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ENE-TYPE CHLORINATION OF OLEFINS WITH DICHLORINE MONOXIDE[1)]

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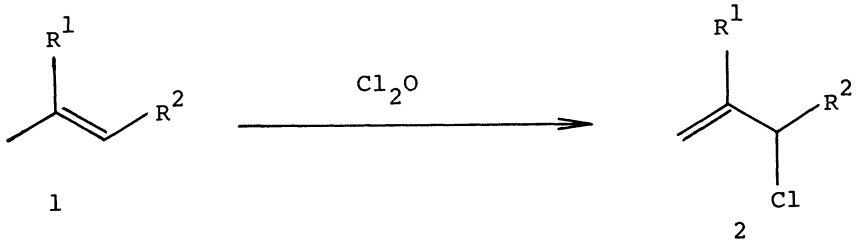
New ene-type chlorination of olefins with dichlorine monoxide (Cl_2O) and its application to the synthesis of chloroazetidinones, key intermediates of penicillin-cephalosporin conversion, are described.

Ene-type chlorination is an important reaction for functionalization of olefins.[2)] In the preceding papers, we have reported electrolytic ene-type chlorination of olefins in a CH_2Cl_2-aqueous NaCl-H_2SO_4-(Pt electrodes) system.[3)] In this connection, we proposed a working hypothesis that Cl_2O is a potential chlorination agent in the electrolysis system, since the electro-generated Cl_2 at the anode would be hydrolyzed in the aqueous phase to give HClO which would, in turn, move to organic phase and generate Cl_2O with loss of water. Recently, it has been reported that Cl_2O is a powerful and selective reagent for the chlorination of side-chain of alkylbenzenes,[4)] while very few results on the chlorination of olefins with Cl_2O have been offered.[5)] This directed our attention to Cl_2O as a potential reagent for the ene-type chlorination of olefins. In this communication, we describe the first demonstration that Cl_2O is an efficient ene-type chlorination agent for olefins under mild conditions.



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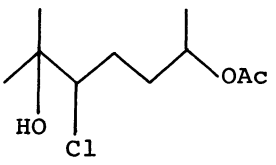
Some of results of the ene-type chlorination of olefins with Cl_2O are shown in Table 1. A typical reaction procedure (entry 1) is as follows: To a solution of 2-methyl-2-hepten-6-yl acetate 1a (0.4 mmol) in diethyl ether (4 ml) was added dropwise a solution of Cl_2O (0.2 mmol) in CCl_4 (1 ml)[6] at room temperature. The mixture was stirred for 15 min and worked up in the usual manner to afford the corresponding allylic chloride 2a in 94% yield. In place of diethyl ether, CH_2Cl_2, benzene, dioxane, and ethyl acetate could be used successfully (yields of 2a > 84%, e.g., entries 2 and 3). The two phase system, CH_2Cl_2-H_2O (1:1), was also examined in order to clarify our working hypothesis on the electrolytic ene-type chlorination,[3] vide supra, and desired product 2a was obtained in an excellent yield (entry 4). In contrast, the use of hydrophilic solvent, such as dioxane, HCOOEt, CH_3CN, and acetone, with water brought about the formation of a considerable amount of chlorohydrin 4 (18-26%) along with the desired 2a (43-65%).

It is notable that each reaction was completed by the use of 0.5 molar equiv. of Cl_2O, indicating that both of the two chlorine atoms of Cl_2O are utilized for the desired ene-type chlorination. Double ene-type chlorination of 1a was performed by using one molar equiv. of Cl_2O in dioxane, yielding dichloride 3a (68%) (entry 5).

As shown in entries 6-8, the highly regioselective chlorination of 1b-d took place to afford the corresponding mono chlorides 2b-d, respectively. These results suggest that the terminal trisubstituted C=C double bonds are much more reactive than the inner or less substituted ones presumably due to the steric and electronic reasons. In fact, under the same conditions as described above, mono or disubstituted olefins, e.g., 5 and 6, afforded no detectable amounts of the ene-type chlorination products but only recovered 5 and 6 (45-67%) along with a complex mixture of decomposition products.[5]



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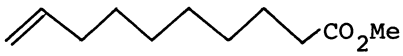

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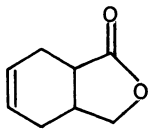

