[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MASSACHUSETTS]

Competitive Reductive *o*-Debenzylation of Ethers and Esters[1]

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A comparison has been made of the susceptibility to Pd-catalyzed hydrogenolysis of different benzyl type groups in ether and ester linkage.

Benzyl type groups could be valuable as protective groups in complex syntheses. One of their advantages is that, once their protective function is accomplished, they can easily be removed by catalytic hydrogenation under mild conditions. For example, $C_6H_5CH_2$—O—R on hydrogenation in the presence of palladium on charcoal gives toluene plus an alcohol.

It would be advantageous in some syntheses to have two benzyl type protective groups which could be removed one at a time. In competitive reductions of tertiary amines containing two different benzyl groups attached to the nitrogen, it was found that the unsubstituted benzyl group was removed by hydrogenolysis in preference to the benzyl groups which contained methyl, chloro, or amino groups in the para positions.[4] In other studies, it was found that the α-naphthylmethyl group was removed in preference to the *p*-phenylbenzyl group, and that the latter is removed in preference to the benzyl group.[5] Thus in an amine containing the four groups, α-naphthylmethyl, *p*-phenylbenzyl, benzyl, and *p*-methylbenzyl, attached to nitrogen, it is to be expected that the four could be removed stepwise by catalytic hydrogenation in the order in which they are listed above.

It was the object of this work to determine whether comparable selectivity could be obtained in the ether and ester series. Accordingly, the cyclohexyl ethers of the above four groups were prepared and competitively hydrogenolyzed. Also benzyl acetate and α-naphthylmethyl acetate were competitively hydrogenolyzed with each other and with these ethers.

In the competitive reductive debenzylation of ethers, summarized in Table I, it was found that the order of ease of cleavage of benzyl groups which was established for tertiary amines holds in the case of the ethers also, except that the α-naphthylmethyl group could not be cleaved from its ether linkage under the conditions used. In the presence of α-naphthylmethyl cyclohexyl ether, even the benzyl cyclohexyl ether could not be reduced. The possibility that the α-naphthylmethyl cyclohexyl ether used in these experiments contained some poison was eliminated when it was found that benzyl acetate or α-naphthylmethyl acetate mixed with this ether were hydrogenated easily with cleavage of the ester group.

Although the order of ease of cleavage of the benzyl type groups in ether linkage was the same as that established for amines, 100% selectivity was not obtained in any case. Thus when benzyl cyclohexyl ether and *p*-phenylbenzyl cyclohexyl ether were simultaneously hydrogenated (No. 1 in Table I), *p*-methylbiphenyl was isolated in greater yield than toluene, but both were obtained in significant quantities. These results offer little encouragement for the use under these conditions of selective debenzylation of benzyl type protective groups in ether linkage.

The result with the two esters studied was more encouraging. When benzyl acetate was reduced competitively with α-naphthylmethyl acetate (No. 4), it was found that the α-naphthylmethyl group was cleaved with almost complete selectivity However, benzyl benzoate and benzyl acetate showed no selectivity of reduction between themselves (No. 5), indicating that the acid portion of the ester does not exert much effect on selectivity.

A comparison of the ease of cleavage of benzyl type groups in ester linkage with those in ether linkage showed that the esters are preferentially cleaved. Thus when benzyl benzoate and benzyl cyclohexyl ether were simultaneously hydrogenated (No. 6), the ester was practically completely cleaved, while the ether was apparently not attacked at all, since no cyclohexanol could be detected among the reduction products. Also, as is to be expected, when a mixture of α-naphthylmethyl acetate and benzyl cyclohexyl ether was hydrogenated (No. 7), the ester was completely cleaved, while the ether was not attacked, since no toluene or cyclohexanol could be detected among the reduction products. When benzyl benzoate was simultaneously hydrogenated with α-naphthylmethyl cyclohexyl ether (No. 8), again

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[4] R. Baltzly and J. S. Buck, *J. Am. Chem. Soc.*, **65**, 1984 (1943). R. Baltzly and P. B. Russell, *J. Am. Chem. Soc.*, **72**, 3410 (1950); *J. Am. Chem. Soc.*, **75**, 5598 (1953).

