*Tetrahedron.* Vol. 30, pp. 1155 to 1160. Pergamon Press 1974. Printed in Great Britain

# THE RACEMIZATION OF AN OPTICALLY ACTIVE SULFILIMINE AND OPTICALLY ACTIVE AMINOSULFONIUM SALTS

D. DARWISH[a] and S. K. DATTA[b,*]

Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada

(*Received in the USA* 17 *July* 1973; *Received in the UK for publication* 1 *October* 1973)

**Abstract**—The racemization of an optically active sulfilimine and optically active aminosulfonium salts was kinetically measured. The mechanism of the racemization of optically active sulfilimine (-)-**1** has been established. The activation parameters for the racemization of (-)-**1** and (-)-**7** were calculated. A plausible pathway for the decomposition of (-)-**6**, (-)-**7** and (-)-**8** with tetra-n-butylammonium bromide in the presence of methyl ethyl ketone to provide 3-*p*-tolylthio-2-butanone **22** is proposed.

We wish to report on the racemization of (-)- S - methyl - S - *p* - tolyl - N - *p* - toluenesulfonylsulfilimine (-)-**1**[1], (-)- methyl - *p* - tolyl - N - methyl - *p* - tolylsulfonylaminosulfonium trifluoromethanesulfonate (-)-7 and (-) - methyl - *p* - tolyl - N - methyl - *p* - tolylsulfonylaminosulfonium 2,4,6 - trinitrobenzenesulfonate (-)-**8**. The first-order polarimetric rate constants for the racemization of (-)-**1** in dry ethanol and methyl ethyl ketone are summarized in Table 1.

There are two mechanisms which could account for the racemization of (-)-**1**. These are (i) heterolytic nitrogen–sulfur bond cleavage to yield a nitrene **2** and a sulfide **3** which could recombine to form racemic sulfilimine and (ii) pyramidal inversion about the central sulfur atom analogous to the inversion of an ammonia molecule.

In order to determine the mechanism of the racemization of (-)-**1**, the rate constant was measured in the presence of an equivalent amount of *p*-t-butylphenyl methyl sulfide **4**[2] in methyl ethyl ketone as solvent at 90·0°. The addition of **4** to (-)-**1** had no effect on the rate constant for the racemization of (-)-**1**. The compound (-)-**1** showed no decomposition under the conditions required for the racemization. Isolation of the racemic sulfilimine in quantitative yield and the complete recovery of **4** after 10 half-lives for the racemization of (-)-**1** offers strong argument against the formation of a nitrene **2** which could have led to the formation of another new sulfilimine **5**. The NMR of the reaction mixture indicated the presence of only **1** and **4**.

All this evidence supports the suggestion that the racemization of (-)-**1** must be independent of heterolysis and is consistent with a pyramidal inversion mechanism. The activation parameters for the racemization of (-)-**1** are

$$\Delta E\alpha\dagger = 29{\cdot}39 \text{ kcal/mole}$$
$$\Delta H\dagger = 28{\cdot}71 \text{ kcal/mole}$$
$$\Delta S\dagger = -1{\cdot}08 \text{ ev.}$$

The mechanisms for the racemization of the sulfonium salts, ylide and sulfoxides have been discussed in the literature.[3-5] The activation enthalpies for racemization are 25–29 kcal for several sulfonium salts,[3-5] 35–43 kcal for sulfoxides[6] and 23·3 kcal for ethylmethylsulfonium phenacylide.[4] Hence it is

[a] Deceased April 15, 1973.

[b] Postdoctoral fellow, 1969–1971.

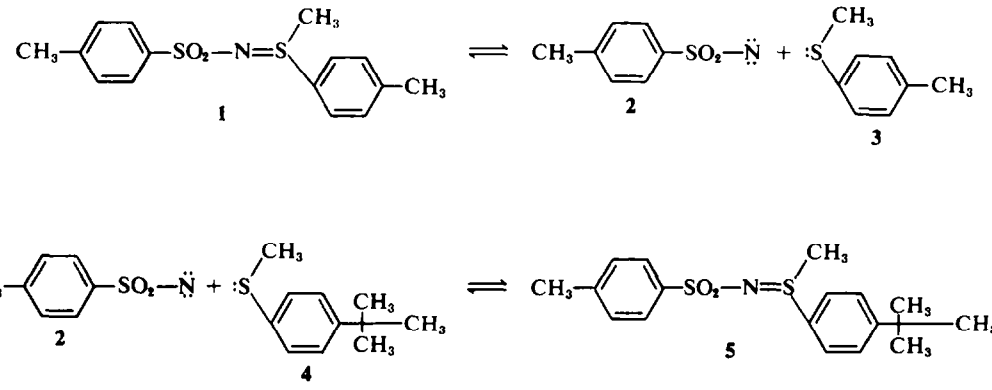
*Present address: Department of Chemistry, University of Sherbrooke, Sherbrooke, Quebec, Canada.

