246. *Reaction Kinetics and the Walden Inversion. Part XI.*[1] *Steric Course of Bimolecular Nucleophilic Substitution by a Neutral Nucleophile on a Neutral Substrate.*

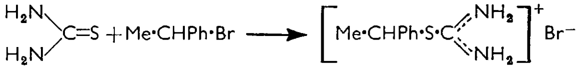
By H. M. R. Hoffmann and (the late) E. D. Hughes.

It is shown that an S_N2 reaction of charge-type 2 (neutral nucleophile and neutral substrate), namely, that of thiourea with 1-phenylethyl bromide to give 1-phenylethylthiouronium bromide, proceeds with quantitative inversion. A stereospecific conversion of (+)-1-phenylethyl bromide into (−)-1-phenylethanethiol is in complete agreement with the two-step correlation of Part IX. Ancillary studies are described which lead to the elimination of disturbances that would have obscured the stereochemical results.

Although it has become generally accepted that a reaction proceeding by mechanism S_N2 necessarily entails Walden inversion, there is, nevertheless, no compelling example of this rule for the stereochemical course of a substitution of charge-type 2,[2] *i.e.*, the formation of an 'onium salt from a neutral nucleophile and a neutral substrate. The stereochemical work quoted in the literature for this charge-type is scant and far from being quantitative. Using tertiary amines as nucleophiles and 1-methylheptyl bromobenzene-*p*-sulphonate as substrate, optically active quaternary ammonium salts were obtained,[3] which were unstable and whose configuration and optical purity relative to the reactant were unknown. The reaction of 1-phenylethyl bromide with dimethyl sulphide,[4] which is quoted in text-books,[5] was carried out without a solvent and without kinetic control, and proceeded with an unspecified amount of inversion and racemisation.

The best investigated example so far, seems to be the reaction of 1-methylheptyl bromide and of 1-methylphenethyl toluene-*p*-sulphonate with thiourea in ethanol.[6] Although the optical purity of the products is unknown, it appears that a large amount of inversion occurred, the exact proportion of which, however, would have to be determined by an independent stereospecific correlation of reactants with products, or a resolution of the products.

For our example, we have again chosen thiourea as the neutral nucleophile and 1-phenylethyl bromide * as the substrate in acetonitrile solvent:



$$(H_2N)_2C{=}S + Me{\cdot}CHPh{\cdot}Br \longrightarrow \left[Me{\cdot}CHPh{\cdot}S{\cdot}C\begin{matrix}NH_2\\NH_2\end{matrix}\right]^+ Br^-$$

There are several advantages in using thiourea rather than a sulphide[4] or an amine:[3] (i) Thiourea is one of the strongest neutral nucleophiles towards saturated carbon that is available;[7] (ii) In contrast to sulphonium halides, the thiouronium salts crystallise readily; (iii) Thiouronium salts can be easily converted into thiols; (iv) The positive charge in thiouronium salts is remote from the alkyl residue, rendering $S{\cdot}C(NH_2)_2^+$ a much poorer leaving group than SMe_2^+. This effect should stabilise thiouronium salts relative to sulphonium salts.

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* The 1-phenylethyl was preferred to the 1-methylheptyl system because the former had to be investigated for charge-type 4 (cf. Part XII). In Part VIII (*J.*, 1960, 800), charge-types 2 and 3 were inadvertently crossed over.

[1] Part X, Hoffmann, preceding paper.

[2] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953.

[3] Cary, Vitcha, and Shriner, *J. Org. Chem.*, 1937, **1**, 280.

[4] Siegel and Graefe, *J. Amer. Chem. Soc.*, 1953, **75**, 4521.

[5] Hine, " Physical Organic Chemistry," McGraw-Hill, New York, 1962, p. 128; Eliel in " Steric Effects in Organic Chemistry," ed. Newman, Wiley, New York, 1956, p. 68.

[6] Arcus and Hallgarten, *J.*, 1956, 2987.

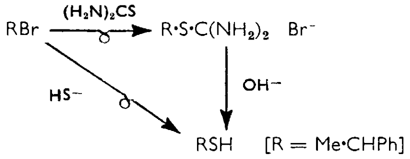
[7] Edwards and Pearson, *J. Amer. Chem. Soc.*, 1962, **84**, 16.