[5] H. Dahn, U. Solms, and P. Zoller, *Helv. Chim. Acta*, **35**, 2117 (1952).

TABLE I

COMPETITIVE REDUCTION OF BENZYL ETHERS AND ESTERS

Expt. No.	Starting Materials	Moles	H_2 Absorbed, Moles	Time, Min.	Products Isolated	Yield, Mole %
1.	Ph benz-O-Cx[a] plus Benzyl cyclohexyl ether	0.05 0.05	0.05	2.5	$p\text{-}C_6H_5\text{-}C_6H_4\text{-}CH_3$ Toluene Cyclohexanol	51.2 30.3 68
2.	Me benz-O-Cx[b] plus Benzyl cyclohexyl ether	0.1 0.1	0.1	3.0	p-Xylene Toluene	29.1 41.3
3.	Ph benz-O-Cx[a] plus Me benz-O-Cx[b]	0.05 0.05	0.05	8	$p\text{-}C_6H_5\text{-}C_6H_4\text{-}CH_3$ p-Xylene	50.5 29.1
4.	Men-O-Ac[c] plus Benzyl acetate	0.1 0.1	0.1	154[e]	α-Methylnaphthalene Toluene	84.5 2.2
5.	Benzyl benzoate plus Benzyl acetate	0.1 0.1	0.1	111[f]	Benzoic acid Total acid	41.0[h] 88.5[i]
6.	Benzyl benzoate plus Benzyl cyclohexyl ether	0.1 0.1	0.1	30[f]	Benzoic acid Cyclohexanol	85.5[i] 0.0
7.	Men-O-Ac[a] plus Benzyl cyclohexyl ether	0.05 0.05	0.05	1	α-Methylnaphthalene Toluene	76.0 0.0
8.	Men-O-Cx[d] plus Benzyl benzoate	0.05 0.05	0.05	105[g]	Cyclohexanol Toluene Benzoic acid	0.0 56.5 63.8[h]
9.	Ph benz-O-Cx[a] plus Benzyl acetate	0.05 0.05	0.05	3	$p\text{-}C_6H_5\text{-}C_6H_4\text{-}CH_3$ Cyclohexanol Toluene	34.5 26 45.6

[a] Ph benz-O-Cx is p-phenylbenzyl cyclohexyl ether. [b] Me benz-O-Cx is p-methylbenzyl cyclohexyl ether. [c] Men-O-Ac is α-naphthylmethyl acetate. [d] Men-O-Cx is α-naphthylmethyl cyclohexyl ether. [e] Four g. of catalyst used. [f] One g. of catalyst used. [g] Three g. of catalyst used. [h] By isolation. [i] By titration.

the ester was completely cleaved, and the ether was untouched, in accordance with expectations, since the ether could not be reduced alone under these conditions.

However, when the most easily cleaved ether, p-phenylbenzyl cyclohexyl ether, and the less easily cleaved ester, benzyl acetate, were hydrogenated together (No. 9), it was found that the selectivity of reduction was not complete. To be sure, the ester was cleaved to a greater extent, but a 35% yield of p-methylbiphenyl was also isolated, indicating at least this much ether cleavage.

At first glance it may appear anomalous that the α-naphthylmethyl group, which is considered to be the "most easily cleaved" of all benzyl type groups in hydrogenolysis of tertiary amines and quaternary ammonium bases, is not cleaved at all in its ether linkage. The explanation of this fact rests on the observation of Dahn *et al.*,[5] that although the naphthylmethyl group in a competitive reduction is preferentially cleaved, it gives the slowest reactions of all the benzyl type groups with which they worked. This is explained by assuming that the selectivity of reduction is governed by the degree of adsorption of the compound on the palladium catalyst, and not by the speed of hydrogenation. Thus, apparently α-naphthylmethyl cyclohexyl ether is adsorbed very strongly on the catalyst, but its rate of hydrogenation is impracticably slow.

