Neighboring-Group Replacement Reactions of Substituted Phenylcyclohexyl Tosylates

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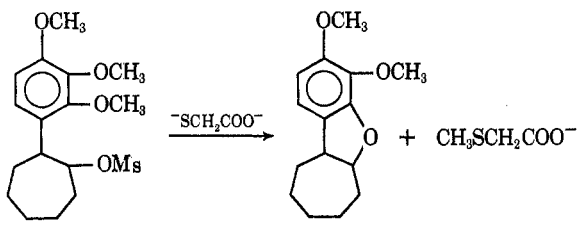
Received May 27, 1970

Tosylates of *trans*-2-(2′,3′-dimethoxyphenyl)-, (2′,3′,4′-trimethoxyphenyl)-, (2′,5′-dimethoxyphenyl)-, (2′,6′-dimethoxyphenyl)-, (2′,4′-dimethoxyphenyl)-, (3′,4′-dimethoxyphenyl)-, (2′-methoxyphenyl)-, (3′-methoxyphenyl)-, and (4′-methoxyphenyl)cyclohexanols were treated with the dipotassium salt of mercaptoacetic acid in methanol at relative concentrations of 2:1 and 50:1 (anion:tosylate). Neighboring-group replacement of the tosyl group with subsequent formation of the furan derivative predominated in all displacements where an *o*-methoxyl substituent was involved at low anion to tosylate ratios (2:1) with the exception of *trans*-2-(2′,4′-dimethoxyphenyl)cyclohexyl tosylate which favored simple displacement. At high anion to tosylate ratios (50:1), the simple displacement reaction was favored with decreased neighboring-group partcipation and increased elimination. The simple displacement reaction of tosylates with an *o*- or a *p*-methoxyl substituent gave the *trans*-sulfide acid (retention of configuration) at low anion concentration (2:1) while at the higher ratio (50:1) inversion of configuration occurred to give the cis acids. However, those tosylates with an *o*- and a *p*-methoxyl group gave retention of configuration at both ratios. The substituted 3-phenylcyclohexenes were the predominant olefins formed in practically all cases.

The participation of methoxyl groups in numerous solvolysis reactions was summarized by Winstein, *et al.*,[1] in 1958. Methoxyl participation was also shown in the reaction of *trans*-2-(2′,3′,4′-trimethoxyphenyl)cycloheptyl methanesulfonate (I) with the dipotassium salt of mercaptoacetic acid where 5a,7,8,9,10,10a-hexahydro-3,4-dimethoxy-6*H*-benzo[*b*]cyclohepta[*d*]furan (II)[2] was the main product. The above results in the



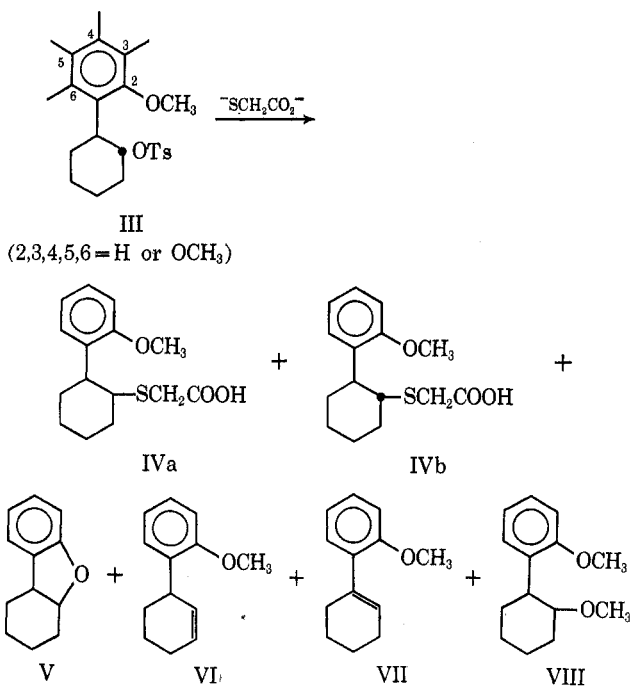
I II

seven-membered-ring system along with the low yield of 2-(2′,3′-dimethoxyphenyl)cyclohexanemercaptoacetic acid resulting from the treatment of 2-(2′,3′-dimethoxyphenyl)cyclohexyl *p*-toluenesulfonate with the dipotassium salt of mercaptoacetic acid led us to investigate the effect of the methoxyl groups on displacement reactions in the substituted phenylcyclohexane system.

