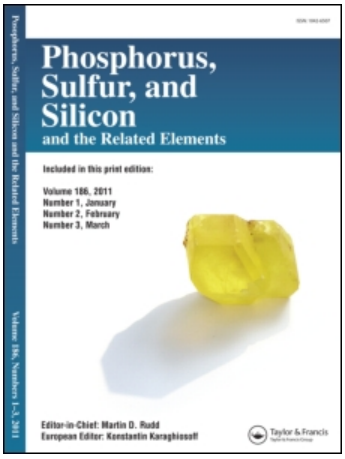

Phosphorus, Sulfur, and Silicon and the Related Elements

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Nucleophilic Substitution of 1-Phenyl-2-Phenyl Telluropropane to Yield 2-Halo-1-Phenylpropanes

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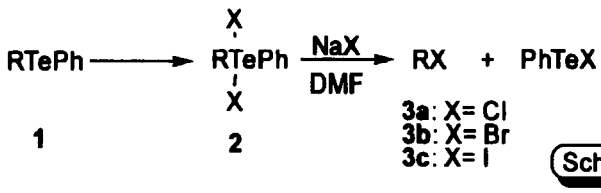
Mechanism of a novel transformation of the alkyl phenyltellurides to alkyl halides via nucleophilic substitution of the phenyltelluro group in organotelluriums is studied on the basis of kinetics and stereochemistry using the titled chiral substrate. The results obtained strongly suggest that the substitutions proceed via S_N2 mechanism with Walden inversion and very low Arrhenius' energies of activation.

Keywords: Chiral Organotelluriums; Alkyl Phenyltellurides; Alkyl Halides; Facile Transformation; S_N2 Reaction; Walden Inversion

Tellurium, a main group element sitting on the 5th row of 16th group, has metallic as well as nonmetallic character and shows variable valences including hypervalency. Recently organotellurium compounds attracted much attention from the viewpoint of development of new synthetic methodology and synthesis of new advanced materials.[1,2] In 1982 we have reported a novel and facile transformation of alkyl phenyltellurides (**1**) to alkyl halides (**3**) via substitution of the PhTe group in organotelluriums (**2**).[3] In this paper the results of mechanistic studies, kinetics and stereochemistry, of this reaction (Scheme 1) are described to show that the substitutions proceed via S_N2 mechanism with Walden inversion and very low Arrhenius' energies of activation.



Scheme 1

Optical active substrate was prepared as follows; 1-Phenyl-2-propanol (**4**) was prepared by the reaction of propylene oxide and PhMgBr [4] and optically resolved via the hydrogen phthalate.[5] The (+)-enatiomer (4, $[\alpha]_D^{25}$=+38.55°(c 2.1, $CHCl_3$)), determined to have S configuration[6], was converted to the corresponding (S)-(+)-tosylate (m.p. 69.0-69.5°C, $[\alpha]_D^{25}$=+25.82°(c 1.5, $CHCl_3$)), by the conventional pyridine-tosyl chloride method.[7] (-)-1-Phenyl-2-phenyltelluropropane (1, R= $PhCH_2$-$CH(CH_3)$-, pale brown oil, 78% yield, $[\alpha]_D^{25}$= -51.07°(c 1.6, $CHCl_3$)), was prepared by the reaction of (S)-(+)-tosylate and benzenetellurolate anion generated from diphenyl ditelluride and

$NaBH_4$.[8] The absolute configuration of (-)-**1** (R= $PhCH_2CH(CH_3)$-) was assumed to be R, because the reaction proceeded with S_N2 substitution of tosyloxy group by highly nucleophilic $PhTe^-$, i.e. inversion of configuration. According to the reported method[3], (R)-(-)-**1** thus obtained was submitted to the halogenation reactions (Scheme 2). The results were summarized in Table 1. To determine the absolute configuration of the products, (R)-(-)-**3a-c** and (S)-(+)-**3a** were prepared by both known S_Ni and S_N2[9] reactions using $SOCl_2$ and Mitsunobu's procedure[10] (Scheme 2 and Table 2). By direct and careful comparison of specific rotations of these reaction products, the stereochemistry of (+)-halides obtained from (R)-(-)-telluride (**1**) were firmly established to be (S). That means even numbers of inversion occur through the process from (S)-(+)-**4** to (S)-(+)-**3**. These results strongly suggest that in this novel reaction the phenyltelluro group is substituted by halide ions under S_N2 mechanism with Walden inversion.

