# Competing Reactions in the Regeneration of Alcohols from Tosylates with Aromatic Radical Anions

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The recovery of alcohols from alkyl tosylates by cathodic reduction has found use in organic synthesis because chiral alcohols are recovered without racemization.[2] However, competing change into dialkyl ethers[2] and hydrocarbons[3] was found to reduce the yield of alcohols.

Recently, reactions of tosylates with aromatic radical anions have been proposed as a better method for the recovery of alcohols which were in fact obtained in high yields, free from competing products, from simple alkyl tosylates such as cyclohexyl tosylate.[4]

We were interested in comparing the heterogeneous (cathodic) method[2,3] with the homogenous (radical anion) one[4] just for those tosylates where cathodic reduction was known to give competing formation of hydrocarbons.[2]

Thus, we closely imitated the procedure reported for the reduction of simple alkyl tosylates by sodium naphthalene in tetrahydrofuran.[4] In fact, we were able to obtain cyclohexanol in high yield from cyclohexyl tosylate (Table I) as reported previously.[4] However, with *p*-methylbenzyl tosylate, under similar conditions, *p*-methylbenzyl alcohol was obtained in only 31% yield, along with *p*-xylene, 22%, 1,2-bis(*p*-methylbenzyl)ethane, 19%, traces of bis(*p*-methylbenzyl) ether, and toluene.

With benzhydryl tosylate and sodium naphthalene we obtained benzhydrol in 39% yield, along with diphenylmethane, 24%, 1,1′,2,2′-tetraphenylethane, 12%, and traces of dibenzhydryl ether.

With allyl tosylate and sodium naphthalene we obtained both allyl alcohol, 45%, and propene, 3%.

Changing to a less powerful reducing radical anion, like sodium anthracene in tetrahydrofuran,[5] the product distribution was only slightly affected relative to that above in the case of benzhydryl tosylate (Table I). In contrast, with *p*-methylbenzyl tosylate, formation of *p*-methylbenzyl alcohol was enhanced (74%), that of *p*-xylene was depressed (11%), and finally, the ethane derivative was not detectable at all. Control experiments with our batches of sodium anthracene in tetrahydrofurane and cyclohexyl tosylate led to cyclohexanol in a higher yield, 71% (table I), than in the original work (ca. 50%).[4]

Comparing the heterogeneous[2,3] with the homogeneous reduction,[4] it is striking that dialkyl ethers are important products from both *p*-methylbenzyl and allyl tosylate only

**Table I. Reaction of Tosylates ROTs (ca. $2 \times 10^{-2}$ M) in THF at Room Temperature with a Fourfold Molar Excess of Sodium Naphthalene (NaN) or Sodium Anthracene (NaA)**

| reagents | | | products (% on initial ROTs)[a] | | | | |
|---|---|---|---|---|---|---|---|
| R | arene radical anion | ROH | RH | RR | ROR | $PhCH_3$ |
| $C_6H_{11}$[b] | NaN | 98 | | | | 94 |
| $C_6H_{11}$[b] | NaA | 71 | | | | 90 |
| *p*-$MeC_6H_4CH_2$[b] | NaN | 31 | 22 | 19 | traces | 71 |
| *p*-$MeC_6H_4CH_2$[b] | NaA | 74 | 11 | | | 8 |
| $Ph_2CH$ | NaN | 39 | 24 | 12 | traces | 48 |
| $Ph_2CH$ | NaA | 51 | 26 | 17 | 0.8 | 48 |
| $CH_2$=$CHCH_2$ | NaN | 45 | 3 | | | 67 |

[a] GC analysis. [b] Analysis by cyclic voltammetry of the starting solution of tosylate, just before reaction with the radical anion, showed an effective purity for the tosylate of >90%.

