23-Acetyltigogenin (IIIg).—After dissolving 0.5 g. of potassium in 40 ml. of *t*-butyl alcohol, 1.0 g. of II was added and the resulting mixture was heated at reflux temperature for 15 hours. Following dilution with water (50 ml.), the solution was extracted with ethyl acetate and the extracts were washed with water, dried over sodium sulfate and evaporated to dryness. The residue (0.75 g.) was chromatographed over 30 g. of neutral alumina. Elution with benzene provided 0.51 g., m.p. 215–220°. Several crystallizations from acetone–hexane followed by sublimation at 215° (0.04 mm.) gave the analytical sample, m.p. 221–223°, $[\alpha]_D$ −94°, λ_{max}^{KBr} 5.85 and 5.92 μ, $\lambda_{max}^{CHCl_3}$ 5.89 μ (infrareds recorded on material from the same sample).

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 75.49; H, 9.94.

23-Acetyltigogenin Acetate (IIIh).—Compound IIIg (0.55 g.) was acetylated by the previously described conditions. The crude product was recrystallized from methanol–acetone to give 0.52 g. of crystals, m.p. 129–130°. Several recrystallizations from the same solvent pair provided the pure acetate, m.p. 149–150°, $[\alpha]_D$ −96°, λ_{max}^{KBr} 5.76 and 5.87 μ.

Anal. Calcd. for $C_{31}H_{48}O_5$: C, 74.36; H, 9.66; O, 15.98. Found: C, 74.76; H, 9.84; O, 15.76.

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA, CHARLOTTESVILLE, VIRGINIA]

Intramolecular S–O and S–N Acetyl Transfer Reactions

BY R. BRUCE MARTIN AND REGINA I. HEDRICK

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Specific base catalyzed intramolecular acetyl transfer from sulfur to oxygen proceeds about 30 times faster in S-acetylmercaptoethanol than in the corresponding propyl compound. Intramolecular acetyl transfer from sulfur to nitrogen in S-acetylmercaptoethylamine exhibits inverse dependence on hydrogen ion concentration at low *p*H and is general base catalyzed at high *p*H. A detailed mechanism for S–N transfer including dehydration to yield methylthiazoline is presented and absolute values for all rate constants are either evaluated or estimated.

Acetyl transfer from sulfur to oxygen occurs readily in the series[1] $CH_3COS(CH_2)_nOH$ when n is 2 or 3 and not at all when n is 4. For $n = 3$, the equilibrium constant[2] for S–O transfer if 56 at 39°. Acetyl transfer from sulfur to nitrogen takes place in the series[3] $CH_3COS(CH_2)_nNH_3^+$ when n is 2 or 3, but little or no transfer is detected when n is 4, 6 or 10. The equilibrium constant for S–N transfer is *p*H dependent.[4,5] The above results implicate intermediate ring formation in both S–O and S–N transfer reactions. In this paper further investigations of the transfer reactions are reported, including *p*H, temperature and catalytic studies. Finally, a detailed mechanism of S–N transfer is presented which can account for all the observations on S–N acetyl transfer reactions and on methylthiazoline and methylthiazine hydrolysis studies.[4,5]

Experimental

S-acetylmercaptoethanol[6] had b.p. 116–119° (26 mm.) and an absorption maximum with $\epsilon_{232} = 4400$ in aqueous solutions. S-acetylmercaptopropanol had b.p. 79° (1.2 mm.) and exhibited an absorption maximum with $\epsilon_{232} = 4260$ in aqueous solutions. This molar extinction coefficient agrees well with a value determined in ethanol[1] but differs from $\epsilon_{235} = 5200$ reported in 0.01 *N* HCl.[2]

S-Acetyl-β-mercaptoethylamine HCl[7] was prepared as previously[4] and had m.p. 145° and a maximum with $\epsilon_{229} = 4260$. S-Acetylcysteine ethyl ester hydrochloride required more vigorous conditions for its preparation. Fifteen ml. of acetyl chloride was added to 5 g. of L-cysteine ethyl ester hydrochloride and the heterogeneous mixture was refluxed at 50° for about 1.5 hr. Upon boiling off the excess acetyl chloride, the remaining white crystalline solid was washed several times with dry ether and recrystallized from absolute ethanol. The final product had m.p. 116–117° and an absorption maximum with $\epsilon_{229} = 3800$.

