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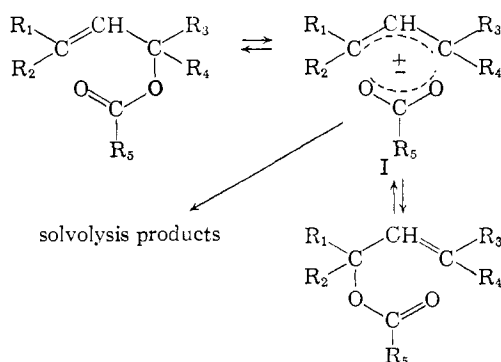
## Rearrangement of Allylic Thiobenzoates

BY STANLEY G. SMITH

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The allylic rearrangement of allyl, crotyl and  $\alpha$ -methylallyl thionbenzoates to thiolbenzoates has been studied in a variety of solvents. It was found that isomerization occurs only *ca.* ten times faster in acetic acid than in cyclohexane. This low sensitivity to the ionizing power of the solvent has been attributed to a small difference in charge separation between ground state and transition state.

The isomeric rearrangement accompanying solvolysis of esters of allylic alcohols has been extensively studied.<sup>1,2</sup> On the basis of a detailed analysis of the effect of solvents and temperature on racemization, solvolysis and isotopic exchange rate constants, Goering and co-workers<sup>1b</sup> have suggested that in polar solvents solvolysis and isomeric rearrangement proceed through a common intermediate (I) with allylic systems such as 5-methyl-2-cyclohexyl<sup>3-6</sup> and  $\alpha,\gamma$ -dimethylallyl.<sup>7,8</sup> The intermediate I has been described as an ion pair.



In the case of rearrangement of esters of allylic alcohols in relatively non-polar solvents such as chlorobenzene<sup>9</sup> (e.g.,  $\alpha$ -phenylallyl *p*-nitrobenzoate<sup>9</sup>) it is difficult to distinguish between an ion-pair and a more concerted mechanism from the existing data. However, it has been suggested<sup>10</sup> on the basis of the sensitivity of such isomerizations to the ionizing power of the medium<sup>11,12</sup> that such reactions probably proceed through a highly polar transition state.

(1) (a) R. H. DeWolfe and W. G. Young, *Chem. Revs.*, **56**, 753 (1956); (b) H. L. Goering, *Rec. Chem. Prog.*, **21**, 109 (1960); (c) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 586.

(2) (a) R. A. Snee, *J. Am. Chem. Soc.*, **82**, 426 (1960); (b) R. A. Snee and A. M. Rosenberg, *ibid.*, **83**, 895 (1961).

(3) H. L. Goering, J. P. Blanchard and E. F. Silversmith, *ibid.*, **76**, 5409 (1954).

(4) H. L. Goering and E. F. Silversmith, *ibid.*, **77**, 1129 (1955).

(5) H. L. Goering and E. F. Silversmith, *ibid.*, **77**, 6249 (1955).

(6) H. L. Goering and J. T. Doi, *ibid.*, **82**, 5850 (1960).

(7) H. L. Goering and R. W. Greiner, *ibid.*, **79**, 3464 (1957).

(8) H. L. Goering and M. M. Pombo, *ibid.*, **82**, 2515 (1960).

(9) (a) E. A. Braude and D. W. Turner, *Chemistry & Industry*, 1223 (1955); (b) E. A. Braude, D. W. Turner and E. S. Wright, *J. Chem. Soc.*, 2396 (1958).

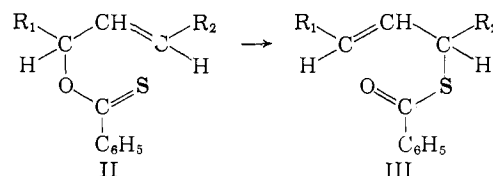
(10) S. Winstein and G. C. Robinson, *J. Am. Chem. Soc.*, **80**, 169 (1958).

(11) (a) J. Meisenheimer, W. Schmade and G. Schäfer, *Ann.*, **501**, 131 (1933); (b) A. G. Catchpole and E. D. Hughes, *J. Chem. Soc.*, 1 (1948).

(12) S. G. Smith, A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, **83**, 618 (1961).

Winstein<sup>13</sup> has pointed out that one should anticipate a spectrum of merging ion-pair and non-ionic cyclic rearrangement mechanisms. Recently, several examples of the latter type, which involve very little charge separation in the transition state, have been reported. For example, the allylic rearrangement of  $\alpha,\alpha$ -dimethylallyl azide<sup>14</sup> and the isomerization of allylic thiocyanates to isothiocyanates<sup>15,16</sup> display very small sensitivities to solvent ionizing power indicative of a relatively non-polar transition state.

