Chimica Techno Acta
published by Ural Federal University
eISSN 2411-1414; chimicatechnoacta.ru

LETTER
2021, vol. 8(4), № 20218408
DOI: 10.15826/chimtech.2021.8.4.08

Deoxydichlorination of aldehydes catalyzed by Diphenyl sulfoxide

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This short communication (letter) belongs to the MOSM2021 Special Issue.

Abstract

The diphenyl sulfoxide-catalyzed conversion of aldehydes to 1,1-dichlorides is reported. The reaction proceeds via a sulfurous (IV)-catalysis manifold in which diphenyl sulfoxide turnover is achieved using oxalyl chloride as a consumable reagent.

Keywords

aldehydes
Lewis base catalysis
organocatalysis
diphenyl sulfoxide

Received: 31.10.2021
Revised: 17.11.2021
Accepted: 01.12.2021
Available online: 03.12.2021

1. Introduction

Nucleophilic substitutions S_N are general chemical transformations, as they allow, for example, strategic building of C–Cl, C–O, C–N and C–C bonds [1–10]. In addition, geminal dihalides, especially dichlorides, are important intermediates in chemical synthesis, and the traditional synthesis protocols are often limited in terms of cost efficiency and waste balance [11, 12]. However, research in this area is at an early stage in the study of such catalytic reaction. Although by now several effective protocols for the preparation of dichlorides from aldehydes catalyzed by a Lewis base have been disclosed [13, 14], all possibilities for studying these reactions have not yet been realized (Scheme 1).

Dichlorides – important class of intermediates in organic synthesis. They were used for alkenylation of carbonyl compounds [15, 16], cyclopropanation and epoxidation [17–19], dimerization [20, 21] and others [22–25]. In addition, geminal dichlorides are encountered as structural motifs in polyhalogenated natural products [26, 27] (Fig. 1).

2. Experimental

Yields are given for isolated products showing one spot on a TLC plate and no impurities detectable in the NMR spectrum. The identity of the products prepared by different methods was checked by comparison of their NMR spectra.

^{1}H and ^{13}C NMR spectra were recorded at 400 MHz for ^{1}H and 100 MHz for ^{13}C NMR at room temperature; the chemical shifts (δ) were measured in ppm with respect to the solvent ($CDCl_3$, ^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.16 ppm; [D6] DMSO, ^{1}H: δ = 2.50 ppm, ^{13}C: δ = 39.52 ppm). Coupling constants (*J*) are given in Hertz. Splitting patterns of apparent multiplets associated with an averaged coupling constants were designated as *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *sept* (septet), *m* (multiplet), *dd* (doublet of doublets) and *br* (broadened). Melting points were determined with a «Stuart SMP 30», the values are uncorrected. Flash chromatography was performed on silica gel Macherey Nagel (40–63 μm).

Reaction progress was monitored by GC/MS analysis and thin layer chromatography (TLC) on aluminum backed plates with Merck Kiesel 60 F254 silica gel. The TLC plates were visualized either by UV radiation at a wavelength of 254 nm, or stained by exposure to a Dragendorff's reagent or potassium permanganate aqueous solution. All the reactions were carried out using dried and freshly distilled solvent.

2.1. General method for synthesis of dichlorides from aldehyde

Diphenyl sulfoxide (Ph_2SO) (40 mg, 0.2 mmol, 0.1 equiv, 10 mol.%) and aldehyde 1 (2 mmol, 1 equiv) were dissolved in 15 mL of anhydrous toluene in a 25 mL round bottom flask equipped with a magnetic stirring bar. The resulting solution was treated dropwise with neat oxalyl chloride (0.26 mL, 3 mmol, 1.5 equiv (chlorine source))

using an adjustable volume pipette (0.1–1.0 mL), followed by the temperature increase up to 100 °C; the mixture was stirred for 6 h. The reaction progress was monitored by GC-MS. After the reaction was complete, the solution was filtered and concentrated in vacuum. The crude mixture thus obtained was purified by flash chromatography on silica (petroleum ether/Et_2O – 19/1).

2.1.1. (Dichloromethyl)benzene 4a

Obtained from 1a (212 mg, 2 mmol), diphenyl sulfoxide (Ph_2SO) (40 mg, 0.2 mmol, 0.1 equiv, 10 mol.%), and oxalyl chloride (0.26 mL, 3 mmol, 1.5 equiv), in anhydrous toluene (15 mL). Colorless oil (242 mg, 75%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 6.75 (s, 1H, CH), 7.44 (m, 3H, H_{Ar}), 7.66 (m, 2H, H_{Ar}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 72.0, 126.2, 128.8, 123.0, 140.4.

