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Cyanuric Chloride-Mediated Synthesis of Allylic Chloride—*ipso*- versus *tele*-Substitution

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Abstract: Synthesis of unsymmetrical allylic chlorides has been accomplished using cyanuric chloride in combination with DMF through *ipso*-substitution and *tele*-substitution by judicious choice of the substituents at appropriate positions of unsymmetrical allyl alcohols, taking care of their electronic and steric properties.

Keywords: allylic chloride, electrophilic halogenating agent, regioselectivity, substitution

INTRODUCTION

Conversion of allylic alcohols to the corresponding chlorides is an important organic transformation^[1] that often brings about allylic rearrangement along with normal substitution. Numerous reagents^[1–3] have been developed for this purpose where the product spread often depends upon the nature of the substrates as well as the reagents. There are also few reports of allylic chlorination^[4] of simple olefins, but the products are complicated because of simultaneous side reactions such as vinylic chlorination, addition of chlorine across the double bond and regioisomeric allylic halogenation. We report herein a mild, cost-effective, and operationally simple protocol using cyanuric chloride^[5] (TCT) in combination with DMF for the conversion of unsymmetrically substituted

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allylic alcohols to chlorides (Scheme 1) where the product spread depends on the electronic and steric nature of the substitutens (Table 1).

It appears (entries 1, 2, 4, and 5 in Table 1) that the addition of chlorine occurs in such a way that it experiences less steric hindrance. Accordingly, ipso- (entries 1 and 2 in Table 1) and tele-substitution (entries 4 and 5 in Table 1) took place. Another driving force for this differential behavior is the newly formed double bond with extended conjugation with the aromatic ring, rendering extra stabilization. This is supported from the fact that 3° -allylic alcohol underwent in situ elimination to yield the conjugated diene in good yield (entry 3 in Table 1). Steric factor seems to play an important role as reflected in complete *tele*-substitution (entry 6 in Table 1) where attainment of extended conjugation is not possible. Competitive steric interactions between the alkyl substituents have been reflected in the product spread (entries 7 and 8 in Table 1). It is interesting to note that the presence of an electron-withdrawing group (e.g., COOMe) at the allylic position with respect to the OH group has a strong influence on the outcome of the reaction; ipso-substitution occurs preferentially over the tele-substitution (entry 9 in Table 1) despite the possibility of gaining extra stabilization of the product due to extended conjugation. This may be due to the destabilizing role of the COOMe group to accommodate the incipient electron-deficient center at the carbon to which it is attached where the incoming nucleophile would attack, leading to tele-substitution. Aryl homoallylic alcohol underwent predominant ipso-substitution as expected (entry 10 in Table 1) because there is no question of attainment of extended conjugation. Aryl-substituted-1,3-diene was obtained as the minor product in this case through elimination (entry 10 in Table 1). Therefore, a novel method has been developed for the regioselective synthesis of unsymmetrical allyl chlorides from easily accessible precursors using readily available reagents under mild reaction conditions.

EXPERIMENTAL

General Procedure for the Reaction of Allylic Alcohols with TCT/DMF

2,4,6-Trichloro-1,3,5-triazine (274 mg, 1.5 mmol) was added with vigorous stirring to anhydrous DMF (0.4 mL) at $0-5^{\circ}$ C. Stirring was continued for

Entry	Substrate	Product	Time (min)	Yield $(\%)^a$
1	Ph~~OH	Ph Cl	60	80
2	Me	Me	60	75
3	Ph OH Me	Ph Cl Me	60	70
5	Ph OH	Ph	00	70
4	Me OH I	Ph Cl	50	79
5	Ph OH	cı	120	73
	Ph	Ph Me		
6	OH	Cl	50	71
7	ОН	Cl Me	60	74 (30:70) ^b
	Me			
8	OH	Cl + Cl	60	72 (67:33) ^b
	Me	Me Me Me		
9	Ph COOMe	Cl + Cl	50	81 (83:17) ^b
10	OH		50	84 (86:14) ^b
	Ph	Ph Ph		

Table 1. Reaction of Cyanuric Chloride with unsymmetrical allylic alcohols

^aYields refer to those of isolated products, characterized spectroscopically.

^bRatio of products determined by ¹H NMR.

30 min at room temperature while a white precipitate was obtained. A solution of the substrate allylic alcohol (1 mmol) in anhydrous dichloromethane (2.0 mL) was added dropwise to it. The reaction mixture was stirred at room temperature for 2 h until completion of the reaction (monitored with thinlayer chromatography on silica gel). Then diethyl ether (6 mL) was added to the reaction mixture, which was stirred for 10 min, filtered, and the solid residue was repeatedly washed with ether (3×10 mL). The combined organic extract was washed with saturated aqueous sodium carbonate solution (2×10 mL) and brine (1×10 mL) and dried over anhydrous sodium sulfate. The solvent was evaporated to furnish the crude product. The products, if needed, were further purified by filtration chromatography on a short column of silica gel using hexane as eluent.

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