Results

The tosylates IX–XVII (Table I) were displaced with the dipotassium salt of mercaptoacetic acid in methanol (56°) for 72 hr at two ratios of anion:tosylate (2:1 and 50:1). The reaction mixtures were separated into two fractions, base-soluble and base-insoluble. Scheme I illustrates the products which were identified. The cis and trans acids (IVa,b) represent the base soluble fractions formed from the reaction of the tosylate with the anion; the cis acid is formed by displacement with inversion of configuration and the trans acid by displacement with retention of configuration. The base-insoluble fraction contains (1) the furan derivative (V) from the neighboring-group replacement by the *o*-methoxyl group, (2) the olefins (VI, VII) by elimination, and (3) the methyl ether (VIII) from solvolysis. The cyclic

SCHEME I



ethers listed in Table II were identified by their nmr absorption spectra. The proton absorption between τ 5.30 and 5.39 was assigned to the proton α to the cyclic ether oxygen.[2-4] Integration of the methoxyl protons indicated that, in the formation of the cyclic compound, one methyl group was lost for each compound. The methylene protons of each compound integrated correctly for eight protons. We were unable to determine the characteristics of the 2,4-dimethoxy derivative because of very low yields of base-insoluble material.

We were unable to obtain pure samples of all methyl ethers. However, in those cases where pure samples were analyzed by nmr, the proton absorption at τ 6.12–6.20 was assigned to the methoxyl group attached to the benzene ring and the absorption at τ 6.85–6.89 to the methoxyl group attached to the cyclohexane ring. The spectra integrated correctly for the methyl ether. We

(1) S. Winstein, E. Allred, R. Heck, and R. Glick, *Tetrahedron*, **3**, 1 (1958).
(2) F. J. Lotspeich, *J. Org. Chem.*, **33**, 3316 (1968).
(3) S. D. Darling and K. D. Wills, *ibid.*, **32**, 2794 (1967).
(4) W. Fulmor, J. E. Lancaster, G. O. Martin, J. J. Brown, C. F. Howell, C. T. Nora, and R. A. Hardy, Jr., *J. Amer. Chem. Soc.*, **89**, 3322 (1967).

TABLE I

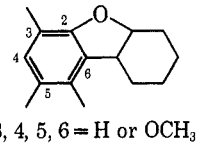
YIELDS OF THE IMPORTANT PRODUCTS FROM THE DISPLACEMENT REACTIONS OF METHOXY-SUBSTITUTED PHENYLCYCLOHEXYL *p*-TOLUENESULFONATES

Compd	Ring substituent	% yield	% IV	% V	% VI	% VII	% VIII	% recovered III	% cis/ % trans acid	Ratio of anion: tosylate
IX	2-OCH_3	102	11.77	47.30	15.66	<1	24.99	0	27/73	2:1
	2-OCH_3	100	42.42	21.03	32.60	0	3.97	0	78/22	50:1
X	2,3-OCH_3	97	6.17	87.50	4.44	2.22	0	0	58/42	2:1
	2,3-OCH_3	101	25.06	45.70	26.28	0	3.13	0	100/0	50:1
XI	2,3,4-OCH_3	107	31.10	48.70	5.69	1.70	12.84	0	0/100	2:1
	2,3,4-OCH_3	96	45.27	27.49	24.00	<1	3.06	0	0/100	50:1
XII	2,5-OCH_3	98	6.07	67.42	8.06	4.92	13.37	0	*a*	2:1
	2,5-OCH_3	100	40.78	30.51	27.29	<1	1.29	0		50:1
XIII	2,6-OCH_3	98	7.30	82.60	7.30	2.79	0	0	*b*	2:1
	2,6-OCH_3	98	0	83.30	12.36	4.34	0	0		50:1
XIV	2,4-OCH_3	85	64.52	8.57	0	3.71	23.00	0	0/100	2:1
	2,4-OCH_3	104	78.20	5.45	15.19	0	1.32	0	0/100	50:1
XV	4-OCH_3	94	23.18	0	0	0	33.03	43.68	18/82	2:1
	4-OCH_3	100	63.94	0	35.09	0	<1	0	85/15	50:1
XVI	3,4-OCH_3	107	22.30	0	0	0	16.02	61.67	31/69	2:1
	3,4-OCH_3	101	64.86	0	33.59	<1	1.24	0	97/3	50:1
XVII	3-OCH_3	85	19.26	0	0	0	0	80.74	100/0	2:1
	3-OCH_3	106	45.58	0	41.84	4.52	8.16	0	100/0	50:1

