Tetrahedron. Vol. 30, pp. 2087 to 2092. Pergamon Press 1974. Printed in Great Britain

THE ROLES OF HETERO ATOMS IN SOLVOLYTIC REACTIONS—II

TRANSANNULAR PARTICIPATION BY NEIGHBOURING SULPHUR ATOM

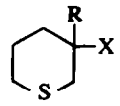
S. IKEGAMI,* T. ASAI,[a] K. TSUNEOKA, S. MATSUMURA[b] and S. AKABOSHI
Division of Pharmaceutical Chemistry, National Institute of Radiological Sciences, Anagawa, Chibashi, Japan

(*Received in Japan* 6 *July* 1973; *Received in the UK for publication* 20 *February* 1974)

Abstract—Esters of sulphur-containing 5- and 6-membered heterocycles, tetrahydro-3- and 4-thiopyranol and their 3- and 4-methyl, phenyl derivatives, and tetrahydro-2-thiophenemethanol, were synthesized. The solvolysis of β-thioesters in 80% aqueous acetone resulted in strong transannular S-participation and the products of solvolysis substantiated formation of bicyclic episulphonium ion intermediates. Such participation is considered to be present even in a tertiary system. On the other hand, γ-thioesters were solvolysed without any transannular S-participation.

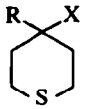
INTRODUCTION

Two different types of nitrogen effects, (a) direct nucleophilic participation to a carbonium ion and (b) intramolecular catalysis in ester hydrolysis, demonstrate the importance of unshared electrons of nitrogen in solvolytic reactions.[1,2] Similarly, solvolytic displacement reactions in mustard-type compounds, in which S-participation is important, have been investigated by many workers.[3] An S atom having unshared electrons similar to nitrogen shows similar but very different effect. The present report concerns the solvolysis of tetrahydro - 3 - and - 4 - thiopyranol derivatives (**1d, e, f, 2d, e, f**) and tetrahydro - 2 - thiophenemethanol *p*-nitrobenzoate (**3b**).



