# Solvolysis of 6,7-Dimethoxy-1,2-dimethyl-*exo*-2-benzonorbornenyl Derivatives. Evidence for an Unsymmetrical Benzonorbornenyl Nonclassical Intermediate

Harlan L. Goering,* Chiu-Shan Chang, and Divakar Masilamani

Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. Received August 26, 1977

Abstract: 6,7-Dimethoxy-1,2-dimethyl-*exo*-2-benzonorbornenyl *p*-nitrobenzoate (9-OPNB) and chloride (9-Cl) solvolyze more rapidly than the corresponding unsubstituted 1,2-dimethyl-*exo*-2-benzonorbornenyl derivatives (6-OPNB and 6-Cl) by factors of from 16 (9-OPNB in 90% acetone) to 131 (methanolysis of 9-Cl). The rate acceleration by the homopara methoxy substituent shows that solvolysis involves assisted ionization in this tertiary *exo*-2-benzonorbornenyl system. Solvolysis of optically active 9-OPNB in 90% acetone gives 6,7-dimethoxy-1-methyl-2-methylenebenzonorbornene (12) with 24–40% retention of configuration and 6,7-dimethoxy-1,2-dimethyl-*exo*-2-benzonorbornenol (9-OH) with 3–4% retention. Results for methanolysis are similar; the E1 and S$_N$1 products (12 and 9-OMe) are formed with 16 and 2% retention. Methanolysis of active 9-Cl also gives slight excess retention of configuration. The kinetic and product studies show that the bridged intermediate formed by assisted ionization is not symmetrical. Evidently, in the 1,2-dimethyl-2-benzonorbornenyl system the unsymmetrical homobenzylic ion (8a and 10) is more stable than a symmetrical bridged species.

Two independent criteria establish that solvolysis of *exo*-2-benzonorbornenyl derivatives (1) involves assisted ionization to give a symmetrical carbonium ion system (2). One of these
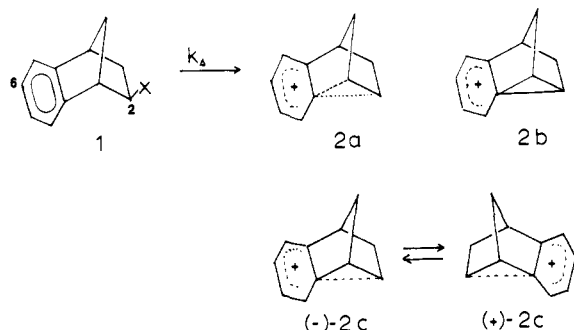

is the effect of substituents in the aromatic ring on solvolytic reactivity[1] and the other is the symmetry properties of the product-forming intermediate.[2] It should also be noted that the large exo/endo rate ratio (~15 000 for acetolysis of the 2-benzonorbornenyl brosylates as compared to ~350 for the 2-norbornyl system) clearly indicates phenyl participation in the exo isomer (1-OBS).[3–6] Or to put it another way, the rate-retarding inductive effect of the aromatic ring is largely offset by anchimeric assistance in the exo, but not in the endo, isomer.

Solvolytic reactivity of *exo*-2-benzonorbornenyl derivatives (1) is sensitive to substituents at C-6, the homopara position. For example, a 6-methoxyl substituent accelerates the rate by factors of 150 (acetolysis of 1-OBS)[1a] to 210 (solvolysis of 1-Cl).[1b,e] A 6-nitro substituent has a dramatic rate-retarding effect.[1c,e] Only minor substituent effects are observed in the endo system. Thus, the substituent effect for the exo epimer is a clear demonstration of aryl participation.

With regard to the symmetry criterion, the pertinent evidence is that optically active 1 gives completely racemic products.[2a] This suggests that solvolysis involves assisted ionization to give a symmetrical bridged carbonium ion system (2) rather than unassisted ionization to give the asymmetric classical ion. Two points of view have been expressed with regard to structural details (symmetry) of the bridged 2-benzonorbornenyl cation involved in solvolytic reactions. One holds that the symmetrical structure 2a is the most stable one,[2,5] the other that 2a is a low-lying transition state connecting enantiomeric

bridged structures (2c).[4,5] We tend to favor a static symmetrical representation (e.g., 2a or 2b[7]) because all evidence[2] indicates that the only capturable intermediate is symmetrical and this seems to be as good as any operational criterion for making such distinctions. It should also be noted that ^{1}H and ^{13}C NMR spectra of the cation under stable ion conditions (−78 °C, superacid) show that the ion is symmetrical on the NMR time scale and that positive charge is delocalized into the aromatic ring.[7] This rules out equilibrating enantiomeric classical ions. The NMR data have been interpreted in terms of a static symmetrical benzonortricyclyl cation (2b).[7]