Table 1

| Concn, M of (-)-**1** | Solvent | Temp. °C | $10^5 k_{\alpha}$, $sec^{-1}$ |
|---|---|---|---|
| 0·010 | dry $C_2H_5OH$ | 90·0 | 1·80 ± 0·01 |
| 0·010 | dry $C_2H_5OH$ | 70·0 | 0·167 ± 0·002 |
| 0·005 | dry $C_2H_5OH$ | 90·0 | 1·78 ± 0·01 |
| 0·005 | $CH_3COC_2H_5$ | 90·0 | 1·61 ± 0·03 |
| 0·005 | $CH_3COC_2H_5$ | 70·0 | 0·155 ± 0·002 |
| 0·010[a] | $CH_3COC_2H_5$ | 90·0 | 1·62 ± 0·01 |

[a] 0·01 M (-)-**1** and 0·01 M **4**.

(i) *Heterolytic nitrogen-sulfur bond cleavage*



(ii) *Pyramidal inversion*

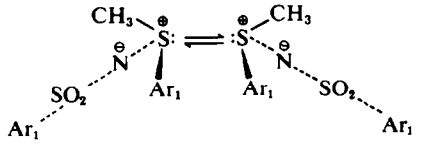


Table 2

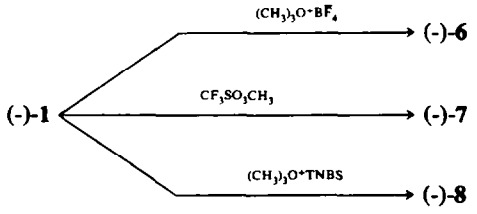
| Concn. M of (-)-1 | Solvent | Temp °C | $10^5 k_a$, $sec^{-1}$ |
|---|---|---|---|
| 0·010[a] | dry EtOH | 70·0 | 1·05 ± 0·02 |
| 0·010[b] | dry EtOH | 70·0 | 1·85 ± 0·048 |

[a] 0·010 M (-)-1 and 12 × 0·010 M $CF_3SO_3H$.
[b] 0·010 M (-)-1 and 24 × 0·010 M $CF_3SO_3H$.
$\lambda_{max}^{EtOH}$ for (-)-1 was 227 nm (log ε 4·34) and $\lambda_{max}^{EtOH}$ for (-)-1 in the presence of 12 and 24 equivalents of $CF_3SO_3H$ was 233 nm (log ε 4·50).

quite clear by the kinetic studies that the barrier to pyramidal inversion in sulfilimine is somewhat higher than that for sulfonium salts in most cases, much lower than barriers found in sulfoxides but higher than the barrier to pyramidal inversion in the sulfonium ylide. Thus sulfilimine would serve as a bridge between the sulfonium salts and the sulfoxides. The rate constants for the decomposition of (-)-**1** in the presence of 12 and 24 equivalents of trifluoromethanesulfonic acid were measured in dry ethanol as solvent at 70·0°. The results are presented in Table 2.

The rate constant for the decomposition of (-)-**1** in the presence of trifluoromethanesulfonic acid could not be measured in methyl ethyl ketone as solvent since the solvent decomposes in the presence of acid. After 10 half-lives for the decomposition of (-)-**1**, methyl *p*-tolyl sulfoxide **9** and *p*-toluenesulfonamide **10** were isolated in almost quantitative yield. This result is not surprising since the aminosulfonium salts decompose in the presence of alcohol, followed by aqueous work-up to form sulfoxides and sulfonamides.

In order to investigate the racemization of the optically active aminosulfonium salts, N-alkylated sulfilimines were prepared in our laboratory. Treatment of (-)-**1** with trimethyloxonium fluoborate,[7] methyl trifluoromethanesulfonate[8] and trimethyloxonium 2,4,6-trinitrobenzenesulfonate[9] in dry methylene chloride gave the corresponding optically active aminosulfonium salts (-)-**6**, (-)-**7** and (-)-**8** in good yields (Scheme 1).