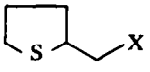
1

a: R = H, X = OH
b: R = Me, X = OH
c: R = Ph, X = OH



2

d: R = H, X = OPNB(X = OTs in 2)
e: R = Me, X = OPNB
f: R = Ph, X = OPNB



3

3a: X = OH
3b: X = OPNB

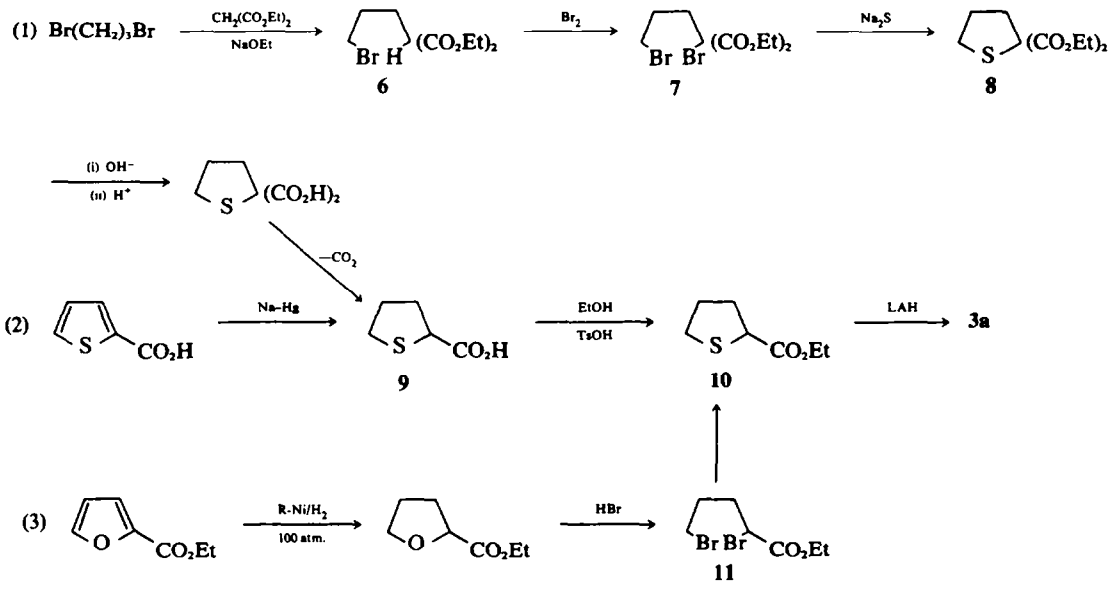
RESULTS AND DISCUSSION

Synthesis of alcohols. Tetrahydrothiopyran - 3 - one (**4**) was synthesized according to Fehnel's procedure[4] by Dieckmann cyclization followed by hydrolysis-decarboxylation. Tetrahydrothiopyran - 4 - one (**5**), which is commercially available, was also prepared from diethyl thiodipropionate by cyclization-decarboxylation.[5] Reduction of both ketones (**4, 5**) with LAH gave the corresponding alcohols (**1a, 2a**).[5,6] Methyl and phenyl tertiary alcohols (**1b, 1c, 2b, 2c**) were obtained from the reactions of the ketones (**4, 5**) with methyl and phenylmagnesium halides.

As the physical and chemical properties of tetrahydro - 2 - thiophenemethanol (**3a**) and its acetyl derivative (*e.g.* GLPC behaviour and b.p.) are very close to those of the 6-membered ring (**1a**), it is considered that separation of both compounds is greatly difficult. In fact, the method that yields the alcohols (**1a, 3a**) in the same route, which was adopted for the preparation of N-containing heterocycles,[1] resulted in failure of separation by distillation. Accordingly, **3a** was prepared by three different ways (Scheme 1) in an attempt to confirm its structure. The synthetic route (2) in Scheme 1, for the preparation of the acid (**9**), is Ernst's procedure.[7] All alcohols (**1a, 1b, 1c, 2b, 2c, 3a**), except **2a**, were converted to *p*-nitrobenzoates in the usual manner; **2a** was converted to *p*-toluenesulfonate.[6c,6d]

[a] A fellow from Medical School, Self-Defence Force, 1971–1973.

[b] A fellow in undergraduate training course from Chiba Institute of Technology (1969).

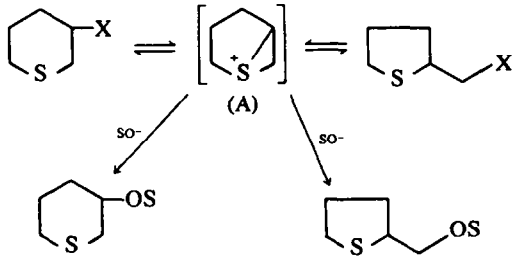


SCHEME 1.

Rates of solvolysis. The chemistry of β-haloalkyl thioethers has been studied in detail because of the importance of "mustard gas." Based on a kinetic study of the relatively rapid aqueous hydrolysis of mustard gas and its analogues,[8,9] thiiranium ions (episulphonium ions) have been proposed as intermediates. These intermediates are also involved either in the reactions of β-hydroxyalkyl thioethers with hydrochloric acid[10] or in the polar additions of sulfenyl halides to double bonds[11] and are usually too reactive to permit isolation unlike the analogous aziridinium ions. Aside from thiiranium ion formation by sulfenyl halide addition, which is the most popular route to supply the ions, the present study was focused on whether or not transannular neighbouring group participation by sulphur in solvolysis gives rise to the ion as an intermediate.[12]

Rates of solvolysis of the various *p*-nitrobenzoates were measured in 80% aqueous acetone and are shown in Table 1. The fast solvolysis rates of **1d** and **3b**, $5{\cdot}9\times10^{6}$ and $5{\cdot}4\times10^{7}$ respectively as compared with the cyclohexyl derivative, are indicative of the magnitude of the participation by sulphur.[13] If these enhanced rates are due to S-participation, both compounds should produce the same thiiranium ion intermediate (A), which in spite of strain, would be relatively stable and attacked by a solvent to give two products. These processes are well substantiated by products from both systems as described later.

It should be noted that solvolysis of β-thioesters proceeds entirely through alkyl-oxygen cleavage resulting in a S_N1 process, in spite of the exclusive cleavage of acyl–oxygen bond in β- and γ-amino esters. This different cleavage is attributed to the



SCHEME 2.

intrinsic difference between the effects of N and S atoms, indicating that the S atom does not contribute to the initial solvation, by which O–CO cleavage will be promoted, when compared with N-containing analogues.[1] On the other hand, transannular β-S-participation to a carbonium ion seems to be greater than β-N-participation as compared with relative rates.