Initial rates of change were measured on a Cary 11 spectrophotometer with a thermostatable absorption cell compartment or on a Radiometer TTT1 *p*H-stat equipped with temperature control. Formate, acetate or phosphate buffers were used at about 10^{-2} *M* concentration and ionic strength was controlled at 0.2 *M* with KCl. Temperature was maintained to 0.1° and is 25.0° unless otherwise specified. Initial rates followed spectrophotometrically were evaluated by log $(A_t - A_\infty)$ *vs.* time plots. The A_∞ values were determined from known equilibrium constants,[2,5] but the calculated rate constant is not usually sensitive to the value chosen.

Results

S–O Transfer.—For both S-acetylmercaptoethanol (AME) and S-acetylmercaptopropanol (AMP) the initial rate of disappearance of thioester absorption is first order in ester in the 1–3 × 10^{-4} *M* concentration range. At 25° in solutions 0.02 *N* to 3 *N* HCl the observed rate constants are proportional to the first power of (H^+) with AME disappearing only slightly more rapidly than AMP. Comparison of the rates with those of hydrolysis of thioesters in aqueous solutions[8] indicates that hydrolysis may contribute as much as 20% to the over-all initial rate. Addition of 0.2 *M* glycine at *p*H 2.5 did not accelerate the over-all rate of disappearance of AME. The specific acid catalyzed transfer was not investigated further.

The initial rates of disappearance in basic solutions are inversely proportional to the first power of (H^+) in the range $6.0 < pH < 8.0$ at 25°. The results at 3 temperatures are presented in Table I. The apparent first order rate constant is multiplied by (H^+) to obtain a *p*H independent constant. The observed activation energy ΔE and the ap-

(1) J. S. Harding and L. N. Owen, *J. Chem. Soc.*, 1528, 1536 (1954).
(2) W. P. Jencks, S. Cordes and J. Carriuolo, *J. Biol. Chem.*, **235**, 3608 (1960).
(3) T. Wieland and H. Hornig, *Ann.*, **600**, 12 (1956).
(4) R. B. Martin, S. Lowey, E. L. Elson and J. T. Edsall, *J. Am. Chem. Soc.*, **81**, 5089 (1959).
(5) R. B. Martin and A. Parcell, *ibid.*, **83**, 4830 (1961).
(6) P. Nylen and A. Olsen, *Svensk Kem. Tidskr.*, **53**, 274 (1941); *Chem. Absir.*, **36**, 753 (1942).
(7) T. Wieland and E. Bokelmann, *Ann.*, **576**, 20 (1952).
(8) L. H. Noda, S. A. Kuby and H. A. Lardy, *J. Am. Chem. Soc.*, **75**, 913 (1953).

parent entropy of activation also are recorded. Comparison with the hydrolysis rates of thioesters[8] indicates the contribution of hydrolysis to the overall reaction is expected to be negligible. Jencks[2] has reported negligible interference from hydrolysis for AME. A point for AMP obtained by Jencks[2] at 39° by an entirely different method falls above the straight line from which the activation energy was determined. Experiments on AME performed with 0.2 *M* acetate (pH 4.7), THAM (pH 7.0) or borate (pH 9.0) buffers indicate no detectable general catalysis. The same result was obtained for AMP in carbonate buffers.[2]

TABLE I

TRANSFER IN S-ACETYLMERCAPTOETHANOL (AME) AND PROPANOL (AMP)

