

AN ELECTROCHEMICAL CHLORINATIVE ENE-TYPE REACTION OF ISOPRENOIDS

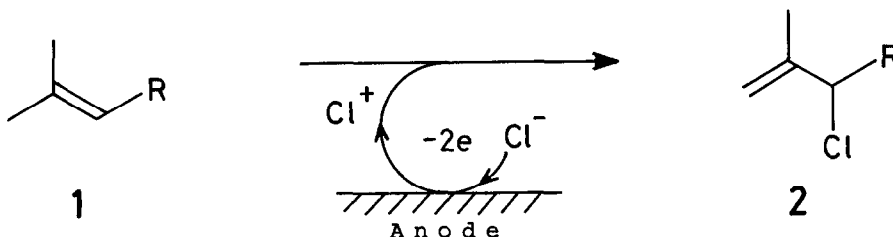
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**ABSTRACT:** The chlorinative ene-type reaction of isoprenoids (1 → 2) has been performed by electrolysis in CH<sub>2</sub>Cl<sub>2</sub>-H<sub>2</sub>O-NaCl system. The reaction provides useful allylic chlorides 2 for terpene synthesis in high yields and is affected strikingly by the nature of halide ions and solvents. dl-Theaspirane 21 was prepared from α-dihydroionol via the electrolysis.

In the course of our study on functionalization by electrochemically generated halonium ions, we succeeded in development of a novel regio- and chemoselective chlorinative ene-type reaction (1 → 2), which is valuable for the preparation of allylic chlorides 2<sup>1)</sup> and found that the product-selectivity of the electrolysis is highly concerned to the choice of halide ions and solvents.



So far the chemistry of electrochemically generated halonium ions is concerned, bromide<sup>2)</sup> and iodide<sup>3)</sup> ions have been extensively employed, but very few has been known on the chemistry of the electrochemically generated chloronium ions.<sup>4)</sup>

In contrast to the bromide ion promoted electrochemical epoxidation in MeCN - H<sub>2</sub>O,<sup>2a)</sup> the chlorinative ene-type reaction (1 → 2) was extensively facilitated by use of CH<sub>2</sub>Cl<sub>2</sub> - H<sub>2</sub>O - NaCl system. A typical electrolysis is as follows; A mixture of dehydrolinalyl acetate 3 (50 mg) and NaCl (150 mg) dissolved in CH<sub>2</sub>Cl<sub>2</sub> (6 ml) - H<sub>2</sub>O (3 ml) was electrolyzed by using Pt foils (1.5 x 3 cm<sup>2</sup>) at constant current (50 mA, for 4 h) in an undivided cell (diam. 3.5, height 10 cm) at room temperature.

The electrochemical chlorinative ene-type reaction (3 → 4, 91%) is more straightforward procedure than the usual NCS method in CH<sub>2</sub>Cl<sub>2</sub> (81%).<sup>1), 4)</sup> The effect of halide ions is noteworthy. Thus, sodium chloride in CH<sub>2</sub>Cl<sub>2</sub> - H<sub>2</sub>O gave 4 exclusively (entry 1, Table 1), but sodium bromide afforded a mixture (4, 5, and 6, entry 2). The absence of dichloride 6 even in the presence of large excess amount of chloride ion (entry 1) is sharply in contrast to the result obtained by using sodium bromide (entry 2), suggesting that attack of the electrochemically generated chloronium ion or hypochlorite to a double bond and deprotonation from methyl group proceed concertedly in CH<sub>2</sub>Cl<sub>2</sub> - H<sub>2</sub>O. The effect of solvents is also remarkable. Thus, electrolysis with NaCl in MeCN - H<sub>2</sub>O produced a mixture of 4, 5, and 7 (entry 4), while the use of NaBr (less than one equivalent to 3) in MeCN - H<sub>2</sub>O promoted epoxidation of 3, preferentially.

The terminal trisubstituted double bond of isoprenoids 4, 9, 10, 11, 12, 13, and 14 are exclusively more reactive than vinylic and internal double bonds. Acetyl, ethynyl, carbomethoxyl, and sulfonyl groups are inert in the course of the electrolysis. However, behavior of hydroxy-compounds (R = H) 4, 8, 9, 10, 11, and 12 is somewhat complex and the yields are lower than those of the corresponding acetates. Carvone suffers the chlorination at the isopropenyl moiety to give 15 (75%). Dimethyl 4-cyclohexene-1,2-dicarboxylate provided chlorohydrin 16 (75%) as a major product along with the desired chloride 17 (17%). The low yield of 17 is presumably due to lack of the proton at C-3 properly oriented for the concerted deprotonation. The newly built isopropenyl moiety is not reactive in the electrolytic condition because of the strong electron-withdrawing nature of chlorine atom.