Contrary to this strong β-S-participation with 10^{6}–10^{7} orders of magnitude of rate enhancement to the corresponding carbon system, γ-S-participation is not important. The ester (**2d**) was solvolysed as slowly as the cyclohexyl derivative by a factor of 0·1. Recently, Ohno and Ohnishi[14] have observed transannular β- and γ-S-participations to cyano tertiary radicals in system **1** and **2**. The β-S-participation in radical reactions, as might be expected, is much smaller than that in solvolysis, but it is of interest that the S atom contributes to the stabilisation of a radical at the γ-position. In contrast, Paquette[15] has pointed out, on the basis of spectroscopical evidence, that S–CO interaction of tetrahydro-γ-thiopyron is absent or at best ex-

Table 1. Rates of solvolysis of S-containing cycloalkyl *p*-nitrobenzoates in 80% aqueous acetone[a]

Compd	Pseudo first-order rate constant $k \times 10^6$ sec^{-1} 150°	125°	100°	75°	50°	$\Delta H^{\neq}$ kcal/mole	$\Delta S^{\neq}$ e.u.	Rel. rate at 50°		
Cyclohexyl					$2{\cdot}8 \times 10^{-9}$[b]			1·0		
1d[c]		67·8	6·14		0·0166[e]	27·6	−8·9	$5{\cdot}9 \times 10^6$	1·0	
2d[d]			73·1	4·60	0·189[e]	27·8	−3·3			
					$2{\cdot}9 \times 10^{-10}$[e]			0·1		1·0
3b[f]		238	28·5		0·152[e]	24·3	−15	$5{\cdot}4 \times 10^7$		
1e			207	18·2	1·09[e]	24·4	−10		66	
1f				651	40·1	24·3	−3·7		2,400	
2e	29·5	2·34			$1{\cdot}10 \times 10^{-4}$[e]	33·1	−1·6			$3{\cdot}8 \times 10^5$
2f		113	9·13		$1{\cdot}84 \times 10^{-2}$[e]	29·0	−4·4			$6{\cdot}3 \times 10^7$

[a] All rates and physical parameters were calculated using a computer with an appropriate program. [b] *cf* Ref 1. [c] Rate of methanolysis: $k = 1{\cdot}11 \times 10^{-4}$ sec^{-1} (125°), $9{\cdot}35 \times 10^{-6}$ sec^{-1} (100°); $\Delta H^{\neq} = 28{\cdot}4$ kcal . mole^{-1}; $\Delta S^{\neq} = -5{\cdot}8$ e.u. [d] Rate of the tosylate. Rate of methanolysis: $k = 1{\cdot}43 \times 10^{-4}$ sec^{-1} (100°), $7{\cdot}56 \times 10^{-6}$ sec^{-1} (75°); $\Delta H^{\neq} = 29{\cdot}7$ kcal . mole^{-1}, $\Delta S^{\neq} = 2{\cdot}9$ e.u. [e] Rate of the *p*-nitrobenzoate calculated using a factor of $k_{T_s}/k_{PNB} = 6{\cdot}6 \times 10^8$ (See Ref 1). [f] Rate of methanolysis: $k = 4{\cdot}06 \times 10^{-4}$ sec^{-1} (125°), $4{\cdot}26 \times 10^{-5}$ sec^{-1} (100°); $\Delta H^{\neq} = 25{\cdot}9$ kcal . mole^{-1}, $\Delta S^{\neq} = -9{\cdot}7$ e.u. [g] Rate extrapolated from the rates at higher temperatures.

tremely weak. Even though γ-S-participation is present in radical reactions, its absence in solvolysis would be due to the difference of solvent (or reaction condition) used.