	AME	AMP
15.0°	7.6×10^{-13} sec.$^{-1}$ *M*	.....
18.2°	.....	0.40×10^{-13} sec.$^{-1}$ *M*
25.0°	31×10^{-13} sec.$^{-1}$ *M*	1.1×10^{-13} sec.$^{-1}$ *M*
35.0°	105×10^{-13} sec.$^{-1}$ *M*	3.2×10^{-13} sec.$^{-1}$ *M*
ΔE, kcal./mole	23 ± 1	22
$\Delta S\neq$, e.u.	−38	−49

S–N Transfer.—The initial rate of disappearance of ester was always first order in ester in the 1–30 $\times 10^{-4}$ *M* concentration range. Initial rates were followed spectrophotometrically at pH < 3 and in the pH-stat at pH > 3 since a proton is liberated for each mole of the N-acetyl derivative formed. The results obtained in aqueous solutions at several temperatures are shown in Fig. 1. Comparison with rate constants for base catalysis of hydrolysis of thioesters[8] indicates that hydrolysis is negligible compared to the rapid S–N transfer reaction.

The unit slope of Fig. 1 in the pH 2.5 region implicates a reaction inversely proportional to (H^+), the plateau region is ascribed to general base catalysis by H_2O, and the pH 5 region of unit slope is assigned to general base catalysis by OH^-. Addition of 0.2, 0.3 or 0.4 *M* boric acid or phenol to solutions in the pH-stat in the range 3.2 < pH < 4.0 accelerated the initial rate of disappearance in an amount proportional to the concentration of the basic form of the conjugate acid–base pair. Addition of boric acid also accelerated the reaction in the pH 5 region. General base catalysis by formate was observed spectrophotometrically at pH 3.6. A plot of the logarithm of the catalytic coefficients for the bases H_2O, formate, borate, phenolate and hydroxide *vs.* pKa yields a Brønsted plot similar to those reported for other acylations.[9] No significant general catalysis was observed in the pH 2.5 region. Addition of Zn^{++} so that the ratio of concentrations of thioester to Zn^{++} was 2 gave no alteration in the rate of thioester disappearance in the pH stat at pH 5.5.

The results presented graphically in Fig. 1 are summarized in Table II. For mechanistic reasons to appear in the discussion the apparent rate constant is multiplied by (H^+) in the low pH region to give the pH independent values in the second column of Table II. The plateau region values are recorded directly in column 3. In the high pH region the apparent rate constant is divided by (OH^-) to give the pH independent second order rate constants in the fourth column of Table II. The values of pKw used were 14.35, 14.00 and 13.68 at 15°, 25° and 35°, respectively. Finally, the activation energies for each pH region are tabulated. The apparent entropy of activation for the low pH region is −19 e.u.

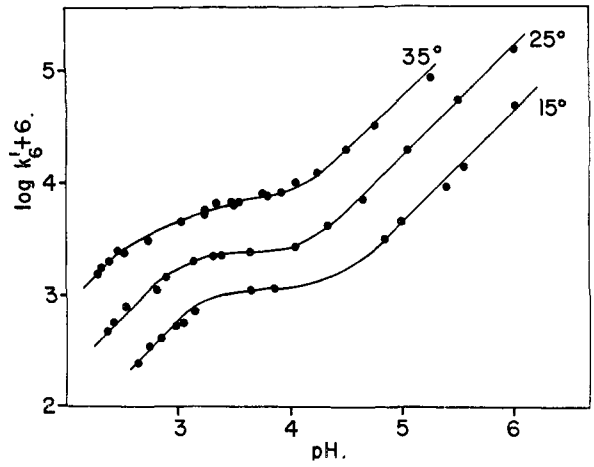


Fig. 1.—Logarithm of the observed rate constant in min.$^{-1}$ *vs.* pH for the initial rate of disappearance of S-acetyl-β-mercaptoethylamine.

