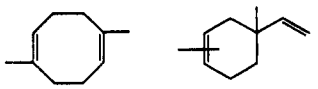

3 4

The conversion **1** → **2** was carried out by hydroboration with 1 *M* disiamylborane in THF at 0°. Alkaline peroxide oxidation of the organoborane gave the desired product in 52% yield. Purification was accomplished by preparative glpc on a 6 ft × 0.25 in. 30% SE-30 on 80–100 Chromosorb W column at 120°. The material isolated by this method proved to be identical with an authentic sample.[8]

Finally, the method promises to be useful for the syntheses of various analogs of **2**. Thus, *cis*-2-vinyl-1-cyclobutaneethanol was produced from *cis*-1,2-divinylcyclobutane with disiamylborane.

Acknowledgment. We gratefully acknowledge the Research Corporation for financial support of this work.

(8) We thank Dr. R. C. Gueldner for providing spectral data and a sample of grandisol. The following 60-MHz nmr spectrum in CCl_4 with a TMS internal reference was observed: δ 1.18 (s, 3 H), ~1.3–2.2 (m, 6 H), 1.68 (s, 3 H), 2.53 (t, 1 H), 2.67 (s, 1 H, a concentration dependent OH), 3.55 (t, 2 H), 6.62 (s, 1 H), and 6.8 (s, 1 H). The identity of this substance was confirmed by comparison of this spectrum with the one provided by Dr. Gueldner and by comparison of its glpc retention time with an authentic sample on an SE-30 column. The structure **1** was further confirmed by bioassaying, which showed activity equal to natural grandisol.

(9) National Defense Education Act Fellow, 1970–present.

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Stereochemical Outcome of a 1,3-Sulfur Migration

Sir:

Rearrangements involving novel 1,3-sulfur migrations have recently been observed with certain dihydro-1,4-thiazines.[1] For example, methyl (6*S*)-5,5-dimethyl-4-thia-1-azabicyclo[4.1.0]hept-2-ene-3-carboxylate (**1**) was converted into methyl (3*R*)-3,4-dihydro-3-isopropenyl-2*H*-1,4-thiazine-6-carboxylate (**3**) in boiling toluene. A study of the rearrangement of **1**, specifically monodeuterated at the 7-methylene group, is expected to provide insight into the mechanism of the reaction. We now describe the results of this investigation.

One approach to the synthesis of the specifically labeled aziridine, *e.g.*, **2**, involves the stereoselective reduction of **7** to **10**. A preliminary experiment established that **9**,[2] mp 81–82°, $[\alpha]D$ +158° ($CHCl_3$), which was prepared (24%) from **11** by the method of Perron, *et al.*,[3] underwent rearrangement[4] to **5** (85%) in the presence of methanolic sodium methoxide. Derivative **5** can be converted into **1** by way of **6**.[1]

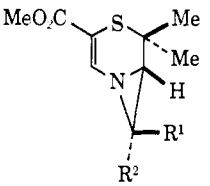
(1) A. R. Dunn and R. J. Stoodley, *Chem. Commun.*, 1169, 1368 (1969); *J. Chem. Soc., Perkin Trans. 1*, 2509 (1972).

(2) The composition of all new compounds was confirmed by elemental analysis or by mass spectroscopy. Structural assignments are based on ir and nmr evidence.

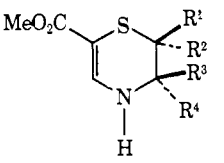
(3) Y. G. Perron, L. B. Crast, J. M. Essery, R. R. Fraser, J. C. Godfrey, G. T. Holdrege, W. F. Minor, M. E. Neubert, R. A. Partyka, and L. C. Cheney, *J. Med. Chem.*, 7, 483 (1964).

(4) I. McMillan and R. J. Stoodley, *Tetrahedron Lett.*, 1205 (1966); *J. Chem. Soc. C*, 2533 (1968).

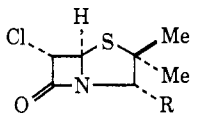
Attempts to prepare **7** by oxidation[5] of **9** and by reduction[6] of **11** were unsuccessful. However, the following route proved to be satisfactory. 6α-Chloropenicillanoyldiazomethane[2] (**12**), mp 93–95° dec, $[\alpha]D$ +400° ($CHCl_3$), was prepared (76%) from **11** in the usual manner.[7] When heated with 1 *N* sulfuric acid in dioxane, **12** afforded (52% after silica gel chromatography) the syrupy ketol[2] **13**, $[\alpha]D$ +235° ($CHCl_3$), which was reduced by sodium borohydride to a mixture (3:2 by nmr spectroscopy) of diols **14** (21%). The mixture was fractionated by silica gel chromatography to give the major diol[2] as a syrup, $[\alpha]D$ +137° ($CHCl_3$), and the minor diol,[2] mp 76–77°, $[\alpha]D$ +129° ($CHCl_3$). The diols (individually or as a mixture) were oxidatively cleaved by 1 mol equiv of sodium periodate in aqueous dioxane to the syrupy aldehyde **7** (71%), which was reduced to **9** (29%) by actively fermenting yeast.[8]