**Table II. Cathodic Reduction of Tosylates[1]**

| ROTs ($10^2$ M) | solvent | supporting electrolyte (0.1 M) | electrolysis potential (vs. SCE) | electron no.[a] | product yields | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | ROH | ROR | RH | RR | $PhCH_3$ | HCOOR |
| $CH_2$=$CHCH_2$ (4.24) | DMF | TEAP | -2.40 | 2 | 63.4 | | | | absent | |
| $CH_2$=$CHCH_2$ (3.46) | AN | TEAP | -2.43 | | 49.5 | | | 15 | 2 | |
| *p*-$MeC_6H_4CH_2$ (0.98) | DMF | TEAP | -2.21 | 2 | 70 | absent | 30 | | absent | |
| *p*-$MeC_6H_4CH_2$ (1.94) | AN | TEAP | -2.36 | | 45.9 | 21 | 24 | traces | | 42.5 |
| $(C_6H_5)_2CH$ (1.39) | DMF | TEAP | -1.59 | | 24 | traces | | | | |
| $(C_6H_5)_2CH$ (2.37) | AN | TEAP | -1.70 | 1 | 54.3 | 38.1 | | traces | | 63 |
| $(C_6H_5)_2CH$ (1.96) | DMF | GP | -1.46 | | 38 | traces | | | | |
| $(C_6H_5)_2CH$ (3.91) | AN | GP | -1.25 | 0.9 | 21 | 43.3 | 11.8 | | | |

[a] The number of electrons depends on the extent of the electrolysis. We report in the table the mean value. A more extensive treatment of this point will be reported later. Data for electrolysis of cyclohexyl tosylate are reported in ref 2.

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(5) $E_{1/2}$ (vs. SCE) = 1.96 and -2.50 V for sodium anthracene and sodium naphthalene, respectively, in dioxane–water (G. J. Hoijstink and J. van Schooten, *Recl. Trav. Chim. Pays-Bas*, 71, 1089 (1952)).

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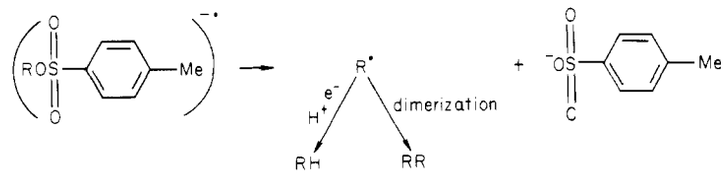
Scheme I




under heterogeneous conditions (Table I and ref 3). However, other differences in the product distribution cannot be ascribed, on the basis of the available data, to the different methods, the heterogeneous or the homogenous one, used. In fact, for example, *p*-methylbenzyl tosylate gave 1,2-bis(*p*-methylbenzyl)ethane only in the reduction by sodium naphthalene, while both the cathodic and the sodium anthracene reduction[3] gave only *p*-methylbenzyl alcohol and *p*-xylene (Table I).

In conclusion, it is clear that after reduction of the tosylate to its radical anion, cleavage will occur along the weakest bond, giving a delocalized radical. This is the case of benzyl, benzhydryl, and allyl tosylate, where a stabilized alkyl radical R· is formed. The latter can then be further reduced to the hydrocarbon RH (Scheme I). There is, in fact, ample precedent to such a behavior with both benzyl benzoates[6] and benzyl ethers and acetates.[7]

The factors leading to the ethane derivatives RR (Table I) can be less clearly identified on the basis of the present data. In fact, among the factors leading to production of ethane derivatives, it is clear that not only does the nature of the reducing agent (heterogeneous vs. homogeneous) play an important role, but so does the strength of the reducing agent under homogeneous conditions (see Table I). Whether in the homogeneous reduction of tosylates the ethane derivatives R–R come from dimerization[3] of the radical R· or rather from attack of the carbanion $R^-$ on unreacted tosylate has yet to be established.