The 2-methyl-*exo*-2-benzonorbornenyl system (3) has been investigated to determine if changing structure from secondary to tertiary results in change from assisted (k_Δ) to unassisted (k_c) solvolysis.[8] In other systems, replacement of an α hydrogen by a methyl substituent increases unassisted ionization (k_c) about 10^8 fold[9] and k_Δ about 10^2–10^3 fold.[10] Thus if k_Δ/k_c (anchimeric acceleration) is <10^5 for the secondary *exo*-2-benzonorbornenyl system (1), unassisted ionization might dominate in the tertiary system (3).
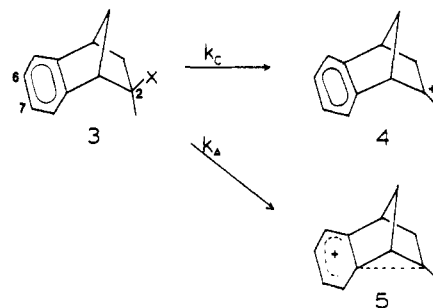
In the earlier work[8] it was observed that a 6-methoxyl substituent in 3 increases the rate of solvolysis of the tertiary *exo*-*p*-nitrobenzoate (3-OPNB) by a factor of 17. Only a minor effect is observed with the endo epimer. Clearly, solvolysis of 6-methoxy-3 involves assisted ionization. The situation for the parent tertiary system (3) is not clear because the 6-methoxyl may cause a switch from unassisted solvolysis ($k_c > k_\Delta$) for 3 to assisted solvolysis ($k_\Delta > k_c$) for 6-methoxy-3. In the tertiary 2-methyl-2-benzonorbornenyl system the symmetry criterion is not applicable.

Recently, we investigated the 1,2-dimethyl-*exo*-2-benzonorbornenyl (6) system.[11] In this tertiary 2-benzonorbornenyl

Table I. Titrimetric (k_t) and Polarimetric (k_α) Rate Constants for Solvolysis of 9-OPNB

Temp, °C	$10^3 k_t$, min^{-1}	$10^3 k_\alpha$, min$^{-1 a}$
	A. 90% Acetone (v/v)[b]	
78.3	0.125 ± 0.001[c]	0.206 ± 0.001[c]
100.1	1.20 ± 0.01[c]	2.25 ± 0.01
123.4	10.6 ± 0.2[c]	
	B. Methanol[d]	
78.3	1.18 ± 0.05	1.64 ± 0.01[e]
68.4	0.363 ± 0.005	0.544 ± 0.01[e]

[a] Solvent contained ~20% excess 2,6-lutidine. [b] Substrate concentration ~0.02 M. [c] Average of two or more independent experiments. [d] Substrate concentration 0.0038 M. [e] Average of constants for rotations at four wavelengths.

Table II. Rate Constants for Methanolysis of 9-Cl

Temp, °C	$10^3 k_t$,[a,b] min^{-1}	$10^3 k_\alpha$,[c] min^{-1}
0.00	6.08 ± 0.06	
10.15	20.78 ± 0.7[b]	31.3 ± 1.6[e]
10.15	20.81 ± 0.8[d]	35.0 ± 1.0[f]
17.00	45.0 ± 1	

[a] Substrate concentration 0.0032 M. [b] Solution kept basic; small increments of NaOCH₃ added when end point reached. [c] Substrate concentration 0.102 M. [d] Reaction mixture acidic except when titrated. [e] 2,6-Lutidine concentration 0.103 M. [f] 2,6-Lutidine concentration 0.2 M.

system the additional 1-methyl substituent restores the symmetry criterion. Since the 1-methyl substituent has only a small accelerating effect in **6** (~5)[12] and in the tertiary 5-norbornen-2-yl (~3)[12] and 2-norbornyl (~4)[13] systems, it appears that this substituent has no significant effect on the nature of the ionization. The small effect of the 1-methyl substituent is consistent with assisted[10] as well as unassisted solvolysis.

In our earlier work[11] we observed that solvolysis of optically active **6-OPNB** and **6-Cl** gives active E1 (57–81% retention) and S$_N$1 products (3–9% retention) and concluded that solvolysis involves the asymmetric classical ion (**7**) and that evidently ionization changes from assisted in the secondary 2-benzonorbornenyl system (**1**) to unassisted in the tertiary system **7**. This cavalier conclusion was based on the assumption that the bridged homobenzylic ion is symmetrical (**8b** or **8c**).
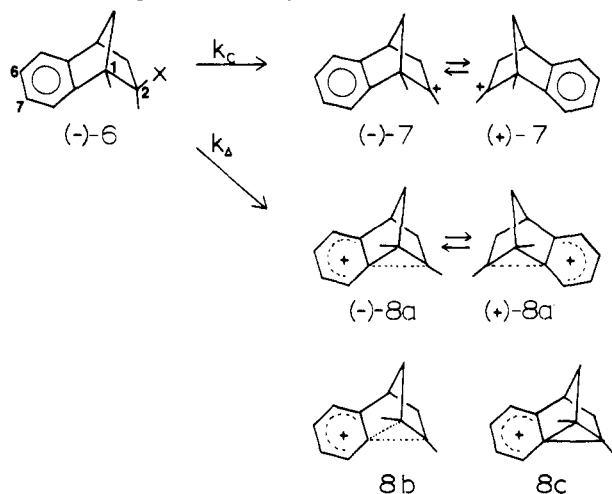
We now present evidence that this assumption is not valid and that in fact in the 1,2-dimethyl-*exo*-2-benzonorbornenyl system the delocalized homobenzylic bridged ion evidently is unsymmetrical (**8a**) and thus, formation of active product from active **6** does not rule out assisted ionization.