Similar studies on S-acetylcysteine ethyl ester yield curves like those of Fig. 1 except that the low pH region of unit slope sets in only at pH < 2 where ester hydrolysis and thiazoline ring formation also occur. At 25° in the plateau region the value corresponding to those in the third column of Table II is 7.1×10^{-5} sec.$^{-1}$. Similarly in the high pH region the values of the second order pH independent rate constants are 3.0×10^5, 5.9×10^5 and 9.6×10^5 sec.$^{-1}$ M^{-1} at 15, 25 and 35°, respectively, yielding an apparent activation energy of 10 kcal./mole. Thus the general base catalyzed rate of transfer of S-acetylcysteine ethyl ester proceeds about twice as fast as transfer in S-acetyl-β-mercaptoethylamine and with a similar activation energy.

Discussion

S–O Transfer.—Evidently any mechanism of transfer in basic solutions must be first order in ester and inverse first order in (H^+), proceed *via* a cyclic intermediate, and not be subject to general catalysis. A mechanism satisfying these requirements as drawn for AME is shown by formulas A → C, where K_3 and K_4 are acid ionization constants. When a steady state equation for the cyclic intermediate is written, the observed rate constant for the initial rate of disappearance of thioester is given by

$$k' = k_{11}K_3/[(H^+)(1 + k_{12}/k_{13})] \qquad (1)$$

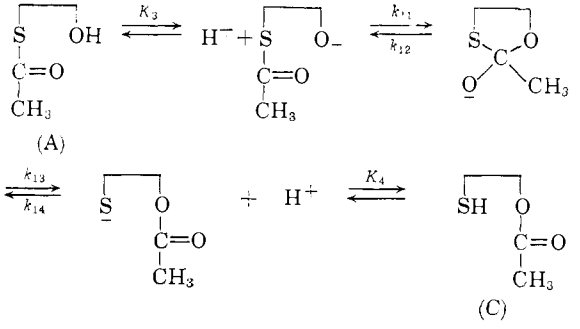
which fits the requirements of S–O transfer reac

(9) T. C. Bruice and R. Lapinski, *J. Am. Chem. Soc.*, **80**, 2265 (1958); W. P. Jencks and J. Carriuolo, *ibid.*, **82**, 1778 (1960).

TABLE II

TRANSFER IN S-ACETYLMERCAPTOETHYLAMINE

	Low pH	Plateau	High pH
15.0°	9.4×10^{-9} sec.$^{-1}$ M	1.6×10^{-5} sec.$^{-1}$	1.6×10^{5} sec.$^{-1}$ M^{-1}
25.0°	34×10^{-9} sec.$^{-1}$ M	4.0×10^{-5} sec.$^{-1}$	2.8×10^{5} sec.$^{-1}$ M^{-1}
35.0°	127×10^{-9} sec.$^{-1}$ M	11.0×10^{-5} sec.$^{-1}$	4.9×10^{5} sec.$^{-1}$ M^{-1}
ΔE, kcal./mole	23	16	10



(A) (C)