[a] Isomers could not be separated; nmr showed acid at low concentration to be primarily the trans isomer, at high concentration the cis isomer. [b] Isomers could not be identified due to low yields.

TABLE II

PROTON NMR DATA FOR CYCLIC ETHERS[a]



3, 4, 5, 6 = H or OCH_3

Compd	Registry no.	Proton α to O of cyclic ether
No substitution	13524-79-3	5.30 (1 H)
3-OCH_3	27124-66-9	5.31 (1 H)
3,4-Di-OCH_3	27124-67-0	5.29 (1 H)
5-OCH_3	27124-68-1	5.38 (1 H)
6-OCH_3	27124-69-2	5.39 (1 H)

[a] Expressed as τ values.

were also able to decrease the formation of this product by increasing the concentration of anion.

Characterization of the cis and trans acids was based on their nmr spectra. The *trans*-sulfide acids were identified by a doublet between τ 6.89 and 7.19 representing the methylene hydrogens between the sulfur and carboxy group of the side chain.[5] The corresponding protons for the *cis*-sulfide acids showed a quartet centered between τ 7.40 and 7.58. Nmr data for the cis acids are given in Table III.

To establish the ratio of cis and trans isomers, the methyl esters of all base-soluble products were prepared and analyzed by glc. The cis isomers were identified by comparison with standards prepared by a known procedure and the ratio of cis–trans isomers was determined by peak areas. Although we were unable to separate the isomers of 2-(2′,5′-dimethoxyphenyl)cyclohexanemercaptoacetic acid, the nmr indicated that the trans acid was primarily formed at low-anion concentration and the cis at high-anion concentrations.

(5) F. J. Lotspeich and S. Karickhoff, *J. Org. Chem.*, **31**, 2183 (1966).

Discussion

The products obtained from the displacement reactions reported in Table I can be rationalized by considering Scheme II. Compound IX (2-methoxy) gives a 47% yield of cyclic ether at low-anion concentration and is postulated to react through intermediate C. The formation of this intermediate would require the tosyl and phenyl groups to exist in axial positions.[6] The cyclic ether is formed after displacement of the methoxyl methyl group by the anion 2. Compound XIII (2,6-dimethoxy) with two methoxyl groups available for participation has a greater tendency to form intermediate C and gives an 83% yield of the cyclic ether.

Compounds X (2,3-dimethoxy) and XII (2,5-dimethoxy) form 87 and 67% of the cyclic compound, respectively, at low-anion concentration. The methoxyl groups, which are either ortho or para to the participating methoxyl substituent in these compounds, increase the electron density of the participating methoxyl group and thus facilitate the formation of intermediate C as well as stabilizing the intermediate. The role of the 3-methoxyl group is also evident in the case of compounds XI (2,3,4-trimethoxy) and XIV (2,4-dimethoxy) where the yield of cyclic ether is 49 and 9%, respectively. The relatively low yield of the cyclic ether from compound XI compared to compounds X and XII is undoubtedly due to the presence of the *p*-methoxyl group which facilitates the formation of the "phenonium ion" and results in an increased formation of sulfide acid with a consequent decrease of cyclic ether.