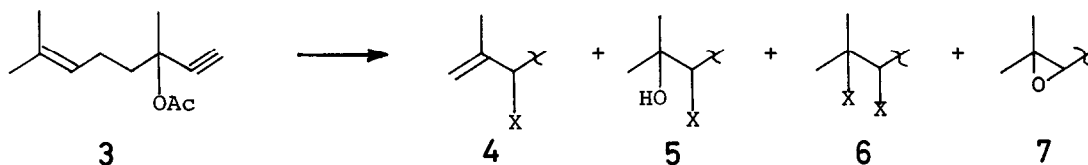
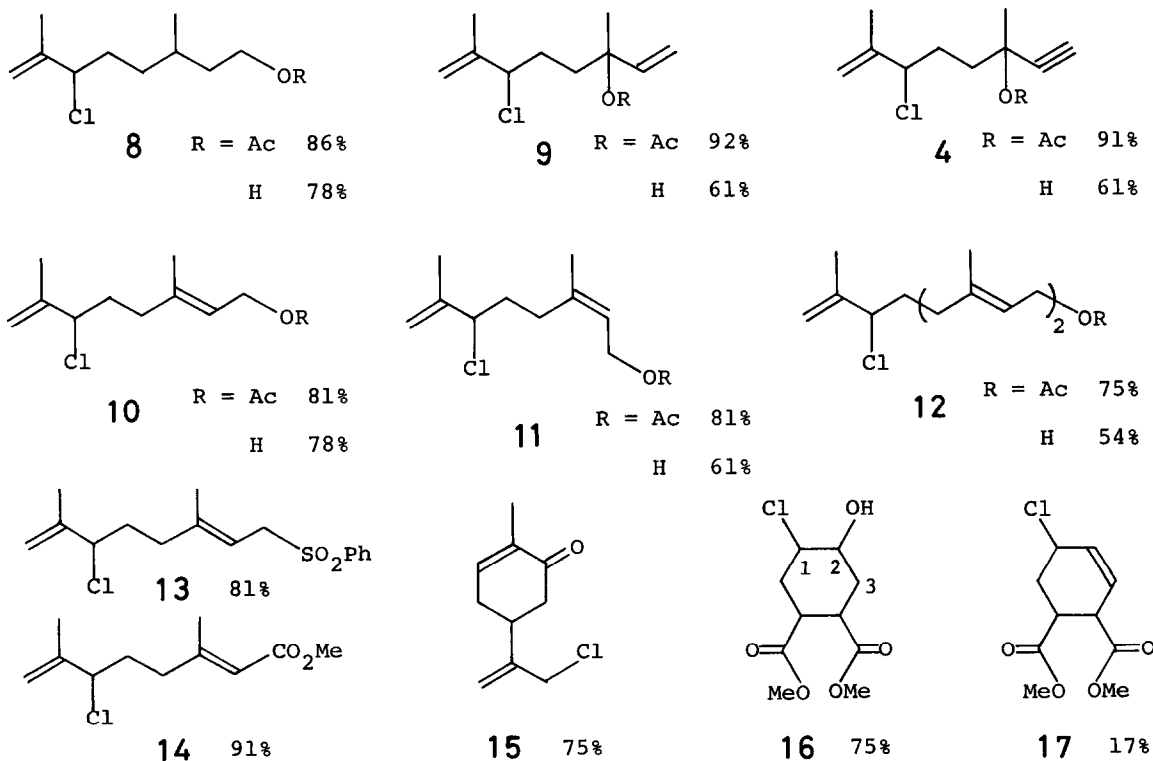


