Revision of Azoxy Assignments in LL-BH872α and Elaiomycin Based on Circular Dichroism Studies on Synthetic Azoxy Compounds

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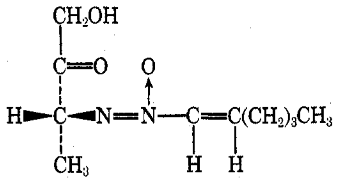
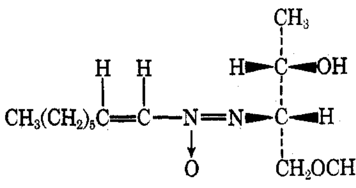
The previous cis and trans assignments of the azoxy chromophores in elaiomycin and LL-BH872α, respectively, have been shown to be in error. Both optical antipodes of *ONN*-1-cyclohexylazoxyethane have been prepared and the synthetic compounds have the same configuration of the azoxy chromophore as the two natural products as shown by CD curves. The optical antipodes of *ONN*-1-phenylazoxyethane have also been prepared. The CD curves of these materials are complex; nevertheless an assignment of the azoxy Cotton effect has been made. The rotational strength of this Cotton effect is greatly enhanced due to coupling between the azoxy and homoconjugated phenyl systems.

The antibiotics LL-BH872α and elaiomycin have been described[1] as (3*R*)-1-hydroxy-3-(1′-*cis*-hexenyl-*trans*-azoxy)-2-butanone and (2*S*,3*S*)-4-methoxy-3-(1′-*cis*-octenyl-*cis*-azoxy)-2-butanol, respectively.

The configurational assignments of the azoxy chromophores in these natural products were based on the notion that the configuration of the adjacent asymmetric carbon atoms in each material was the same (D). In fact, the carbon atoms in question are of opposite configuration. The original correlations of these asymmetric centers were made with the amino acids D-alanine[2] and D-threonine,[3] respectively, but different rather than corresponding substituents were related with the amino acid carboxyl groups. Specifically, the hydroxy methyl ketone substituent of LL-BH872α, I (which corresponds to the ethanolic substituent of elaiomycin II), was related to the carboxyl group of D-alanine while the methyl methyl ether of substituent of II (corresponding to the methyl substituent of I) was related to the carboxyl group of D-threonine. This pitfall, although overlooked in the original assignments of configuration in LL-BH872α and elaiomycin, is well known,[4] and Neuberger[5] suggested a simple method to avoid it, namely, that in correlations with amino acids the substituent of the higher state of oxidation should be deemed to have been formed by replacing the carboxyl group of the amino acid. Since the asymmetric carbon atoms adjacent to the azoxy chromophores in I and II are of opposite absolute configuration, the observed opposite Cotton effects of azoxy chromophores in these compounds are normal and the invocation of opposite configurations of these chromophores was in error.

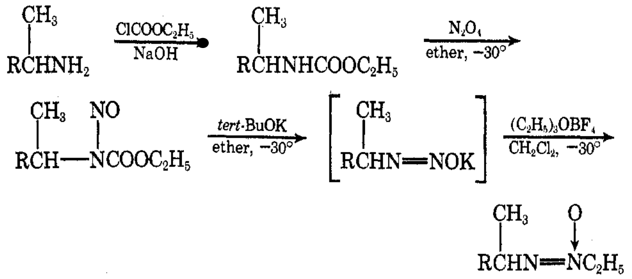


I



II

Recently Moss and Landon[6] described useful methods which are outlined below for the preparation of azoxy compounds. With the idea in mind of examining the azoxy assignments in the antibiotics I and II, we prepared both optical antipodes of the azoxy compounds where the R substituents were cyclohexyl and phenyl groups, respectively.