In order to demonstrate the presence or absence of β- and γ-S-participations, the solvolysis of esters substituted by Me and Ph groups were examined. Solvolysis of tertiary systems, **1** and **2**, indicated the very strong effect produced by sulphur in β-thio derivatives. As shown in Table 1, tertiary phenyl ester (**1f**) was solvolysed 2400 times faster than the corresponding secondary derivative (**1d**), whereas γ-thio derivative (**2f**) underwent solvolysis at a rate by a factor of $6{\cdot}3 \times 10^7$ which may indicate the absence of any neighbouring participation. It is generally recognized that the magnitude of participation diminishes with increasing stability of a carbonium ion at a reaction centre.[16] Brown and Rei[17] have reported that rate ratios of k_{Ph}/k_H in systems of isopropyl, α-phenethyl, and benzhydryl chlorides are $2{\cdot}5 \times 10^8$, 9×10^4, and 1×10^4 respectively. Apparently, phenyl resonance to the reaction centre contributes to the stabilisation of the carbonium ion, so that substituent effects are minimized. Similarly, the replacement of the 7-hydrogen by a Ph group in *anti*-7-norbornenyl system, which shows 10^{11} rate enhancement to 7-norbornyl derivative by double bond participation, merely causes the rate to increase by a factor of ~3000.[18] The smallest rate ratio (k_{Ph}/k_H) of system **1** observed at present reveals that β-S-participation would be the greatest. Substituent effects of Me and Ph groups are summarized in Table 2 with pertinent data.

Similar effects are shown by the solvolysis of methyl substituted ester (**1e**). Systems in which participation is not involved are usually solvolysed with a factor of 10^4–10^5 by replacing an H by a Me group. A Me substituent in the system **1** increased the rate only by a factor of 66, even though the Me effect of the benzhydryl derivative which is a strongly resonance-stabilised species produces a 346 times faster rate. Also, methyl and phenyl tertiary *p*-nitrobenzoates (**1e**, **1f**) underwent solvolysis at faster rates than the corresponding cyclohexyl derivatives by factors of 620 and 91 (Table 3). As expected, the relative rate of **1e** decreased by replacing an H by a Me group.

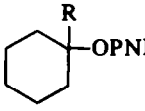
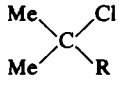
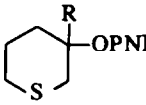
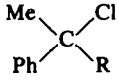
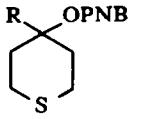
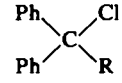
However, the fact that enhanced rates were still observed in the Me and Ph substituents suggests that a sulphide group in the β-position stabilises a tertiary carbonium ion. Substituent effects in γ-thioesters (**2e**, **2f**), by comparison of relative rates, are similar to those of cyclohexyl derivatives, thus indicating that S has no effect in secondary system as well as in tertiary systems. A slight rate retardation, 0·1–0·05, would not be considered important, but it is difficult to reason why rates are slower than those of cyclohexyl derivatives.

Solvolysis product. The products of solvolysis in 80% aqueous acetone were analysed on GLPC. The results are shown in Table 4.

The *p*-nitrobenzoates (**1d**, **3b**) gave the same two products in similar ratios. This indicates that solvolysis of both compounds (**1d**, **3b**) proceeded *via* the same intermediate formed exclusively by strong S-participation (Scheme 2) and not as a result of oxygen–acyl bond cleavage as observed for N-containing analogues. Furthermore, that O–CO cleavage did not take place was confirmed by infinity titer in methanolysis, which was in accord with a calculated titer.

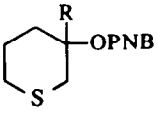
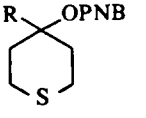
Free energy of activation is calculated for both compounds (**1d**, **3b**), i.e., 30·5 kcal for **1d** and 29·0 kcal for **3d**. In addition, based on the distribution of kinetically controlled products, there is obtained 1 kcal/mole as an energy difference between both transition states. Therefore, the more

Table 2. Summary of methyl and phenyl substituent effects in solvolysis

Compd	Rate ratio (50°)[a] Me/H	Ph/Me	Compd	Rate ratio (25°)[b] Me/H	Ph/Me
	620,000[d]	190		55,000	4,580
	66	37		1,800	50
	384,000[d]	167		346	29

[a] Hydrolysis in 80% aq acetone. [b] Ethanolysis (Ref 17). [c] See Ref 17; Brown and Rei report 33,000 for Me/H and 1,900 for Ph/Me in ethanolysis of the chlorides. [d] Compared with rate of PNB calculated from rate of the tosylate measured for R = H.