In this paper, the effect of solvent ionizing power on the isomerization of allylic thionbenzoates (II) to allylic thiolbenzoates (III) will be presented.



## Results and Discussion

Allyl,  $\alpha$ -methylallyl and crotyl thionbenzoates were prepared by the action of the sodium salts of the corresponding alcohols on thiobenzoyl chloride.<sup>17</sup> These thion esters display strong infrared absorption<sup>18</sup> at 1270 and 1230  $\text{cm}^{-1}$ . The visible absorption spectrum of these compounds shows one band with  $\lambda_{\text{max}}$  420 ( $\epsilon$  97  $\pm$  4, cyclohexane).

Facile rearrangement of allylic thion esters to thiol esters is indicated by the observation that the characteristic yellow color of allyl thionbenzoate disappears when a neat sample is maintained at 100° for 70 hours. In addition, after being heated, the infrared absorption spectrum no longer shows bands characteristic of the thionester; instead, the spectrum is identical with that of its allylic isomer, allyl thiolbenzoate. Similarly, after one hour at 100° the infrared absorption spectrum of  $\alpha$ -methylallyl thionbenzoate was found to be essentially identical with that of its allylic isomer, crotyl thiolbenzoate.

(13) Discussion, "Symposium on Molecular Rearrangements," Queen Mary College, University of London; *Nature*, **173**, 898 (1954).

(14) A. Gagneux, S. Winstein and W. G. Young, *J. Am. Chem. Soc.*, **82**, 5956 (1960).

(15) A. Iliceto, A. Fava and V. Mazzucato, *Tetrahedron Letters*, **11**, 27 (1960).

(16) P. A. S. Smith and D. W. Emerson, *J. Am. Chem. Soc.*, **82**, 3076 (1960).

(17) H. Staudinger and J. Siegmant, *Helv. Chim. Acta*, **3**, 824 (1920).

(18) L. J. Bellamy and P. E. Rogosch [*J. Chem. Soc.*, 2218 (1960)] report that the C=S group frequency for dithioesters is near 1200  $\text{cm}^{-1}$ .

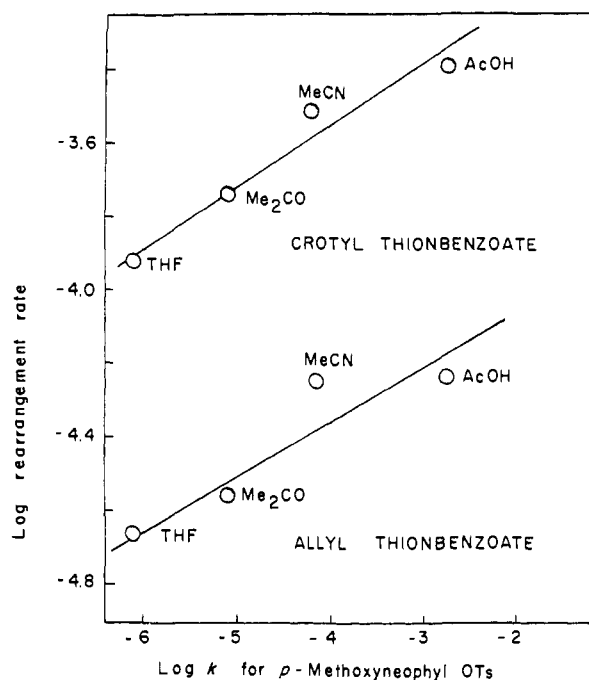


Fig. 1.—Plot of  $\log k$  for rearrangement vs.  $\log k$  for *p*-methoxyneophyl OTs.

The thion to thiol isomerization indicated by the changes in the infrared absorption spectrum upon heating allyl and  $\alpha$ -methylallyl thionbenzoates is conveniently followed in a variety of solvents by measuring the absorbance at  $420\text{ m}\mu$  as a function of time. From such data satisfactory integrated first-order rate constants for the allylic rearrangement may be calculated. This is illustrated in Table I for the case of the isomerization of allyl thionbenzoate to allyl thiolbenzoate in chlorobenzene at  $100.0^\circ$ .

