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DIRECT CHLORINATION OF SATURATED CYCLIC ETHERS USING TRICHLOROISOCYANURIC ACID

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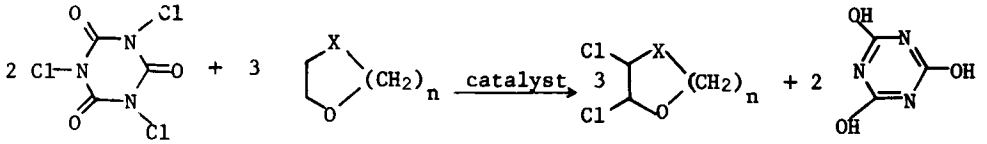
Allylic chlorination using trichloroisocyanuric acid [1,3,5-trichloro-2,4,6-trioxohexahydro-*s*-triazine (1)] has been described by Ziegler.[2] The synthetic utility of this reagent as a convenient laboratory substitute for chlorine in hypohalogenations[3] and nuclear or benzylic chlorinations[4] has recently been demonstrated. In addition, its use in the direct conversion of saturated aliphatic ethers to esters has been described.[5]

The chlorination of tetrahydrofuran (3) and tetrahydropyran (4) with 1 provided the corresponding *trans*-2,3-dichloro derivatives 3a and 4a in *ca.* 28% yield.[3] Consequently, it seemed desirable to extend the scope and limitations of this chlorination procedure.



1 — 2, n = 2, X = O — 2a, *trans*; 2b, *cis* — 5
3, n = 1, X = CH_2 — 3a, *trans*
4, n = 2, X = CH_2 — 4a, *trans*

The investigation was initiated by reacting 1 with *p*-dioxane (2). The reaction of *p*-dioxane and other cyclic ethers with *t*-butyl hypochlorite has been reported.[6] However, the chlorination products were not characterized for *p*-dioxane. We were unable to find any other report of the use of N-chloro compounds or hypohalites to chlorinate *p*-dioxane. Preliminary experiments indicated that at temperatures <50°, 2 was unreactive, i.e. <5% of

chlorinated products were isolated, even in the presence of I_2 or $SnCl_2$ catalyst. However, 1 reacts smoothly with 2 at 90-95° to give a mixture of *trans* and *cis*-2,3-dichloro-*p*-dioxanes (2a and 2b in 53% yield). Cyanuric acid (5) was recovered in >95% yield. The 2,3-structure of the product was shown unequivocally by its reaction with silver acetate to give a 62% yield of the known diacetate of 2,3-*p*-dioxanediol (6).[7] That the reaction product was indeed a mixture of 2a and 2b was shown by ir[8a] and nmr analysis.[8b] In an attempt to gain additional information concerning optimum reaction conditions and selective substitution in this reaction, several other experiments were carried out. The results are summarized in Table I.

TABLE I

CHLORINATION OF *p*-DIOXANE

Temp (°C)	Reaction time (hr)	Catalyst	% Yield, 2a and 2b[a]
90-95	4	-	53
90-95	5	-	49
80-85	1.5	I_2	72
80-85	3	I_2	62
80-85	1.5	$SnCl_2$	65
0-5	4	Hν	49[b,c]

[a] Nmr analysis of all mixtures of 2a and 2b indicates a composition of *ca.* 90% 2a and 10% 2b. [b] This reaction was carried out in a photochemical reactor[9] using equimolar quantities of 1 and 2 with excess CCl_4 as solvent. [c] 2,5-Dichloro-*p*-dioxane (7) was also isolated in 18% yield.

These data indicate that the optimum reaction time for the uncatalyzed reaction at 90-95° is 4 hr, since the yield decreased slightly for longer reaction times, presumably due to decomposition. An analogous situation seems operative in the iodine chloride catalyzed reaction. It should also

be noted that an increase in yield is observed when catalysts are employed. Some selective substitution is indicated by the isolation of 7 from the photochemical reaction.

Since the direct chlorination of 3 and 4 using 1 without catalysis had been studied, we decided to investigate the effect of various catalysts on these reactions. The results are shown in Table II. These catalyzed chlorinations proceed smoothly at room temperature, the yields being increased *ca.* 27% when I_2 is utilized and significantly increased when other catalysts are employed.