The last point was confirmed experimentally. Whereas the dimethyl-1-phenylethylsulphonium cation decomposed by an E 1 reaction ($t_{\frac{1}{2}} = 410$ min.) in acetonitrile at 59·8° (cf. Part XII), no such elimination was observed for the 1-phenylethylthiouronium salt under identical conditions; it appears that thiourea, in order to be a leaving group, requires either a resonance-stabilised alkyl residue and S_N1 conditions, or help from attack of a strong nucleophile.[8] Table 1 summarises the kinetic experiments for the formation of the thiouronium salt. The reaction is clearly first-order with respect to the nucleophile and first-order in substrate, *i.e.*, second-order overall. It therefore proceeds by an S_N2 mechanism. The relative configurations and optical purities of reactant and product were obtained by way of 1-phenylethanethiol, resulting in the following Walden cycle.

TABLE 1.

First-order (k_1 in sec.$^{-1}$) and second-order velocity constants (k_2 in l. mole^{-1} sec.$^{-1}$) for the reaction of thiourea with 1-phenylethyl bromide in acetonitrile at 59·8°.

$[(H_2N)_2CS]_0$ (moles l.$^{-1}$)	0·096	0·116	0·039	0·203	0·109	0·115	0·169
$[Me\cdot CHPh\cdot Br]_0$ (moles l.$^{-1}$)...	0·097	0·043	0·113	0·048	0·045	0·046	0·056
$k_1 \times 10^4$	1·18	1·52	0·40	3·24	1·40	1·65	2·69
$k_2 \times 10^3$	1·71	1·55	1·69	1·71	1·52	1·56	1·62



Scheme 1.

Although 1-phenylethyl bromide and 1-phenylethanethiol have already been linked[9] by way of methyl 1-phenylethyl sulphide, we made this additional check and converted the alkyl bromide directly into the thiol. The kinetic study of this reaction was complicated by the proton-transfer:

$$RSH + HS^- \rightleftharpoons RS^- + H_2S$$

resulting in competition of thiolate ion with hydrosulphide ion for the substrate, to give the symmetrical sulphide, as an important side-reaction:

$$RS^- + RBr \longrightarrow RSR + Br^-$$

However, it is safe to assume that the displacement by hydrosulphide ion is bimolecular, and that its rate is about the same as those measured for the substitutions by thiolate ion which are described in the preceding Parts of this series. The side-reaction was suppressed by working with a five-fold excess of sodium hydrogen sulphide and saturating the reaction solution with hydrogen sulphide before addition of 1-phenylethyl bromide. From (+)-1-phenylethyl bromide, α_D^{20} 88·9°, the thiol, α_D^{20} −56·8°, was isolated, corresponding to 52·5% optical purity[9] (all values for α in this Paper refer to neat liquids and l 1 dm., unless stated otherwise). 1-Phenylethyl bromide therefore has α_D^{20} (max.) 169°. This figure is in excellent agreement with the value, α_D^{20} (max.) 170°, obtained from the " detour " by way of methyl 1-phenylethyl sulphide,[9] and it further demonstrates that all the steps described have been carried out with complete preservation of optical purity.

Finally, the rotation of the 1-phenylethylthiouronium salt had to be correlated with that of the thiol. Although in the stereochemical experiment the formation of the thiouronium salt was followed in acetonitrile in order to obtain clean kinetics, this solvent was not found suitable for large-scale preparations of the salt, since the thiouronium

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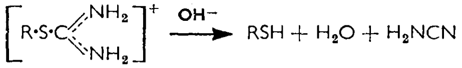
[8] Saville, *Proc. Chem. Soc.*, 1961, 214.

[9] Part IX, Hoffmann and Hughes, *J.*, 1964, 1244.

bromide was not sufficiently optically stable on prolonged heating with an excess of thiourea, and the bromide ion which is formed caused racemisation of the unreacted 1-phenylethyl bromide (see below). By contrast, when 95% aqueous ethanol and 1-phenylethyl chloride,[4] instead of bromide, was used, a product with 77% net inversion was obtained, although the reaction mixture had to be kept at 73° for 20 hr. This method was used preparatively. It appears that the protic solvent, 95% ethanol, stabilises the ground state of the thiouronium salt relative to a possible transition state in which the positive charge is spread, and simultaneously makes chloride ion a comparatively poor nucleophile towards 1-phenylethyl chloride.[10]

The alkaline hydrolysis of the thiouronium salt should not disturb the bonds of the asymmetric carbon atom:



$$\left[R{\cdot}S{\cdot}C{\begin{smallmatrix}NH_2\\NH_2\end{smallmatrix}}\right]^+ \xrightarrow{OH^-} RSH + H_2O + H_2NCN$$

However, our initial experiments, as well as the correlation given in the literature,[4] were in error. Two reasons can account for this.