Table 1. Effect of Halide Ions and Solvents in Halogenative Ene-Type Reaction

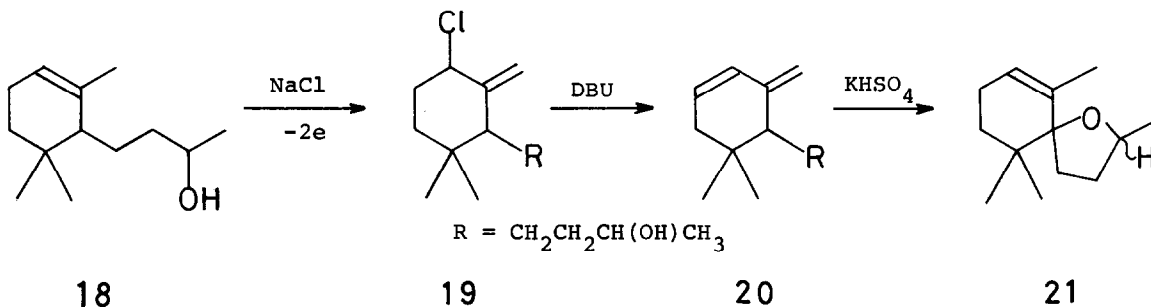
Entry	Solvent	Halide Salt MX	Product (%) <sup>a</sup>			
			<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>
1	CH <sub>2</sub> Cl <sub>2</sub> - H <sub>2</sub> O <sup>c</sup>	NaCl (12 eq) <sup>b</sup>	91	0	0	0
2	CH <sub>2</sub> Cl <sub>2</sub> - H <sub>2</sub> O <sup>c</sup>	NaBr (19 eq)	37	15	37	0
3	CH <sub>2</sub> Cl <sub>2</sub>	Et <sub>4</sub> NCl (1.1 eq)	79	0	0	0
4	CH <sub>3</sub> CN - H <sub>2</sub> O <sup>d</sup>	NaCl (12 eq)	20	24	0	20
5	CH <sub>3</sub> CN - H <sub>2</sub> O <sup>d</sup>	NaBr (1 eq)	0	0	6	82
6	CH <sub>3</sub> CN - H <sub>2</sub> O <sup>d</sup>	NaBr (4 eq)	0	8	21	65

a) isolated yield ; b) mole equivalent to substrate ; c) CH<sub>2</sub>Cl<sub>2</sub>-H<sub>2</sub>O (6ml:3ml)

d) CH<sub>3</sub>CN - H<sub>2</sub>O (7 ml:2 ml)



The chlorinative ene-type reaction and subsequent dehydrochlorination is a great use for diene preparation (18  $\rightarrow$  20) which leads to dl-theaspirane 21. Thus, electrolysis of 18 provided 19 (77%) which was dehydrochlorinated by the action with DBU in DMF, affording 20 (70%).<sup>6)</sup> Cyclization of 20 by Ohno's method ( $\text{KHSO}_4$ )<sup>6)</sup> gave 21 as an epimeric mixture at C-2 (1:1 by HPLC) and its IR,  $^1\text{H-NMR}$  and MS spectra are consistent with those of the authentic sample.<sup>7)</sup>



## References and Notes

- 1) For instance, the compound 8 (R=H) prepared by calcium hypochlorite catalyzed reaction in the presence of dry ice was converted into rose oxide. S. D. Hegde, M. K. Vogel, J. Saddler, T. Hrinyo, N. Rockwell, H. Haynes, M. Oliver, and J. Woliasky, *Tetrahedron Lett.*, 441(1980).
- 2) (a) S. Torii, K. Uneyama, M. Ono, H. Tazawa, and S. Matsunami, *Tetrahedron Lett.*, 1122(1979); (b) S. Torii, K. Uneyama, and M. Ono, *ibid.*, 2653, 2741 (1980); (c) S. Torii, K. Uneyama, and K. Handa, *ibid.*, 1863 (1980); (d) T. Shono, Y. Matsumura, J. Hayashi, and M. Mizoguchi, *ibid.*, 1867 (1980); (e) W. Schmidt and E. Steckan, *Angew. Chem. Int. Ed., Engl.*, 17, 1554 (1979); (f) S. Torii, H. Tanaka, and M. Ukida, *J. Org. Chem.*, 44, 1554 (1979); (g) S. Torii, H. Tanaka, and N. Sayo, *ibid.*, 44, 2938 (1979).
- 3) (a) S. Torii, N. Sayo, and H. Tanaka, *Tetrahedron Lett.*, 4471 (1979); (b) T. Shono, Y. Matsumura, J. Hayashi, and M. Mizoguchi, *ibid.*, 165 (1979); (c) L. L. Miller and B. F. Watkins, *ibid.*, 4495 (1974).
- 4) Epoxidation of simple olefins is affected by sodium chloride promoted electrolysis. J. A. M. Leduc, U. S. Patent, 3,288,692, Nov. 29 (1966); N. L. Weiberg and H. R. Weiberg, *Chem. Rev.*, 68, 449 (1968).
- 5) Selenium-catalyzed chlorination with NCS is reported. T. Hori and K. B. Sharpless, *J. Org. Chem.*, 44, 4204 (1979).
- 6) The compound 20 was prepared by photochemical oxygen oxidation of acetate of 18 followed by chlorination with  $\text{SOCl}_2$ , dehydrochlorination with DBU, and reduction with  $\text{LiAlH}_4$ . H. Ohkawa, S. Kobayashi, and M. Ohno, Preprint of 24 th Conference on Chemistry of Terpene, Essential Oil, and Aromatics, 1980, Kooriyama, Japan.
- 7) K. Roman, K. Annemaria, and L. Dietman, *Helv. Chem. Acta*, 61, 387 (1978) and references cited therein.

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