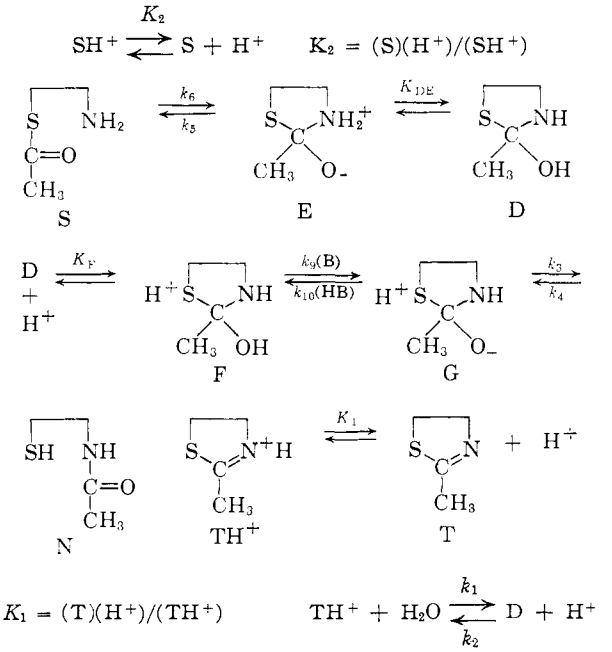
tions. At equilibrium

$$K_{os} = 56 = \frac{(C)}{(A)} = \frac{k_{11}k_{13}K_3}{k_{12}k_{14}K_4}$$

For purposes of estimation K_3 may be taken as 10^{-16}, K_4 as 10^{-9} and k_{11}/k_{14} as about 1/20 from results on the relative reactivities of thiolate and alkoxide ions.[10] Then apparently $k_{12}/k_{13} \simeq 10^{-10}$ so that equation 1 reduces to $k' = k_{11}K_3/(H^+)$. The $k'(H^+)$ product is recorded in Table I.

With assumed equal values of K_3 for AME and AMP, ring closure is about 30 times faster for the 5-membered than for the 6-membered ring. The corresponding factor is about 65 in S–N and N–S transfer reactions.[5] The greater negative entropy term in Table I for AMP is consistent with greater loss of rotational freedom in formation of a six membered cyclic intermediate. More information may be inferred only if the thermodynamic quantities for the K_3 ionization are known. Due to the lack of more appropriate data, the values are assumed to be similar to those for water, $\Delta H = 13.5$ kcal./mole and $\Delta S = -27$ e.u. Combination of these values with those recorded in Table I yields $\Delta E \simeq 9$ and 8 kcal./mole and $\Delta S^{\pm} \simeq -11$ and -22 e.u. for k_{11} in AME and AMP, respectively. The negative values of $\Delta S^{\pm}$ are consistent with ring formation in the activated complex of the k_{11} reaction. Finally, if K_3 is estimated as 10^{-16} then $k_{11} \simeq 3 \times 10^4$ sec^{-1} for AME at 25°.

S–N Transfer.—A mechanism for S–N transfer must account for first order disappearance of ester, proceed *via* a cyclic intermediate, be consistent with Fig. 1 and general base catalysis in the plateau and high pH regions and no general catalysis in the low pH region, explain inhibition of hydrolysis in acid solutions of thiazoline and thiazine compounds[4,5] with a pH independent ratio of initial S-acetyl appearance to thiazoline disappearance[5] and account for general base catalysis only on the basic, descending side of the bell shaped hydrolysis curve for thiazoline.[5] Apparently sufficient information is available so that severe restrictions are imposed on the choice of mechanisms. A mechanism consistent with all the information currently available as written for S-acetyl-β-mercaptoethylamine(S) is



where the large K's are equilibrium constants and the small k's rate constants, and the steady state approximation is considered applicable to intermediates D through G. Define: $K_{DE} = (D)/(E)$, $K_F = (D)(H^+)/(F)$, $K_G = (G)(H^+)/(F)$ and $K_B = (B)(H^+)/(HB)$ where B is the basic and HB and the acidic component of a catalytic system. The constants k_1, k_2, k_4, k_6, K_1 and K_2 have the same meaning as before[4,5] whereas the former k_3 and k_5 (now denoted by primes) are given by $k_3' = k_3 K_G/K_F$ and $k_5' = k_5/K_{DE}$.

The apparent rate constant k_6' for the initial rate of disappearance of SH^+ where N is the only product is given by

$$k_6' = \frac{k_6K_2k_3k_9(B)(H^+)K_{DE}}{(H^+)[k_3k_9(B)(H^+)K_{DE} + K_Fk_{10}(HB)k_5 + K_F k_3k_5]} \quad (2)$$

Under the conditions studied in this paper appreciable thiazoline formation does not take place. Thus k_6' of equation 2 accounts for the curves of Fig. 1. In solutions of high acidity where the only

(10) M. L. Bender, *Chem. Revs.*, **60**, 63 (1960).