Then we proceed to analyze the reaction kinetically. Racemic **4** was converted to dl-**1** via dl-tosylate. Racemic **1** was first transformed to Te(IV) derivatives in situ and then reacted with sodium halides as reported [3] in DMF. The halides produced were analyzed quantitatively by gas chromatography with regard to time[11]. Halogenation reactions were carried out at 20°C, 30°C, and 45°C[12]. As a typical example, the results of bromination are shown in Fig. 1, 2, and 3. Time dependence of bromide yielded at 20°C is shown in Fig. 1. The data of 20°C was analyzed by the second order rate equation (Eq. 1) and found to exist a good linear relationship as shown in Fig. 2, particularly in the initial stage of the reaction. From the linearity shown, second order rate constant, k_2, could be calculated. By the essentially same procedures, k_2

values at 30°C and 45°C for bromination were calculated. Those values obtained for chlorination and iodination at the same temperatures are summarized in Table 3. To obtain Arrhenius's energy of activation (E_{act}) for bromination, log k_2 values are plotted against 1/T (Fig. 3). Again a good linearity was obtained as expected by the Arrhenius's equation (2). So the activation energy can be obtained to be 12.4 kcal/mol from the slope. The Ea values for chlorination and iodination are also obtained (Table 4). Reactivities of halide ions seem to be different from those in usual polar reactions. It may be due to the effects of a dipolar aprotic solvent (DMF) used in this research[13]. In conclusion, our results clearly show that these reactions proceed smoothly via S_N2 mechanism with inversion of configuration.

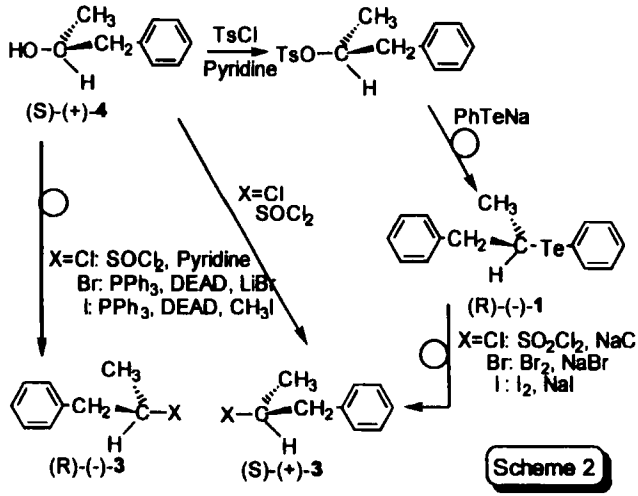


TABLE 1. Conversion of (R)-(-)-**1** to (S)-(+)-**3** and specific rotations of the products

Reagent	Conditions	Product	Yield(%)	$[\alpha]_D^{25}(°)$
SO_2Cl_2	60°C, 24h	**3a**	34.0	+7.86
SO_2Cl_2, NaCl	50°C, 2.5 days	**3a**	50.2	+23.09
Br_2, NaBr	rt, 2.5 days	**3b**	77.9	+29.18
I_2, NaI	rt, 2.5 days	**3c**	77.5	+42.09

TABLE 2 Conversion of (S)-(+)-**4** to (S)-(+)- or (R)-(-)-**3** and specific rotations

Reagent	Conditions	Product	Yield(%)	[α]D25(°)
$SOCl_2$	rt, 24h, 30°C, 2h	(S)-(+)-**3a**	65	+25.46
$SOCl_2$, pyridine	65°C, 6h	(R)-(-)-**3a**	29	-24.24
PPh_3, DEAD*, LiBr	rt, 24h	(R)-(-)-**3b**	32	-30.02
PPh_3, DEAD*, CH_3I	rt, 24h	(R)-(-)-**3c**	40	-43.33

*DEAD = Diethyl azodicarboxylate

$$k_2t = (1/b_\infty)ln\{(b - b_\infty)(b - x)/(b - b_\infty - x)b\} \quad (1)$$

where,

k_2: second order rate constant, t: time (min),

b: initial concentration of telluride, b_∞: end concentration of telluride,

x: reacted concentration of telluride (= halide concentration produced)

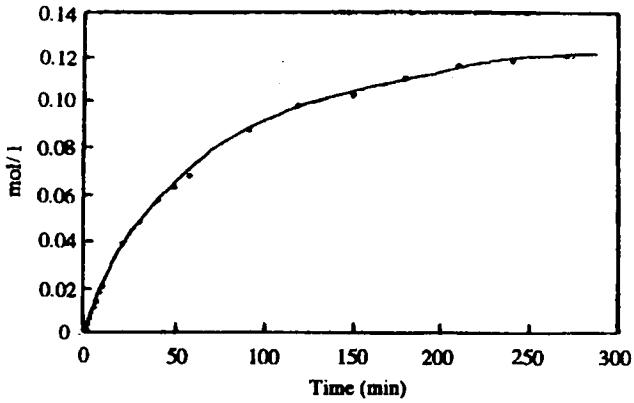


FIGURE 1. Time dependence of bromide yield at 20°C

TABLE 3. Rate constants (k_2, min^{-1} . mol^{-1} . l) of halogenation

Temperature (°C)	Chlorination	Bromination	Iodination
20	0.039	0.104	0.073
30	0.059	0.151	0.302
45	0.100	0.543	0.543

$$ln\ k_2 = A - E_{act}/RT \quad or \quad \log k_2 = 0.4343\ (A - E_{act}/RT) \qquad (2)$$

where, Ea and A are the activation energy and a constant, respectively.