Table 3. Summary of solvolysis rates relative to cyclohexyl derivatives

Compd	R = H	R = Me	R = Ph
	$5{\cdot}8 \times 10^6$	620	91
	1/10[a]	1/16	1/24

[a] Compared with rate of tosylate.

Table 4. Products of solvolysis in 80% aqueous acetone

Compd	Yield, %[a]	1a	3a	2a	12[b]
1d	94	81·9	18·1		
3d	92	82·0	18·0		
2d				22·7	77·3

[a] GLPC yield. [b] 5,6-Dihydro-2H-thiopyran.

stable isomer at the ground state is not **3b** but **1d** by 2·5 kcal/mole. If this energy difference is applied to the alcohols (**1a**, **3a**), this value would become important in the preparation of both alcohols by an ionic process.

The methyl derivative (**1e**) yielded quantitatively the corresponding alcohol (**1b**), together with a slight unknown single peak on GLPC. Probably, the minor product would be 2 - methyltetrahydro - 2 - thiophenemethanol by consideration of the products in the acid-catalysed opening of epoxides.[19]

EXPERIMENTAL

All m.ps are corrected. All b.ps are uncorrected. IR spectra were recorded on a Hitachi-Perkin-Elmer Model 225 (Grating) spectrometer. Mass spectra were taken by a reservoir method on a Hitachi mass spectrometer Model RMS-4 performed with the target current, 70 μA and the chamber voltage, 70 eV.

Ethyl (3-bromopropyl)malonate **6**. To a soln of Na metal (5·75 g; 250 matom) in 120 ml of abs EtOH, a soln of diethyl malonate (40 g; 250mmol) in 50 ml of abs EtOH was added dropwise with mechanical stirring, then the soln was refluxed for 1·5 h. After cooling, to a soln of 1,3-dibromopropane (50·5 g; 250 mmol) in 50 ml of abs EtOH, the soln of sodiomalonate prepared before use was added dropwise and the mixture was stirred for 1 h at room temp and heated under reflux for 1·5 h. Filtration and evaporation left an oil, which was extracted with $CHCl_3$ and the extract was washed with H_2O few times and dried over $MgSO_4$. After removal of the solvent, a residue was distilled under reduced pressure to give a fraction of b.p. 121–123°/2 mmHg (11·5 g, 16% yield), n_D^{20} 1·4538. Lit, b.p. 153–154°/9 mmHg,[20] 158–160°/14 mmHg.[21]

Diethyl (3-bromopropyl)bromomalonate **7**. To a soln of **6** (30 g; 107 mmol) in 100 ml of anhyd Et_2O, Br_2 (17·1 g; 107 mmol) was added dropwise with magnetic stirring under ice-cooling. The mixture was refluxed for 1 h, then washed with sat $NaHCO_3$ aq after cooling and dried over $MgSO_4$. Evaporation of the solvent left an oil which was distilled *in vacuo* to yield colorless oil of 30·1 g (yield, 78%), b.p. 88–90°/0·01 mmHg, n_D^{20} 1·4842. Mass spectrum showed to be dibromo compound; *m/e*: 358, 360·362 (M^+). Lit, b.p. 176–177·5°/13 mmHg,[22] 177°/11 mmHg, n_D^{20} 1·4842.[21]

Diethyl tetrahydrothiophene - 2,2 - dicarboxylate **8**. To

a soln of 7 (25 g; 70 mmol) in 40 ml of abs EtOH, a suspended soln of anhyd Na_2S (7·1 g; 91 mmol) in 120 ml of abs EtOH was added dropwise with magnetical stirring under ice-cooling. Then the mixture was stirred for additional 2 h under cooling and 200 ml of anhyd Et_2O was added to it. The organic layer was separated from NaBr by decantation and after removal of the solvent, the resulting oil was distilled to give colorless oil of 11·1 g (69% yield), b.p. 120–121°/2 mmHg, n_D^{20} 1·4783. IR (film): 1740 cm^{-1} (C=O); Mass, *m/e* (%): 232 (22, M^+) 159 (96, $M^+ - CO_2Et$), 87 (100, $M^+ - 2CO_2Et$). (Found: C, 51·49; H, 6·89; S, 13·50. $C_{10}H_{16}O_4S$. Calc: C, 51·71; H, 6·94; S, 13·80).