In the present work we have examined the 6,7-dimethoxy-1,2-dimethyl-*exo*-2-benzonorbornenyl system (**9**)[14,15] and
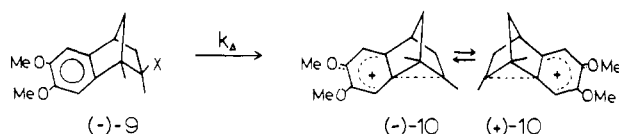
from the rate-accelerating effect of the methoxyl substituents (the entire effect is due to the homopara methoxyl substituent)[16] it is apparent that solvolysis of **9** involves anchimeric assistance. However, optically active **9** also gives active E1 and S$_N$1 products which shows that assisted ionization leads to an unsymmetrical intermediate.

The preparation of racemic and optically active 6,7-dimethoxy-1,2-dimethyl-*exo*-2-benzonorbornenyl derivatives (**9**) and determination of absolute rotations and configurations have been described elsewhere.[14,15] In the present work we were interested in the effect of the C-6 (homopara) methoxyl substituent on solvolytic reactivity and symmetry properties of the product-forming intermediate. The reason for the additional 7-methoxyl substituent in **9** is that an optically active precursor for **9** can readily be prepared by asymmetric hydroboration[14] whereas the optically active system with a single 6-methoxyl substituent would presumably involve a resolution. In other work we have shown that in both secondary and tertiary 2-benzonorbornenyl systems, the effect of 6,7-dimethoxy substituents is the same as that of a single 6-methoxyl substituent for both exo and endo isomers.[16] Thus the additional 7-methoxyl substituent in **9** does not interfere with the electronic effect of the homopara 6-methoxyl group.

Titrimetric (k_t) and polarimetric (k_α) rate constants for solvolysis of 9-OPNB[14] in 90% (v/v) aqueous acetone and methanol are presented in Table I. All rates are first order and in each case $k_\alpha > k_t$. This shows that solvolysis is accompanied by internal return that results in re-formation of racemic substrate.

For the polarimetric experiments, a slight excess of 2,6-lutidine was added to the solvent to neutralize the acid produced by solvolysis. Under these conditions initially formed products are optically stable. Without lutidine, active products undergo subsequent racemization which disturbs the polarimetric measurements. In both 90% acetone and methanol, k_α was unaffected by variation of 2,6-lutidine concentration over the range 0.02 (slight excess) to 0.04 M (twofold excess). Thus in these cases presumably the lutidine has no effect on the rate of solvolysis (k_t).

Kinetic data for the methanolysis of 9-Cl[15] are shown in Table II. Again good first-order behavior was observed. Relatively high concentrations of 9-Cl (~0.1 M) were required for the polarimetric measurements because of the low optical purity and rotation of the chloride.[15] At these concentrations k_α increases with lutidine concentration, and presumably in this case k_α would be somewhat lower under conditions of the titrimetric experiments.

Relative solvolytic reactivities of 1,2-dimethyl-*exo*-2-norbornyl (**11**), 1,2-dimethyl-*exo*-2-benzonorbornenyl (**6**), and 6,7-dimethoxy-1,2-dimethyl-*exo*-2-benzonorbornenyl (**9**) *p*-nitrobenzoate and chlorides are presented in Table III. For these comparisons, temperatures were selected to eliminate or minimize extrapolation of rate constants. The tertiary norbornyl system (**11**) is included to illustrate the magnitudes of the net rate-retarding effect of the aromatic ring in the tertiary 2-benzonorbornenyl systems.

These data show that in every case, the homopara 6-methoxyl substituent in **9** has an appreciable rate-accelerating effect. The methoxy substitutents increase k_t by factors of 16 for solvolysis of 9-OPNB in 90% acetone and 131 for methanolysis of 9-Cl. In this connection it is significant that the chlorides

Table III. Rates and Relative Rates of Solvolysis of Tertiary *exo*-2-Norbornyl (**11**) and *exo*-2-Benzonorbornyl Derivatives (**6** and **9**)