acid is hydronium ion, equation 2 becomes

$$k_6' = \frac{k_6K_2k_3K_GK_{DE}}{(H^+)[k_3K_GK_{DE} + K_Fk_5]} \quad (3)$$

which is analogous to

$$k_6' = \frac{k_6K_2k_3'}{(H^+)[k_3' + k_5']} \quad (4)$$

of previous work where all the constants of equation 4 have the same definition except k_3' and k_5' which are unprimed in the other accounts.[4,5] The ratio $k_3'/(k_3' + k_5') = 0.45$ corresponds to the partitioning of the cyclic intermediate and is fairly temperature independent.[5] Thus $k_6K_2 = 7.5 \times 10^{-8}$ sec.$^{-1}$ M at 25°.

Since $pK_2 \simeq 9.1$,[5] $k_6 = 94$ sec.$^{-1}$, a value which is about 300 times less than the estimated k_{11} value for AME. Thus alkoxide ion is more nucleophilic toward aliphatic thioesters than an amine if steric factors involved in 5 membered ring formation are comparable for the two compounds and if the approximation made in estimating k_{11} is not too inaccurate. Steric factors are probably not too important because comparison of k_{11} for AMP with k_6 for the thiazine system[5] reveals about a 700 fold difference, but even more approximations are required to derive the latter value, and the difference between the two estimates is not significant.

As with the case of S–O transfer the thermodynamic functions for K_2 are not known but may be approximated in this case by those for ethanolamine[11] where $\Delta H = 12$ kcal./mole and $\Delta S = -3$ e.u. Hence for the ring closure step k_6 from the S-acetyl derivative, $\Delta E \simeq 11$ kcal./mole and $\Delta S^{\ddagger} \simeq -15$ e.u. The latter value is more negative than the -11 e.u. estimated for AME of the same ring size because the k_6 step involves the creation of two new charges with consequent solvent orientation whereas no new charges are created in the k_{11} step.

In solutions of low acidity equation 2 becomes

$$k_6' = \frac{k_5K_2k_9(B)K_{DE}}{K_Fk_5} \quad (5)$$

which accounts for general base catalysis, by H_2O in the plateau region and by OH^- in the high pH region of the curves of Fig. 1. Since the absolute rate constants of elementary reactions in solution have been determined by fast reaction techniques and summarized,[12] estimation of the absolute values rather than ratios[4,5] of the rate constants in the proposed mechanism is possible if the acid ionization constants of the several intermediates may be approximated. To some extent errors in the last approximation will cancel, if self-consistent values are used, because the equilibrium constants appear in both numerator and denominator. In the plateau region where water is the base in equation 5, $k_9(B) \simeq 10^{-3}$ (55) and taking $K_{DE} \simeq 10^3$, $K_F \simeq 10^2$, yields $k_5 \simeq 10^{-3}$ sec.$^{-1}$, since the other constants are already known.

From the known equilibrium constant for S–N transfer in this system,[5] $K_{NS} = 0.045 = (N)(H^+)/(SH^+) = k_6K_2k_3K_{DE}K_G/k_4k_5K_F$, substitution of known values[5] for k_6K_2 and k_4 yields $k_3K_{DE}K_G/k_5K_F \simeq 1$. If K_G is taken as 10^{-11}, then $k_3 \simeq 10^{10}$. $k_5 \simeq 10^7$ sec.$^{-1}$. Since the equilibrium constant for thiazoline formation is also known,[5] $K_{ST} = 11 = \frac{(SH^+)}{(TH^+)} = k_1k_5/k_6K_2K_{DE}k_2$, the absolute value of k_2 may be estimated to be 2×10^{-5} sec.$^{-1}$ M^{-1} because, all the other constants in the equilibrium expression are either known or have been approximated. Thus the absolute values of all the constants in the S–N transfer mechanism are accurately known[5] or have been estimated. The values quoted are all possible if not even reasonable ones. Estimation can be easily extended to include the thiazine system.[5]