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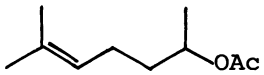
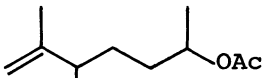
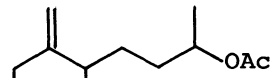
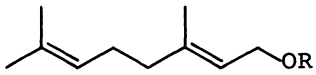
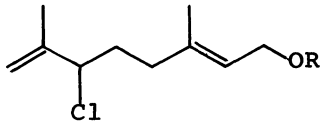
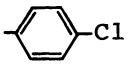
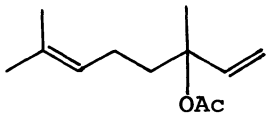
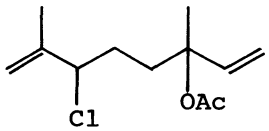
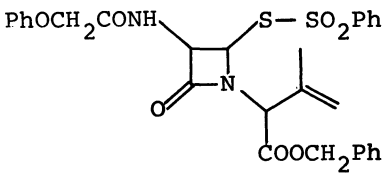
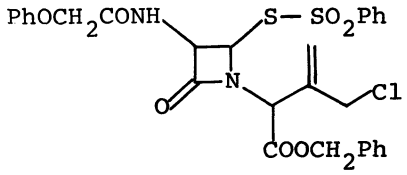
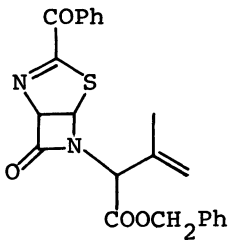
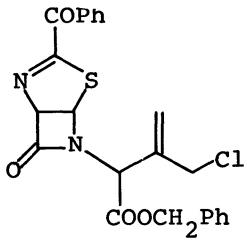
Next, the ene-type chlorination with Cl_2O was extended with success to the chlorination of azetidinone derivatives 1e and 1f (entries 9-11), which is a key step of the penicillin-cephalosporin conversion recently reported from this laboratory.[7] Thus, treatment of 1e with Cl_2O (0.65 molar equiv.) in ethyl acetate and diethyl ether at room temperature for 10 min afforded the corresponding chloride 2e in 90-93% yields (entries 9 and 10). On the other hand, chlorination of thiazoline-azetidinone 1f with Cl_2O was carried out in a two-phase solution of CCl_4-CH_2Cl_2-H_2O (1/1/1)[8] to simulate the electrolysis conditions, vide supra. After 10 min reaction and work-up, the corresponding chloride 2f was obtained in 85% yield (entry 11).

Table 1. Ene-Type Chlorination with Cl_2O [a]

Entry	Substrate	Solvent	Product (Yield / %)[b]	
				
1	1a	Et_2O	2a (94)	3a (—)
2		CH_2Cl_2	(93)	(—)
3		dioxane	(84)	(6)
4		CH_2Cl_2-H_2O (1/1)	(91)	(—)
5[c]		dioxane	(3)	(68)
				
6	1b R = Ac	Et_2O	2b (85)	
7	1c R = 	Et_2O	2c (97)	
				
8	1d	Et_2O	2d (90)	
				
9	1e	EtOAc	2e (90)	
10		Et_2O	(93)	
				
11	1f	CH_2Cl_2-H_2O (1/1)	2f (85)	

a) Carried out by treatment with a CCl_4 solution of Cl_2O (0.5 molar equiv.) at room temperature for 15 min. b) Isolated yields after column chromatography (SiO_2). c) One molar equiv. of Cl_2O was used.

As demonstrated above, Cl_2O is an excellent reagent for the ene-type chlorination of olefins and it is very likely that Cl_2O is one of the active chlorinating species in the two-phase electrolytic chlorination.[3] Studies on the scope and limitation of this reagent for ene-type chlorination and on its application are in progress.

References

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4) F. D. Marsh, W. B. Farnham, J. D. Sam, and B. D. Smart, J. Am. Chem. Soc., 104, 4680 (1982).
5) J. J. Renard and H. I. Bolker, Chem. Rev., 76, 487 (1981).
6) A CCl_4 solution of Cl_2O was prepared according to the reported procedure: G. H. Cady, Inorg. Synth., 5, 156 (1957).
7) S. Torii, H. Tanaka, M. Sasaoka, N. Saitoh, T. Siroi, and J. Nokami, Tetrahedron Lett., 23, 2495 (1982), and see also Refs. 3b-c.
8) In this two-phase system, Cl_2O would be hydrolyzed in the aqueous phase to give an equilibrium mixture: $Cl_2O + H_2O \rightleftarrows 2\ HClO$. It is likely that Cl_2O migrates into the organic phase by liquid-liquid extraction and reacts with 1f efficiently, since Cl_2O is several times more soluble in CH_2Cl_2-CCl_4 than the aqueous phase: S. Goldshmidt, Ber., 52 B, 753 (1919).

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