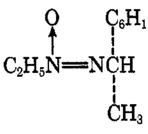


$$R\overset{CH_3}{\overset{|}{C}}HNH_2 \xrightarrow[NaOH]{ClCOOC_2H_5} R\overset{CH_3}{\overset{|}{C}}HNHCOOC_2H_5 \xrightarrow[\text{ether, }-30^\circ]{N_2O_4}$$

$$R\overset{CH_3}{\overset{|}{C}}H{-}\overset{NO}{\overset{|}{N}}COOC_2H_5 \xrightarrow[\text{ether, }-30^\circ]{tert\text{-BuOK}} \left[R\overset{CH_3}{\overset{|}{C}}HN{=}NOK\right] \xrightarrow[CH_2Cl_2,\ -30^\circ]{(C_2H_5)_3OBF_4} R\overset{CH_3}{\overset{|}{C}}HN{=}\overset{\overset{O}{\downarrow}}{N}C_2H_5$$

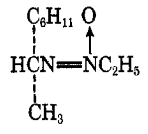
As was anticipated, we had more trouble with the isolation and purification of the cyclohexyl compound than with those of the phenyl series. The urethanes of both series were low-melting solids which yielded readily to purification by adsorption chromatography. The phenyl nitrosourethanes could be obtained analytically pure by partition chromatography over diatomaceous earth using the system heptane saturated with acetonitrile followed by low-pressure, short-path distillation. The corresponding cyclohexyl compounds were not amenable to either low pressure distillation or glc because of their instability and consequently we could not obtain analytically pure samples of these intermediates. Fortunately, the azoxy compounds of the cyclohexyl series are stable compounds and may be purified by glc.

The compounds (*S*)-*ONN*-1-cyclohexylazoxyethane[7] and its R enantiomorph are represented by the Fisher projections III and IV. The CD curves of compounds



$$C_2H_5\overset{\overset{O}{\uparrow}}{N}{=}N\overset{C_6H_{11}}{\underset{CH_3}{C}}H$$

III



$$H\overset{C_6H_{11}}{\underset{CH_3}{C}}N{=}\overset{\overset{O}{\uparrow}}{N}C_2H_5$$

IV

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[1] W. J. McGahren and M. P. Kunstmann, *J. Amer. Chem. Soc.*, **92**, 1587 (1970).

[2] W. J. McGahren and M. P. Kunstmann, *ibid.*, **91**, 2808 (1969).

[3] C. L. Stevens, B. T. Gillis, and T. H. Haskell, *ibid.*, **81**, 1435 (1959).

[4] D. W. Slocum, D. Sugarman, and S. P. Tucker, *J. Chem. Educ.*, **48**, 597 (1971).

[5] A. Neuberger, *Advan. Protein Chem.*, **4**, 297 (1948).

[6] R. A. Moss and M. J. Landon, *Tetrahedron Lett.*, 3869 (1969).

[7] NNO denotes that the group attached to NO is unprimed whereas ONN would denote that this group would be primed.[8]

[8] Former Chemical Abstracts practice as stated in the introduction to Vol. 56 (1961) defined the unprimed group as always being attached to NO.