The ability of the α-naphthylmethyl cyclohexyl ether to prevent the reduction of benzyl cyclohexyl ether is explained on the same basis: the menaphthyl ether is adsorbed so much more strongly that it occupies all the available catalytic sites on the catalyst, leaving none available for the benzyl ether.

EXPERIMENTAL

Reductions. The Parr Adams Pressure Reaction Apparatus was used throughout this work. Reductions were carried out with an overpressure of three atmospheres of hydrogen. A drop of 7 pounds was equivalent to 0.1 mole of hydrogen absorbed. In all cases either 0.05 or 0.1 mole of compound dissolved in 100 ml. of ether was taken for hydrogenation. The hydrogenation catalyst used was 10% Palladium on Darco (made by The American Platinum Works, Newark, N.J.).

For each 0.1 mole of compound taken for hydrogenation, six grams of catalyst were used, except that with the esters, smaller quantities were used, as noted in Table I.

When the desired amount of hydrogen had been absorbed, the catalyst was filtered off and washed with ether. In some cases where acetic and/or benzoic acid had been produced during hydrogenation, a titration was performed to determine the amount of acid, after which the acid was extracted with sodium hydroxide. Then the non-acidic products were separated by distillation in a micro apparatus fitted with a small Vigreux column.

Benzyl benzoate and *benzyl acetate* were obtained commercially.

Benzyl cyclohexyl ether was prepared by the method of

Jarrousse,[6] from cyclohexanol and benzyl chloride in the presence of 55% sodium hydroxide and triethylamine at 50–55°. Yield of benzyl cyclohexyl ether, b.p. 164° (37 mm.), 141° (18 mm.), 132° (12 mm.), was 70%.

p-Xylyl bromide, b.p. 85–95° (4 mm.), m.p. 34–35° (needles from ethanol), was prepared in 44% yield by sunlight initiated bromination of *p*-xylene in carbon tetrachloride solution.

p-Xylyl cyclohexyl ether. Cyclohexanol (10.0 g., 0.1 mole) was added to a stirred mixture of 25 ml. of absolute ether and 3.9 g. (0.1 mole) of sodamide. Then 18.5 g. (0.1 mole) of *p*-xylyl bromide was added dropwise. The reaction was stirred in an oil bath at 70° for 21 hr. Then water was added to dissolve the sodium salt and the organic layer was extracted with ether. The ether layer was washed with water, dried with magnesium sulfate, and distilled. *p*-Xylyl cyclohexyl ether, b.p. 114° (4 mm.), was obtained in 44% yield.

Anal. Calcd. for $C_{14}H_{20}O$: C, 82.28; H, 9.87. Found: C, 79.92; H, 9.60.

4-Phenyl benzyl alcohol was made from 4-bromodiphenyl by the Grignard reaction.[7]

4-Chloromethyl diphenyl was made from the alcohol and thionyl chloride.[7]

p-Phenylbenzyl cyclohexyl ether, b.p. 160–167° (5 mm.), m.p. 84–86° (colorless plates from ethanol), was made by two methods. It was made from cyclohexanol and 4-chloromethyl diphenyl in 41% yield by the method described above for *p*-xylyl cyclohexyl ether: and it was made in 47% yield by the method of Jarrousse[6] described above for benzyl cyclohexyl ether.

1-Chloromethyl naphthalene was made by the method of Coles and Dodds.[8] *α-Naphthylmethanol* was made in 75% yield by hydrolysis of 1-chloromethylnaphthalene and in 45% yield by the Grignard reaction *via* alpha-bromonaphthalene according to Bourquelot and Bridel.[9] *α-Naphthylmethyl acetate*, b.p. 142–143° (4 mm.), 172–173° (13 mm.), was made in 24% yield by direct reaction of acetyl chloride with the alcohol. Acetic anhydride would not react with α-naphthylmethanol in the absence of a catalyst; and in the presence of sulfuric acid only polymeric products could be obtained.