TABLE I

REARRANGEMENT OF  $0.0111\text{ M}$  ALLYL THIONBENZOATE TO ALLYL THIOLBENZOATE IN CHLOROBENZENE AT  $100.0^\circ$

Time, $10^{-4}$ sec.	$A^a$	Reacn., %	$10^3 k_1, ^b$ sec. $^{-1}$
..	1.045	..	..
1.09	0.838	19.8	2.02
1.86	.715	31.6	2.04
2.52	.612	41.4	2.12
3.21	.530	49.3	2.12
7.302	.176	83.2	2.44
9.99	.132	87.4	2.07
12.45	.057	94.5	2.34
27.36	.015	98.6	
86.40	.013	98.8	

<sup>a</sup> Absorbance at  $420\text{ m}\mu$ . <sup>b</sup> Integrated first order rate constant.

In the run summarized in Table I, ca. 2% of the original absorption at  $420\text{ m}\mu$  was still present after about 10 half-lives. It is not yet clear whether this small residual absorption, which is typical of the runs reported here, is a good measure of the position of equilibrium or if it represents an absorbing impurity. However, it is evident that the thiol esters are considerably more stable than the corresponding thion esters.

The first-order rate constants ( $k_1$ ) for the rearrangement of allyl, crotyl and  $\alpha$ -methylallyl thionbenzoates in a variety of solvents at  $100.0^\circ$  are summarized in Table II. These rate constants were calculated from the least squares slope of a plot of  $\log(A_t - A_\infty)$  versus time, where  $A_t$  is the absorbance at time  $t$  and  $A_\infty$  is the absorbance after about ten half-lives.

From the rate constants summarized in Table II, it is apparent that the isomerization of allylic thionbenzoates is not very sensitive to the ionizing power<sup>12</sup> of the medium, rearrangement proceeding only about ten times faster in acetic acid than in cyclohexane.

TABLE II

SUMMARY OF REARRANGEMENT RATE CONSTANTS FOR SOME ALLYLIC THIONBENZOATES AT  $100.0^\circ$

Solvent	$10^3 k_1, \text{sec.}^{-1}$		
	Allyl	Crotyl	$\alpha$ -Methylallyl
AcOH	0.567	3.72	30.7
MeCN	.576	3.15	30.2
Me <sub>2</sub> CO	.273	1.81	16.6
C <sub>6</sub> H <sub>5</sub> Cl	.224	1.27	13.8
(CH <sub>2</sub> ) <sub>6</sub> O	.218	1.20	12.0
C <sub>6</sub> H <sub>12</sub>	.117	0.362	4.11

The effect of solvent on the rate of this rearrangement may be correlated with Winstein's<sup>12</sup> scale of solvent ionizing powers. This scale is based on the ionization rate of *p*-methoxyneophyl *p*-toluenesulfonate. As illustrated in Fig. 1,  $\log k_1$  is correlated quite well by the logarithm of the ionization rate of *p*-methoxyneophyl *p*-toluenesulfonate, a straight line of slope  $a$  being obtained. The least squares slopes  $a$  of this linear relation, eq. 1,<sup>12</sup> for allyl, crotyl and  $\alpha$ -methylallyl are summarized in Table III.

TABLE III

SENSITIVITY OF SEVERAL ALLYLIC REARRANGEMENTS TO SOLVENT IONIZING POWER

Substrate	Solvent sensitivity parameter $a$
<i>cis</i> -5-Methyl-2-cyclohexenyl acid phthalate <sup>4</sup>	0.94 <sup>a</sup>
1-Phenylallyl-3,4,5-tribromobenzoate <sup>11</sup>	.57 <sup>b</sup>
$\alpha, \alpha$ -Dimethylallyl azide <sup>14</sup>	.12 <sup>c</sup>
Allyl thionbenzoate	.13
Crotyl thionbenzoate	.15
$\alpha$ -Methylallyl thionbenzoate	.13

<sup>a</sup> Based upon the reported<sup>4</sup> rate of racemization in 80% and 90% aqueous acetone. <sup>b</sup> See ref. 12 for solvents. <sup>c</sup> Based upon rearrangement rates<sup>14</sup> in acetic acid, 80% ethanol, ethanol, acetone and ether.

