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A Base-induced Elimination Reaction of Phenylsulfonylacetates. II. Effects of the Base and the Solvent on the Stereochemistry of Elimination

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The base-induced elimination reaction[1] of 1,2-diphenylethyl phenylsulfonylacetate was investigated in a variety of base–solvent systems. A stronger base was found to facilitate *syn* elimination. The addition of crown ether caused a remarkable change in the stereochemistry of elimination from *syn* to *anti*. In aprotic solvents, an overwhelming *syn* elimination was observed.

In the preceding paper we reported that 1,2-diphenylethyl phenylsulfonylacetate (**1**) undergoes β-elimination with potassium *t*-butoxide in *t*-butyl alcohol, predominantly through a *syn* pathway.[1] An intervention of a carbanion intermediate was described, and a cyclic transition state for the *syn* elimination was proposed. It was also suggested that an ion pair or an ion aggregate more or less controlled the stereochemistry of elimination.

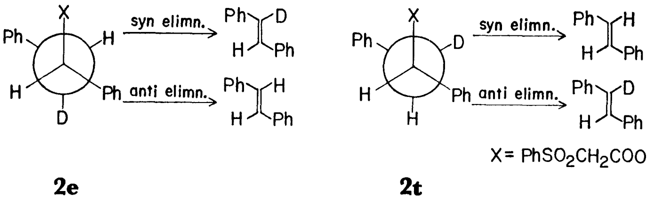
Pedersen[2] has shown that cyclic polyethers containing from five to ten oxygen atoms can form stable complexes with a potassium ion as well as with other cations. Recently, the cyclic polyethers have been used in studies of bimolecular elimination reactions exhibiting *syn–anti* dichotomy, and a pronounced effect of base ion-pairing and association on the stereochemistry of β-eliminations has been observed.[3–5] The present paper will deal with the effect of base association on the stereochemistry of the base-induced carbanionic elimination from 1,2-diphenylethyl phenylsulfonylacetate. Dicyclohexyl-18-crown-6 ether (**3**) was employed as a mechanistic probe.

Results and Discussion

The stereochemistry of elimination from 1,2-diphenylethyl phenylsulfonylacetate ($PhSO_2CH_2COOCHPh$-CH_2Ph, **1**) was examined under a variety of conditions. Four base–solvent systems, KOH–aq.EtOH, MeOK–MeOH, EtOK–EtOH, and *t*-BuOK–*t*-BuOH, were employed, as well as systems of *t*-BuOK in THF and DMF. The substrates examined in the present investigation were *dl-erythro-* and *dl-threo-*2-deuterio-1,2-diphenylethyl phenylsulfonylacetates (**2e** and **2t**). The reaction products from **1** and **2** were *trans*-stilbene, 1,2-diphenylethanol, and methyl phenyl sulfone. The deuterium content of *trans*-stilbene was examined in order to find out the stereochemical course of elimination. If the elimination were to occur in a *syn* fashion, **2e** should give *trans*-stilbene-α-*d* and **2t** should give *trans*-stilbene with no deuterium, while if it were to occur in an *anti* fashion, **2e** should give *trans*-stilbene with no deuterium and **2t** should give *trans*-stilbene-α-*d*.[1] Table 1 shows the results. The yield of *trans*-stilbene is also shown.

In protic solvents (water, methanol, ethanol, and *t*-butyl alcohol), the deuterium content of *trans*-stilbene produced from **2e** increases with the following order of base–solvent systems. KOH–aq.EtOH, MeOK–MeOH, EtOK–EtOH, *t*-BuOK–*t*-BuOH, while that produced from **2t** decreases with the same order; that is, the stereochemical course of the elimination reaction from **2** with potassium *t*-butoxide in *t*-butyl alcohol is more *syn*-favored. Since *t*-butoxide is stronger as a base, it seems to be more effective to form a carbanion positioned α to the sulfonyl group of the substrate. The fact that the *syn* elimination reaction is caused by this carbanion was pointed out in the preceding paper.[1] These observations imply that the *syn* elimination from **2** is facilitated by the use of a stronger base, *t*-butoxide, in a solvent of a low dielectric constant, *t*-butyl alcohol. In addition, an ion pairing or ion aggregation of the base must be operating in the present base–solvent system, because it was necessary to employ a rather high base concentration in order to bring about the reaction effectively. It was suggested by Závada and Svoboda[6] that both the dissociated and ion-paired bases take part in the elimination reactions of cycloalkyl tosylates simultaneously; the former prefers an *anti* elimination, and the latter, a *syn*. Very recently, evidence has been presented to indicate that the base association is one of the essential requisites for *syn* elimination by using a macrocyclic polyether.[3–5] Macrocyclic polyethers (crown ethers) are known to co-ordinate with alkali metal cations; hence, they convert contact ion pairs into separated ions.[7,8] Accordingly, the effect of dicyclohexyl-18-crown-6 ether (**3**) was investigated.