Compd	k_t, min^{-1}	Rel rate	k_α, min^{-1}	Rel rate
	A. Methanolysis, 78 °C			
11-OPNB[a]	4.35×10^{-3}	79	7.08×10^{-3}	95
6-OPNB[b]	5.50×10^{-5}	1	7.45×10^{-5}	1
9-OPNB[c]	1.14×10^{-3}	21	1.59×10^{-3}	21
	B. Methanolysis, 17 °C			
11-Cl[d]	8.8×10^{-2}	256		
6-Cl[b]	3.43×10^{-4}	1		
9-Cl[e]	4.50×10^{-2}	131		
	C. 90% Acetone, 100 °C			
11-OPNB[f]	7.99×10^{-3}	104	1.07×10^{-2}	118
6-OPNB[g]	7.62×10^{-5}	1	9.03×10^{-5}	1
9-OPNB[c]	1.20×10^{-3}	16	2.25×10^{-3}	25

[a] Taken from data in ref 17. [b] Extrapolated from data in ref 11. [c] Taken from Table I. [d] Extrapolated from data in ref 18. [e] Taken from Table II. [f] Taken from ref 17. [g] Taken from ref 11.

are much more reactive than the *p*-nitrobenzoates. Extrapolation of k_t for methanolysis to 50 °C shows that the chlorides are more reactive than the corresponding *p*-nitrobenzoates by factors of $10^{4.5}$ for **11**, $10^{4.2}$ for **6**, and $10^{4.6}$ for **9**. Thus, the


11
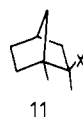
effect of the homopara methoxy substituent is relatively insensitive to large variations in reactivity that result from changing the leaving group.

The magnitude of the dimethoxy substituent effect for solvolysis of **9-OPNB** in 90% acetone (16-fold increase in k_t) is essentially the same as that observed earlier for the 2-methyl-2-benzonorbornenyl system (**3**) (17-fold increase in k_t).[16] A single 6-methoxyl substituent in 3-OPNB also increases k_t 17-fold for solvolysis in 50% acetone.[8]
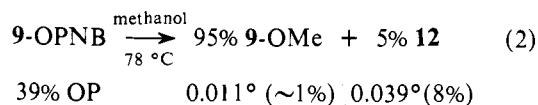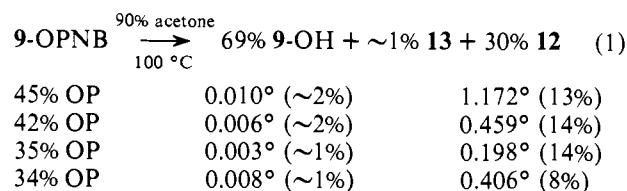
From the rate-accelerating effect of the methoxyl substituents in **9** it is apparent that aryl participation is involved in this tertiary *exo*-2-benzonorbornenyl system. Moreover, there is evidence that ionization has not changed from unassisted (k_c) for **6** to assisted (k_Δ) for **9**. The effect of the homopara methoxyl substituent is essentially the same for solvolysis in methanol, 50% acetone, and 90% acetone even though there is a large difference in overall rates. It seems unlikely that solvent effects are the same for k_c and k_Δ and one would expect a different substituent effect for different solvents if both types of ionization were involved. From this we conclude that solvolysis of **6**, as well as solvolysis of **9**, involves assisted ionization. In this connection it is significant that under stable ion conditions, the 1,2-dimethyl-2-benzonorbornenyl cation is symmetrical on the NMR time scale.[19] Moreover, the ^{13}C NMR spectrum indicates that some positive charge (although less than for the secondary 2-benzonorbornenyl system) is delocalized into the aromatic ring. This is supporting evidence that solvolysis of **6** involves equilibrating enantiomeric bridged ions (**8**) instead of equilibrating classical ions (**7**).

Under conditions of the polarimetric experiments solvolysis of **9-OPNB**[14] in 90% acetone at 100 °C gives 69% **9-OH**,[14] 30% 6,7-dimethoxy-1-methyl-2-methylenebenzonorbornene (**12**),[14,15] and about 1% of a second E1 product, 6,7-dimethoxy-1,2-dimethylbenzonorbornadiene (**13**). In methanol the products are 95% **9-OCH₃**, 5% **12**, and a trace of **13**. Methanolysis of **9-Cl**[15] gives 98% **9-OCH₃**, 1.5% **12**, and ~0.5% **13**. In all cases the product believed to be **13** was formed in
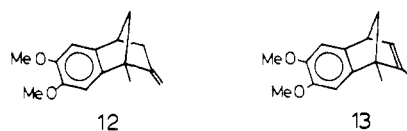
amounts too small for positive identification. Product compositions were determined by capillary GC.