1, $R^1 = R^2 = H$
2, $R^1 = D$; $R^2 = H$



3, $R^1 = R^2 = R^4 = H$; $R^3 = CMe{=}CH_2$
4, $R^1 = R^4 = H$; $R^2 = D$; $R^3 = CMe{=}CH_2$
5, $R^1 = R^2 = Me$; $R^3 = H$; $R^4 = CH_2OH$
6, $R^1 = R^2 = Me$; $R^3 = H$; $R^4 = CH_2OTs$



7, R = CHO
8, R = CDO
9, R = CH_2OH
10, R = CHDOH
11, R = CO_2H
12, R = $COCHN_2$
13, R = $COCH_2OH$
14, R = $CHOHCH_2OH$
15, R = $CDOHCH_2OH$

Sodium borodeuteride reduction of **13** gave a mixture of the monodeuterated diols **15**, which was converted into **8** by sodium periodate. The last derivative was reduced by Mosher's procedure[8] to **10**, which was transformed into **2**. The aziridine was *ca.* 77% monodeuterated and *ca.* 23% undeuterated on the basis of mass spectroscopy. Nmr spectroscopy corroborated this result (*ca.* 73% monodeuterated) and indicated that the deuterium resided at the 7-exo position[9] [τ ($CDCl_3$) 8.18 (d, 1 H, $J_{6,7\text{-endo}}$ = 3.5 Hz, 7-*endo*-H), 7.70 (d, 0.27 H, $J_{6,7\text{-exo}}$ = 4.6 Hz, 7-*exo*-H), 7.25 (d, 1 H, separation = 3.4 Hz, 6-H)]. On the assumption that the configuration of the exocyclic methylene group of **6** is inverted[10] during the formation of **1**, **10** possesses the *S* configuration, in accord with previous work.[11]

(5) C. W. Rees and R. C. Storr, *Chem. Commun.*, 1305 (1968); R. E. Partch, *Tetrahedron Lett.*, 3071 (1964); J. D. Albright and L. Goldman, *J. Amer. Chem. Soc.*, 87, 4214 (1965); K. E. Pfitzner and J. G. Moffat, *J. Amer. Chem. Soc.*, 87, 5670 (1965); M. M. Baizer, *J. Org. Chem.*, 25, 670 (1960).

(6) W. J. Gottstein, G. E. Bocian, L. B. Crast, K. Dadabo, J. M. Essery, J. C. Godfrey, and L. C. Cheney, *J. Org. Chem.*, 31, 1922 (1966).

(7) B. G. Ramsay and R. J. Stoodley, *J. Chem. Soc. C*, 1319 (1969).

(8) V. E. Althouse, K. Veda, and H. S. Mosher, *J. Amer. Chem. Soc.*, 82, 5938 (1960).

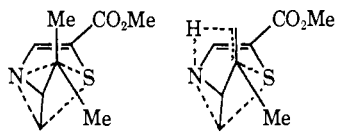
(9) A. R. Dunn and R. J. Stoodley, *Tetrahedron Lett.*, 3367 (1969).

(10) O. C. Dermer and G. E. Ham, "Ethylenimine and Other Aziridines: Chemistry and Applications," Academic Press, London, 1969.

(11) D. Arigoni and E. L. Eliel, *Top. Stereochem.*, 4, 127 (1969).

The monodeuterated aziridine **2** was heated in toluene for 4 days[1] to give **4** (30% after silica gel chromatography), which was converted into the sulfoxide[12] without loss of deuterium; the isotope was located at the 2α position of the sulfoxide by nmr spectroscopy [τ ($CDCl_3$) 7.70 (d, 0.73 H, $J_{2\beta,3}$ = 13.2 Hz, t, 0.27 H, $J_{2\alpha,2\beta}$ = $J_{2\beta,3}$ = 13.2 Hz, 2β-H), 7.00 (d of d, 0.27 H, $J_{2\alpha,2\beta}$ = 13.2, $J_{2\alpha,3}$ = 3.0 Hz, 2α-H)].

The isomerization of **2** to **4** illustrates that the 1,3-sulfur migration occurs so that the new carbon–sulfur bond is formed with retention of configuration. This result, although not excluding nonconcerted pathways, is consistent with a concerted reorganization, in which the aziridine reacts in its thermodynamically unfavorable conformation[9] *via* a transition state such as **16** or **17**. In the former event, **18** is an intermediate in the reaction, which represents an example of a [4.4]-dyotropic shift.[13]



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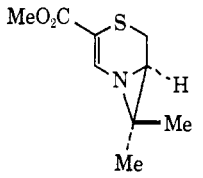
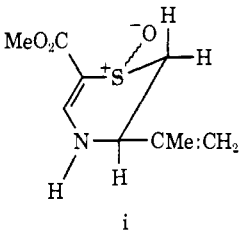


18

Acknowledgments. We thank Mr. P. Kelly for the mass spectral determinations, Dr. N. M. S. Hill for measuring the 90-MHz nmr spectra, and the Science Research Council for a research studentship (to J. K.).