Tetrahydrothiophene - 2 - carboxylic acid **9**. (**a**) Dicarboxylate **8** (1·44 g; 6·2 mmol) was saponified in 90% EtOH containing NaOH (0·99 g; 25 mmol) by heating under reflux for 1 h. The ppt obtained was dissolved in a small volume of H_2O and the soln was acidified with conc HCl soln, then extracted with Et_2O several times. After drying the extract, evaporation left colorless crystals of 0·59 g (yield, 51%), m.p. 132–133° (dec), which was easily decarboxylated at 140° to give monocarboxylic acid (**9**) of 0·52 g. This crude product solidified under ice-cooling but melted at room temp and was supplied to esterification without further purification. Lit, m.p. 51°.[7] (**b**) 2-Thiophenecarboxylic acid was hydrogenated with Na–Hg according to Ernst's procedure.[7] Crude product obtained in 90% yield was identical with the product prepared in the method **a** by comparison of their IR spectra. Because of a large amount of loss on purification, the crude acid was esterified without purification.

Ethyl tetrahydrothiophene - 2 - carboxylate **10**. (a) A soln of crude **9** (6·8 g; 51 mmol) dissolved in 60 ml of EtOH was heated under reflux in the presence of a trace amount of *p*-TsOH for 50 h. After removal of the solvent, the resulting oil was distilled under reduced pressure to give colorless oil of 4·4 g (53% yield), b.p. 64–76°/4 mmHg, n_D^{20} 1·4489. Lit, b.p. 98–99°/14 mmHg,[7b] 102·5–104°/11 mmHg.[22]

(b) The cyclization of **9** with Na_2S was carried out in the procedure similar to the preparation of **8**. The ester (**10**) was obtained in 61% yield and its IR spectrum was superimposable with that of the product prepared in the method **a**.

Tetrahydrothiophene - 2 - methanol **3a**. To a soln of LAH (0·6 g; 15 mmol) in 40 ml of anhyd Et_2O was added a soln of **10** 2·4 g; 15 mmol) in Et_2O under N_2 and the mixture was heated under reflux for 1 h. Decomposition of an excess of LAH and a complex with H_2O–NaOH and filtration gave colorless soln, which was dried over $MgSO_4$ and evaporated to leave an oil. Distillation under reduced pressure gave 1·2 g (yield, 68%) of colorless oil, b.p. 70–71°/3 mmHg, n_D^{20} 1·5222. Lit reports b.p. 96–97°/10 mmHg, n_D^{20} 1·5286 for the optically active alcohol.[24]

Ethyl 2,5-dibromovalerate **11**. Gaseous HBr generated from the reaction of Br_2 with tetraline was passed into a soln of ethyl tetrahydrofuroate (46·1 g; 0·32 mol) dissolved in 40 ml of glacial AcOH. After saturation with HBr, the soln was allowed to stand at room temp for 2 days and then poured into ice-water. Organic layer was extracted with Et_2O and the extract was washed with 10% Na_2CO_3 aq until alkaline, dried over $MgSO_4$ and evaporated to leave a colorless oil, which was distilled to afford 13·1 g (14% yield) of a colorless oil, b.p. 98–99°/2 mmHg. Lit, b.p. 111–112°/5 mmHg.[25]

Grignard reaction to tetrahydrothiopyran - 3 - and 4 - ones. To a stirred etherial soln of Grignard reagent (30% excess to ketone) prepared from the reaction of MeI or PhBr with Mg under N_2, was added dropwise a soln of ketone (3·5 g; 0·03 mol) dissolved in 10 ml of anhyd Et_2O at room temp. The mixture was stirred overnight and poured into a cold saturated NH_4Cl aq.

The etherial layer was separated, dried and evaporated to leave almost pure tertiary alcohol in satisfactory yield. Careful removal of ether under atmospheric pressure using a Viglex column was needed for the isolation of **1b**. If not so, the yield decreases unfavorably because of its volatility. Yield and physical constant are shown in Table 5.

Conversion of alcohol to p-nitrobenzoate. To a soln of 3–10 mmoles of alcohol dissolved in 3–10 ml of anhyd pyridine was added portionwise an equimolar amount of *p*-nitrobenzoyl chloride under ice-cooling. Then the soln was allowed to stirr at room temp for 1–7 days and poured into ice-water. Ester solidified by an aid of scratch was assembled by filtration and after dryness *in vacuo*, recrystallised from hexane or benzene or their mixed solvents to give pure *p*-nitrobenzoate in moderate yield. Elemental analysis and m.p. are shown in Table 6.