The conditions for the product studies were the same as for the polarimetric measurements. Product distributions are summarized by eq 1 and 2 and data for solvolysis of optically active **9-OPNB**[14] are presented under these equations. For each experiment, the optical purity of the **9-OPNB** and observed rotations (measurable to within 0.001°) and optical purities[14] of the S_N1 and E1 products are shown. The indicated optical purities of **9-OPNB** have been corrected for racemization that results from ion-pair return by multiplication of the initial optical purity (84% for the first experiment) by k_t/k_α.[20] The optical purities of the products were determined by comparison of the indicated observed rotations of chloroform solutions, with values calculated from the absolute rotations[14] for the same conditions.

$$\text{9-OPNB} \xrightarrow[\text{100 °C}]{\text{90\% acetone}} 69\% \text{ 9-OH} + \sim1\% \text{ 13} + 30\% \text{ 12} \quad (1)$$

45% OP	0.010° (~2%)	1.172° (13%)
42% OP	0.006° (~2%)	0.459° (14%)
35% OP	0.003° (~1%)	0.198° (14%)
34% OP	0.008° (~1%)	0.406° (8%)

$$\text{9-OPNB} \xrightarrow[\text{78 °C}]{\text{methanol}} 95\% \text{ 9-OMe} + 5\% \text{ 12} \quad (2)$$

39% OP   0.011° (~1%)   0.039°(8%)

In some experiments products were isolated by preparative GC and in others by preparative TLC. After purification by sublimation, samples were shown to be homogenous by capillary GC and by spectral properties. In all cases the origins of the observed optical activities were established by comparison of ORD properties with those of authentic active samples.[14]

Products were isolated after 8–10 solvolytic half-lives. In a control experiment, racemic **9-OPNB** was solvolyzed in 90% acetone containing sufficient optically active **12**, the E1 product, to give a measurable rotation. There was no detectable change in rotation over a period of 10 half-lives. The same results were obtained when active **9-OH** (S_N1 product) was added at the outset. Similar results were observed for methanolysis. Thus, the initially formed products are optically stable under conditions of the product studies.

As shown by the data under eq 1 and 2, solvolysis of optically active **9-OPNB** gives active S_N1 and E1 products. In 90% acetone **9-OH** and **12** are formed with 3–5 and 24–40% retention, respectively. For methanolysis the S_N1 product (**9-OCH₃**) and E1 product (**12**) are formed with about 3 and 21% retention of configuration.

Methanolysis of optically active **9-Cl**[15] also leads to S_N1 product (**9-OCH₃**) with some excess retention of configuration. Not enough E1 product is formed for isolation. The chloride could not be obtained with high optical purity[15] and purification resulted in additional racemization. The homogenous samples available for the product studies were only about 8% optically pure and correction for ion-pair return lowers the average optical purity for solvolysis to ~5%. Rotations of isolated homogenous samples of **9-OCH₃** were too low for meaningful quantitative determinations. However, in all cases small rotations corresponding to a few percent retention were observed.

The kinetic studies (substituent effect) clearly show that solvolysis of **9** involves assisted ionization and the product studies show that an unsymmetrical product-forming inter-

mediate is involved. Presumably ionization leads to the unsymmetrical bridged homobenzylic ion (10) and the partial loss of configuration results from interconversion of enantiomeric cations in competition with product formation. The results of the product studies are similar to those reported earlier for the parent 1,2-dimethyl-*exo*-2-benzonorbornenyl system (6)[11] with regard to retention of configuration in the E1 and S_N1 products. In each case the E1 product is more active than the S_N1 product. This is also observed with 1,2-dimethyl-*exo*-2-norbornyl (11)[17,18] and 1,2-dimethyl-5-norbornen-*exo*-2-yl systems.[12]

As noted earlier,[11,12] the different amounts of retention for E1 and S_N1 products shows that they are derived from different intermediates. The present results for 9, as well as the results for 6, are accommodated by a mechanism proposed earlier[22] in which most, if not all, of the E1 product is derived from the initially formed intimate ion pair and the S_N1 product is formed from a solvent-separated ion pair or a dissociated carbonium ion. According to this interpretation, the additional dissociation required for solvent capture is accompanied by additional racemization. The somewhat larger loss of configuration for solvolysis of 9 than for solvolysis of 6 suggests that the barrier for interconversion of the enantiomeric bridged ion is lowered by a homopara methoxyl substituent.

It should be noted that in systems such as 6 and 9, substrate re-formed by ion pair return is presumably at least as active as the E1 product. Thus, lower limits for the rate constants for total ionization are $k_\alpha/0.7$ for solvolysis of 9-OPNB and $k_\alpha/0.3$ for solvolysis of 6-OPNB.

Experimental Section

Optical rotations were determined with a Perkin-Elmer 141 polarimeter and NMR spectra were obtained with a JEOL MH-100 spectrometer.

Materials. Methanol and 90% acetone were prepared as described earlier.[12] The preparation of racemic and optically active 6,7-dimethoxy-1,2-dimethyl-*exo*-2-benzonorbornenyl *p*-nitrobenzoate (9-OPNB)[14] and chloride (9-Cl)[15] have been described elsewhere. Absolute configurations and rotations of 9 and the solvolysis products have been established[14,15] and the structural illustrations show the correct absolute configurations.

