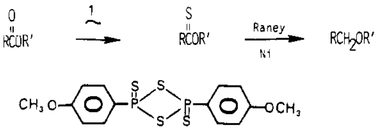
New Conversion of Esters to Ethers and Its Application to the Preparation of Furano-18-crown-6

Summary: Thionoesters which are readily prepared from esters can be desulfurized with Raney nickel to form the corresponding ethers. This new synthetic pathway to convert esters to ethers avoids many of the steric and functional limitations of known methods and appears to be a general method for this conversion.

Sir: For the past several years we have been interested in the reduction of the carbonyl function of esters as a synthetic pathway to form ethers. This reduction would permit the preparation of a variety of known and unknown crown ethers from the corresponding crown ether–diester analogues whose preparation is frequently much easier to achieve.[1-3] Pettit and his co-workers have used a variety of borohydride reagents (all of which lead to the formation of diborane in situ) to reduce some hindered esters to form ethers.[4,5] Tsurugi and his co-workers found that trichlorosilane in the presence of ultraviolet radiation reduced esters of primary and secondary alcohols to the corresponding ethers.[6,7] The application of these methods to the reduction of crown ether–diester compounds to form the crown ethers was unsuccessful.[8] A recent report of the high-yield conversion of esters to thionoesters[9] has prompted us to investigate the thionation and desulfurization of a variety of simple esters as an alternate pathway to convert esters to ethers. Using this procedure, we have also reduced a furano crown ether–diester compound to the furano crown ether.

Thionation of the esters was performed according to the recently reported method of Pedersen and co-workers[9] by using 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide (1) which was readily prepared from phosphorus pentasulfide and anisole.[10] Desulfurization was carried out over Raney nickel at −10 to −30 °C in a suitable aprotic solvent. Aqueous solvents gave only benzaldehyde in the desulfurization of ethyl thionobenzoate while in ethanol, benzaldehyde diethyl acetal was the major product. The conversion of methyl benzoate to methyl benzyl ether is given below.



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A mixture of 0.5 g (0.037 mol) of methyl benzoate, 2.0 g of 1, and 4 mL of anhydrous xylene was refluxed in a nitrogen atmosphere until a TLC analysis showed that the ester had reacted (nearly 24 h). The orange material was mixed with 2–3 g of silica gel, and the xylene was removed by evaporation. The adsorbed silica gel was then added to a column of about 40 g of silica gel, and the column was eluted with hexane. When the orange thionoester band started to elute, the solvent was changed to ether/hexane (2:98). After the solvent was removed from the orange eluant, 5 mL of ether was added, and the ether solution was dried over molecular sieves for at least 1 h.

Table I. Preparation of Ethers from Esters by Thionation–Desulfurization

ester (RC(O)OR′)		thionation time, h	% ether (RCH_2OR')[a]
R	R′		
Ph	Me	24	63[b]
Ph	Et	25	59
Ph	*i*-Pr	25	69
Ph	*t*-Bu	*c*	
Ph	Ph	24	34
p-NO_2Ph	Me	*c*	
p-MeOPh	Me	4.5	66
Ph	$CH_2CH_2OCH_3$	*c*	
t-Bu	Et	8[d]	66
2-thienyl	Et	1	*e*
2-furanyl	Me	1.5	37
2-pyridyl	Me	*c*	
diglycolyl	Et	*f*	5

[a] Yield determined by multiple VPC analyses of the desulfurized reaction mixture by using an internal standard. Yields are based on the amount of starting ester and therefore correspond to the overall conversion of ester to ether. Products were collected from the chromatograph and characterized by comparison of IR, NMR, or mass spectral properties to reported values. [b] A 33% yield was obtained by distillation of a preparative-scale reaction. The forerun and pot contained an additional 6% and 5%, respectively, as determined by VPC analysis. [c] No thionoester was isolated. [d] Thionation was carried out in a Teflon-lined bomb with benzene solvent at 155 °C. [e] Ethyl pentyl ether was obtained as the major product. [f] Thionation was performed in toluene for 7 h. A poor yield was observed due to polymerization of the thionating reagent.

About 10 g of wet Raney nickel was placed in a centrifuge tube and then washed 10 times with anhydrous ethanol followed by 10 washes with anhydrous ether. The Raney nickel was then stored under 5 mL of anhydrous ether, and the mixture was dried with molecular sieves for at least 1 h. The thionoester–ether solution and the Raney nickel–ether mixture were each cooled to −15 °C and then mixed together. The resulting mixture was shaken while the temperature was kept below about −10 °C until the orange color disappeared (about 3 min). At high temperatures, the methyl benzyl ether product is reduced to toluene. The mixture was then centrifuged and decanted. The Raney nickel was washed with five portions of anhydrous ether. **Caution**: the Raney nickel must be kept under solvent at all times since it becomes pyrophoric when exposed to air. The combined ether solutions were evaporated to a 5-mL volume and analyzed by gas chromatography using an internal standard. The results for a number of reductions are shown in Table I. The IR and NMR spectra of the isolated methyl benzyl ether were identical with those of an authentic sample.

Table I shows that unlike Pettit's borohydride procedure,[5] the thionation–desulfurization method allows esters of primary and secondary alcohols to be reduced in good yields (~60–70%). This method is also superior to Tsurugi's photochemical reduction[7] in that aromatic substrates are also reduced in good yields.

The limiting step of this procedure appears to be the thionation reaction. *tert*-Butyl benzoate failed to undergo thionation due to either steric hindrance or an acid-cata-

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(1) Maas, G. E.; Bradshaw, J. S.; Izatt, R. M.; Christensen, J. J. *J. Org. Chem.* **1977**, *42*, 3937–3941.