(i) Thiols are readily oxidised in alkaline solution in the presence of oxygen to give disulphides:

$$2Me{\cdot}CHPh{\cdot}S^- + \tfrac{1}{2}O_2 + H_2O \longrightarrow Me{\cdot}CHPh{\cdot}S{\cdot}S{\cdot}CHPh{\cdot}Me + 2OH^-$$

The disulphide bridge is flanked by two α-hydrogen atoms which are each made labile by a phenyl group and by an adjacent sulphur atom (because of the easy expansion of the sulphur valency shell[11]). Therefore, the two labilised α-hydrogen atoms could be abstracted by base during the steam-distillation of the thiol, with formation of a racemised carbanion. Subsequent thiol–disulphide interchange,[12] according to

$$R^*S^- + RS{\cdot}SR \rightleftharpoons RS^- + R^*S{\cdot}SR$$

would lead to partly racemised thiol. We prevented these oxidative side-reactions by performing our later experiments in an atmosphere of nitrogen at room temperature.

(ii) There was some difficulty in obtaining an optically homogeneous sample of the crystalline thiouronium salt. Unless identical material is used for optical rotatory measurement both on the salt in solution and for its hydrolysis to thiol, the results will be in error. This difficulty was overcome by taking samples for both estimations from an aqueous solution of the thiouronium salt. Thus a molecular rotation for (+)-1-phenylethylthiouronium chloride of $[M]_D^{20}$ 131° (in water) was found to be equivalent to a rotation of α_D^{20} 41·4° for (+)-1-phenylethanethiol (38·2% optically pure[9]). The molecular rotation of the optically pure thiouronium salt is therefore $[M]_D^{20}$ (max.) 342° (in water). The reaction between thiourea and 1-phenylethyl bromide was then investigated stereochemically. An initial experiment with approximately equal concentrations of nucleophile (0·122 moles $l.^{-1}$) and substrate (0·166 moles $l.^{-1}$) carried out under kinetic conditions, gave 96% racemisation and only 4% net inversion; the product 1-phenylethylthiouronium bromide was isolated after 60% reaction. This suggested that an important side-reaction also occurred, which was found to be the bimolecular symmetrical exchange:

$$Br^- + (+)\text{-}RBr \underset{k_2'}{\overset{k_2'}{\rightleftharpoons}} (-)\text{-}RBr + Br^- \qquad [R = Me{\cdot}CHPh]$$

As the bromide-ion concentration builds up during the reaction, this bimolecular racemisation becomes more and more important. The unimolecular rate of racemisation (from reversible ionisation) can be safely neglected under our conditions ($k_1 \approx 1{\cdot}3 \times 10^{-5}$ sec.$^{-1}$

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[10] Parker, *J.*, 1961, 1328.

[11] Cilento, *Chem. Rev.*, 1960, **60**, 147.

[12] Parker and Kharasch, *Chem. Rev.*, 1959, **59**, 583.

from initial rates). The observed bimolecular rate constants for racemisation are shown in Table 2.

TABLE 2.

Rates of racemisation of (+)-1-phenylethyl bromide by inactive 1-phenylethylthiouronium bromide and by lithium bromide in acetonitrile at 59·8°.