Kinetic Studies. A. Solvolysis of 6,7-Dimethoxy-1,2-dimethyl-*exo*-2-benzonorbornenyl *p*-Nitrobenzoate (9-OPNB). The titrimetric (k_t) and polarimetric (k_α) rate constants in Table I were determined by a standard ampule technique described earlier.[12,23] Reactions were followed to ~75% completion and good first-order behavior was observed in all cases. A control experiment demonstrated that under the conditions for methanolysis of 9-OPNB, *p*-nitrobenzoic acid produced by solvolysis does not undergo detectable esterification with the solvent (no change in titer when a 0.02 M solution of *p*-nitrobenzoic acid in methanol is heated for a period corresponding to 10 half-lives).

In the polarimetric exteriments, optical activity was not completely lost provided that 1 equiv of 2,6-lutidine was present. In a typical experiment the observed rotation, α_{436}^{25}, changed from an initial value of $-1.457°$ to a final value of $-0.131°$. The constant final value indicates that initially formed optically active products are optically stable under these conditions. This was confirmed by control experiments outlined below.

B. Methanolysis of 6,7-Dimethoxy-1,2-dimethyl-*exo*-2-benzonorbornenyl Chloride (9-Cl). The apparatus[23] used for the titrimetric rates consisted of a glass-jacketed 100-mL volumetric flask containing a magnetic stirring bar and a microburet with a long tip that extended into the jacketed (thermostated) neck of the volumetric flask. The temperature of the stirred reaction mixture in the flask and of the contents of the buret tip was controlled by circulating thermostated fluid through the jacket of the well-insulated apparatus.

In a typical experiment, 50 mL of purified methanol,[12] containing lacmoid indicator, was placed in the volumetric flask. After temperature equilibration at 10.15 °C, 42.8 mg (0.160 mmol) of 9-Cl, mp 47–49 °C,[14] was added to the stirred solution and the buret was put in place. The reaction was followed by periodic titration of the entire reaction mixture with 0.03 M sodium methoxide in methanol. Thus

the solvent was unchanged by titration. The zero point titer (after complete mixing and temperature equilibration) was 0.008 mL and the final titer (after 10 half-lives) was 5.290 mL. Good first-order behavior was observed and rate constants were reproducible. The same method was used previously to determine k_t for methanolysis of 6-Cl[11] and 11-Cl.[18]

Variation of the amount of excess titrant has no effect on k_t. The rate is the same if the solution is kept basic (adding varying amounts of titrant as soon as the end point is reached) as if the solution is kept acidic (careful periodic titrations of the acid reaction mixture).

The polarimetric rates were determined with a thermostated 1-dm all-glass jacketed polarimeter tube. Because of low rotations, higher concentrations (~0.1 M) were required than for the titrimetric rates (~0.003 M). In a typical experiment, 30.0 mg (0.112 mmol) of (−)-9-Cl[15] was added to 1.10 mL of cold (~10 °C) methanol containing 12.1 mg (0.113 mmol) of 2,6-lutidine. This solution was placed in a jacketed polarimeter tube and after temperature equilibration at 10.15 °C the observed rotation was α_{589} $-0.196°$. The final rotation after 10 half-lives for k_t was α_{589} $-0.086°$. Good first-order behavior was observed and k_α was reproducible. The final rotation was constant for an extended period. As shown in Table II, when the amount of 2,6-lutidine was doubled (0.2 M), k_α increased about 10%.

Product Studies. A. Solvolysis of 9-OPNB and 9-Cl. Conditions, including substrate and 2,6-lutidine concentration, were the same as for the corresponding polarimetric experiments included in Tables I and II. In typical cases, 50-mL batches of solution, sealed in heavy-walled ampules, were placed in a thermostat for 8 half-lives. Most of the solvent was removed under reduced pressure and the residue extracted with ether. The ether solution was extracted with aqueous sodium bicarbonate and washed with water. After drying (Drierite) the extract was concentrated. For solvolysis of 9-OPNB in 90% acetone the product composition (eq 1) was determined by capillary GC (SE-30 containing 2% Carbowax, 50 ft, oven and injector at 140 °C). Consistent results were obtained for a number of independent experiments.

For solvolysis of optically active 9-OPNB in 90% acetone, homogenous samples of 9-OH and 12 were isolated by preparative GC (10% FAPP on 45/60 Chromosorb W, 5 ft × ¼ in., 140 °C) or by preparative TLC (E. Merck, 0.25-mm silica gel F-254 precoated plates) with 1:4 ether–hexane. Observed R_f values: 9-OH (0.33), 13 (0.53), 12 (0.77). Capillary GC showed that homogeneous samples were obtained by both methods.

For methanolysis of 9-OPNB, product compositions were also determined by capillary GC (SE-30, 100 ft) and homogeneous samples of 9-OCH₃ and 12 were separated by preparative GC (10% QF-1, 5 ft × ¼ in., 140 °C). The same methods were used for methanolysis of 9-Cl.