2.1.2. 1-(Dichloromethyl)-4-methylbenzene 4b

Obtained from 1b (240 mg, 2 mmol), diphenyl sulfoxide (Ph_2SO) (40 mg, 0.2 mmol, 0.1 equiv, 10 mol.%), and oxalyl chloride (0.26 mL, 3 mmol, 1.5 equiv), in anhydrous toluene (15 mL). Colorless oil (278 mg, 80%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.40 (s, 3H, CH_3), 6.68 (s, 1H, CH), 7.23 (m, 2H, H_{Ar}), 7.48 (m, 2H, H_{Ar}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 21.7, 71.6, 126.1, 129.3, 137.5, 140.9.

2.1.3. 1-Bromo-4-(dichloromethyl)benzene 4c

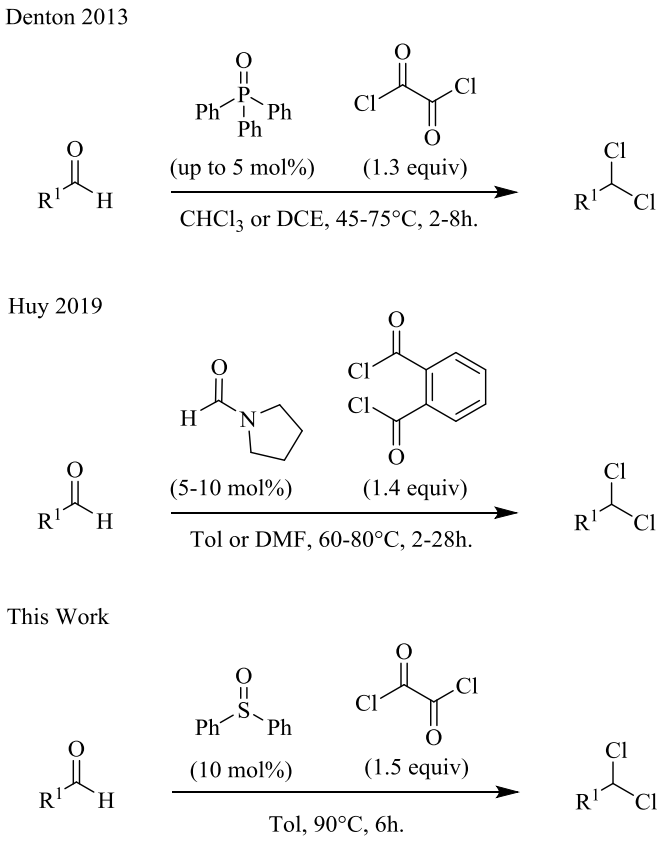
Obtained from 1c (370 mg, 2 mmol), diphenyl sulfoxide (Ph_2SO) (40 mg, 0.2 mmol, 0.1 equiv, 10 mol.%), and oxalyl chloride (0.26 mL, 3 mmol, 1.5 equiv), in anhydrous toluene (15 mL). Colorless oil (345 mg, 72%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 6.68 (s, 1H, CH), 7.46 (m, 2H, H_{Ar}), 7.55 (m, 2H, H_{Ar}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 72.0, 124.3, 128.0, 131.9, 139.4.

2.1.4. 1-(Dichloromethyl)-4-nitrobenzene 4d

Obtained from 1d (302 mg, 2 mmol), diphenyl sulfoxide (Ph_2SO) (40 mg, 0.2 mmol, 0.1 equiv, 10 mol.%), and oxalyl chloride (0.26 mL, 3 mmol, 1.5 equiv), in anhydrous toluene (15 mL). Colorless oil (259 mg, 63%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 6.78 (s, 1H, CH), 7.78 (m, 2H, H_{Ar}), 8.29 (m, 2H, H_{Ar}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 70.2, 124.5, 127.9, 146.6, 149.2.