## Experimental Section

In order to aid comparison of data for homogeneous and heterogeneous reductions, we include here experimental details for our previous electrochemical reduction of the present tosylates.[3]

**Chemicals.** The tosylates were synthesized according to reported procedures: cyclohexyl-,[8] *p*-methylbenzyl,[9] benzhydryl-,[10] and allyl tosylate.[11] Reaction products were isolated and compared with authentical samples: cyclohexanol (Merck), *p*-methylbenzyl alcohol (Merck), benzhydrol (Fluka), allyl alcohol (Merck), *p*-xylene (C. Erba), diphenylmethane (Merck), propene (Merck), 1,2-di-*p*-benzylethane,[12] 1,2-dibenzhydrylethane,[13] bis(*p*-methylbenzyl) ether,[14] and dibenzhydryl ether.[8] Tetrahydrofuran (THF) (C. Erba) was distilled from lithium aluminum hydride. Dimethylformamide (DMF) (C. Erba) was distilled over molecular sieves. Acetonitrile (AN) (C. Erba) was distilled over $P_2O_5$ and then fractionated over calcium hydride. Tetraethylammonium perchlorate (TEAP) (C. Erba for polarography) was dried at 80° C in vacuo. Guanidinium perchlorate (GP) was prepared by treatment of guanidinium chloride with excess sodium hydroxide, extracting with ether, and neutralizing with $HClO_4$. The salt was dried in vacuo at 80 °C.

**General Procedure for the Reduction of Tosylates by Radical Anions.** The method of ref 4 was closely imitated using a 4:1 molar excess of the radical anion over the tosylate.

**General Procedure for the Cathodic Reduction of Tosylates.** Electrolyses were carried out at constant potential by means of an AMEL model 552 potentiostat coupled to an AMEL 721 digital integrator. Anodic and cathodic compartments were separated by means of a glass frit. The working electrode was a mercury pool. The auxiliary electrode was a platinum wire which was flat coiled parallel to the mercury pool. The reference electrode was silver–0.1 M silver perchlorate in AN. Electrolysis potentials are referred to the saturated calomel electrode (SCE). The electrolysis solution, which was accurately flushed with dry nitrogen, was stirred by a magnetic bar. The extent of the electrolysis was monitored by cyclic voltammetry on a dropping mercury electrode which was lodged within the electrolytic cell. The supporting electyrolyte was 0.1 M. Data for the electrolyses[3] are reported in Table II.

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**Registry No.** Cyclohexyl tosylate, 953-91-3; *p*-methylbenzyl tosylate, 4606-98-8; benzhydryl tosylate, 5435-24-5; allyl tosylate, 4873-09-0; cyclohexanol, 108-93-0; toluene, 108-88-3; *p*-methylbenzyl alcohol, 589-18-4; *p*-xylene, 106-42-3; bis(*p*-methylbenzyl)ethane, 7568-23-2; bis(*p*-methylbenzyl) ether, 38460-98-9; benzhydrol, 91-01-0; diphenylmethane, 101-81-5; 1,1′,2,2′-tetraphenylethane, 632-50-8; dibenzhydryl ether, 574-42-5; allyl alcohol, 107-18-6; propene, 115-07-1; sodium naphthalene, 3481-12-7; sodium anthracene, 12261-48-2; 1,5-hexadiene, 592-42-7; benzhydryl formate, 66680-81-7.

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## Formation of $CH_2Cl_2$-Soluble Urea Derivatives during Solid-Phase Peptide Synthesis with Unsymmetrical Carbodiimides

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Dicyclohexylcarbodiimide (DCC) (Ia) is by far the most utilized coupling reagent in solid phase peptide synthesis.[1] Yet, with DCC it is difficult to wash out the precipitated dicyclohexylurea IIa before the next deprotection step[2] due to its poor solubility in $CH_2Cl_2$. Unfortunately, IIa, which remains inside the resin, is most soluble in solvents like alcohols that shrink the resin. In any case, these washings can only be performed after the coupling. Last but not least, these washings are time and solvent consuming, and the polymer has to be thoroughly washed afterwards with $CH_2Cl_2$ to prevent side reactions.[3]

In 1976, Sarantakis[4] briefly reported the synthesis of a cyclic undecapeptide, using diisopropylcarbodiimide (Ib).

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