[$Me·CHPh·S·C(NH_2)_2^+$ Br^-] (moles l.$^{-1}$)	$k_2' \times 10^3$ (l. mole^{-1} sec.$^{-1}$)	Degree of dissociation (α)
0·0128	5·45	0·21
0·0064	6·09	0·27
0·00285	10·6	0·41

[LiBr] (moles l.$^{-1}$)	$k_2^0 \times 10^3$ (l. mole^{-1} sec.$^{-1}$)	Degree of dissociation (α)
0·00878	26·2	1·0
0·00740	25·3	1·0 (cf. ref. 10)

The fact that k_2' is not constant for the racemisation with 1-phenylethylthiouronium bromide can be rationalised by making $k_2' = \alpha k_2^0$, *i.e.*, by allowing for the degree of dissociation, α, of the ion-paired thiouronium bromide in a way originally suggested by Acree;[10] k_2^0 is the true bimolecular rate constant for " free " bromide ion, and was estimated by using dilute solutions of completely dissociated lithium bromide in acetonitrile. As can be seen, the thiouronium bromide has comparatively little tendency to dissociate, as is consistent with its low solubility in acetonitrile (a saturated solution was only 0·013M at room temperature). For a kinetic run, α cannot be estimated accurately; it will be decreased by added thiourea and also as the concentration of 1-phenylethylthiouronium bromide increases. However, k_2' can be at best as great as the value for complete dissociation; therefore, $k_2' = 2{\cdot}58 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$ is a safe upper limit, and is assumed for the subsequent discussion.

Total inversion in a bimolecular substitution of charge-type 2 would require the following reactions (Scheme 2), in which the expressions below the chemical symbols are concentrations at an arbitrary time.

$$\underset{(a-x)}{\mathrm{N}} + \underset{y}{(+)\text{-}\mathrm{RX}} \xrightarrow{k_2} \underset{z}{(-)\text{-}\mathrm{RN}^+} + \underset{x}{\mathrm{X}^-} \qquad (1)$$

$$\underset{(a-x)}{\mathrm{N}} + \underset{(b-x-y)}{(-)\text{-}\mathrm{RX}} \xrightarrow{k_2} \underset{(x-z)}{(+)\text{-}\mathrm{RN}^+} + \underset{x}{\mathrm{X}^-} \qquad (2)$$

$$\mathrm{X}^- + \underset{y}{(+)\text{-}\mathrm{RX}} \underset{k_2'}{\overset{k_2'}{\rightleftharpoons}} \underset{(b-x-y)}{(-)\text{-}\mathrm{RX}} + \underset{x}{\mathrm{X}^-} \qquad (3)$$

Scheme 2.

Reactions (1) and (2) represent the main reaction, *i.e.*, the formation of the thiouronium bromide (RN^+) from alkyl bromide (RX) and thiourea (N). Reaction (3) allows for the simultaneous and reversible racemisation of unreacted 1-phenylethyl bromide by the bromide ion formed. It follows (see Appendix) that:

$$\frac{[(-)\text{-}\mathrm{RN}^+]}{[(+)\text{-}\mathrm{RN}^+] + [(-)\text{-}\mathrm{RN}^+]} = \frac{[(+)\text{-}\mathrm{RX}]_0}{[(+)\text{-}\mathrm{RX}]_0 + [(-)\text{-}\mathrm{RX}]_0}\cdot f,$$

where $$f = 1 - \frac{k_2'\,x^2}{3ak_2}\left(\frac{1}{b} - \frac{1}{2[(+)\text{-}\mathrm{RX}]_0}\right)\left(1 + \frac{a+b}{2ab}\,x + \ldots .\right)$$

Higher terms in x can be neglected. Assuming that $[(+)\text{-}\mathrm{RX}]_0 > [(-)\text{-}\mathrm{RX}]_0$, and neglecting the factor f for the time being, this equation implies the following: inverted product : total amount of product = initial amount of reactant of opposite rotation : total initial amount of reactant. This is a mathematical restatement of the S_N2 rule, and is to be expected because the S_N2 rule is implicit in all three equations of Scheme 2. The factor f allows for racemisation through halide exchange, *i.e.*, reaction (3) of Scheme 2, and it is smaller than, or equal to, unity. If f equals, or is close to, unity side-reaction (3) is excluded, *i.e.*, reactant and product should have the same optical purity. In order to suppress reaction (3) f must be kept as near to unity as possible. This can be achieved by (i) taking a large initial concentration of nucleophile, *i.e.*, by making "a" in the denominator comparatively large, and (ii) stopping the reaction during its initial stages, *i.e.*, by keeping "x" in the numerator comparatively small.