The importance of the "phenonium ion" in these reactions is emphasized by the fact that compounds XI (2,3,4-trimethoxy) and XIV (2,4-dimethoxy) form only *trans*-sulfide acids (retained configuration) at both low- and high-anion concentration, whereas the other tosylates yield increasing amounts of *cis*-sulfide acid at high-anion concentration. The *o*-methoxyl group without

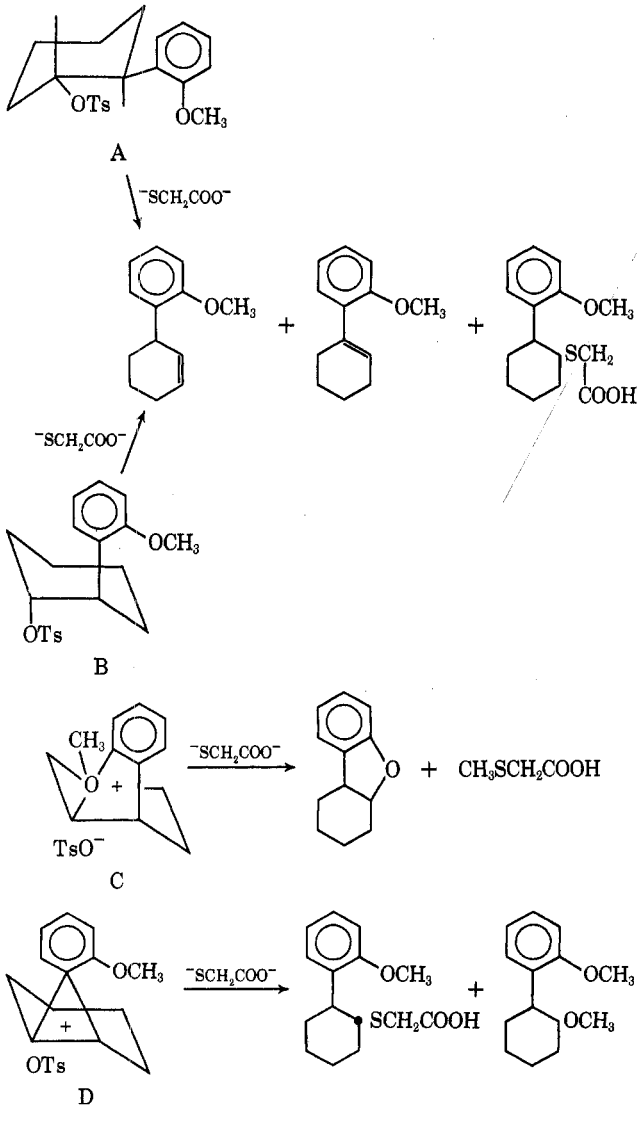
(6) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 229.

TABLE III
PROTON NMR DATA[a]

Compd[b]	Aromatic	Cyclohexane	Tertiary	$-SCH_2-$	$-OCH_3$
		Substituted *cis*-Sulfide Acids			
2, 3, 4	3.27 (q)	8.05, 8.40	6.60, 6.83	7.44 (q)	6.13, 6.22
3, 4	3.20 (q)	7.80–8.80	6.59, 6.91	7.40 (q)	6.12, 6.15
2, 3	3.13–3.20 (m)[c]	8.05, 8.42	6.58, 6.71	7.46 (q)	6.19, 6.22
2, 5	3.16–3.28 (m)	8.03, 8.38	6.48, 6.73	7.50 (q)	6.21, 6.25
2, 4	2.77–3.58 (m)	8.00, 8.39	6.48, 6.75	7.45 (q)	6.22
4	2.71–3.22 (m)	7.92, 8.32	6.67, 6.95	7.41 (q)	6.23
2	2.82–3.14 (m)	8.00, 8.35	6.47, 6.72	7.58 (q)	6.22
3	2.75–3.15 (m)	7.69–8.80	6.67, 6.95	7.42 (q)	6.22
		Substituted *trans*-Sulfide Acids from Tosylate Displacement			
2, 3, 4	3.23 (q)	7.90–8.90	7.03, 7.73	6.89, 6.98 (d)[c]	6.10, 6.13, 6.17
3, 4	3.18, 3.22 (m)	7.80–8.80		7.11, 7.19 (d)	6.12, 6.16
2, 3	3.03, 3.10 (m)	7.85–8.85		6.93, 7.00 (d)	6.13, 6.15
2, 5	3.16–3.28 (m)	7.80–8.90		6.95, 7.00 (d)	6.19, 6.22
2, 4	3.42–3.57 (m)	7.90–8.80		6.91, 6.97 (d)	6.18
4	2.89–3.23 (m)	7.90–8.82		7.09, 7.18 (d)	6.22
2	2.70–3.19 (m)	7.90–8.86		6.99, 7.05 (d)	6.23

[a] Expressed as τ values. [b] The compound is designated by the methoxyl substitution pattern of the aromatic ring. [c] q = quartet; m = multiplet; d = doublet.