SCHEME 1

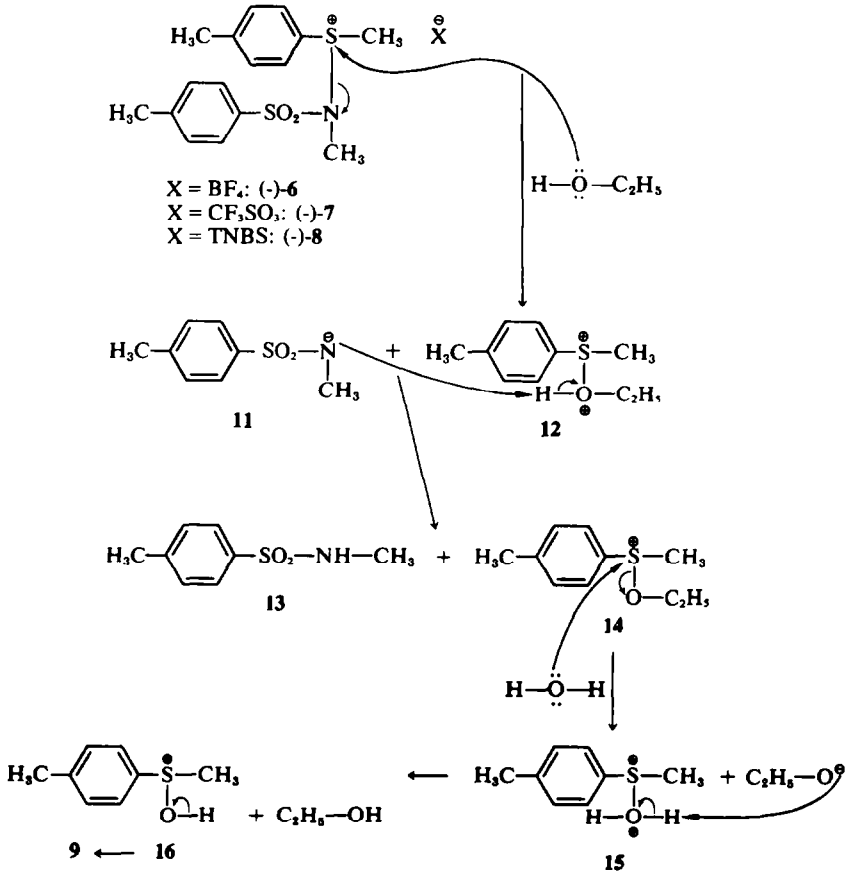
These salts (-)-**6**, (-)-**7** and (-)-**8** were readily attacked by alcohol followed by aqueous work-up to provide methyl *p*-tolyl sulfoxide **9** and N - methyl - *p* - toluenesulfonamide **13**. Johnson *et al.*[10] also observed that the aminosulfonium salts were attacked by aqueous base. As soon as the salts (-)-**6**, (-)-**7** and (-)-**8** were dissolved in alcohol, they gave positive rotation indicating the decomposition of the aminosulfonium salts presumably due to the reaction with alcohol to form alkoxysulfonium salts which had been confirmed by comparison with an authentic sample. Storage of the solution at room temperature resulted in a zero rotation after a week. The treatment of the alkoxysulfonium salts with water gave the sulfoxide **9**. Obviously, backside nucleophilic displacement on the sulfonium sulfur proceeded to give the sulfoxide with inversion of configuration. Conversion of the aminosulfonium salts into **9** and **13** can be readily explained in Scheme 2.

When tetra - n - butylammonium bromide was added to the aminosulfonium salts (-)-**6**, (-)-**7** and (-)-**8** at room temperature in equimolecular amounts in methyl ethyl ketone, the salts decomposed within a few minutes. The decomposition products were isolated and proved to be **13** and 3 - *p* - tolylthio - 2 - butanone **22**. A possible reaction path which is comprehensible for the above results is shown in Scheme 3.