B. Control Experiments. To 5 mL of a 0.02 M solution of racemic 9-OPNB containing a 20% excess of 2,6-lutidine was added 125 mg of (−)-12. This solution had α_{546} $-5.416°$. After heating for 65 h at 100 °C (6.5 half-lives) the rotation was α_{546} $-5.406°$.

In a parallel experiments, 39.7 mg of (−)-9-OH was added instead of active 12. The rotation of the solution was α_{546} $-0.276°$. After heating for 65 h at 100 °C the rotation was the same. These experiments show that the products are optically stable under the conditions of the product studies.

Similar experiments showed that the products are optically stable under conditions of methanolysis of active 9-OPNB and 9-Cl. It was also shown that the compositions of synthetic mixtures of 9-OH (or 9-OCH₃), 12, and 13 are not changed by heating for 10 half-lives with the amount of *p*-nitrobenzoic acid producted by solvolysis.

References and Notes

(1) (a) D. V. Braddon, G. A. Wiley, J. Dirlam, and S. Winstein, *J. Am. Chem. Soc.*, **90**, 1901 (1968); (b) H. Tanida, H. Ishitobi, and T. Irie, *ibid.*, **90**, 2688 (1968); (c) H. Tanida, H. Ishitobi, T. Irie, and T. Tsushima, *ibid.*, **91**, 4512 (1969); (d) H. Tanida, *Acc. Chem. Res.*, **1**, 239 (1968); (e) H. C. Brown and G. L. Tritle, *J. Am. Chem. Soc.*, **90**, 2689 (1968).
(2) (a) W. P. Giddings and J. Dirlam, *J. Am. Chem. Soc.*, **85**, 3900 (1963); J. P. Dirlam, A. Diaz, S. Winstein, W. R. Giddings, and G. C. Hanson, *Tetrahedron Lett.*, 3133 (1969); (b) S. J. Cristol and J. M. Sullivan, *J. Am. Chem. Soc.*, **93**, 1967 (1971).
(3) P. D. Bartlett and W. P. Giddings, *J. Am. Chem. Soc.*, **82**, 1240 (1960).

(4) P. R. Story and B. C. Clark, Jr., in "Carbonium Ions", Vol. III, G. Olah and P. v. R. Schleyer, Ed., Wiley, New York, N.Y., 1972, Chapter 23.

(5) P. D. Bartlett, "Nonclassical Ions", W. A. Benjamin, New York, N.Y., 1955, p 314.

(6) C. J. Lancelot, D. J. Cram, and P. v. R. Schleyer in ref 4, Chapter 27.

(7) G. A. Olah and G. Liang, *J. Am. Chem. Soc.*, **97**, 2236 (1975).

(8) J. P. Dirlam and S. Winstein, *J. Am. Chem. Soc.*, **91**, 5905 (1969).

(9) J. L. Fry, J. M. Harris, R. C. Bingham, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **92**, 2540 (1970); P. G. Gassman and J. M. Pascone, *ibid.*, **95**, 7801 (1973).

(10) R. M. Coates and E. R. Fretz, *J. Am. Chem. Soc.*, **99**, 297 (1977).

(11) H. L. Goering, C.-S. Chang, and J. V. Clevenger, *J. Am. Chem. Soc.*, **96**, 7602 (1974).

(12) H. L. Goering and C.-S. Chang, *J. Am. Chem. Soc.*, **99**, 1547 (1977).

(13) H. C. Brown and M. H. Rei, *J. Am. Chem. Soc.*, **86**, 5004 (1964).

(14) H. L. Goering, A. C. Backus, C.-S. Chang, and D. Masilamani, *J. Org. Chem.*, **40**, 1533 (1975).

(15) H. L. Goering, C.-S. Chang, and J. V. Clevenger, *J. Org. Chem.*, **41**, 4023 (1976).

(16) H. L. Goering, D. C. K. Chang, and W.-S. Chang, *J. Org. Chem.*, **42**, 1145 (1977).

(17) H. L. Goering and K. Humski, *J. Am. Chem. Soc.*, **90**, 6213 (1968).

(18) H. L. Goering and J. V. Clevenger, *J. Am. Chem. Soc.*, **94**, 1010 (1972).

(19) G. A. Olah and G. Liang, *J. Am. Chem. Soc.*, **98**, 6304 (1976).

(20) S. Winstein and D. Trifan, *J. Am. Chem. Soc.*, **74**, 1154 (1952).

(21) H. L. Goering and K. Humski, *J. Org. Chem.*, **40**, 920 (1975).

(22) H. L. Goering, G. S. Koermer, and E. C. Linsay, *J. Am. Chem. Soc.*, **93**, 1230 (1971).

(23) J. V. Clevenger, Ph.D. Thesis, University of Wisconsin, Madison, Wis., 1971.