SCHEME II



doubt contributes to the retention of configuration of the sulfide acids in these compounds (XI and XIV) since the *p*-methoxyl group by itself (compound XV) is unable to prevent an inversion in configuration even at low-anion concentration. The *o*-methoxyl substituent probably exerts its influence on the formation of sulfide acid *via* the "phenonium ion" since the 2,6-dimethoxy compound (XIII), which reacts through the "methoxonium ion" C, yields no sulfide acid at high-anion concentration and only 7% sulfide acid at low-anion concentration.

The electron-withdrawing effect of the *m*-methoxyl group is evident when compound XV (4-methoxy), which gives a high yield of *trans*-sulfide acid (retained configuration), is compared to compound XVI (3,4-dimethoxy), which gives a lower yield of *trans*-sulfide acid. The *m*-methoxy compound (XVII) is unable to form intermediate C and gives only *cis*-sulfide acid (inversion of configuration).

The solvolysis reaction at low-anion concentration occurs most readily with those compounds capable of forming intermediate D. The 3-methoxy compound (XVII) gives no solvolysis product and supports the above reasoning. The fact that compound IX (2-methoxy) undergoes solvolysis (25%) further supports the previous contention that the *o*-methoxyl group contributes to the formation of the "phenonium ion" as well as participating directly in anchimeric assistance.

At low-anion concentration trans elimination is favored in the case of compounds IX–XIV and substituted 3-phenylcyclohexenes are formed. These results would be expected from the work of Eliel and Ro,[7] who found that axial tosylates undergo appreciable bimolecular elimination, whereas the equatorial tosylates react more slowly. Cristol and Stermitz[8] also reported that trans elimination was favored over cis elimination in the base-induced elimination of *trans*-phenylcyclohexyl *p*-toluenesulfonate. From these reports and a consideration of Scheme II, it is easy to see that conformer B would not only contribute to the formation of the "phenonium ion" and "methoxonium ion" but would also be the major conformer contributing to the formation of the 3-phenylcyclohexenes. In this conformer, the axial

(7) E. L. Eliel and R. S. Ro, *J. Amer. Chem. Soc.*, **79**, 5995 (1957).
(8) S. J. Cristol and F. R. Stermitz, *ibid.*, **82**, 4692 (1960).

hydrogen on carbon number 6 would be eliminated with the axial sulfonate group.

In general, the results observed at high-anion concentration can be explained on the basis of increased attack by the anion on conformer B. This is supported by the results with the 3-methoxy compound where only 20% of the compound reacted at the low-anion concentration, but a complete reaction was observed at high-anion concentration with 3-(3′-methoxyphenyl)cyclohexene being the main olefin.

Experimental Section

Melting points were taken using a Nalge–Axelrod melting point apparatus and are uncorrected. All elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Nmr spectra were recorded on a Varian A-60 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Glc data were recorded on a Microtek 220 with a hydrogen flame detector. All samples were analyzed on two or more columns. All percentages were calculated from peak areas. The following columns were used: 20% silicone oil on 60–80 AW Chromosorb P; 12% Apiezon L–8% tetracyanoethyl pentaerythritol on 100–110 Anakrom ABS; 3% SE-30 on 110–120 Anakrom SD; 3% Apiezon L on 110–120 Anakrom SD; and 3% Carbowax 20M on 110–120 Anakrom SD.

Substituted *trans*-2-Phenylcyclohexanols.—The alcohols were prepared by the addition of the phenyllithium derivative to cyclohexene oxide in diethyl ether according to the procedure of Lotspeich and Karickhoff.[5]

Substituted *trans*-2-Phenylcyclohexyl *p*-Toluenesulfonates.—The tosylates were prepared from the trans alcohols by a procedure reported previously.[5] Elemental analyses are given in Table IV.

TABLE IV

Compd	Mp, °C	C, % Calcd	C, % Found	H, % Calcd	H, % Found
IX	98–99	66.67	66.36	6.67	6.69
X	113–114	64.59	64.79	6.71	6.78
XII[a]	83–85	64.59	64.79	6.71	6.86
XIII	90–93	64.59	64.56	6.71	6.67
XIV	89–92	64.59	64.15	6.71	6.52
XV	116–118	66.67	66.42	6.67	6.72
XVI	92–95	64.59	64.63	6.71	6.71
XVII	96–97	66.67	66.51	6.67	6.67

[a] Compound XI is a known compound.