(2) Bradshaw, J. S.; Maas, G. E.; Lamb, J. D.; Izatt, R. M.; Christensen, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 467–474.

(3) Bradshaw, J. S.; Maas, G. E.; Izatt, R. M.; Christensen, J. J. *Chem. Rev.* **1979**, *79*, 37–52.

(4) Pettit, G. R.; Kasturi, T. R. *J. Org. Chem.* **1960**, *25*, 875–876.

(5) Pettit, G. R.; Piatak, D. M. *J. Org. Chem.* **1962**, *27*, 2127–2130.

(6) Tsurugi, J.; Nakao, R.; Fukumoto, T. *J. Am. Chem. Soc.* **1969**, *91*, 4587–4588.

(7) Nagata, Y.; Dohmaru, T.; Tsurugi, J. *J. Org. Chem.* **1973**, *38*, 795–799.

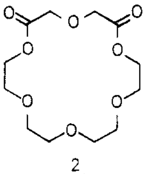
(8) Maas, G. E. Ph.D. Dissertation, Brigham Young University, 1979.

(9) Pedersen, B. S.; Scheibye, S.; Clausen, K.; Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 293–297.

(10) Pedersen, B. S.; Scheibye, S.; Nilsson, N. H.; Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 223–228.

0022-3263/81/1946-0831$01.00/0

lyzed decomposition of the ester. Compounds with electron-withdrawing substituents conjugated to the ester carbonyl failed to react (cf. methyl *p*-nitrobenzoate, methyl picolinate), while conjugated electron-donating groups increased the rate of the reaction (cf. methyl *p*-methoxybenzoate, methyl furoate). In keeping with the known electrophilic reactions of the phosphorous atoms in related systems,[11,12] we have interpreted these results as being indicative of a mechanism involving nucleophilic attack by the carbonyl oxygen on the phosphorus of the thionating reagent. We have also observed that esters containing ether functionality are difficult to thionate (cf. diethyl diglycolate, β-methoxyethyl benzoate). We believe this is caused by competition between the carbonyl oxygen and the more basic ether oxygen for the electrophilic phosphorous. In agreement with this observation, the simple crown ether–diester 2 failed to undergo thionation.



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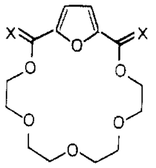

3 X = O

4 X = S

5 X = H_2

However, the more reactive furano crown ether–diester 3 was thionated in a good yield (83%) to give dithiono crown ether 4, a yellow solid, mp 125–126 °C.[13] Compound 4 was desulfurized in a poor yield (15%) to give furano-18-crown-6 (5) a known compound.[14] Compound 4 is the first of a new series of crown compounds containing the thionoester function. Thiono crown compounds may be interesting complexing agents themselves as well as intermediates in the preparation of crown ethers.

This procedure for reducing esters to ethers appears to be the most general method available to date. Future work will include a more detailed investigation of the scope of this reduction. We also plan to prepare more thiono crown compounds in order to evaluate their complexation properties as well as to study their desulfurization to form the corresponding crown ethers.

Acknowledgment. The authors thank Mr. J. S. Gebhard and Mr. J. H. Colter for the synthesis of some of the thionoesters. Support from National Science Foundation Grant CHE-8000059 is also acknowledged.

Registry No. 1, 19172-47-5; 3, 72638-75-6; 4, 76190-21-1; 5, 53914-85-5; PhC(O)OMe, 93-58-3; PhC(O)OEt, 93-89-0; PhC(O)O-*i*-Pr, 939-48-0; PhC(O)O-*t*-Bu, 774-65-2; PhC(O)OPh, 93-99-2; *p*-NO_2PhC(O)OMe, 619-50-1; *p*-MeOPhC(O)OMe, 121-98-2; PhC(O)-$OCH_2CH_2OCH_3$, 5451-71-8; *t*-BuC(O)OEt, 3938-95-2; (2-C_4H_3S)C-(O)OEt, 2810-04-0; (2-C_4H_3O)C(O)OMe, 611-13-2; (2-C_5H_4N)C(O)-OMe, 2459-07-6; EtOCOCOCH_2OCH_2COC(O)OEt, 76190-22-2; PhC-(S)OMe, 5873-86-9; PhC(S)OEt, 936-61-8; PhC(S)O-*i*-Pr, 40669-41-8; PhC(S)OPh, 16911-57-2; *p*-MeOPhC(S)OMe, 5925-50-8; *t*-BuC(S)-OEt, 58287-47-1; (2-C_4H_3S)C(S)OEt, 13749-76-3; (2-C_4H_3O)C(S)-OMe, 76190-23-3; EtOC(S)COCH_2OCH_2COC(S)OEt, 76190-24-4; PhCH_2OMe, 538-86-3; PhCH_2OEt, 539-30-0; PhCH_2O-*i*-Pr, 937-54-2; PhCH_2OPh, 946-80-5; *p*-MeOPhCH_2OMe, 1515-81-7; *t*-BuCH_2OEt, 17348-57-1; ethyl pentyl ether, 17952-11-3; (2-C_4H_3O)CH_2OMe, 13679-46-4; EtOCH_2COCH_2OCH_2COCH_2OEt, 76190-25-5.

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Received October 8, 1980

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(11) Corbridge, D. E. C. "Phosphorus: An Outline of its Chemistry, Biochemistry and Technology"; Elsevier: New York, 1978; Chapter 7.

(12) Almasi, L. In "Sulfur in Organic and Inorganic Chemistry"; Senning, A., Ed.; Marcel Dekker: New York, 1971; Chapter 4.

(13) Satisfactory IR, NMR, and combustion analyses were obtained. The melting point is uncorrected.

(14) Timko, J. M.; Moore, S. S.; Walba, D. M.; Hiberty, P. C.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 4207–4219.

(15) Contribution no. 235.