The mechanism proposed in this paper for S–N transfer reactions includes and extends the formulation previously presented.[4,5] Under conditions where base catalysis of S–N transfer is not important, the earlier presentation is simpler. When considering thiazoline hydrolysis,[5] in particular, no great benefit is usually derived from consideration of the extended mechanism presented here. For instance, the ratio of the initial rate of appearance of S-acetyl to the initial rate of disappearance of thiazoline in an initial solution of the latter is given by

$$-\frac{d(SH^+)}{d(TH^+)} = \frac{k_5/K_{DE}}{k_5/K_{DE} + k_3K_G/K_F} = \frac{k_5'}{k_5' + k_3'}$$

which is independent of (H^+) in either the extended or previous[4,5] (primes) formulations. The mechanism proposed here may also be applied to intermolecular acyl transfer reactions.

The extended mechanism of this paper is evidently not required when considering the oxazoline system and O–N transfer reactions because the latter do not seem to be general base catalyzed[13] even at pH 8. Once formed, the breakdown of intermediate G to yield N might be expected to be much less rapid when oxygen is substituted for sulfur with the result that intermediates F and G are in equilibrium to much higher pH values. If the equilibrium constants between the intermediates are not affected much by substitution of oxygen for sulfur, the conclusion is that $k_3 < 10^2$ sec.$^{-1}$ in the oxazoline system. If the k_2 values for the two systems are the same comparison of the k_3'/k_2 ratios[13] yields $k_3 \simeq 40$ sec.$^{-1}$ in the oxazoline system. This low value accounts for the pronounced partitioning of the intermediates in favor of the ester rather than the amide product in the oxazoline system.[13]

Two features of the S–N transfer system have made possible estimation of the absolute values of the rate constants. The dehydration byproduct of transfer, methylthiazoline, provides a handle for evaluation of the partitioning of the intermediate to yield ester or amide.[4,5] This advantage also is utilized for O–N transfer by a study of methyloxazoline disappearance.[13] By contrast, the partition-

(11) R. G. Bates and G. D. Pinching, *J. Research Natl. Bur. Standards*, **46**, 349 (1951).

(12) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, New York, 1959, page 120.

(13) R. B. Martin and A. Parcell, *J. Am. Chem. Soc.*, **83**, 4835 (1961).

ing of the cyclic intermediate in S–O transfer had to be estimated by more indirect methods. Isotopic exchange experiments provide one of the few tools for evaluation of partitioning in intermolecular reactions. Demonstration of general base catalysis for S–N transfer and a knowledge of reaction rates of fast proton transfer reactions permit evaluation of the absolute rate constants in this system. In the O–N transfer system, general base catalysis presumably occurs only at high *p*H where intermolecular reaction effects would be competitive with intramolecular transfer.

Finally, the question of retention or inversion of configuration in acyl transfer reactions has received considerable attention.[14] The mechanism proposed here involves retention of configuration. In S → N, N → S, O → S and O → N transfer reactions, inversion of configuration would yield different products than assumed here. The identical equilibrium results obtained by starting with more than one of the reactants in the thiazoline[5] or oxazoline[13] systems would seem to rule out any kind of inversion mechanism for these systems. In S → O and N → O transfer both mechanisms would yield the same products in aqueous solutions, but a retention mechanism is favored by analogy with the other similar transfer reactions considered here.

Acknowledgment.—This research was supported by grants from the National Science Foundation and the National Institutes of Health.

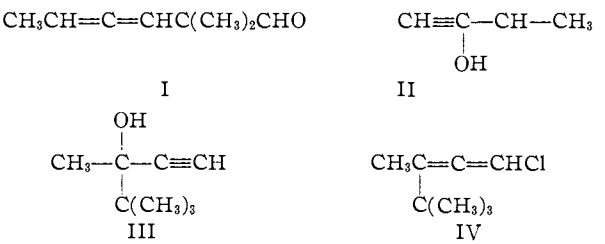
(14) For instance, L. H. Welsh, *ibid.*, **71**, 3500 (1949); G. E. McCasland, *ibid.*, **73**, 2295 (1951); E. E. van Tamelen, *ibid.*, **73**, 5773 (1951); G. Fodor and J. Kiss, *J. Chem. Soc.*, 1589 (1952); S. Winstein and R. Boschan, *J. Am. Chem. Soc.*, **72**, 4669 (1950).