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 77.92; H, 6.04. Found: C, 76.94; H, 6.13.

α-Naphthylmethyl cyclohexyl ether was made in 27% yield from the chloride and cyclohexanol by the method of Jarrousse[4] described above for benzyl cyclohexyl ether. The compound is described in the literature[10] as a liquid, b.p. 165–166° (0.8 mm.). It was found in this work to be a solid, m.p. 40–41.5° (needles from ethanol), b.p. 176–177° (6 mm.).

Anal. Calcd. for $C_{17}H_{20}O$: C, 84.89; H, 8.39; M. W. 240.2. Found: C, 84.64; H, 8.21; M. W. 244.0.

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(6) J. Jarrousse, *Compt. rend.*, 232, 1424 (1951).

(7) S. Goldschmidt, P. Modderman, and G. A. Overbeek, *Rec. trav. chim.*, 69, 1109 (1950).

(8) H. W. Coles and M. L. Dodds, *J. Am. Chem. Soc.*, 60, 853 (1938).

(9) E. Bourquelot and M. Bridel, *Compt. rend.*, 168, 323 (1919).

(10) W. Kruyt and H. Veldstra, *Landbouwk. Tijdschr.*, 63, 398 (1951); *Chem. Abstr.*, 55, 7287 (1951).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Heterocyclic Vinyl Ethers. XIII. The Reaction of 2,5-Diphenyl-1,4-dithiadiene with *n*-Butyllithium and Dimethyl Sulfate[1]

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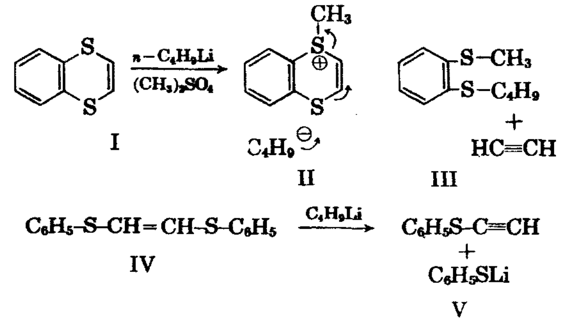
2,5-Diphenyl-1,4-dithiadiene (VI) does not react appreciably with *n*-butyllithium in ether at 0°; however, when dimethyl sulfate is present a substitution-elimination reaction occurs leading to phenylacetylene and the sulfides VIII and IX. VIII was shown to be a major component of the mixed sulfides, by alkaline hydrolysis of the corresponding crude sulfone to benzyl *n*-butyl sulfone (XII). It appears that the cleavage of the dithiadiene ring to acetylenes and alicyclic ethylenic sulfides is a general reaction, for both VI and benzo-1,4-dithiadiene (I) react similarly, and in a manner different from their open chain analogs.

The reaction of the ethylenic sulfides VIII and IX with phenyllithium was studied, and cleavage of the expected acetylenic sulfides to phenylacetylene was observed.

It has been previously shown that benzo-1,4-dithiadiene (I) does not undergo appreciable metalation by reaction with butyllithium in ether at 0°. However, when such reaction mixtures are treated with alkylating agents, a substitution-elimination reaction occurs (II), leading to the formation of acetylene and sulfides such as III. The open chain analogs of I, *cis* or *trans* bis-(phenylmercapto)-ethylene (IV), on the other hand, react rapidly with butyllithium in ether at 0° to give high yields of phenylmercaptoacetylene and lithium thiophenolate. The presence of dimethyl sulfate



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(2) From the M.S. Thesis of M. T. Kneller, University of Minnesota ,1958.

(3) W. E. Parham and Paul L. Stright, *J. Am. Chem. Soc.*, 78, 4783 (1956).