Kinetic measurement. The procedures were similar to those used for the related compounds previously described.[1a] The 80% aqueous acetone used as solvent was prepared by mixing 80 parts by volume of acetone (purified according to Fieser's procedure) with 20 parts by volume of water at 20° and adjusted to yield a rate of solvolysis identical within the experimental uncertainty of ±3% with that observed for 1-phenylcyclohexyl *p*-nitrobenzoate.[26] Rate constants were calculated by least-squares linear regression analysis to first-order rate expression. The enthalpy and entropy of activation were obtained by Eyring's absolute rate equation using a computer (TOSBAC 3400).

Analysis of solvolysis products. Solvolytic technique were similar to those used for rate measurements in 80% aqueous acetone. After allowing in a temp-controlled bath for more than 10 half-lives, an equimolar amount of acetophenone was added to the soln as an internal standard for GLPC analysis and the soln was dehydrated by anhyd K_2CO_3. Products were analysed under the follow-

Table 5

Compd	Yield, %	m.p. (b.p.)	n_D^{20}	Lit, m.p. (b.p.)
1b	71	(111–112°/42 mmHg)	1·5187	—
1c	82	64–65°		64–65°[a]
2b	78	42–42·5°, (76–80°/6 mmHg)		45·5°, (54–55°/1 mmHg)[b]
2c	85	76–77°		75–76°[a]

[a] R. F. Noylor, *J. Chem. Soc.* 2749 (1949). [b] A. Luttringhaus, S. Kabuss, H. Prinzbach and F. Langenbucher, *Liebig's Ann.* **653**, 195 (1962).

Table 6

PNB	m.p., °C	Formula	Analysis Calcd. C	H	N	S	Found C	H	N	S
1d	67–68	$C_{12}H_{13}NO_4S$	53·92	4·90	5·24	12·00	53·62	4·90	5·20	11·80
3b	86–87	$C_{12}H_{13}NO_4S$					53·94	4·90	5·32	12·00
1e	96–97	$C_{13}H_{15}NO_4S$	55·90	5·37	4·98	11·40	55·61	5·40	4·90	11·41
2e	128–129	$C_{13}H_{15}NO_4S$					55·87	5·37	4·86	
1f	131–132	$C_{18}H_{17}NO_4S$	62·95	4·99	4·08	9·33	62·65	5·01	3·97	9·04
2f	162·5–163·5	$C_{18}H_{17}NO_4S$					62·94	5·01	3·94	

ing gas chromatographical condition. Varian gas chromatograph Model 1400 (single column, FID) was performed with 8 feet × ⅛" glass spiral tubing packed with 10% by weight of diethylene glycol adipate supported on acid-washed 80–100 mesh chromosorb W. The column was controlled at 110° with a flow rate of 20 ml/min of N_2. Under these conditions **1a** and **3a** showed peaks at 52·0 min and 47·8 min of retention time respectively and their peaks were analysed quantitatively by comparison with an internal standard using DISC integrator equipped with a recorder. Peaks of **2a** and **12** appeared at 16·3 min and 4·0 min respectively using the same column controlled at 80°.

Acknowledgements—We are indebted to Dr. S. Saito, Tokyo Research Laboratory, Tanabe Seiyaku Co., LTD, for microanalyses. We thank Mr. M. Uoji for measurements of IR spectra and members of the computer room of the institute for the arrangement of rate calculation.