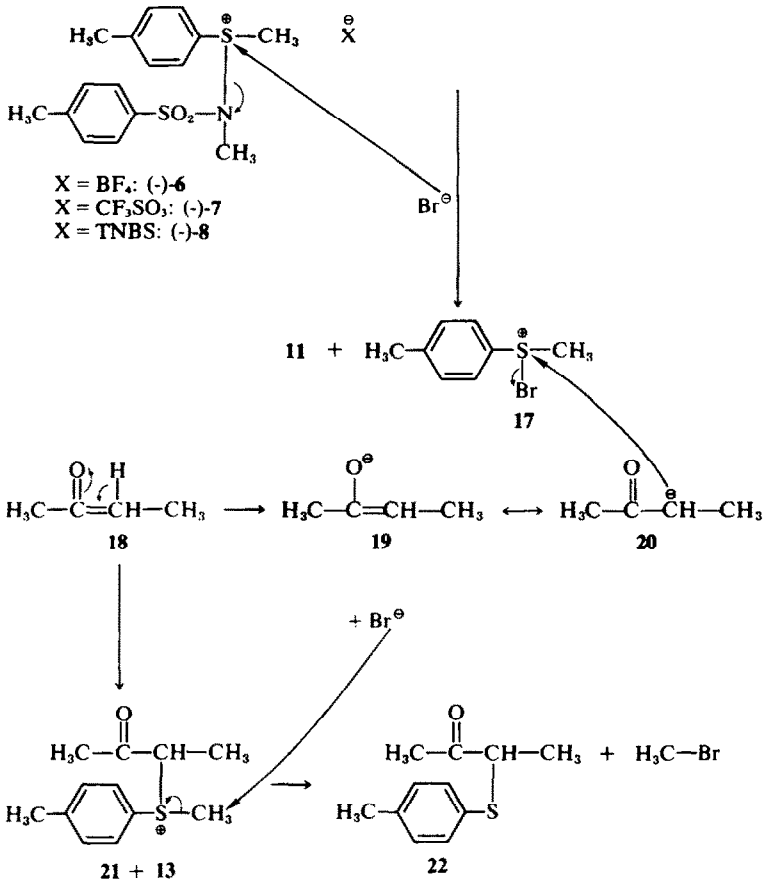
Since (-)-**6** decomposed during the kinetic investigation on racemization, we concentrated our attention on (-)-**7**. The first-order polarimetric rate constants for the reacemization of (-)-**7** were determined up to 3 half-lives after which the optical rotation could not be measured due to the color of the solution. Addition of the impurities tetra - n - butylammonium bromide and **13** to (-)-**7** in 0·10 : 1·0 ratio in methyl ethyl ketone as solvent increased the rate of racemization though not in an appreciable amount. A summary of the first-order polarimetric rate constants for the racemization of (-)-**7** is presented in Table 3.

The activation parameters for the racemization of (-)-**7** are

$$\Delta E\alpha\dagger = 26{\cdot}55 \text{ kcal/mole}$$
$$\Delta H\dagger = 25{\cdot}82 \text{ kcal/mole}$$
$$\Delta S\dagger = -1{\cdot}08 \text{ ev.}$$




SCHEME 2




SCHEME 3

Table 3

| Concn., M of (-)-7 | Solvent | Temp. °C | $10^4 k_a$, $sec^{-1}$ |
|---|---|---|---|
| 0·0155 | $CH_3COC_2H_5$ | 70·0 | 0·751 ± 0·030 |
| 0·0155 | $CH_3COC_2H_5$ | 90·0 | 6·46 ± 0·30 |
| 0·0228[a] | $CH_3COC_2H_5$ | 70·0 | 0·785 ± 0·020 |
| 0·0227[b] | $CH_3COC_2H_5$ | 70·0 | 0·770 ± 0·025 |
| 0·0310 | $CH_3COC_2H_5$ | 90·0 | 6·44 ± 0·27 |

[a] 0·0228 M (-)-7 and 0·00228 M 13.
[b] 0·0227 M (-)-7 and 0·00227 M tetra-n-butylammonium bromide.