2.1.5. (E)-(3,3-Dichloroprop-1-en-1-yl)benzene 4e

Obtained from 1e (264 mg, 2 mmol), diphenyl sulfoxide (Ph_2SO) (40 mg, 0.2 mmol, 0.1 equiv, 10 mol.%), and oxalyl chloride (0.26 mL, 3 mmol, 1.5 equiv), in anhydrous toluene (15 mL). Colorless oil (286 mg, 77%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 6.34 (*d*, *J* = 7.6 Hz, 1H, CH), 6.39 (*dd*, *J* = 14.7 and 7.6 Hz, 1H, CH), 6.72 (*d*, *J* = 14.7 Hz, 1H, CH), 7.41 (m, 5H, H_{Ar}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 73.5, 127.0, 128.2, 129.1, 129.3, 132.5, 134.9.



Scheme 1 Deoxydichlorination of aldehydes to 1,1-dichlorides

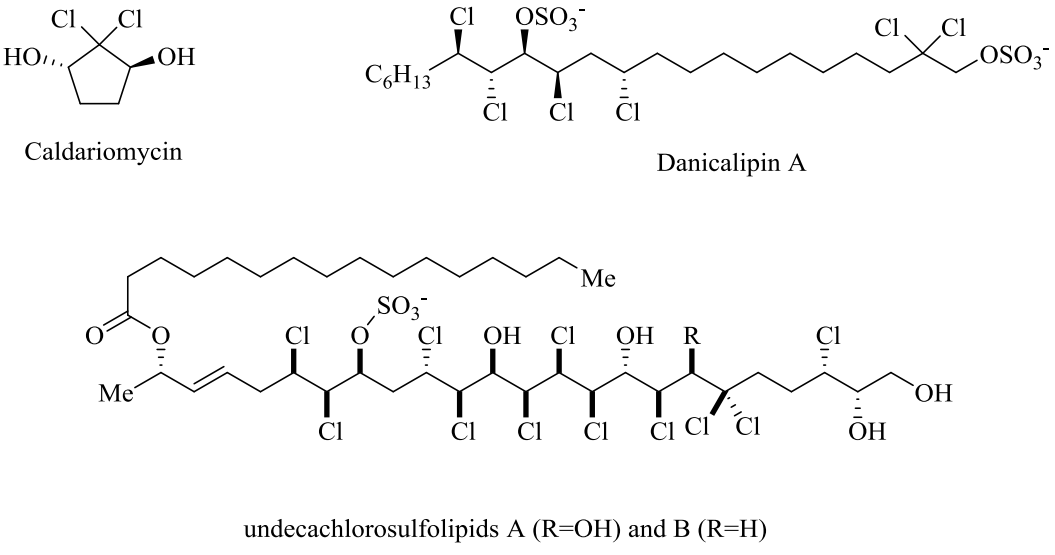
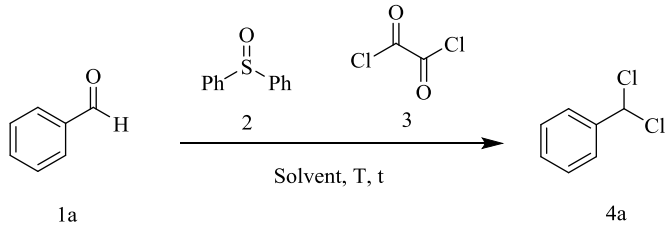


Fig. 1 Natural products including a fragment of dichlorides

3. Results and discussion

The investigation commenced with establishing the best conditions for the deoxydichlorination of aldehydes, employing benzaldehyde 1a as a model substrate (Scheme 2). First, the role of each reagent was evaluated. Oxalyl chloride on its own did not produce (Dichloromethyl)benzene 4a (Table 1, entry 1). The use of stoichiometric quantities of Ph_2SO and $(COCl)_2$ in acetonitrile resulted in low conversion of 1a into 4a (entry 2). With 10 mol.% Ph_2SO and 1 equiv of oxalyl chloride, 4a was formed in 15% conversion (entry 3), which increased to 51% after change the solvent on toluene (entry 4). The up of the temperature to 100 °C and use 1.5 equiv of oxalyl chloride to give the best results of conversion to 92% (entry 11).



