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CONVERSION OF METHYLENEDIOXYBENZENE DERIVATIVES INTO 2-METHOXYPHENOL DERIVATIVES

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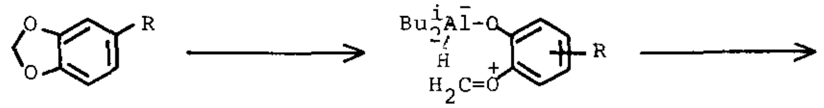
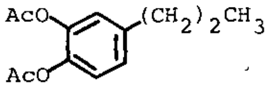
Abstract-----Methylenedioxybenzene derivatives are reductively cleft with diisobutylaluminum hydride to give 2-methoxyphenol derivatives. Concurrent hydroalumination occurs when a substrate contains an olefinic bond in a side chain.

Cleavage of aromatic methylenedioxy compounds into 2-methoxyphenol derivatives is synthetically interesting especially in the preparation of a number of isoquinoline alkaloids containing such groups in molecule[1]. Moreover, the cleavage is biosynthetically interesting because of the reverse process is believed to occur in plant[2]. We now report here the cleavage of some methylenedioxybenzene with diisobutylaluminum hydride to give 2-methoxyphenol derivatives[3].



(1) a : R=H
b : R=CHO
c : $R=CH_2CH=CH_2$
d : R=CH=CHMe
e : $R=CH_2CH_2Me$

(2)



(3) a : R=H
b : $R=CH_2OH$
c : $R=C_3H_6AlBu^i_2$

(4) a : $R=CH_2OAc$
b : $R=(CH_2)_2Me$

(5)

Treatment of methylenedioxybenzene (1a) with three equivalents of diisobutylaluminum hydride in toluene at reflux temperature for 3 h allowed complete cleavage of the methylenedioxy group to give guaiacol (3a) in 75 % yield. Piperonal (1b), on the same treatment using five equivalents of the hydride reagent, followed by treating the reaction mixture with an excess amount of acetic anhydride at 0°C- ambient temperature, afforded an inseparable mixture (ca. 2:1) of the diacetates (4a, R=4) and (4a, R=5)[4] in 51 % overall yield. Since piperonyl alcohol could be detected in the first stage of the reaction, reduction of the carbonyl group was apparently preceded by cleavage of the methylenedioxy group.

Non-regioselective cleavage was also observed in the reaction of safrol (1c), isosafrol (1d), and 4-n-propylmethylenedioxybenzene (1e) which gave an inseparable mixture (ca. 1:1) of monoacetates (4b)[4] in 48 ; 42, and 44 % yield, respectively, on treatment with 5.5-6 equivalents of diisobutylaluminum hydride in toluene at 60°C, followed by acetic anhydride. Under these conditions hydroalumination and protodealumination occurred concurrently with the reductive cleavage of the methylenedioxy group and acetylation via a mixture of alanes (3). In these cases the diacetate (5) could be isolated as a by-product in about 10 % yield[5,6].

The reaction is assumed to proceed via a betaine intermediate (2) formed by an action of diisobutylaluminum hydride as a Lewis acid. Although high regioselectivity was not observed in the cleavage reaction, the finding may be useful in the synthesis of the isoquinoline alkaloids for the reversion of a methylenedioxy group into its biosynthetically preceding group.

REFERENCES AND NOTES:

1. For example: T. Kametani, *The Chemistry of The Isoquinoline Alkaloids*, Vol. 2, The Sendai Institute of Heterocyclic Chemistry, Sendai, 1974.
2. Cf. M. Shamma, The Isoquinoline Alkaloids, Academic Press, New York, 1972, pp. 214-215.
3. Reductive cleavage of some acetals with diisobutylaluminum hydride has been reported. See, a) E. Winterfeldt, Synthesis, 1975, 617. b) S. Takano, M. Akiyama, S. Sato, and K. Ogasawara, Chemistry Lett., 1983, in press.
4. Structures were assingned by comparing the ^{1}H-nmr spectrum with those of authentic materials and by tlc behaviors.
5. Reductive cleavage of methyl phenyl ethers with diisobutylaluminum hydride has been reported. See ref. 3a).
6. Ir (neat): ν_{max} 1770 cm^{-1}. ^{1}H-nmr: δ 0.94 (3H, t, J=7Hz), 1.62 (2H, m), 2.23 (6H, s), 2.56 (2H, t, J=8Hz), 7.00 (3H, m) ppm.

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