Again the importance of using a strong nucleophile is emphasised, k_2 being in the denominator. The calculation of f allows one to lay down quantitatively the conditions for exclusion of racemisation through attack by bromide ion upon unreacted 1-phenylethyl bromide. It was calculated that a ten-fold excess of nucleophile over substrate concentration, and the following of the reaction for only 25% of its path, were sufficient to over-ride this side-reaction completely. These conditions were chosen experimentally (cf. Table 3). From the values $a = 0{\cdot}356$, $b = 0{\cdot}033$, and $x = 0{\cdot}0083$ moles l.$^{-1}$, $[(+)\text{-RX}]_0 = 0{\cdot}0025$ (moles l.$^{-1}$), *i.e.*, 52·6% optical purity, and, furthermore, since $k_2' = 2{\cdot}58 \times 10^{-2}$ and $k_2 = 1{\cdot}62 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$, we calculate $f = 0{\cdot}99$. Since k_2' is almost certainly smaller, f should be even nearer to unity.

TABLE 3.

The reaction of thiourea with (+)-1-phenylethyl bromide in acetonitrile at 59·8°.

$[(H_2N)_2CS]_0$ (moles l.$^{-1}$)	$[\text{Me·CHPh·Br}]_0$ (moles l.$^{-1}$)	Optical rotations Me·CH(Ph)·Br α_D^{20}	 $\text{Me·CHPh·S·C(NH}_2)_2^+\ \text{Br}^-$ $[M]_D^{20}$ (in water)
0·356	0·033	88·9°	−183°
0·352	0·038	88·9	−182

The rotation of the product, as calculated by assuming 100% inversion, is $[M]_D^{20} = -342 \times 88{\cdot}9/169 = -180°$. This value is in excellent agreement with experiment (Table 3), and indicates that complete inversion occurs in this S_N2 reaction of charge-type 2.

EXPERIMENTAL

Materials.—Thiourea (B.D.H. material, 99—101% purity) was recrystallised from absolute ethanol. Sodium hydrogen sulphide was prepared as described.[13] Commercial acetonitrile was refluxed for 2 hr. over phosphorus pentoxide and then distilled from the flask using a splash-trap; it had b. p. 81·4—81·5°/760 mm. The distilled material was pure by gas-chromatographic standards, and contained no trace of acid as checked by an unsuccessful attempt to neutralise tri-n-butylamine in 90% chloroform–10% glacial acetic acid, using Crystal Violet as indicator.

Analytical Methods.—All liquid compounds were checked for purity by infrared spectroscopy. Thiouronium salts were estimated [14] in aqueous solutions by using the cation-exchange resin Zeo-Karb 225(H) and titrating the liberated acid [indicator, Bromocresol Green–Methyl Red 3 : 1]. No blank-correction was required when the resin was washed with distilled water before running individual samples through it.

Conversion of (+)-1-*Phenylethyl Bromide into* (−)-1-*Phenylethanethiol.*—(+)-Phenylethyl bromide,[9] α_D^{20} 88·9° (2·04 g.), in an ethanol solution (60 ml.) saturated with hydrogen sulphide and containing sodium hydrogen sulphide (3·17 g.), was kept at 45° for 20 min. and (−)-1-phenylethanethiol was isolated after acidification, as described [9] for methyl 1-phenylethyl sulphide. It had α_D^{20} −56·78° and distilled at 57°/1·2 mm. leaving a residue of di-(1-phenylethyl) sulphide.

(+)-1-*Phenylethylthiouronium Chloride.*[4]—(−)-1-Phenylethyl chloride,[9] α_D^{20} −63·2° (5·13 g.), and thiourea (2·79 g.) were dissolved in 95% aqueous ethanol (20 ml.) and kept at 73° for 20 hr. After evaporation of the solvent, the residue was taken up in ethanol–acetone (1 : 1),

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[13] Teichert and Klemm, *Z. anorg. Chem.*, 1939, **117**, 93.