Scheme 2 The reaction for optimization of the conditions

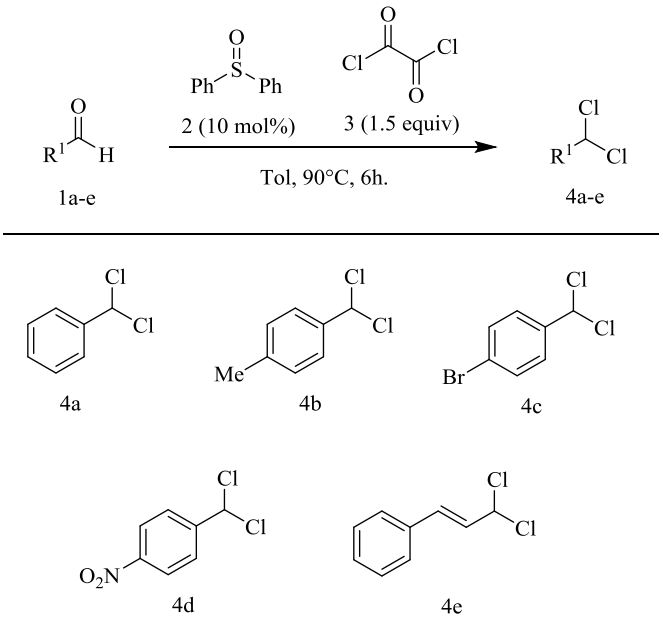
Table 1 Optimization of the reaction conditions

Entry	Equiv of $(COCl)_2$	Ph_2SO, mol.%	Solvent	*T*, °C	*t*, h	*Conv.*, %[b]
1	1	–	MeCN	50	1	0
2	1	100	MeCN	50	1	19
3	1	10	MeCN	50	6	15
4	1	10	Tol	50	6	53
5	1	10	DCM	40	6	10
6	1	10	DCE	50	6	18
7	1	10	THF	50	6	37
8	1	10	Et_2O	30	6	4
9	1	10	Tol	100	6	85
10	1	10	Tol	100	12	88
11	1.5	10	Tol	100	6	92

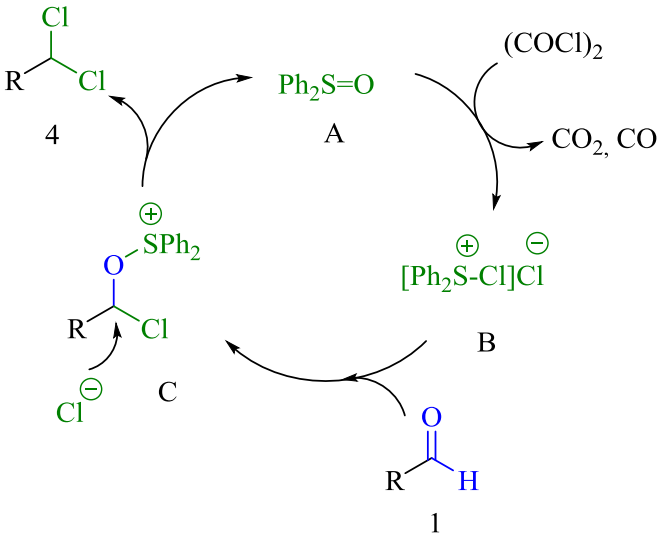
[a]General conditions: 1a (0.2 mmol), Ph_2SO, dry solvent (1 mL), dropwise addition of neat $(COCl)_2$. The reactions were carried out for 1–12 h before an aliquot (50 μL) was taken, quenched with aqueous solvent (1 mL), and analyzed by GC.
[b]Conversion to 4a was calculated from GC.

The substrate scope was investigated next. As shown in Scheme 3, the reaction work well with different type of aromatic aldehydes, including donor and acceptor substituents at the fourth position of the ring. The use of cinnamaldehyde under the reaction conditions also showed good results.

The proposed mechanism is depicted in Scheme 4. We think that the catalytic cycle start with quick formation of the intermediate chlorodiphenylsulfonium chloride (B) upon treatment of diphenyl sulfoxide (A) with $(COCl)_2$. Previously, a similar process was carried out by Denton with triphenylphosphine oxide as a catalyst [14]. Next, in the catalytic cycle, the intermediate B reacts with the aldehyde 1 via oxygen to form the intermediate C, which then undergoes elimination to furnish the geminal dichloride 4 and regenerate the catalyst A.



Scheme 3 Deoxydichlorination of aldehydes catalyzed by Diphenyl sulfoxide



Scheme 4 Proposed mechanism

4. Conclusions

We have developed a highly expedient protocol for a catalytic deoxydichlorination of aldehydes under conditions of a catalytic Swern Oxidation catalyzed by diphenyl sulfoxide. The salient features of the method are: (i) operational simplicity, (ii) low catalyst loading (10 mol.%), (iii) medium reaction times and (iv) mild conditions.

Acknowledgments

The authors thank Russian Science Foundation for grant 20-73-00081.

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