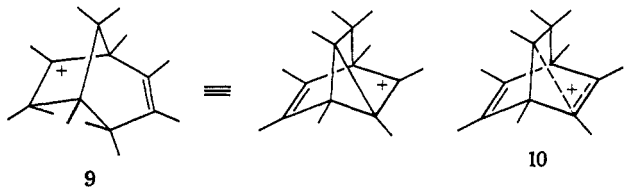
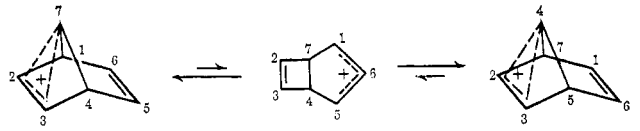
Scheme I is a formalism for rationalizing the nmr results; the intermediate ion **8** may, however, better be represented by structure **9** or **10**.[14]



9 **10**

We call attention to the complementary relationship between our results and those observed several years ago on the 7-norbornadienyl cation (**11**).[15] There a



11 **12** **11′**

stepwise circumambulatory motion of five carbons (1, 6, 5, 4, 7) with respect to the two "bound" vinyl carbons (2, 3) was rationalized *via* the [3.2.0] allylic ion **12**. Ion **12** was not observed at −78° in the nmr spectrum, the only detectable ion being **11**. When the ring system is expanded by one carbon atom, as we report here, the converse obtains; only the allylic ion (*i.e.*, **5**) can be observed by nmr; the intermediate ion (**8–10**) goes undetected. This inversion in the relative stabilities of the ions is reasonable since the cationic site is now "off-center" with respect to the stabilizing double bond (see **10**).

The mechanism by which **5** is formed from **4** is being investigated.

Acknowledgment. We are indebted to the National Science Foundation and the National Institutes of Health for financial support and to Professors Max T. Rogers and D. G. Farnum for stimulating discussions.

(14) H. Hogeveen and C. J. Gaasbeek, *Recl. Trav. Chim. Pays-Bas*, **88**, 367 (1969).

(15) R. K. Lustgarten, M. Brookhart, and S. Winstein, *J. Amer. Chem. Soc.*, **89**, 6350 (1967).

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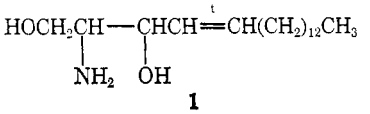
A Stereoselective Synthesis of D-*erythro*-Sphingosine

Sir:

We would like to report a short, highly stereoselective synthesis of D-*erythro*-sphingosine (**1**) (1,3-dihydroxy-

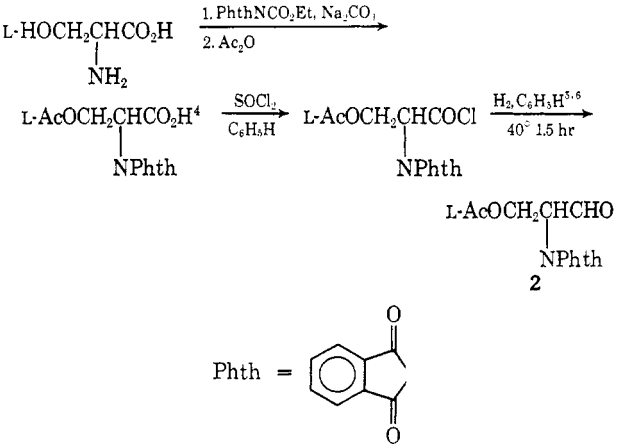


1

2-aminooctadec-2-*trans*-ene), the most widely occurring of the sphingolipid bases.[1] The attractive features of this novel synthesis, not shared in combination by those previously reported,[2] are its brevity, the direct formation of a chiral product with predominantly the correct stereochemistry, and its potential for ready adaptation to the synthesis of other homologs, ceramides, cerebrosides, and more complex sphingolipids.

The synthesis involves the simple conversion of the commercially available L-serine whose chiral center corresponds to that of sphingosine (**1**)[3] to the L-aldehyde **2**[7] by N-phthaloylation, O-acetylation, acid chloride formation, and catalytic hydrogenation as indicated in Scheme I.

Scheme I



Addition (*ca.* 15 min) of 6.6 g of the chiral aldehyde **2**[7] in 30 ml of benzene–ether (2:1) to 0.024 mol of *trans*-pentadecenyldiisobutylalane in hexane (40 ml)[8] at 5–10° and allowing an additional hour for warming to room temperature furnished directly D-*erythro*-*O*-acetyl-*N*-phthaloylsphingosine (**3**)[9] (1.5 g) obtained as an oil, $[\alpha]_D$ +3.3° (*c* 0.37, EtOH),[10] along with the unnatural threo isomer **4** (0.4 g), mp 55–63°.[11] The

(2) The various chemical approaches to the synthesis of the sphingolipid bases reported to date have been recently reviewed: D. Schapiro, "Chemistry of Sphingolipids," Hermann, Paris, 1969.

