ring, indicated that the three-carbon chain of propiophenone remained intact during pyrolysis. Labeling of one of the N-methyl groups of **9** with ^{14}C, followed by pyrolysis, gave **12**, in which one-third of the original activity was retained. Thus, the γ carbon (4C) of the pyridine nucleus must be derived from the trimethylamine moiety of the quaternary fluoroborate.

Phenylazirine, which has been isolated during studies of the Neber rearrangement,[4] was not detected nor was its expected dimerization product, 2,5-diphenylpyrazine.[10] Products arising from C–N skeletal rearrangement were not detected, which implies that either the incipient intermediate **2** does not form or, if formed, it does not undergo rearrangement under the conditions used.

Investigations of the synthetic utility and mechanism of these pyrolysis reactions are being continued.

Acknowledgment. Mass spectroscopic analyses were performed by Nathan M. Ingber in the laboratories of The Standard Oil Co., Cleveland, Ohio.

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An Unequivocal Ozonide Stereoisomer Assignment

Sir:

The formation of both *cis*- and *trans*-ozonides upon ozonolysis of olefinic materials has now been reported by a number of workers.[1–8] In those cases where individual ozonide stereoisomer assignments have been reported they have been based upon some combination of infrared, nmr, glpc, and chemical reactivity data. Such a combination of data has permitted some reasonable stereoisomer designations to be made. However, it should be noted that in many cases the significant finding is a *dependence* of ozonide[1,2,5–7,9] or cross-ozonide[9] *cis–trans* ratio on olefin *geometry* rather than the specific assignments made. Such assignments are, nevertheless, equivocal, and a more exact method becomes essential in several important cases.

The surprising results reported by Schröder, for example, that *trans*-di-*t*-butylethylene gives 100% *trans*-ozonide while the *cis* isomer gives a 70:30 (*cis*:*trans*) ratio, are based, in part, on the difference in rate of reduction of the ozonides with lithium aluminum hydride, the reasonable assumption being made that the *cis* isomer is more rapidly reduced. A similar difference in rate of reaction of ozonides, this time with triphenylphosphine, was used by Lorenz and Parks[7] to distinguish between the diisopropyl ozonide isomers. Again the underlying assumption is that the *cis*-ozonide will react faster. In the diisopropyl ozonide case the assignment based on chemical reactivity correlated with the glpc data.[7] In the case of the butene-2 ozonides, however, the isomer with the longer glpc retention time, *i.e.*, the alleged *cis* isomer, reacted more slowly with triphenylphosphine. Existing stereoisomer assignments must be regarded as tentative, therefore, with a consequent reduction in their value to the ozonolysis mechanism problem.

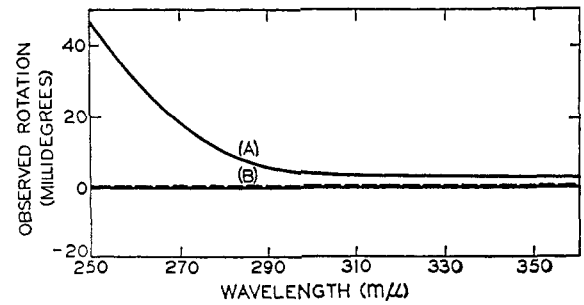

Figure 1. Optical rotatory dispersion curves of the isomeric ozonides of 2,5-dimethylhexene-3 after reaction with brucine. Isomer A is necessarily assigned the *trans* configuration, and B the *cis* configuration.

With increasing attention being given to the use of ozonide *cis*:*trans* ratios as a means of investigating the mechanism of ozonolysis,[9,10] it has become necessary to be able to make this stereochemical assignment on an unequivocal basis. We wish to report an unequivocal assignment of ozonide stereoisomers. The method takes advantage of the fact that the *trans* isomer of a symmetrical ozonide must be a *dl* pair.

Based on our earlier observations[11] that ozonides react rapidly with amines, we have treated each isomer of 2,5-dimethylhexene-3 ozonide (diisopropyl ozonide, I)[12] with less than the anticipated[13] stoichiometric amount of brucine in an attempt at kinetic resolution of the true *trans* isomer. In a typical reaction 100 mg of ozonide was treated with 70 mg of brucine in dichloromethane at −70° for *ca.* 10 min. The reaction mixture was allowed to warm to room temperature and stand for 16 hr. Pentane was then added and the precipitated material filtered off. The unreacted ozonides were isolated from their mother liquors by glpc, identified by comparison with authentic samples, and investigated for optical activity. In order to magnify any optical activity developed we have run ORD curves[14] on both of the recovered ozonides. The results from a typical run are shown in Figure 1. One of the ozonide isomers (isomer A) develops a strong rotation with the beginning of a positive Cotton effect lobe while the other (isomer B) has no rotation. Isomer A is, therefore, unequivocally assigned the

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(13) The mechanism of the reaction between ozonides and amines is still not completely clear. Work on this aspect of the problem is in progress.
(14) The ORD spectra were measured on a Durrum-Jasco Model ORD/UV-5 spectrophotometer and ORD recorder using a 0.5 *M* solution of ozonide in hexane.

trans configuration. This assignment is in accord with that made previously on the basis of infrared, nmr, glpc, and chemical reactivity data. The latter criteria may now be used with more confidence for making stereoisomer assignments.