Our work was then extended to study the racemization of (-)-8. The racemization of (-)-8 with 0·0160 M of concentration at 70·0° in methyl ethyl ketone as solvent proceeded with the rate constant of $(4·12 \pm 0·10) \times 10^{-5}$ $sec^{-1}$. It was thus observed that an electron releasing group, such as a Me group, attached to the nitrogen in sulfilimine increased the rate of racemization of the compound. Structural studies[10] on the aminosulfonium salt suggest the $sp^2$ hybridized nitrogen and significant p–d$\pi$ bonding in the aminosulfonium salt. The dihedral angle between the $sp^3$ lone pair on sulfur and p lone pair on nitrogen in the aminosulfonium salt was found[10] to be in the vicinity of 90° at which point there should be a minimum lone-pair lone-pair repulsion. Substantial (2p–3d)$\pi$ bonding was also postulated[5] in sulfilimine as it is in the case of sulfoxides. The difference in inversion rate between the sulfilimine and aminosulfonium salts could be accounted for by assuming that the much greater

electron density on the nitrogen in the sulfilimine relative to that in aminosulfonium salts slows down the inversion process. At the present time it is difficult to provide conclusive evidence regarding the pronounced effect of the electronegativity on the pyramidal stability of the sulfilimine and aminosulfonium salts. However, the combined effects of p–d$\pi$ bonding, lone pair-lone pair interactions and the electronegativity of the nitrogen substituent are expected to play a crucial role in the inversion rate of the sulfilimine and aminosulfonium salts. At the transition state for inversion the electronic repulsion between the unshared electron pairs on the sulfur and nitrogen of the sulfilimine will be greater than in the ground state. In the aminosulfonium salts such repulsion will be lower in comparison to sulfilimine.

## EXPERIMENTAL

The NMR spectra were recorded in a A-60A Varian spectrometer with TMS as internal standard, and are reported on the $\delta$-scale. UV spectra were recorded with a Cary 14M spectrophotometer and the IR spectra were recorded with a Perkin-Elmer 421 spectrophotometer. Optical rotations were measured at 25° with a Perkin-Elmer 141 polarimeter at 546 nm and jacketed cells. M.ps were taken on a Hershberg Melting point apparatus using a set of Anschutz thermometers.

*Product run for the racemization of* (-)-**1** *in the presence of* **4**. 50 ml of the soln containing 154 mg (0·010 M) of (-)-**1** and 90 mg (0·010 M) of **4** in methyl ethyl ketone was placed in a pressure bottle and immersed in a 90·0° oil bath (the initial rotation the soln was −0·918°). After 10 half-lives (72 h) for the racemization of (-)-**1**, the pressure bottle was cooled in a dry ice-acetone bath. The solvent was removed on a rotary evaporator to give 240 mg of a pale yellow solid, which was washed several times with ether to give 145 mg of racemic sulfilimine, m.p. 120–124°, identified by comparison of the NMR and IR spectra with those of an authentic sample. Removal of the solvent from the washings gave 95 mg of oil which contained **4** and a trace of racemic sulfilimine (confirmed by comparison with authentic samples). Repeated crystallization from pentane gave 85 mg of **4**, m.p. 31–33° (lit.[2] m.p. 30–33°). The mother liquor gave 8 mg of an oil which was identified as a mixture of racemic sulfilimine and **4**. The recovery of racemic sulfilimine and **4** was quantitative.

*Product run for the decomposition of* (-)-**1** *in the presence of trifluoromethanesulfonic acid* (12 *equivts*) *in dry ethanol.* A pressure bottle containing 100 ml of a soln of 307 mg (0·010 M) of (-)-**1** and 1·8 g (12 × 0·010 M) trifluoromethanesulfonic acid in dry EtOH was immersed in a 70·0° oil bath (the initial rotation of the soln was −0·910°). After 9 days for the decomposition of (-)-**1** under these conditions the pressure bottle was cooled in a dry ice–acetone bath. The soln at this stage had a rotation of +0·090°. The acid from the mixture was carefully neutralized with $Na_2CO_3$ and the resulting soln was concentrated under reduced pressure (rotary evaporator) below 45°. This mixture was poured into ice-water and extracted several times with ether. Evaporation of the combined ether extracts left 150 mg of a yellow solid, m.p. 65–72°. The IR and NMR spectra of this material were identical with those of an authentic sample of methyl *p*-tolyl solfoxide. This solid was recrystallized several times from n-pentane-ether to afford 40 mg of light yellow crystals, m.p. 70–74°, $[\alpha]_{546}^{25}$ + 100° (*c* 0·20, acetone). Evaporation of the solvent from the mother liquor gave 125 mg of a yellow solid, the rotation of which could not be measured since the soln was opaque in the polarimeter cell in acetone solvent. The aqueous soln was evaporated to dryness on a water-bath and the residue was extracted 3 times with ether. The ether extracts gave 165 mg of a white solid, m.p. 132–134°, identified as **10** by mixed m.p. and comparison of IR and NMR spectra with those of an authentic sample.