[14] Vogel, "Elementary Practical Organic Chemistry," Longmans, London, 1958, p. 805.

filtered from dust, and reprecipitated by agitation with an excess of purified benzene on a shaking machine. This procedure was repeated twice. The product, consisting of unreacted thiourea and optically active 1-phenylethylthiouronium chloride, was washed with anhydrous ether, dried, and dissolved in water (80 ml.). Two 5 ml. samples were run through Zeo-Karb 225(H) resin and titrated for hydrochloric acid. They consumed (i) 9·58 ml. and (ii) 9·57 ml. of 0·1N-sodiumhydroxide. A third portion of the solution was used in measuring the rotation [observed: α_D 10·07° (l 4 dm. in water)]; this rotation was not influenced by added salts. The molecular rotation of the thiouronium salt is therefore given by $[M]_D^{20} = 10{\cdot}07/(9{\cdot}58 \times 20 \times 10^{-4} \times 4) = 131{\cdot}2°$ (in water). The residual solution was used for the preparation of (+)-1-phenylethanethiol; the solution was shaken for 3 min. with 30% potassium hydroxide solution (10 ml.) in an atmosphere of nitrogen at room temperature, acidified with dilute hydrochloric acid, and twice extracted with pentane. The pentane solution was washed with water, and evaporated; distillation gave (+)-1-phenylethanethiol, b. p. 57°/1·2 mm., α_D^{20} 41·4°.*

Measurement of Rates of Racemisation of (+)-1-*Phenylethyl Bromide by Inactive* 1-*Phenylethylthiouronium Bromide and by Lithium Bromide, in Acetonitrile at* 59·8°.—These rates were measured with a polarimeter tube (l, 4 dm.) equipped with a jacket through which water at 59·8°, from the thermostat (which was covered with a film of oil to minimise the evaporation of water), was circulated. The lagging of the tube was heated electrically to 55° and the tubing was kept as short as possible. The flow rate was controlled with a clamp at the delivery head. After the reaction solution had been introduced into the thermostated polarimeter tube, *ca.* 12 min. passed before the heating-haze of the solution disappeared and readings could be taken. They are reproducible to *ca.* ±0·02°. The rate of racemisation of optically active 1-phenylethyl bromide by lithium bromide, and the unimolecular rate of racemisation, were measured in the same way. The results of a typical run are shown in Table 4.

TABLE 4.

Racemisation of (+)-1-phenylethyl bromide by inactive 1-phenylethylthiouronium bromide in acetonitrile at 59·8°.

$[\mathrm{Me{\cdot}CHPh{\cdot}S{\cdot}C(NH_2)_2^{-}\ Br^{-}}] = 0{\cdot}0128$ moles l.$^{-1}$; $[\mathrm{Me{\cdot}CHPh{\cdot}Br}] = 0{\cdot}143$ moles l.$^{-1}$.

Time (min.)	15	20	25	30	35	40	45	50
α_t	2·04	1·94	1·86	1·79	1·71	1·62	1·57	1·50
Time (min.)	55	60	65	70	75	80		
α_t	1·45	1·38	1·33	1·29	1·23	1·18		

A first-order plot of ln α against t gave a straight line of slope $2k_2'[\mathrm{Br}^-]$ (cf. Hughes *et al.*, *J.*, 1938, 209); therefore $k_2' = 5{\cdot}45 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$.

The Reaction of Thiourea with 1-*Phenylethyl Bromide in Acetonitrile at* 59·8°.—*Kinetic investigation.* The reaction was carried out in sealed tubes. Timed samples were quenched in carbon tetrachloride (50 ml.); thiourea and the thiouronium bromide, which precipitated, were extracted with ice-cold water (50 ml.), run through Zeo-Karb 225(H) resin, and washed. The thiourea present did not interfere in the titration of hydrobromic acid. The results of all runs are compiled in Table 1.

Stereochemical investigation. (i) *Equal concentrations of nucleophile and substrate.* (+)-1-Phenylethyl bromide, α_D^{20} 135·4° (2·16 g.), and thiourea (0·928 g.), in acetonitrile (100 ml.) were kept at 59·8° for 160 min. The reaction mixture was concentrated at reduced pressure and (−)-1-phenylethylthiouronium bromide at once crystallised, m. p. 157°, $\alpha_D = -0{\cdot}05_5°$ [l, 0·5 dm.; c, 4·890 (in water)], $[M]_D^{20}$ −9·9° (in water). A determination with another sample gave $[M]_D^{20}$ −9·4°.

(ii) *A ten-fold excess of nucleophile over substrate concentration.* A solution of thiourea (2·71 g.) in acetonitrile (90 ml.), superheated in a closed flask to 100° to effect solution, was cooled to 55°, mixed quickly with a solution of (+)-1-phenylethyl bromide, α_D^{20} 88·9° (0·611 g.), in acetonitrile (10 ml.), and kept at 59·8° for 7 min. The reaction mixture was run into cold AnalaR carbon tetrachloride (100 ml.), and the precipitate was extracted with ice-cold water

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* The correlation in the literature [4] is in error; it was reported that 1-phenylethanethiol (α_D^{23} −40·44°) was obtained from 1-phenylethylthiouronium chloride {$[M]_D^{20}$ −102° (in water)}.