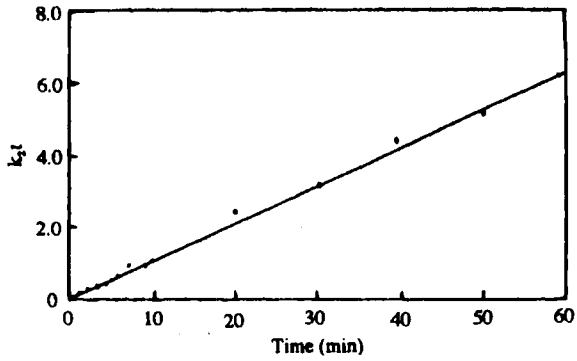


FIGURE 2. Determination of k_2

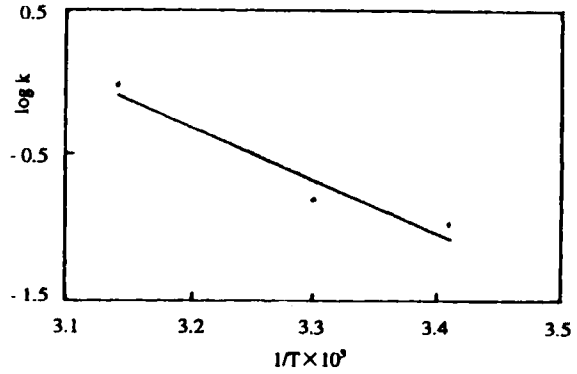


FIGURE 3. Relationship of k_2 versus 1/T

TABLE 4. Activation Energy (E_{act})

Halogenation	E_{act} (kcal/mol)
Chlorination	7.6
Bromination	12.4
Iodination	14.3

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[8] Under argon atmosphere and shield of light, $NaBH_4$ (0.90 g, 23.8 mmol) dissolved in degassed EtOH (20 mL) was added dropwise to an ice-cooled abs. THF (40 mL) solution containing PhTeTePh (3.24 g, 7.92 mmol) and stirred for 1hr with ice-cooling to obtain a clear colorless solution. To the solution cooled to –40°C, tosylate (**4**, 2.30 g, 7.92 mmol) dissolved in abs. THF (10 mL) was added dropwise. The mixture was stirred for 2h at –40°C and for 2 days further at rt. After addition of crushed ice (ca 50 g) and 2 M HCl aq (100 mL), the reaction mixture was extracted with CH_2Cl_2 (100 mL × 3). The combined extracts were washed with 1 M HCl, brine and water successively and dried over anhydrous $MgSO_4$. After filtration the extract was concentrated under reduced pressure to yield a yellow brown oil. The oil was purified by preparative GPC LC equipped with a recycle system (Japan Analytical Industry Co. Ltd., Model LC-908 carrying JAIGEL-1H and 2H columns, solvent: $CHCl_3$) to yield pure **1** (2.00 g, 77.8%) as a pale brown oil of retention volume 210 mL. ^1H NMR (400 MHz, $CDCl_3$): δ 1.54 (d, J=7.0 Hz, 3H, CH_3), 2.92 (dd, J_{gem}=13.7 Hz, J_{vic}=8.9, 1H, CH_2), 3.12 (dd, J_{gem}=13.7 Hz, J_{vic}=6.3 Hz, 1H, CH_2), 3.68 (sext, J=7.5 Hz, 1H, CH), 7.03–7.31 (m, 8H, Ar-H), 7.78 (dd, Jo=7.86 Hz, Jm=1.14 Hz, 2H, Ar-H).

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[11] Conditions of GC analysis are as follows. Machine: Shimadzu GC, Model GC-14B with FID detector; Column: J&W Scientific DB-5 (30 m) capillary column; Operating conditions: injection port 180°C, column 120°C, detector 180°C, carrier gas; nitrogen for column; Internal standard: 2,3-Dimethylnitrobenzene, retention time 7.1 min.; Retention times: chloride 3.9 min., bromide 5.4 min., iodide 8.3 min.; Response factors to the standard: chloride 0.82, bromide 1.06, iodide 1.17; GC peaks were integrated and their intensities were printed out digitally by Shimadzu Chromatopac C-R3A.

[12] Chlorination reaction was carried out and analyzed also at 60°C and essentially similar results were obtained.

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