(-)- *Methyl* - p - *tolyl* - N - *methyl* - p - *tolylsulfonylaminosulfonium fluoborate* (-)-**6**. To a soln of 3 g of (-)-**1** in 25 ml dry methylene chloride was added 3 g trimethyloxonium fluoborate[7] (Meerwein's reagent). After stirring at room temp for 12 h, the unreacted Meerwein's reagent was filtered off. Removal of the solvent afforded syrupy oil. Crystallization of the oil from methylene chloride-ether gave 4g of the salt, m.p. 84–85°, yield 100%; $[\alpha]_{546}^{245}$ − 5° (*c* 1·0, methyl ethyl ketone); UV: $\lambda_{max}^{CH_2Cl_2}$ 245 nm (log $\epsilon$ 4·31); NMR ($CD_2Cl_2$): 7·45–7·95 (8 aromatic protons, m), 3·55 (S-Me, s), 3·05 (N-Me, s) and 2·5 (two C-aromatic Me protons, s); (Found: C, 46·79; H, 4·99; N, 3·42; S, 15·80. Calc for $C_{16}H_{20}N_1S_2O_2BF_4$: C, 46·96; H, 4·88; N, 3·42; S, 15·67%).

(-)- *Methyl* - p - *tolyl* - N - *methyl* - p - *tolylsulfonylaminosulfonium trifluoromethanesulfonate* (-)-**7**. To 1 g of (-)-**1** in 50 ml dry methylene chloride was added 0·8 g methyl trifluoromethanesulfonate[8] and stirred at room temp for 24 h. Removal of the solvent and excess methyl trifluoromethanesulfonate provided 1·532 g (99%) of glassy solid; $[\alpha]_{546}^{25}$ − 17° (*c* 1·6, methyl ethyl ketone). All attempts to recrystallize this material proved futile. UV: $\lambda_{max}^{CH_2Cl_2}$ 245 nm (log $\epsilon$ 4·22); NMR ($CDCl_3$): 7·3–7·9 (8 aromatic protons, m), 3·53 (S-Me, s), 3·02 (N-Me, s) and 2·4–2·46 (two C-aromatic Me protons, broad singlet); (Found: C, 43·43; H, 4·31; N, 3·06; S, 20·55. Calc for $C_{17}H_{20}N_1S_3O_5F_3$; C, 43·31; H, 4·24; N, 2·97; S, 20·38%).

(-)-*Methyl* - p - *tolyl* - N - *methyl* - p - *tolylsulfonyl* - *aminosulfonium* 2,4,6-*trinitrobenzenesulfonate* (-)-**8**. To 1 g of (-)-**1** in 60 ml dry methylene chloride was added 8 g trimethyloxonium 2,4,6-trinitrobenzenesulfonate[9] and stirred at room temp for 24 h. The soln was filtered to remove the unreacted reagent. Removal of solvent gave 3·1 g of yellow white residue. The solid product was treated with 15 ml dry methylene chloride and kept in the refrigerator for 24 h to precipitate the unreacted reagent. The mixture was filtered and the solvent removed to give 1·95 g of white solid, m.p. 124–128°. Recrystallization from methylene chloride-ether afforded white crystals, m.p. 127–128°; $[\alpha]_{546}^{25}$ − 8·3° (*c* 0·6, methyl ethyl ketone); IR(KBr): 3420, 1540, 1350, 1250 and 1240 cm$^{-1}$; NMR ($CDCl_3$): 8·40 (2,4,6-$(NO_2)_3$-Ar$\langle^{H}_{H}$, 2H, s), 7·2–7·8 (Ar-H, 8H, m), 3·52 (S-Me, s), 2·98 (N-Me, s) and 2·4 (Two C-aromatic Me protons, s); (Found C, 43·20; H, 3·73; N, 9·23; S, 15·54. Calc for $C_{22}H_{22}N_4S_3O_{11}$: C, 42·99; H, 3·58; N, 9·12; S, 15·63%).