(12) Oxidation of **3** by sodium periodate gave (89%) a single sulfoxide:[2] mp 154–156° dec; $[\alpha]_D$ +291° (EtOH); nmr τ ($CDCl_3$) 7.70 (t, 1 H, $J_{2\alpha,2\beta}$ = $J_{2\beta,3}$ = 13.2 Hz, 2β-H), 7.00 (d of d, 1 H, $J_{2\alpha,2\beta}$ = 13.2, $J_{2\alpha,3}$ = 3.0 Hz, 2α-H). The configurational and conformational features of 3-substituted-3,4-dihydro-6-methoxycarbonyl-2*H*-1,4-thiazine 1-oxides will be discussed elsewhere (J. Kitchin and R. J. Stoodley, *Tetrahedron*, submitted for publication). However, the magnitudes of the vicinal coupling constants of the sulfoxide of **3** indicate that the sofa conformer i is adopted in solution. For a discussion of the conformational properties of 3-substituted-3,4-dihydro-6-methoxycarbonyl-2*H*-1,4-thiazines see A. R. Dunn and R. J. Stoodley, *Tetrahedron*, **28**, 3315 (1972).



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(13) M. Reetz, *Angew. Chem., Int. Ed. Engl.*, 11, 129 (1972).

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Received January 29, 1973

Conversion of Amides to Thiol Acids and Isothiocyanates. A Novel Method for Breaking of the Amide Bond

Sir:

Of all the derivatives of the carboxylic group, an amide bond is the hardest to break hydrolytically. In many instances extreme conditions, such as heating with very concentrated acids or bases, have to be employed.

We have discovered a new method of breaking primary or secondary amides under anhydrous conditions and at room temperature. The products are a thiol acid and an isothiocyanate, which can be easily converted to an amine. Tertiary amides are stable under those conditions, and indeed the solvent of choice is a 1:1 mixture of *N*,*N*-dimethylacetamide and benzene. The amide is first converted to the corresponding anion by sodium hydride, carbon disulfide is added, and the reaction is finished after 90 min at room temperature, even in the case of aromatic amides, which are notoriously hard to hydrolyze by the usual methods.

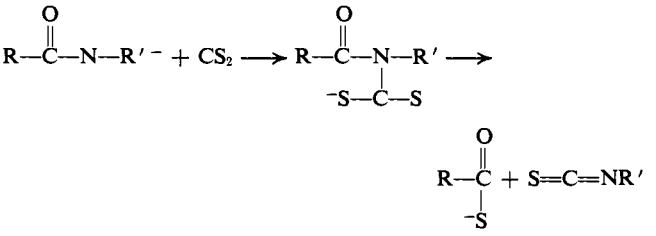
The reaction can be represented as follows. In the case of primary amide

$$RCONH_2 \xrightarrow{NaH} RCONH^- \xrightarrow[NaH]{CS_2} RCOS^- + NCS^-$$

In the case of a secondary amide

$$RCONHR' \xrightarrow{NaH} RCONR'^- \xrightarrow{CS_2} RCOS^- + S{=}C{=}NR'$$

We propose the following mechanism



Similar mechanisms were proposed for the conversion of imides by carbon disulfide to thio ketones[1,2] known in the aromatic series. A similar reaction in the aliphatic series was carried out recently by one of the authors (I. S.) in the laboratory of Professor D. M. R. Barton

$$[(CH_3)_3Cl_2C{=}NH \xrightarrow[2.\ CS_2]{1.\ MeLi} [(CH_3)_3Cl_2C{=}S$$

The thiol acids obtained from our reaction can be easily isolated in good yields. In case of very volatile thiol acids it may be convenient to oxidize them *in situ* to the less volatile diacyl disulfides. The isothiocyanates can be easily isolated in the aromatic series, but more generally they are either hydrolyzed *in situ* to the corresponding amines, or isolated as thioureas after reaction with aniline. The primary and secondary amides which reacted are given in Tables I and II.

Table I. Primary Amides, $RCONH_2$

R	Yield of RCOSH, %
C_6H_5	80
$C_6H_5CH_2$	65
1-Naphthyl	70
CH_3	65[a]

[a] Isolated diacetyl disulfide, bp 110° (20 mm).

The general procedure for secondary amides is as follows. To a suspension of 2.5 g (50 mmol) of sodium hydride (53% suspension in mineral oil) in 40 ml of *dry* dimethylacetamide and 40 ml of dry benzene, 50 mmol

(1) R. Ahmed and W. Lwowski, *Tetrahedron Lett.*, 3611 (1969).
(2) H. B. Williams, R. N. Yarborough, K. L. Crochet, and D. W. Wells, *Tetrahedron*, **26**, 817 (1970).