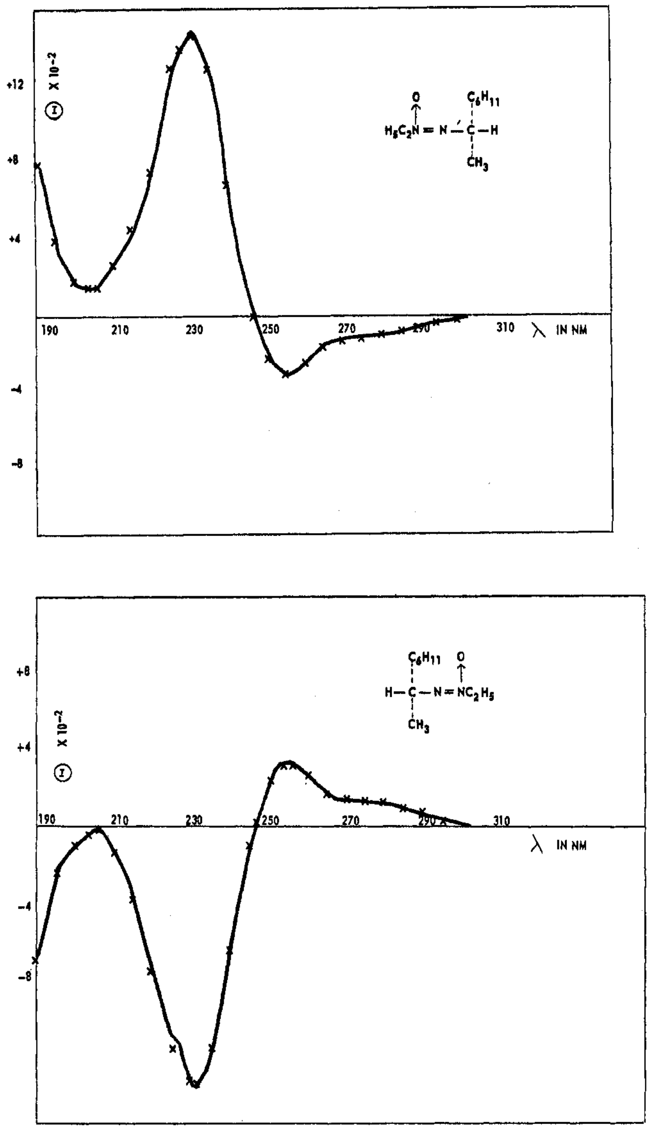


Figure 1.—CD curves of (*S*)-*ONN*-1-cyclohexylazoxyethane (above) and (*R*)-*ONN*-1-cyclohexylazoxyethane (below) in cyclohexane.

III and IV are shown in Figure 1. The S compound III has a Cotton effect $[\theta]_{232}$ $+1.47 \times 10^3$, which matches in sign, location, and magnitude that of II.[1] The antipodal IV has a Cotton effect $[\theta]_{232}$ -1.36×10^3, which corresponds in location and sign with that of I. This agreement between the signs and locations of the Cotton effects of the two natural products with those of the corresponding synthetic antipodal azoxy compounds establishes beyond reasonable doubt the same configuration for all four azoxy chromophores. As indicated by Freeman,[9] this configuration is most likely to be the trans form.

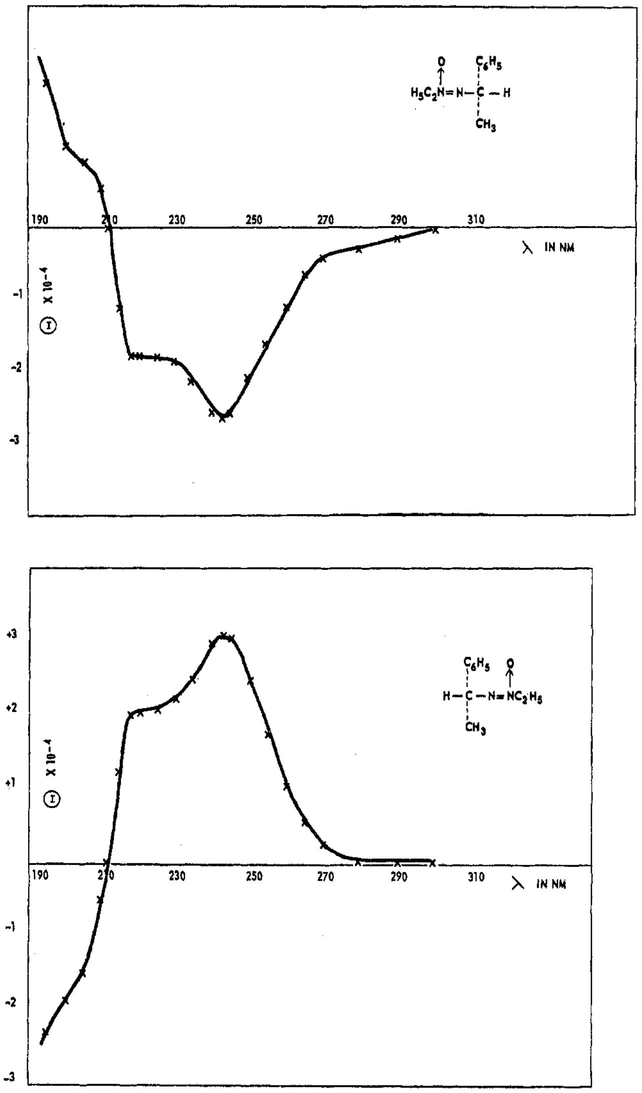
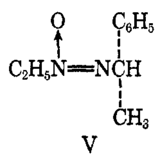
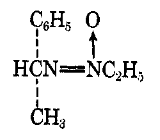


Figure 2.—CD curves of (*S*)-*ONN*-1-phenylazoxyethane (above) and (*R*)-*ONN*-1-phenylazoxyethane (below) in cyclohexane.