(3) R. M. Burton, M. A. Sodd, and R. O. Brady, *J. Biol. Chem.*, **233**, 1053 (1958).

(4) J. C. Sheehan, M. Goodman, and G. P. Hess, *J. Amer. Chem. Soc.*, **78**, 1367 (1956).

(5) The conditions used are a modification of those described by W. Foye and W. E. Lange, *J. Amer. Pharm. Ass. Sci. Ed.*, **45**, 742 (1956).

(6) The optical rotation of triacetyl-D-*erythro*-sphingosine prepared from **1** obtained below ($[\alpha]_D$ −10.6° (*c* 0.3, $CHCl_3$)) is in essential agreement with the literature value (*Beilstein III*, **4**, 855) indicating that the hydrogenation of the acid chloride to produce **2** proceeded without racemization. By contrast, H. Seki, *et al.* (*Chem. Pharm. Bull.*, **20**, 361 (1972)), report that extensive racemization occurred during the catalytic hydrogenation of alkoxyformic anhydrides of *N*-acetylamino acids.

(7) Obtained as a colorless oil. A comparison of intensity ratios of the aldehydic proton and the phthaloyl and $-CH_2CH-$ protons indicated the crude product to contain *ca.* 50% of the desired aldehyde.

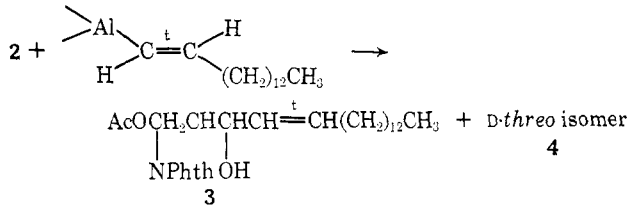
(8) H. Newman, *Tetrahedron Lett.*, 4571 (1971).

(9) The apparent change in configuration of C-2 from L in the serine derivatives to D in sphingosine and its derivatives is actually the result of a change in reference origin. In the former series, as with all amino acids, the molecule is, according to convention, oriented in two dimensions with its carboxyl group up. This puts the amino group having the L optical configuration on the left. In the latter series, the terminal OH is oriented upward. This now places the same amino function on the right, therefore, the D optical configuration.

(10) Satisfactory analytical data were obtained for this compound.

(11) After further thick-layer chromatographic purification (2-mm silica gel; C_6H_6–EtOAc, 9:1) of the product isolated from the partition chromatogram. Since Re tlc of this product still showed slight contamination with a slightly faster running impurity, its optical rotation was not measured. Unequivocal characterization of **4** was accomplished by converting it exclusively to the known *N*-acetyl-D-*threo*-sphinganine (E. F. Jenny and C. A. Grob, *Helv. Chim. Acta*, **36**, 1454 (1953)) by catalytic hydrogenation, followed by blocking group removal as described in the main discussion and then N-acetylation (by the method of R. C. Gaver and C. C. Sweeley, *J. Amer. Chem. Soc.*, **88**, 3643 (1966)).

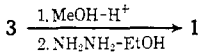
(1) For recent reviews, see: (a) K. A. Karlsson, *Lipids*, **5**, 878 (1970); (b) J. Kiss, *Advan. Carbohyd. Chem. Biochem.*, **24**, 381 (1969); (c) P. Morell and P. Braun, *J. Lipid Res.*, **13**, 293 (1972).



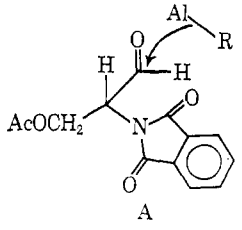
isomers were readily separated by partition chromatography.[12]

This reaction is a further example of our recently reported method[8] for the preparation of trans allylic alcohols stereospecifically from the reaction of aldehydes and ketones and vinylalanes.

Removal of the blocking groups from **3** was accomplished (96% yield) preferentially int wo stages,[13] *viz.* methanolysis in the presence of a trace of acid to remove the acetoxy substituent followed by hydrazinolysis to remove the phthaloyl group to give D-*erythro*-sphingosine (**1**).[6,14]



The aldehyde **2** showed a sharp singlet in its nmr spectrum at δ 9.68 due to the aldehyde proton, suggesting conformation A for this aldehyde, in which the



A

dihedral angle between the aldehydic proton and the one on the α carbon would be *ca.* 90° and as a result show a minimum spin–spin coupling.[16] Preferential attack of this conformation by the organometallic from the least-hindered topside as indicated by the arrow would give predominantly the erythro isomer **3**.[17]

Acknowledgments. The author thanks Mr. J. Baker for the partition chromatography, Mr. L. Brancone and staff for the microanalyses, and Mr. L. Fulmor and staff for the nmr spectra and optical rotation measurements.

