**), 23%] under similar conditions (2 equiv. BuLi, -25 to -20 °C for 4 h and then -15 °C for 40 h). The intramolecular cyclization proceeded efficiently with the *meso*-diphenylethylene acetal (**3**) under milder conditions (2 equiv. BuLi, -50 to -40 °C for 20 min and then -30 to -25 °C for 20 min) to give (**8**) in 90% yield together with $PhCH_2COPh$ (92%). These results, coupled with the following facts, indicate that the reactions involve attack of the dithian carbanion on the acetal carbon atom with concomitant hydride shift at the acetal group [structure (**A**)]. The *o*-phenylene acetal (**4**) and the dimethyl acetal (**5**) did not undergo cyclization under the same conditions as for (**2**) (2 equiv. BuLi) [recovered (**4**) and (**5**), 85 and 80%, respectively]; the same treatment of the ethylene acetal (**7**) followed by work-up with deuterium oxide also led to recovery (85%) of unchanged (**7**) containing no deuterium. In view of the easy removal of the acetal-alkoxy leaving group, the present formation of 2-hydroxycyclobutanone equivalents is significant, and provides a new and useful route to 1,4-diketones and cyclopentenones as illustrated below.



THP = tetrahydropyran-2-yl



(**A**)

Compound (**8**), on treatment with dihydropyran and dry toluene-*p*-sulphonic acid [0 °C (bath temp.), 30 min], formed the tetrahydropyranyl ether (**9**) in 97% yield, which was hydrolysed with mercury(II) chloride in the presence of mercury(II) oxide and calcium carbonate in 80% aqueous acetonitrile (reflux, 1·5 h)[4] to yield the cyclobutanone (**11**), ν_{max} (neat) 1791 cm^{-1}, quantitatively. Grignard reaction of (**11**) with hexyl- and but-3-enylmagnesium bromides,[5] followed by oxidation with periodic acid (3 equiv.) in aqueous THF (room temp., 20 h), produced the 4-keto-aldehydes (**12**) and (**13**), respectively, which were immediately cyclized with base (1% aqueous NaOH, 50—60 °C, 30 min)[6] to give 2-pentyl- and 2-allylcyclopent-2-enones,[7] (**14**) and (**15**), in 45 and 42% overall yields, respectively. Compounds (**14**) and (**15**) were transformed by the known procedure into dihydrojasmone[7] and allylrethrone.[7,8]

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[1] *E.g.*, D. Seebach, N. R. Jones, and E. J. Corey, *J. Org. Chem.*, 1968, **33**, 300; B. M. Trost, D. Keeley, and M. J. Bogdanowicz, *J. Amer. Chem. Soc.*, 1973, **95**, 3068; J. E. Baldwin, G. A. Hofle, and O. W. Lever, Jr., *ibid.*, 1974, **96**, 7125; B. M. Trost, M. Preckel, and L. M. Leichter, *ibid.*, 1975, **97**, 2224; K. Ogura, M. Yamamoto, M. Suzuki, and G. Tsuchihashi, *Tetrahedron Letters*, 1974, 3653.

[2] *E.g.*, G. Büchi and H. Wüest, *J. Org. Chem.*, 1966, **31**, 977; E. J. Corey and L. S. Hegedus, *J. Amer. Chem. Soc.*, 1969, **91**, 4926; J. E. McMurry and J. Melton, *ibid.*, 1971, **93**, 5309; T. Mukaiyama, K. Narasaka, and M. Furusato, *ibid.*, 1972, **94**, 3641; R. A. Ellison and W. D. Woessner, *J.C.S. Chem. Comm.*, 1972, 529; R. C. Cookson and P. J. Persons, *ibid.*, 1976, 990. J. L. Herrmann, J. E. Richman, and R. H. Schlessinger, *Tetrahedron Letters*, 1973, 3275.

[3] Compounds (2) and (6) were prepared by treatment of 3-bromopropanal ethylene acetal (G. Büchi and H. Wüest, *J. Org. Chem.*, 1969, **34**, 1122) and 4-iodobutan-2-one ethylene acetal (B. M. Trost and R. A. Kunz, *J. Org. Chem.*, 1974, **39**, 2475), respectively, with 2-lithio-1,3-dithian in high yields.

[4] *Cf.*, E. J. Corey and R. W. Erickson, *J. Org. Chem.*, 1971, **36**, 3553.

[5] *Cf.*, J. P. Barnier, J. M. Denis, J. Salaum, and J. M. Conia, *Tetrahedron*, 1974, **30**, 1397.

[6] A. I. Meyers and N. Nazarenko, *J. Org. Chem.*, 1973, **38**, 175.

[7] *E.g.*, K. Oshima, H. Yamamoto, and H. Nozaki, *J. Amer. Chem. Soc.*, 1973, **95**, 4446, and refs. cited therein.

[8] *E.g.*, T. Mukaiyama, S. Kobayashi, K. Kamio, and H. Takei, *Chem. Letters*, 1972, 237.