Tosylate Displacement.—The *trans*-tosylates (0.01 mol) were dissolved in methanol (30 ml) along with the dipotassium salt of mercaptoacetic acid at a molar ratio of potassium mercaptoacetate:tosylate of 2:1 or 50:1. The mixture was flushed with nitrogen and the condenser fitted with an oil trap to exclude air. The reaction was heated at 55–58° for 72 hr, and the solvent was removed by a Rinco evaporator. The resulting oil was taken up in ether and the base-soluble fraction was extracted with 5% NaOH.

The acids (base-soluble fraction) were identified by comparison of glc retention times of their methyl esters and nmr spectra of the acids (Table III) to known compounds.

The base-insoluble fraction was subjected to glc to determine the number of components present. The products were then separated on neutral aluminum oxide (Merck) with successive elutions of 100% pentane, 5% diethyl ether in pentane, 10% diethyl ether in pentane, 30% diethyl ether in pentane, 60% diethyl ether in pentane, and 100% diethyl ether. The fractions were checked for purity by glc. The olefins (100% pentane) were identified by comparison with standards and the cyclic compounds (10% diethyl ether in pentane) were identified by nmr (Table II).

Substituted *trans*-2-Phenylcyclohexanemercaptoacetic Acids.—Solid derivatives were prepared from the displacements of tosylates IX, XI, XIV, XVI, and XVII.

trans-2-(2′-Methoxyphenyl)cyclohexanesulfonylacetic acid, mp 135–138°. *Anal.* Calcd for $C_{15}H_{20}O_5S$: C, 57.69; H, 6.60. Found: C, 58.01; H, 6.42.

trans-2-(2′,3′,4′-Trimethoxyphenyl)cyclohexanemercaptoacetic acid (5) and *trans*-methyl 2-(2′,4′-dimethoxylphenyl)cyclohexanemercaptoacetate, mp 56–58°. *Anal.* Calcd for $C_{17}H_{24}O_4S$: C, 62.93; H, 7.46. Found: C, 62.63; H, 7.40.

Methyl *trans*-2-(3′,4′-dimethoxyphenyl)cyclohexanemercaptoacetate, mp 78–81°. *Anal.* Calcd for $C_{17}H_{24}O_4S$: C, 62.93; H, 7.46. Found: C, 62.76; H, 7.47.

cis-2-(3′-Methoxyphenyl)cyclohexanesulfonylacetic acid, mp 118–120° (lit.[9] mp 119–120°).

We were unable to prepare solid derivatives of the acids from tosylates X, XII, and XV. However, their nmr spectra were consistent with the other trans acids. See Table III.

Substituted *cis*-2-Phenylcyclohexylmercaptoacetic Acid.—The cis acids were prepared by the free-radical addition of mercaptoacetic acid to the substituted 1-phenylcyclohexenes with a catalytic amount of benzoyl peroxide.[10,11] Nmr data are given in Table III.

cis-2-(2′,3′,4′-Trimethoxyphenyl)-,[5] *cis*-2-(2′-methoxyphenyl)-, *cis*-2-(3′-methoxyphenyl)-, and *cis*-2-(4′-methoxyphenyl)-cyclohexanemercaptoacetic acids are known compounds.[9]

cis-2-(2′,4′-Dimethoxyphenyl)cyclohexanemercaptoacetic acid, mp 117°. *Anal.* Calcd for $C_{16}H_{22}O_4S$: C, 61.83; H, 7.20. Found: C, 61.91; H, 7.14.

cis-2-(3′,4′-Dimethoxyphenyl)cyclohexanemercaptoacetic acid, mp 121–124°. *Anal.* Calcd for $C_{16}H_{22}O_4S$: C, 62.11; H, 6.84. Found: C, 61.71; H, 7.12.

We were unable to obtain solid derivatives of *cis*-2-(2′,5′-dimethoxyphenyl)- and *cis*-2-(2′,3′-dimethoxyphenyl)cyclohexanemercaptoacetic acids.