The magnitude of the slope  $a$  has been used as a measure of the sensitivity of a reaction to the ionizing power of the medium.<sup>12</sup> It is interesting, therefore, to compare the value of  $a$  obtained

$$\log k_1 = a \log k_{\text{MeONeophyl OTs}} + b \quad (1)$$

from ionization and rearrangement of carboxylic esters with the slope obtained in the thionbenzoate rearrangement correlations. For the racemization of *cis*-5-methyl-2-cyclohexenyl acid phthalate, which is known to isomerize by way of an ion-pair intermediate in polar solvents,  $a$  is 0.94. The allylic rearrangement of 1-phenylallyl-3,4,5-tribromobenzoate has also been shown to be very

sensitive to the nature of the solvent.<sup>12</sup> In this case  $a$  is 0.57.<sup>12</sup> On the other hand,  $a$  is only 0.14 for the allylic rearrangement of thionbenzoates. Apparently these thion esters rearrange by a mechanism which involves very little change in charge separation between the ground state and the transition state.

The effect of  $\alpha$ - and  $\gamma$ -methyl groups on the rate of rearrangement of allyl thionbenzoate is also consistent with a small change in polarity in going to the transition state of the reaction. As is apparent from the data in Table II an  $\alpha$ -methyl group increases rate by a factor of *ca.* 55 and a  $\gamma$ -methyl group increase rate by a factor of about 6. However,  $\alpha$ - or  $\gamma$ -methyl groups are known to increase the reactivity of strongly electron-demanding reactions, such as the solvolysis of allyl chloride in formic acid,<sup>19</sup> by a factor of 10<sup>3</sup>.

### Experimental

**Thiobenzoyl chloride** was prepared as described by Staudinger.<sup>17</sup>

**Allyl Thionbenzoate.**—To a suspension of 1.0 g. of sodium hydride (51.6% NaH) in 20 ml. of ether was added 1.2 g. of allyl alcohol. After stirring for about 15 minutes, freshly distilled thiobenzoyl chloride<sup>17</sup> was added dropwise until a slight red color persisted. The ether solution was then washed with dilute sodium bicarbonate and dried over anhydrous potassium carbonate. Distillation gave 1.9 g. (52%) of a yellow oil, b.p. 84–86° (0.5 mm.). Characteristic infrared bands occurred at 1270(s), 1230(s), 1075(m), 1050(m) and 1030(m) cm.<sup>-1</sup>.

*Anal.* Calcd. for C<sub>10</sub>H<sub>10</sub>OS: C, 67.37; H, 5.65. Found: C, 67.51; H, 5.53.

**Crotyl thionbenzoate** was prepared as described for allyl thionbenzoate from a sample of crotyl alcohol<sup>20</sup>;  $n_D^{25}$  1.4260 (reported<sup>20</sup>  $n_D^{25}$  1.4260). Rapid, short path distillation gave the thionester in 39% yield, b.p. 93–95° (0.3 mm.). The infrared spectrum showed characteristic bands at 1270(s), 1230(s), 1080(m), 1050(m), 1030(m) and 970(m) cm.<sup>-1</sup>.

*Anal.* Calcd. for C<sub>11</sub>H<sub>12</sub>OS: C, 68.71; H, 6.29. Found: C, 68.49; H, 6.35.

(19) C. A. Vernon, *J. Chem. Soc.*, 423 (1954).

(20) W. G. Young, S. H. Sharman and S. Winstein, *J. Am. Chem. Soc.*, **82**, 1376 (1960).

**$\alpha$ -Methylallyl Thionbenzoate.**—The sodium salt of 2.4 g. of  $\alpha$ -methyl allyl alcohol<sup>21</sup> was prepared in 25 ml. of anhydrous tetrahydrofuran with 1.4 g. of 51.6% sodium hydride-oil dispersion. The stirred suspension of the salt was cooled to -20° and 4.2 g. of thiobenzoyl chloride<sup>17</sup> added dropwise. After 15 minutes, the dark brown mixture was poured into ether and washed with dilute aqueous sodium bicarbonate. After drying over potassium carbonate and removal of the solvent at reduced pressure, 4.2 g. of dark oil was obtained. Short path distillation gave 1.5 g. (23%) of the yellow ester, b.p. 80–85° (0.5 mm.). The infrared spectrum showed characteristic bands at 1270(s), 1330(s), 1070(m), 1050(m) and 1030(m) cm.<sup>-1</sup>.

*Anal.* Calcd. for C<sub>11</sub>H<sub>12</sub>OS: C, 68.71; H, 6.29. Found: C, 68.69; H, 6.59.