(12) Celite 545 and heptane–methyl Cellosolve were the support and developing solvent system used, respectively. A third product, D-*erythro*-1-acetoxy-2-phthalimido-3-hydroxyoctadec-4-yne (i) (0.4 g), was also isolated. The order of elution from the column was first **4**, and then **3**, and finally i. All came off between 7 and 11 holdback volumes. The R_f values of these compounds were *ca.* 0.4 on tlc (silica gel; C_6H_5H–EtOAc, 9:1). (No *threo*-i was present. This compound was obtained in connection with another synthetic approach to sphingosine which we investigated (unpublished results) and would have been detected.) The formation of i is presumably the result of the reaction of some $CH_3(CH_2)_2C{\equiv}C{-}Al<$ (ii) present (formed from pentadecyne and diisobutylaluminum hydride in an acid–base reaction) and **2**. The fact that only *erythro*-i formed suggests that the reaction between ii and **2** proceeds stereospecifically. This could, not unreasonably, be attributed to the decreased reactivity of ii compared to its vinylalane analog which results in a still greater selectivity in its reaction with **2** *via* conformation A (see further on in the discussion above).

(13) Direct hydrazinolysis gave a less pure product. We speculate on the basis of its infrared spectrum which showed absorption in the carbonyl region consistent with the presence of N–Ac that direct hydrazinolysis is complicated by O → N acyl transfer which follows the preferential hydrazinolysis of the phthaloyl moiety.

(14) Obtained as a yellow waxy solid; R_f on tlc (silica gel, $CHCl_3$–MeOH–2 *N* NH_4OH, 40:10:1[16]) −0.57. Unequivocal characterization was effected by conversion to the known *O,O,N*-triacetyl-D-*erythro*-sphingosine (*Beilstein III*, **4**, 855) in 92% yield.

(15) P. B. Mendershausen and C. C. Sweeley, *Biochemistry*, **8**, 2633 (1969).

(16) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, p 49.

(17) The recent studies of Hooz[18] and our own unpublished observations indicate organoaluminum additions to carbonyl functions to involve initial coordination of the Al moiety with the carbonyl oxygen followed by attack of the organic moiety at the electron-deficient carbon of the carbonyl component.

(18) J. Hooz and R. B. Layton, *J. Amer. Chem. Soc.*, **93**, 7321 (1971).

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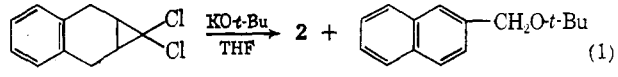
Naphtho[*b*]cyclopropene

Sir:

Although the highly strained but isolable benzocyclopropene (**1**) has been synthesized by two routes,[1] parent members of other aromatic systems incorporating linearly fused cyclopropenes are unknown.[2] We now report the synthesis of naphtho[*b*]cyclopropene (**2**), a compound expected to show a high degree of bond fixation.

1 **2**

Treatment of **3**[3] with an eightfold excess of KO-*t*-Bu in dry THF for 18 hr gives **2** (38% yield) and its solvolysis product **4**, eq 1. Purification of **2**, mp 86–87°,



3 **4** (1)

was accomplished by adsorption chromatography using Florisil (100–200 mesh) and pentane eluent followed by sublimation.

The structural assignment of **2** was based on its spectral and chemical properties: $uv_{max}^{C_6H_{12}}$ 221 nm (ϵ 58,000); ir_{max}^{KBr} 1673 (aromatic double bond) and 843, 745 cm^{-1} (aromatic); mol wt (mass spectrum) 140 (base peak). The nmr spectrum is displayed in Figure 1. The significant feature of this spectrum is the singlet at δ 7.40 assigned to the two central ring protons. Since these protons reside among the remaining four

(1) E. Vogel, W. Grimime, and S. Korte, *Tetrahedron Lett.*, 3625 (1965); W. E. Billups, A. J. Blakeney, and W. Y. Chow, *Chem. Commun.*, 1461 (1971).

(2) The synthesis of 1,1-dichloro-2,7-diphenylnaphtho[*b*]cyclopropene in low yield has just been reported; see A. R. Browne and B. Halton, *J. Chem. Soc., Chem. Commun.*, 1341 (1972). A compound originally believed to be a keto tautomer of naphtho[*b*]cyclopropenediol was later shown not to contain a three-membered ring: L. F. Fieser and M. A. Peters, *J. Amer. Chem. Soc.*, **53**, 4080 (1931); A. R. Bader and M. G. Ettlinger, *ibid.*, **75**, 730 (1953). For interesting synthetic approaches to the naphtho[*b*]cyclopropene system, see M. P. Cava and K. Narasimhan, *J. Org. Chem.*, **36**, 1419 (1971); K. Geibel and J. Heindl, *Tetrahedron Lett.*, 2133 (1970).

(3) Addition of dichlorocarbene (KO-*t*-Bu, $CHCl_3$, 5°) to 1,4-dihydronaphthalene[4] gives **3**, mp 49–51°, in 27% yield: nmr δ 1.97 (m, 2 H), 2.49–3.45 (m, 4 H), and 7.02 (s, 4 H).

(4) E. S. Cook and A. J. Hill, *J. Amer. Chem. Soc.*, **62**, 1995 (1940),