$C_2H_5\overset{\overset{O}{\uparrow}}{N}{=}N\underset{CH_3}{\overset{C_6H_5}{CH}}$

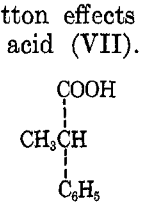
V


$H\underset{CH_3}{\overset{C_6H_5}{C}}N{=}\overset{\overset{O}{\uparrow}}{N}C_2H_5$

VI

The compound (*S*)-*ONN*-1-phenylazoxyethane and its R antipode are given by projections V and VI, respectively, and the CD curves of these materials are illustrated in Figure 2. The uv curve of V or VI shows a strong band at about 210 nm due to the phenyl chromophore which swamps out the azoxy band normally observed around 220 nm. The CD curves are complicated by the presence of Cotton effects due to both chromophores. Similar difficulties have been encountered with regard to the observed Cotton effects in the 200–220 nm region of α-substituted phenylactic acids.[10,11]

Recently, definite assignments[12] have been made for the observed Cotton effects in the CD curve of (*S*)-(+)-hydratropic acid (VII). The strongly positive band at 223 nm is attributed to the n → π* transition of the carboxyl group, while the Cotton effect at 205 nm is said to be due to a π → π* phenyl transition.


$CH_3\underset{C_6H_5}{\overset{COOH}{CH}}$

VII

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[9] J. P. Freeman, *J. Org. Chem.*, **28**, 2508 (1963).

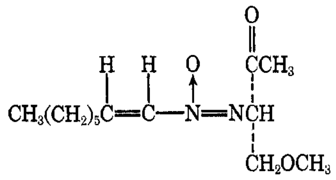
[10] L. Verbit and P. J. Heffron, *Tetrahedron*, **24**, 1231 (1968).

[11] M. Sakota, K. Okita, and Y. Matsui, *Bull. Chem. Soc. Jap.*, **43**, 1138 (1970).

[12] O. Cervinka, L. Hub, and G. Snatzke, *Collect. Czech. Chem. Commun.*, **36**, 1687 (1971).

Two strong positive Cotton effects are clearly visible in the CD curve of VI and possibly two strong negative bands are at least partially visible. We assign the $[\theta]_{220}$ $+2.05 \times 10^4$ effect to the $\pi \rightarrow \pi^*$ transition of the azoxy chromophore. In the more polar trifluoroethanol solvent this Cotton effect moves to $[\theta]_{213}$ $+2.09 \times 10^4$. A blue shift such as this is normally diagnostic of an $n \rightarrow \pi^*$ transition[13] except in the case of certain heteropolar systems.[14]

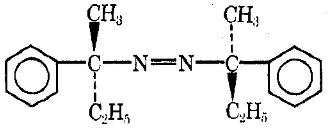
The shift observed here exactly parallels that of the azoxy chromophore of VIII,[1] which moved from 237 nm in cyclohexane to 230 nm in trifluoroethanol. Hence, the assignment of the 220 nm Cotton effect in the curve of VI to the azoxy chromophore is reasonable and it follows that the large effect $[\theta]_{243}$ $+3.14 \times 10^4$ belongs to the phenyl chromophore. In the more polar solvent this band appears at $[\theta]_{242}$ $+2.97 \times 10^4$ and it may be assigned to the phenyl ^1L_b[15] band, since this weak $\pi \rightarrow \pi^*$ transition is normally insensitive to solvent change or blue shifted in more polar solvents.[13]



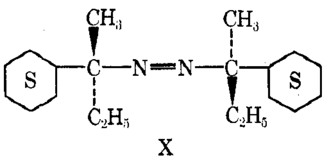
$CH_3(CH_2)_5\overset{H}{C}{=}\overset{H}{C}{-}\overset{O}{\overset{\uparrow}{N}}{=}N\underset{CH_2OCH_3}{C}H{-}\overset{O}{\overset{\|}{C}}CH_3$