The results shown in Table 1 clearly indicate that the



2e **2t**

Scheme 1.

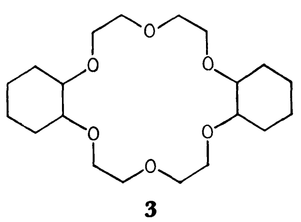


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TABLE 1. DEUTERIUM CONTENTS AND YIELDS OF *trans*-STILBENE OBTAINED FROM *erythro*- AND *threo*-2-DEUTERIO-1,2-DIPHENYLETHYL PHENYLSULFONYLACETATES (**2e** AND **2t**) WITH BASES$^{a)}$

Base	Solvent	From **2e**$^{b)}$		From **2t**$^{b)}$	
		D-content$^{c)}$ (%)	(Yield)$^{d)}$ (%)	D-content$^{c)}$ (%)	(Yield)$^{d)}$ (%)
0.50 M KOH	EtOH–H$_2$O$^{e)}$	70.9 ± 1.4	(7)	56.3 ± 0.9	(7)
0.50 M MeOK	MeOH	71.0 ± 3.7	(9)	52.3 ± 2.8	(10)
0.50 M EtOK	EtOH	72.6 ± 1.4	(14)	51.6 ± 2.6	(12)
0.50 M *t*-BuOK	*t*-BuOH	$82.0 \pm 2.0^{f)}$	(4)	$50.8 \pm 1.7^{f)}$	(3)
1.00 M *t*-BuOK	*t*-BuOH	$82.6 \pm 2.4^{f)}$	(12)	$53.9 \pm 1.1^{f)}$	(11)
0.50 M *t*-BuOK	*t*-BuOH+**3**$^{g)}$	28.5 ± 0.8	(—)	91.2 ± 1.3	(—)
1.00 M *t*-BuOK	*t*-BuOH+**3**$^{h)}$	24.7 ± 1.1	(—)	91.7 ± 3.0	(—)
0.50 M *t*-BuOK	THF	93.8 ± 1.8	(100)	21.4 ± 1.6	(100)
1.00 M *t*-BuOK	THF	102.5 ± 6.3	(100)	23.8 ± 1.7	(100)
0.50 M *t*-BuOK	DMF	97.2 ± 5.7	(100)	41.6 ± 2.4	(100)
1.00 M *t*-BuOK	DMF	98.2 ± 6.8	(100)	37.9 ± 0.9	(100)

a) Reaction temperature was 90.0 °C (1 hr). b) Initial concentration was [substrate]$=5.00 \times 10^{-3}$M. c) Deviations listed are standard deviations. d) Overall yield of *trans*-stilbene. e) EtOH–H$_2$O; 80:20 by volume. f) Taken from Ref. 1. g) Concentration of crown ether **3** was 0.50 M. h) Concentration of crown ether **3** was 1.00 M.

addition of an equimolar amount of the crown ether, **3**, to the reaction mixture effected a remarkable change in the stereochemical course of the elimination. The deuterium contents of *trans*-stilbene produced show that the elimination reaction proceeds, for the most part, in an *anti* fashion in the presence of **3**. Roitman and Cram[8] studied the effect of crown ether on the rates and the stereochemical course of a potassium *t*-butoxide-catalyzed carbanion-generating reaction in *t*-butyl alcohol. They showed that the presence of crown ether dramatically increased the rates of both isotopic exchange and racemization. The occupation of the co-ordination sites of the potassium ion by crown ether was thought to be responsible for the restricted availability of these sites to both the leaving and entering groups in the reaction. Thus, the possibility of the association of a carbanion with the potassium ion complexed with crown ether was suggested.