Substituted 1-Phenylcyclohexenes.—The tertiary alcohols were prepared from the addition of the appropriate phenyl-Grignard or lithium derivative to cyclohexanone and dehydrated to the corresponding olefin with oxalic acid in boiling toluene.[5]

1-(2′,5′-Dimethoxyphenyl)cyclohexene. *Anal.* Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.91; H, 8.35.

1-(2′,6′-Dimethoxyphenyl)cyclohexene. *Anal.* Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.01; H, 8.41.

1-(2′,4′-Dimethoxyphenyl)cyclohexene. *Anal.* Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.45; H, 8.53.

1-(3′,4′-Dimethoxyphenyl)cyclohexene. *Anal.* Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.71; H, 8.39.

The other olefins are known compounds.[5,9]

Substituted 3-Phenylcyclohexenes.—The appropriate substituted phenyl-Grignard or lithium derivative was allowed to react with 3-bromocyclohexene according to the procedure of Schaeffer and Collins[12] (see Table V). The yields of 3-(2′,3′-dimethoxyphenyl)-, 3-(3′,4′-dimethoxyphenyl)-, and 3-(4′-methoxyphenyl)cyclohexene were very low, and we were unable to obtain pure samples for analysis.

Registry No.—IX, 27124-57-8; X, 27124-59-9; XII, 27124-59-0; XIII, 27124-60-3; XIV, 27124-61-4; XV, 20859-18-1; XVI, 27124-63-6; XVII, 27124-64-7; *trans*-2-(2′-methoxyphenyl)cyclohexanesulfonylacetic acid, 27124-76-1; *trans*-2-(2′,3′,4′-trimethoxyphenyl)-cyclohexanemercaptoacetic acid, 6776-94-9; methyl *trans*-2-(2′,4′-dimethoxyphenyl)cyclohexanemercaptoacetate, 27124-78-3; methyl *trans*-2-(3′,4′-dimethoxyphenyl)cyclohexanemercaptoacetate, 27124-79-4; *trans*-2-(2′,3′-dimethoxyphenyl)cyclohexanemercaptoacetic acid,[13] 27124-80-7; *trans*-2-(2′,5′-dimethoxyphenyl)-cyclohexanemercaptoacetic acid,[13] 27124-81-8; *trans*-2-(4′-methoxyphenyl)cyclohexanemercaptoacetic acid,[13] 27124-82-9; *cis*-2-(2′,3′,4′-trimethoxyphenyl)cyclohexanemercaptoacetic acid, 6776-90-5; *cis*-2-(2′-methoxyphenyl)cyclohexanemercaptoacetic acid, 27124-84-1; *cis*-2-(3′-methoxyphenyl)cyclohexanemercaptoacetic acid, 27124-85-2; *cis*-2-(4′-methoxyphenyl)cyclohexanemercaptoacetic acid, 27124-86-3; *cis*-2-(2′,4′-di-

(9) S. Core and F. J. Lotspeich, *J. Med. Chem.*, **12**, 333 (1969).
(10) H. L. Goering, D. I. Relyea, and D. Larsen, *J. Amer. Chem. Soc.*, **78**, 348 (1956).
(11) F. G. Bordwell and W. A. Hewett, *ibid.*, **79**, 3493 (1957).
(12) H. J. Schaeffer and C. J. Collins, *ibid.*, **78**, 124 (1956).
(13) Compound found in Table III.

TABLE V

Compd	Bp (mm) or mp, °C	Formula	Registry no.	Calcd, % C	Calcd, % H	Found, % C	Found, % H
2-OCH_3	74 (0.05)	$C_{13}H_{16}O$	27124-70-5	82.93	8.57	83.08	8.60
3-OCH_3	83 (0.05)	$C_{13}H_{16}O$	27124-71-6	82.93	8.57	82.82	8.62
2,5-OCH_3	93 (0.07)	$C_{14}H_{18}O_2$	27124-72-7	77.03	8.31	76.76	8.34
2,6-OCH_3	68–69.5	$C_{14}H_{18}O_2$	27124-73-8	77.03	8.31	76.81	8.34
2,3,4-OCH_3	110 (0.05)	$C_{15}H_{20}O_3$	27124-74-9	72.55	8.12	72.54	8.09
2,4-OCH_3	108 (0.1)	$C_{14}H_{18}O_2$	27124-75-0	77.03	8.31	77.17	8.29