TABLE II

CHLORINATION OF TETRAHYDROFURAN AND TETRAHYDROPYRAN

Reactant	Reaction time (hr)	Catalyst	% Yield, 3a or 4a
3	1.25	I_2	54
4	1.5	I_2	56
3	1.25	$ZnCl_2$	45
4	1.5	$ZnCl_2$	49
3	1.25	$SnCl_2$	41
4	1.5	$SnCl_2$	45

Chlorination of isochroman (8) with 1 has been reported.[11] Catalysis by I_2 or $ZnCl_2$ increased the yield of 1-chloroisochroman (8a) to 63% from the previously reported 42%. That 8a was indeed the product was shown by conversion to di(1-isochromanyl) ether (9) according to the procedure given by A. Rieche.[12]

EXPERIMENTAL

Trichloroisocyanuric acid is an inexpensive, commercially available compound and was used as received from the Monsanto Corporation, St. Louis, Mo. *p*-Dioxane was purified[13] before use. The other cyclic ethers were

dried by distillation from sodium and subsequently stored over sodium until used. The melting points were taken with a Hoover-Thomas capillary melting point apparatus. The ir spectra were obtained on a Beckman Model 10 spectrophotometer using sodium chloride plates. The nmr spectra were obtained on a Varian H-100 spectrophotometer. The catalysts were reagent grade chemicals and were used as received.

trans and *cis*-2,3-Dichloro-*p*-dioxanes, 2a and 2b.— A 100-ml sample of magnetically stirred *p*-dioxane in a 250-ml three-necked flask equipped with an efficient reflux condenser was preheated to 90-95°. The heating mantle was removed and samll quantities of 1, *ca.* 0.5 g were added at such a rate as to maintain the aforementioned temperature until a total of 46.5 g (0.20 mol) of 1 was added. The addition was complete in 2 hr. The resulting reaction mixture was allowed to stir for 2 hr until a definite brown discoloration appeared. At this point the reaction was stopped and analyzed. During the addition of 1, an intermediate yellow color appeared and rapidly diminished with the concurrent precipitation of 5 and evolution of HCl. The cyanuric acid was removed by filtration and the resulting reaction mixture subjected to vacuum distillation to yield 25 g (53%) of a mixture of 2a and 2b: bp 83-84°/14 mm [lit.[14] 85°/15 mm]. The ir spectrum as a neat liquid shows strong absorption bands at 11.42 μ and 10.55 μ, which are characteristic of 2a and 2b, respectively.[8a] In addition, the nmr spectrum shows a singlet at (CCl_4) τ 4.16, characteristic of the *trans* compound, and a singlet (CCl_4) τ 4.40 characteristic of the *cis* derivative.[8b] The ratio of 2a:2b was 9:1 by nmr analysis. The remaining catalyzed chlorinations of *p*-dioxane listed in Table I were carried out in the same manner, the catalyst (0.20 g) being added to the *p*-dioxane prior to heating.

Diacetate of 2,3-*p*-dioxanediol (6).— The procedure of Boeseken, *et al.* was followed in converting 2a and 2b into 6 in 62% yield which melted

at 103-104° [lit.[7] 103-104°].

2,5-Dichloro-*p*-dioxane (7).— To a 250-ml quartz flask was added 23.24 g (0.10 mol) of 1, 8.80 g (0.10 mol) of 2 and 100 ml of CCl_4. This mixture was illuminated[9] for 4 hr at 0-5° at which time the reaction was stopped and analyzed. No generation of chlorine gas or evolution of hydrogen chloride was noted during the reaction. The cyanuric acid was removed by filtration (95+%) and the resulting reaction mixture subjected to vacuum distillation to yield 11.5 g (49%) of a mixture of 2a and 2b: bp 83-84°/14 mm [lit.[14] 85°/15 mm]. Treatment of the pot residue with petroleum ether (60-68°) resulted in crystallization of 4.2 g (18%) of 7: mp 116-118° [lit.[15] 117-118°]. As reported,[15] 7 did decompose on standing for several days at *ca.* 6°.

trans-2,3-Dichlorotetrahydrofuran (3a).—To 100 ml of magnetically stirred 3, in a 250-ml three-necked flask equipped with a reflux condenser, was added 0.2 g of I_2 and 23.24 g (0.10 mol) of 1 in small quantities, *ca.* 0.5 g, over a period of 2 hr at room temperature. An intermediate yellow color developed and rapidly diminished with the concurrent precipitation of 5. After the addition was complete, the reaction mixture was allowed to stir for 1 hr. The resulting 5 was removed by filtration and nitrogen bubbled through the reaction mixture for 1 hr. Vacuum distillation of the resulting reaction mixture gave 11.4 g (54%) of 3a: bp 60-61°/18 mm [lit.[16] 59-61°/18 mm]. The ir spectra was identical to an authentic sample prepared by the procedure of Crombie and Harper.[16] All catalyzed chlorinations of 3, 4, and 8 were carried out in the same manner with the appropriate catalyst, yielding the corresponding chloro compounds: 3a, 4a, bp 89-90°/20 mm [lit.[3] 89-90°/20 mm], and 8a, bp 117-119°/6 mm [lit.[17] 128°/12.5]. The ir spectrum of 4a was identical to the spectrum of an authentic sample prepared by other methods.[18]

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