A similar concept can account well for the present preferential *anti* elimination observed in the presence of **3** (Table 1). In *t*-butyl alcohol, the potassium ion was thought to associate with the carbanionic center of the substrate. In the presence of crown ether, the added ether must occupy a part of the co-ordination sites of the potassium ion. In the present case, however, the complexed potassium ion is supposed to be still held in the neighborhood of the carbanionic center of the substrate; hence, the carbanion may be prevented from taking the favored position for the intramolecular abstraction of the β-proton at the front face. Undoubtedly, the low dielectric nature of *t*-butyl alcohol plays an important role in the ion pairing between the carbanion and the complexed potassium ion.[9] Furthermore, it is known that a phenylsulfonyl group is one of the functional groups that induce carbanion asymmetry.[10] Consequently, the carbanion positioned α to the sulfonyl group is unable to react at the backside. On the other hand, since ion-paired potassium *t*-butoxide is forced to dissociate more or less by the added crown ether,[7] and since the thus-dissociated *t*-butoxide possesses a much greater kinetic basicity than ion-paired *t*-butoxide,[8] a bimolecular reaction with *t*-butoxide may be accelerated. Therefore, the addition of the crown ether could depress the *syn* elimination reaction and increase the *anti* elimination.

In aprotic solvents (THF and DMF), the deuterium contents of *trans*-stilbene produced indicate that the stereochemical course of the elimination reaction is more *syn*-favored than in *t*-butyl alcohol. Recently, it was reported that, in a bimolecular elimination with potassium *t*-butoxide, both the addition of the crown ether and the change in solvent from *t*-butyl alcohol to DMF operate to increase the *anti* pathway.[3] However, in the present case, the change in solvent from *t*-butyl alcohol to aprotic solvents operates to increase the *syn* pathway. This result can also be explained on the basis of the *syn* elimination mechanism described in the preceding paper.[1] It was shown there that the *syn* elimination requires the carbanion positioned α to the sulfonyl group of the substrate as an effective base. In THF and DMF, the potassium cation must be solvated nucleophilically; hence, the reactivity of the carbanion is increased. Consequently, the *syn* elimination may be highly favored.[11]

No interconversion between **2e** and **2t** was observed with *t*-butoxide in *t*-butyl alcohol.[1] However, in THF and DMF the base-induced interconversion was observed. Preliminary experiments showed that, in the reaction of **2e** with potassium *t*-butoxide in THF or DMF, the recovered ester[12] consisted of **2e** and **2t** (approximately 1 : 1), while in the reaction of **2t** under the same conditions the recovered ester[12] consisted of **2t** only. These results may reasonably be understood in terms of the existence of carbanion intermediates which are responsible for the interconversion of the ester. The kinetic isotope effect will make the rate of *syn* elimination from **2e** faster than that from **2t**. Therefore, the **2e** produced by the isomerization of **2t** is assumed to be exhausted, resulting in the absence of **2e** in the reaction mixture. If this is the case, the *syn* selectivities for **2e** and **2t** must be larger than the values presented in Table 1.[13)]

The reactions of **1** and **2** with potassium *t*-butoxide in DMSO were also examined. However, in DMSO, *trans*-stilbene produced reacted further with the solvent to give secondary products. The details will be reported elsewhere.

Experimental

Materials. Compounds **1**, **2e**, and **2t** have been described previously.[1)] Crown ether **3** (2,5,8,15,18,21-hexaoxatricyclo[20.4.0.0^{9,14}]hexacosane) was prepared as has been described in the literature.[2)]

Solvents and Bases. *t*-Butyl alcohol was purified as previously reported.[1)] Ethanol and methanol were treated with magnesium and distilled twice under anhydrous conditions. Tetrahydrofuran was dried over sodium and distilled from lithium aluminum hydride under anhydrous conditions. *N,N*-dimethylformamide and dimethyl sulfoxide were treated with calcium hydride and distilled under reduced pressure. The alkoxide solutions were prepared from freshly-cut potassium metal and the appropriate alcohol under anhydrous conditions.

Product Analysis. The procedures employed were similar to those described in the preceding paper.[1)] The reactions were performed by the sealed-ampoule technique, and the quantitative analyses of the reaction products were carried out by means of gas chromatography. The deuterium content of *trans*-stilbene was determined by mass spectrometry. The mass spectra were recorded on a Hitachi RM-50GC g.c. mass spectrometer at 70 eV.

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11) One can also anticipate that potassium *t*-butoxide must dissociate more or less in DMF, and that the dissociated *t*-butoxide must operate as a strong base in the *anti* elimination, just as has been observed for usual E2 reactions. However, this is not the case. The reason for those conflicting observations remains to be determined.
12) Unpublished results. Recovered at an about 50% completion of the reaction at 25 °C. Analysis was performed by NMR.
13) Investigations of this problem are now in progress.