**Allyl Thiolbenzoate.**—To a slurry of 6.0 g. of potassium thiobenzoate<sup>22</sup> in 25 ml. of ether was added 3.6 g. of allyl bromide. After stirring for 3 days at room temperature the ether solution was washed with water and dilute aqueous sodium bicarbonate. Distillation gave 4.2 g. (79%) of the desired ester, b.p. 85–86° (0.5 mm.),  $n_D^{25}$  1.5799. Characteristic infrared bands appeared at 1670, 1210 and 920 cm.<sup>-1</sup>.

*Anal.* Calcd. for C<sub>10</sub>H<sub>10</sub>OS: C, 67.37; H, 5.65. Found: C, 67.39; H, 5.59.

**Crotyl Thiolbenzoate.**—Crotyl chloride (9.1 g.) was added to 16 g. of sodium thiobenzoate in 200 ml. of acetone. After standing overnight the solution was poured into water and extracted with several portions of ether. The ether solution was dried over magnesium sulfate and distilled. The yield of ester was 7.5 g. (38%), b.p. 98–100° (0.5 mm.),  $n_D^{25}$  1.5755. Characteristic infrared bands appeared at 1670, 1210, 970 and 920 cm.<sup>-1</sup>.

*Anal.* Calcd. for C<sub>11</sub>H<sub>12</sub>SO: C, 68.71; H, 6.29. Found: C, 68.79; H, 6.29.

**Solvents.**—Acetic acid, acetonitrile, acetone and tetrahydrofuran were purified in the usual manner.<sup>12</sup> Chlorobenzene and cyclohexane were washed with concentrated sulfuric acid followed by water and aqueous sodium carbonate. These solvents were then dried with Linde type 4A Molecular Sieve and distilled.

**Kinetic Procedure.**—All reactions were run in sealed ampoules in a thermostated oil-bath controlled to  $\pm 0.05^\circ$ . At appropriate times samples were removed from the bath, cooled, and examined for absorption at 420 m $\mu$  with a Beckman DU spectrophotometer equipped with a photomultiplier. A slit width of 0.3 mm. was employed.

(21) S. Winstein and W. G. Young, *ibid.*, **58**, 104 (1936).

(22) O. Kym, *Ber.*, **32**, 3533 (1899).

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## COMMUNICATIONS TO THE EDITOR

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### N-GUAN-STREPTOLIDYL GULOSAMINIDE, A DEGRADATION PRODUCT OF THE STREPTOTHRICIN ANTIBIOTIC GROUP

Sir:

Among the various hydrolytic degradation products of streptolin,<sup>1</sup> streptothricin<sup>2</sup> and probably other, similar antibiotics,<sup>3</sup> is found a water soluble amino acid (I) referred to in the past as Compound C<sup>2</sup> or Compound 5.<sup>4</sup> In this Communication we present evidence which defines the

(1) E. E. Smissman, R. W. Sharpe, B. F. Aycock, E. E. van Tamelen and W. H. Peterson, *J. Am. Chem. Soc.*, **75**, 2029 (1953).

(2) H. E. Carter, R. K. Clark, Jr., P. Kohn, J. W. Rothrock, W. R. Taylor, C. A. West, G. B. Whitfield and W. G. Jackson, *ibid.*, **76**, 566 (1954).

(3) *E.g.*, roseothricin: T. Goto, Y. Hirata, S. Hosoya, and N. Komatsu, *Bull. Chem. Soc., Japan*, **30**, no. 7, 729 (1957).

(4) E. E. van Tamelen, J. R. Dyer, H. E. Carter, J. V. Pierce and R. E. Daniels, *J. Am. Chem. Soc.*, **78**, 4817 (1956).

structure of I as N-guan-streptolidyl gulosaminide (II).

Cellulose and charcoal chromatography afforded I as a crystalline dihydrochloride, m.p. 215–220° dec.,  $[\alpha]_D -22.4^\circ$  (*c* 3.00, water) (Found: C, 34.57; H, 6.17; N, 16.20; Cl, 16.70). Amino acid I gave positive Weber (blue) and ninhydrin tests, and negative Sakaguchi, Ehrlich and Elson-Morgan tests. Van Slyke analysis indicated two primary amino functions: C-methyl, O-methyl, N-methyl and  $\alpha$ -amino acid groups were shown to be absent. Prolonged vigorous acid hydrolysis of I resulted in a mixture of streptolidine,<sup>5</sup> gulosamine and 1,6-anhydrogulosamine.<sup>4,6</sup> Substance I

(5) H. E. Carter, *et. al.*, *J. Am. Chem. Soc.*, **83**, 4296 (1961).

(6) This observation is incompatible with the intermolecular ether formulation for I proposed by the Japanese school (ref. 3).