Optical Resolution of Chiral Sulfinyl Compounds via β-Cyclodextrin Inclusion Complexes[1,2]

Marian Mikołajczyk* and Józef Drabowicz

Contribution from the Center of Molecular and Macromolecular Studies, Polish Academy of Sciences, Department of Organic Sulfur Compounds, 90-362 Łódź, Boczna 5, Poland. Received July 1, 1977

Abstract: Direct resolution of chiral sulfoxides, sulfinates, and thiosulfinate *S*-esters by stereospecific inclusion into β-cyclodextrin is described. Optical purities of the partially resolved alkyl aryl and alkyl benzyl sulfoxides do not exceed 15%. The highest stereospecificity of inclusion was observed for isopropyl methanesulfinate, which has been isolated after one inclusion process with 68% optical purity. For the first time simple, optically stable thiosulfinate *S*-esters containing *tert*-butyl groups have been obtained. The influence of steric hindrance on the optical stability of this class of compounds is discussed. The relationship between the chirality at sulfur and optical purity of sulfoxides and the structure of their inclusion complexes with β-cyclodextrin is considered.

The stability of pyramidal arrangement of ligands around the three-coordinate sulfur atom causes the existence of optical isomerism in a large group of suitably substituted sulfinyl compounds of general structure shown below.[3,4] Until now
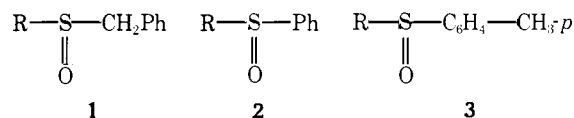

$R^1 \neq R^2$

sulfoxides,[5,6] sulfinates,[3] thiosulfinate *S*-esters,[7] sulfinamides,[8] unsymmetrical sulfites,[9] amido sulfites,[10] and amido thiosulfites[10] belonging to this group of compounds have been obtained in optically active forms. The majority have been prepared mainly by means of the reactions of diastereomeric sulfinates and sulfinamides with organometallic reagents.[6] Some of them have been synthesized by asymmetric oxidation of the corresponding sulfenyl compounds or by means of other asymmetric syntheses.[11]

We now report a novel nonclassical method of resolution of chiral sulfinyl compounds via β-cyclodextrin inclusion complexes.[12] Cyclodextrins (hosts) are optically active since they consist of optically active glucose molecules. Cyclodextrin inclusion compounds with chiral substances (guests) are mixtures of diastereomers which can be formed in unequal amounts, especially when an excess of the included chiral compounds is used. For this reason stereospecific inclusion into cyclodextrins can be applied as a method for resolution of racemic molecules. It is of advantage that it becomes possible to resolve compounds without acidic or basic functional groups which are necessary in the resolution of racemates by the classical method via diastereomeric salts with optically active acids or bases. The use of cyclodextrin as a resolving agent for some chiral carbon compounds was first reported by Cramer.[13] More recently Benschop and Van den Berg[14] described partial

resolution of chiral *O*-alkyl alkylphosphonates, R(RO)P(O)H, via α- and β-cyclodextrin inclusion complexes. In the present paper we describe our studies on the resolution of chiral sulfoxides, sulfinates, and thiosulfinate *S*-esters. We should mention that until the present time 2,5-dithiaspiro[3,3]heptane 2,5-dioxide[15] and ethyl *p*-tolyl sulfoxide[16] were the only chiral sulfur compounds which have been resolved by the nonclassical method by forming diastereomeric metal complexes containing optically active ligands.

Resolution of Chiral Sulfoxides. During the first stage of our work on the resolution of chiral sulfinyl compounds via β-cyclodextrin inclusion compounds we attempted to resolve several alkyl benzyl sulfoxides (**1**), alkyl phenyl sulfoxides (**2**), and alkyl *p*-tolyl sulfoxides (**3**). The choice of sulfoxides for

$$R\text{---}\underset{\underset{O}{\|}}{S}\text{---}CH_2Ph \qquad R\text{---}\underset{\underset{O}{\|}}{S}\text{---}Ph \qquad R\text{---}\underset{\underset{O}{\|}}{S}\text{---}C_6H_4\text{---}CH_3\text{-}p$$

1　　　　　　　　　**2**　　　　　　　　　**3**

these preliminary studies was dictated by two facts. The first is that they are chemically and configurationally stable. Secondly, specific rotations and absolute configurations of enantiomeric sulfoxides are known[4] and for this reason stereospecificity of the inclusion of sulfoxides into β-cyclodextrin may be easily estimated.

Resolution of sulfoxides was carried out according to the standard procedure elaborated by Cramer.[13] The sulfoxides **1, 2,** and **3** in 5-molar excess were added to a 1.5% solution of β-cyclodextrin in water. The precipitated inclusion compounds were decomposed by trichloroethylene–water at 60 °C and the released, included sulfoxides isolated by column chromatography. The optical rotations, optical purities, and absolute configurations of the included sulfoxides are given in Table I.

It was found that the inclusion of sulfoxides **1–3** into β-