*Product run for the racemization of* (-)-**7** *and* (-)-**8**. A 50 ml portion of 0·015 M solution of (-)-**7** or (-)-**8** in methyl ethyl ketone was transferred to a pressure bottle and placed in the 70·0° constant temp bath for 30 h. The pressure bottle was cooled and usual work-up afforded 88–92% yield of the racemic form of (-)-**7** or (-)-**8**, which showed to be identical with an authentic sample (IR and NMR spectra superimposable).

*Decomposition of* (-)-**6**, (-)-**7** *and* (-)-**8** *in the presence of tetra-n-butylammonium bromide in methyl ethyl ketone.* A soln of one of the salts ((-)-**6**–(-)-**8**) (0·015 mole) in 50 ml methyl ethyl ketone was reacted with tetra-n-butylammonium bromide (0·015 mole) at room temp for a few min. After removal of the solvent by rotary evaporator (water-bath at 40°), the residue was poured into water. The oil was taken up in ether and dried ($MgSO_4$). The solvent was removed to give an oil containing a mixture of **13** and **22** in almost equal amount. The IR and NMR of this material were identical with those of a mixture of an equimolecular amount of the authentic samples of N - methyl - *p* - toluenesulfonamide and 3 - *p* - tolylthio - 2 - butanone.[11] The oil was dissolved in pentane–benzene mixture and allowed to crystallize to yield theoretical amount of N - methyl - *p* - toluenesulfonamide, m.p. 78°. Removal of the solvent from the mother liquor gave an oil which was identical with an authentic sample of 3 - *p* - tolylthio - 2 - butanone[11] as shown by comparison of IR and NMR spectra. The yield of **22** was quantitative.

The ketone **22** afforded a 2, 4-dinitrophenylhydrazone, as yellow needles, m.p. 110° from chloroform. (Found: 54·69; H, 4·74; N, 14·99; S, 8·45. Calc for $C_{17}H_{18}N_4O_4S$: C, 54·54; H, 4·81; N, 14·97; S, 8·55%).

*Kinetic measurements.* The optically active sulfilimine and freshly prepared optically active aminosulfonium salts were accurately weighed in a tared volumetric flask. The soln was made up to the mark by addition of solvent. Aliquots of a standard stock soln of one of the impurities **4**, **13** and tetra - n - butylammonium bromide, were added to the accurately weighed sulfilimine or the aminosulfonium salts in a tared volumetric flask and the level of the solution was raised to the mark by addition of the same solvent used in making the standard stock soln. The sealed ampoule technique was used. Each ampoule contained approximately 5·3 ml of soln. The ampoules were placed in a constant temp bath at 70·00 ± 0·02° or 90·00 ± 0·02°. For reactions studied at those temps, the ampoules were quenched in an ice-water bath and then equilibrated to 25°. The integrated first-order rate constants were calculated using the experimental infinity values, usually 100 ± 3% of the theoretical value. The rates were followed to *ca* 85% completion.

## REFERENCES

[1]D. J. Cram, J. Day, D. R. Rayner, D. M. Von Schriltz, D. J. Duchamp and D. C. Garwood, *J. Am. Chem. Soc.* **92**, 7369 (1970)
[2]A. Senning and Sven-Olov Lawesson, *Acta Chimica Scandinavica* **16**, 117 (1952)
[3]D. Darwish, *Mechanism of Reactions of Sulfur Compounds* Vol. **3**, p. 33 (1968) and refs cited
[4]D. Darwish and R. L. Tomilson, *J. Am. Chem. Soc.* **90**, 5938 (1968)
[5]A. Rauk, L. C. Allen and K. Mislow, *Angew Chem.* Internat. Edit. in English Vol. **9**, No. 6, 400 (1970)
[6]D. R. Rayner, E. G. Miller, P. Bickart, A. J. Gordon and K. Mislow, *J. Am. Chem. Soc.* **88**, 3138 (1966)
[7]H. Meerwein, *Org. Syn.* **46**, 120 (1966)
[8]T. Gramstad and R. N. Haszeldine, *J. Chem. Soc.* 180 (1956)
[9]D. J. Pettitt and G. K. Helmkamp, *J. Org. Chem.* **29**, 2702 (1964)
[10]R. E. Cook, M. D. Glick, J. J. Rigau and C. R. Johnson, *J. Am. Chem. Soc.* **93**, 924 (1971) and refs cited
[11]E. G. G. Werner, *Rec. Trav. Chim.* in English **68**, 509 (1949)