REFERENCES

[1a] S. Ikegami, K. Uoji and S. Akaboshi, *Tetrahedron* **30**, 2077 (1974); [b] K. Uoji, Y. Fukunaga and S. Ikegami, *Chem. Pharm. Bull.* In press
[2a] T. C. Bruice and S. J. Benkovic, *Bioorganic Mechanisms*, Vol. 1, Chapter 1. Benjamin, New York, N.Y. (1966); [b] W. P. Jencks, *Catalysis in Chemistry and Enzymology*, Chapters 2, 3, and 10. McGraw-Hill, New York, N.Y. (1969)
[3a] A. Streitwieser, Jr., *Solvolytic Displacement Reactions*, pp. 16–18, 108–110, McGraw-Hill, New York, N.Y. (1962); [b] B. Capon, *Quart. Revs.*, **18**, 45 (1964); [c] K.-D. Gundermann, *Angew. Chem.* **75**, 1194 (1963)
[4] E. A. Fehnel, *J. Am. Chem. Soc.* **74**, 1569 (1952)
[5] E. A. Fehnel and M. Carmack, *Ibid.* **70**, 1813 (1948)
[6a] C. G. Overberger and A. Katchman, *Ibid.* **78**, 1965 (1956); [b] M. Protiva and E. Adlerova, *Chimia*, **12**, 145 (1958); [c] E. Adlerova and M. Protiva, *Coll. Czech. Chem. Comm.* **24**, 1268 (1959)
[7a] F. Ernst, *Chem. Ber.* **20**, 518 (1887); [b] D. J. Cram and T. A. Whitney, *J. Am. Chem. Soc.* **89**, 4651 (1967)
[8] P. D. Bartlett and C. G. Swain, *Ibid.* **71**, 1406 (1949)
[9] A. G. Ogston, E. R. Holiday, J. S. L. Philpot and L. A. Stocken, *Trans. Faraday Soc.* **44**, 45 (1948)
[10] R. C. Fuson, C. C. Price and D. M. Burness, *J. Org. Chem.* **11**, 475 (1946)
[11] For a review, see W. H. Mueller, *Angew. Chem.* Intermat. Edit. **8**, 482 (1969)
[12] S-Participation in solvolysis of various cases have been reported; See Refs [a] V. R. Gaertner, *Tetrahedron Letters* 5919 (1968); [b] H. Morita and S. Oae, *Ibid.* 1347 (1969); [c] H. Hofmann and G. Salbeck, *Angew. Chem. Internat. Edit.* **8**, 456 (1969); [d] M. Hojo, T. Ichi, Y. Tamaru and Z. Yoshida, *J. Am. Chem. Soc.* **91**, 5170 (1969; [e] E. R. de Waard, W. J. Vloon and H. O. Haisman, *Chem. Comm.* 841 (1970); [f] D. L. Coffen and M. L. Lee, *J. Org. Chem.* **35**, 2077 (1970); [g] T. Tsuji, T. Komeno, H. Itani and H. Tanida, *Ibid.* **36**, 1648 (1971)
[13] M. J. Blandamer, H. S. Golinkin and R. E. Robertson, *J. Am. Chem. Soc.* **91**, 2678 (1969) report rate of $1·9 \times 10^5$ for 2-methylthioethyl derivative relative to ethyl bromide
[14] A. Ohno and Y. Ohnishi, *Tetrahedron Letters* 339 (1972)
[15] L. A. Paquette and L. D. Wise, *J. Am. Chem. Soc.* **89**, 6659 (1967)
[16a] H. C. Brown, *Chemistry in Britain* 199 (1966); [b] H. C. Brown, *Chemical and Engineering News*, **45**, 86 (1967); [c] H. C. Brown, *Boranes in Organic Chemistry*, Part III, Cornell Univ. Press, Ithaca, N.Y. (1972)
[17] H. C. Brown and M.-H. Rei, *J. Am. Chem. Soc.* **86**, 5008 (1964)
[18] P. G. Gassman and A. F. Fentiman, Jr., *Ibid.* **91**, 1545 (1969)
[19] J. Ohishi and S. Ikegami, unpublished observation
[20] R. Willstätter and F. Ettlinger, *Liebig* **324**, 91 (1903)
[21] R. Willstätter, *Ber. Chem. Ges.* **33**, 1163 (1900)
[22] R. Willstätter and F. Ettlinger, *Liebig Ann.* **326**, 100 (1903)
[23] A. Kucsman, I. Kapovits, B. Tanacs and A. Nemes, *Acta Chim. Acad. Sci. Hung.* **34**, 87 (1962); *Chem. Abst.* **59**, 556g (1963)
[24] G. Claeson and H. G. Jonsson, *Arkiv för Kemi* **26**, 247 (1966); **31**, 83 (1968)
[25] P. C. Dutta, *Science and Culture* **5**, 560 (1940); *Chem. Abst.* **34**, 6933 (1940)
[26] K. Tsuneoka and S. Ikegami, Manuscript in preparation