COMMUNICATIONS TO THE EDITOR

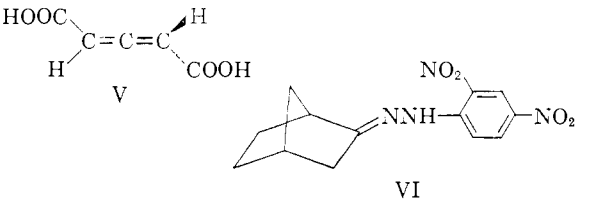
THE ABSOLUTE CONFIGURATION OF PENTADIENDIOIC ACID

Sir:

In the past two years the absolute configurations of two allenic compounds have been deduced by mechanistic correlation with their optically active non-allenic progenitors. Jones, Loder, and Whiting[1] related the allenic aldehyde I to but-3-yn-2-ol (II) of known absolute configuration, and the tentative assignment of Eliel[2] of configuration to III based on Brewster's rules[3] permits the establishment of a similar relationship between that compound and its transformation product IV.[4]



An alternative approach[5] to this problem of allene absolute configuration would be the preparation of an active allene of unknown stereochemistry followed by its transformation into an active compound possessing asymmetric carbon. The absolute geometry of this latter material could then be determined by any of a number of now conventional techniques.[6,7,8] To this end we have partially resolved pentadiendioic (glutinic) acid (V) and converted it into optically active norcamphordinitrophenylhydrazone (VI). The configuration of VI was established by comparison with a sample prepared from optically active norcamphor, the absolute stereochemistry of which was determined recently by Berson.[9] On the basis of the arguments and transformations outlined below (+)glutinic acid is assigned the absolute configuration shown (V). All reactions and proofs of structure were first carried out with racemic compounds, and then the appropriate steps repeated with optically active material.



The Diels–Alder reaction between glutinic acid and cyclopentadiene gave an adduct in over 90% yield, as previously reported.[10] We have separated this by fractional crystallization into approximately equal amounts of two isomeric compounds, one melting 205–207°,[11] and the other 245–246°.[11]

(1) E. R. H. Jones, J. D. Loder, and M. C. Whiting, *Proc. Chem. Soc.*, 180 (1960).

(2) E. L. Eliel, *Tetrahedron Letters*, No. 8, 16 (1960).

(3) J. H. Brewster, *J. Am. Chem. Soc.*, **81**, 5475 (1959).

(4) S. R. Landor and R. Taylor-Smith, *Proc. Chem. Soc.*, 154 (1959).

(5) *Cf.* D. W. Dicker, D. Phil. Thesis, Oxford, 1957.

(6) C. Djerassi, "Optical Rotatory Dispersion, Ch. 10, McGraw-Hill Book Co., New York, N. Y., 1960.

(7) V. Prelog, *Bull. Soc. Chim. France*, 987 (1956).

(8) J. A. Mills and W. Klyne, Ch. 5 in "Progress in Stereochemistry," Vol. 1 (ed. W. Klyne), Butterworths, London, 1954.

(9) Prof. Jerome Berson of the University of Southern California was very kind to provide a copy of his paper prior to publication as well as a sample of resolved norcamphor. It is a pleasure to record here our appreciation of his willing and valuable aid. J. A. Berson, J. S. Walia, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff, and D. Willner, *J. Amer. Chem. Soc.*, **83**, 3986 (1961).

(10) E. R. H. Jones, G. H. Mansfield, and M. C. Whiting, *J. Chem. Soc.*, 4073 (1956).

(11) Satisfactory elementary analysis for carbon and hydrogen was obtained for this compound.