(50 ml.). The aqueous phase was re-extracted with fresh carbon tetrachloride (50 ml.), filtered to remove traces of this solvent, and evaporated to dryness under reduced pressure. The residue was taken up in *ca.* 50 ml. of water; the resulting solution was filtered from dust particles, its rotation was measured, and it was analysed for bromide. Two samples of 10 ml. each were run through Zeo-Karb 225(H) resin and were equivalent to (i) 4·28 ml. and (ii) 4·32 ml. of 0·02N-sodium hydroxide. The rotation was α_D^{20} $-0{\cdot}63$ [l 4 dm., c 0·224 (in water) (average from six readings)], giving $[M]_D^{20} = -0{\cdot}63/(4{\cdot}30 \times 0{\cdot}02 \times 10^{-2} \times 4) = -183°$ (in water).

The experiment was repeated using (+)-1-phenylethyl bromide, α_D^{20} 88·9° (0·351 g.), and thiourea (1·34 g.), in acetonitrile (50 ml.). The solution was kept for 9 min. at 59·8°, and the remaining operations were carried out as above. The residue from the evaporation was taken up in *ca.* 35 ml. of water. 10 ml. of this solution consumed 5·69 ml. of 0·02N-sodium hydroxide. The rotation was α_D^{20} $-0{\cdot}83°$ [(l 4 dm., c 0·297 (in water)], giving $[M]_D^{20} = -182°$ (in water).

APPENDIX

In the system of Scheme 2, let the initial concentrations be:

$$[\mathrm{N}]_0 = a;\ [(+)\text{-RX}]_0 + [(-)\text{-RX}]_0 = b;\ [(+)\text{-RX}]_0 = y_0 > [(-)\text{-RX}]_0,$$

and let the variables x, y, and z denote concentrations at reaction time t:

$$[(+)\text{-RN}^+] + [(-)\text{-RN}^+] = [\mathrm{X}^-] = x;\ [(+)\text{-RX}] = y;\ [(-)\text{-RN}^+] = z.$$

From these variables, all the other concentrations can be derived as shown in Scheme 2. From the rate of disappearance of (+)-RX,

$$-\,\mathrm{d}y/\mathrm{d}t = k_2y(a - x) + k_2'xy - k_2'x(b - x - y),$$

and

$$\mathrm{d}x/\mathrm{d}t = k_2(a - x)(b - x),$$

it follows that:

$$\frac{\mathrm{d}y}{\mathrm{d}x} + \left\{1 + \frac{2k_2'x}{k_2(a - x)}\right\}\frac{y}{b - x} = \frac{k_2'x}{k_2(a - x)}.$$

Integration and observation of the boundary conditions, $x = 0$ for $y = y_0$, lead to:

$$y = (a - x)^{-\alpha-1}(b - x)^{-\beta}\left\{a^{\alpha+1}b^{\beta}y_0 + \frac{k_2'}{k_2}\int(a - x)^{\alpha}(b - x)^{\beta}x\,\mathrm{d}x\right\},$$

where:

$$\alpha = \frac{2ak_2'}{k_2(a - b)} - 1, \text{ and } \beta = -1 - \frac{2bk_2'}{k_2(a - b)}$$

From the rate of formation of (−)-RN⁺,

$$\mathrm{d}z/\mathrm{d}t = k_2y(a - x),$$

and

$$\mathrm{d}x/\mathrm{d}t = k_2(a - x)(b - x),$$

$$\mathrm{d}z/\mathrm{d}x = y/b - x$$

$$= (a - x)^{-\alpha-1}(b - x)^{-\beta-1}\left\{a^{\alpha+1}b^{\beta}y_0 + \frac{k_2'}{k_2}\int(a - x)^{\alpha}(b - x)^{\beta}x\,\mathrm{d}x\right\}.$$

From MacLaurin's theorem, and remembering that $z = 0$ for $x = 0$, one obtains the final equation on page 1255.

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