methoxyphenyl)cyclohexanemercaptoacetic acid, 27124-87-4; *cis*-2-(3′,4′-dimethoxyphenyl)cyclohexanemercaptoacetic acid, 27124-88-5; *cis*-2-(2′,5′-dimethoxyphenyl)cyclohexanemercaptoacetic acid, 27124-89-6; *cis*-2-(2′,3′-dimethoxyphenyl)cyclohexanemercaptoacetic acid, 27124-90-9; 1-(2′,5′-dimethoxyphenyl)cyclohexene, 1848-14-2; 1-(2′,6′-dimethoxyphenyl)cyclohexene, 27124-92-1; 1-(2′,4′-dimethoxyphenyl)cyclohexene, 27098-25-5; 1-(3′,4′-dimethoxyphenyl)cyclohexene, 27124-93-2; *trans*-2-(2′,4′-dimethoxyphenyl)cyclohexanemercaptoacetic acid,[13] 27124-94-3; *trans*-2-(3′,4′-dimethoxyphenyl)cyclohexanemercaptoacetic acid,[13] 27124-95-4; *trans*-2-(2′-methoxyphenyl)cyclohexanemercaptoacetic acid,[13] 27124-96-5.

Acknowledgments.—This investigation was supported by Public Health Service Research Grant No. CA-10270 from the National Institutes of Health.

Stereochemistry of Displacement Reactions at the Neopentyl Carbon. Further Observations on the Triphenylphosphine–Polyhalomethane–Alcohol Reaction[1]

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Received October 20, 1969

$RMe_3CCHDOH$ was prepared by asymmetric reduction of pivaldehyde-*1*-d_1 with isobornyloxymagnesium bromide. Displacement of the tosyl group in (*R*)-$Me_3CCHDOTs$ by acetate ion occurs with 85 ± 17% inversion. Reaction of (*R*)-$Me_3CCHDOH$ with Ph_3P and CCl_4 affords (+)-$Me_3CCHDCl$, assigned the *S* configuration, of greater optical purity than that resulting from chloride displacement on the tosylate. The analogous reaction using CBr_4 affords bromide which seems to be significantly racemized. The characteristics of the title reaction are summarized to point out major differences between it and an SN2 process.

The sluggishness of neopentyl esters or halides to nucleophilic displacement reactions, both SN1 and SN2, is a well-recognized property of that carbon skeletal system. Yet there are several reactions in which "nucleophilic" substitution does occur fairly readily; these reactions have the common property of employing phosphorus-containing reagents and seem to comprise a mechanistically homogenous set.

$$(PhO)_3P + Me_3CCH_2OH + MeI \longrightarrow Me_3CCH_2I^{2,3}$$
$$(+6\%\ EtCMe_2I)$$

$$(PhO)_3P + Me_3CCH_2OH + PhCH_2X \longrightarrow Me_3CCH_2X$$
$$X = I, Br^4$$

$$Ph_3PX_2 + Me_3CCH_2OH \longrightarrow Me_3CCH_2X + Ph_3PO + HX$$
$$X = Br, Cl^5$$

Furthermore, there seems to be no case in which the stereochemistry of substitution in the parent neopentyl system has been studied. We report herein the stereochemical course of the neopentyl alcohol–chloride conversion using triphenylphosphine–carbon tetrachloride and the analogous reaction with CBr_4, a study performed with the hope of gaining further insight into the mechanistic process involved. We also determined the stereochemical course of a typical SN2 reaction of neopentyl tosylate to serve as a reference point for the title reaction.

Results

When the reaction of triphenylphosphine, carbon tetrachloride, and neopentyl alcohol at ambient temperature was monitored by nmr, only the characteristic resonances of reactants and neopentyl chloride were observed. Examination by glpc showed no evidence of formation of isomeric C-5 chlorides. These results are similar to those of Downie, *et al.*[6] We prepared chiral neopentyl-*1*-d_1 alcohol by asymmetric reduction (Scheme I). This afforded low yields of alcohol whose acid phthalate showed a specific rotation, after correc-

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(1) This investigation was made possible by grants from the National Science Foundation and Petroleum Research Fund. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their support.

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