The assignments recently used[9] in speculations on a new mechanism for ozonide formation are also the correct ones; thus this hypothesis gains additional support.

Apart from its importance for the ozonide stereoisomer assignment problem, this appears to be the first example of partial resolution of a *dl*-ozonide. The fact that the active ozonide can be rerun through the gas chromatograph and retain its activity is an initial indication of its stability toward racemization.

Acknowledgment. We are very grateful to Mr. F. P. Hood, III, for his valuable assitance in making the ORD measurements, and to Dr. E. A. Chandross for helpful discussions.

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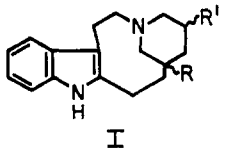
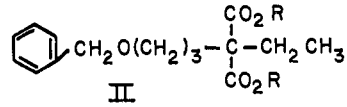
A New Total Synthesis of *dl*-Quebrachamine and *dl*-Aspidospermidine. A General Entry into the Aspidosperma Alkaloids

Sir:

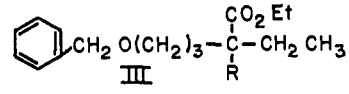
In previous communications[1-3] we described novel transannular cyclizations which provided a synthetic entry into the Aspidosperma, Vinca, and Iboga alkaloids. The complete stereospecificity of these reactions[4,5] has revealed that the compounds such as quebrachamine (I, R = Et; R′ = H), dihydrocleavamine (I, R = H; R′ = Et), and their ester derivatives occupy a central position in providing synthetic pathways to a considerable variety of alkaloids in the above classes. We now report a new total synthesis of *dl*-quebrachamine[6-8] *via* a sequence which we believe to be completely general in its application to the preparation of other nine-membered ring systems.



I



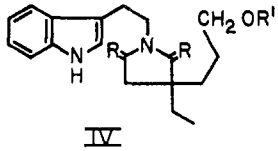
II



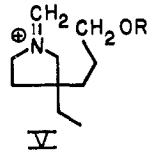
III

Ethyl γ-benzyloxypropylmalonate[9] on treatment with sodium ethoxide and ethyl iodide gave ethyl γ-benzyloxypropylethylmalonate (II, R = Et), bp 220–222° (1.5 mm), which on alkaline hydrolysis gave the diacid[10] (II, R = H), mp 117–120°. This compound was decarboxylated to the monoacid and the latter esterified to give ethyl α-(γ-benzyloxypropyl)butyrate (III, R = H), bp 156–159° (0.25 mm). Alkylation of this ester with triphenylmethylsodium and ethyl bromoacetate gave ethyl α-(γ-benzyloxypropyl)-α-ethylsuccinate (III, R = CH_2CO_2Et) as a viscous liquid.

Condensation of the succinate with tryptamine provided the succinimide (IV, R = O; R′ = $CH_2C_6H_5$), $C_{26}H_{30}N_2O_3$, which showed the following spectral properties: λ_{max}^{MeOH} 221, 275 (sh), 283, and 291 mμ; ν_{CHCl_3} 5.67 and 5.91 μ; nmr signals[11] 3.06 (doublet, α-proton on indole), 5.88 (singlet, $C_6H_5CH_2O$), 6.25 (triplet, CH_2N), 6.68 (triplet, OCH_2CH_2), 7.0 (triplet, CH_2CH_2N), 7.6 (singlet, CH_2CO), 9.27 (triplet, CH_3). Lithium aluminum hydride reduction of the latter yielded the amine (IV, R = H; R′ = $CH_2C_6H_5$) which still exhibited a normal indole absorption in the ultraviolet but had lost the characteristic imide absorption in the infrared spectrum. The molecular formula, $C_{26}H_{34}N_2O$, was established by high-resolution mass spectrometry, which provided the value 390.269 (calculated 390.267). The mass spectrum also revealed the expected fragmentation of the molecule under electron impact to provide the base peak at *m/e* 260 due to the stable ion V (R = $CH_2C_6H_5$).



IV



V

The benzyloxyamine was then treated with excess mercuric acetate in methanol–acetic acid and the crude product, without isolation, reduced immediately with sodium borohydride to give the cyclized amine (VI, R = $CH_2C_6H_5$), $C_{26}H_{32}N_2O$ (Found: mol wt, 388.251. Calcd: mol wt, 388.251): λ_{max}^{MeOH} 273 (sh), 284, and 292 mμ; no nmr signal for the α-proton on the indole ring and a two-proton singlet at τ 8.05 (N–CH_2–C<). This latter datum eliminates the alternative, sterically less favored structure VII for the cyclization product, since this compound must exhibit a multiplet for the methylene protons attached to the basic nitrogen atom. The mass spectrum of VI was completely different from that of the amine IV, and intense peaks at *m/e* 198, 184, 170, 156, etc., were noted. The fragments attributed to these peaks are well known in the mass spectra of indole alkaloids.[12]

Removal of the benzyl group was accomplished by brief treatment of VI (R = $CH_2C_6H_5$) with boron tri-

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