VIII

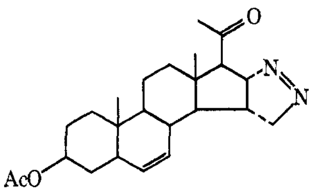
The azoxy Cotton effects of V and VI are about an order of magnitude greater than those exhibited by the same chromophore in II, III, and IV and about the same size as that of I. The enhanced Cotton effect of I[1] was shown to be due to coupling between the azoxy and carbonyl systems. In a similar manner, it can be argued that the enhanced effects in V and VI are due to coupling between the azoxy and homoconjugated phenyl systems. Severn and Kosower[16] prepared and studied the CD curves of the two optically active *trans*-dialkyldiazenes IX and X. The Cotton effects due to the azochromophores of IX and X are approximately given by $[\theta]_{382}$ $+2700$ and $[\theta]_{379}$ $+4200$, respectively. Hence, there is no effective coupling between the $n \rightarrow \pi^*$ transition and the homoconjugated π system, probably because of the large energy difference between the systems. On the other hand, the pyrazoline steroid XI shows unusual rotational strength[17] due to interaction between the azo and carbonyl systems where the energy differences are not so great. In comparing the CD curves of V and VI with those of III and IV and the natural products I and II it is evident that the presence of a phenyl substituent on the asymmetric center inverts the sign of the azoxy Cotton effect. It is well known that the concept which claims that structurally similar compounds of the same absolute configuration give Cotton effects of the same sign[18] is not so clear-cut when one of the substituents is a phenyl group. Brewster and Buta[19] observed that configurationally related 1-substituted indans and α-substituted phenylethyl compounds have ORD curves of mirror image shape.



IX

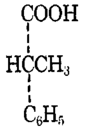


X



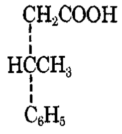
XI

Verbit, *et al.*,[20] have shown that the configurationally related acids XII and XIII have Cotton effects in the 230 nm region which are virtually mirror images of each other. The same authors have examined the $n \rightarrow \pi^*$ carbonyl Cotton effect of XIV and found it to be of opposite sign to that of carbonyl Cotton effect of XV. On the other hand, Verbit and Heffron[10] found that both (*S*)-(+)-α-hydroxyphenylacetic acid and (*S*)-(−)-α-hydroxy-4-methylpentanoic acid have Cotton effects of the same sign in the 220 nm region. It is also evident from the CD curve of VI that the Cotton effect attributed to the ^1L_b band of the phenyl chromophore is inverted while the effect due to the ^1L_a band of the same chromophore is not in comparison with the Cotton effects of the corresponding transitions in (*R*)-α-phenylethylamine (Figure 3).



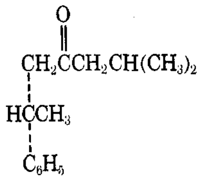
$COOH{-}CH(CH_3){-}C_6H_5$

XII



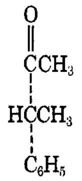
$CH_2COOH{-}CH(CH_3){-}C_6H_5$

XIII



$CH_2\overset{O}{\overset{\|}{C}}CH_2CH(CH_3)_2{-}CH(CH_3){-}C_6H_5$

XIV



$\overset{O}{\overset{\|}{C}}CH_3{-}CH(CH_3){-}C_6H_5$

XV

The cyclohexylazoxy compounds III and IV each give double-humped CD curves as did the natural compounds I and II. An equilibrium involving solvated and unsolvated forms[1,21] reasonably accounted for the appearance of the two oppositely signed CD absorptions of I and II. The CD reversals observed for III and IV do not fit this pattern so well, as the separation of the reverse effects in each curve is about

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[13] H. McConnell, *J. Chem. Phys.*, **20**, 700 (1952).

[14] J. W. Sidman, *Chem. Rev.*, 689 (1958).

[15] P. E. Stevenson, *J. Chem. Educ.*, **41**, 234 (1964).

[16] D. J. Severn and E. M. Kosower, *J. Amer. Chem. Soc.*, **91**, 1710 (1969).

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[19] J. H. Brewster and J. G. Buta, *J. Amer. Chem. Soc.*, **88**, 2233 (1966).

[20] L. Verbit, A. S. Rao, and J. W. Clark-Lewis, *Tetrahedron*, **24**, 5839 (1968).

[21] K. M. Wellman, P. H. A. Laur, W. S. Briggs, A. Moscowitz, and C. Djerassi, *J. Amer. Chem. Soc.*, **87**, 66 (1965).

24 nm instead of the expected 28–32 nm. Severn and Kosower[16] have put forward another explanation of CD reversal based on the assumption that transition from low-energy ground state to low-energy excited state has opposite polarizability to the transition from low-energy ground state to high-level excited state. The argument is developed in connection with an n → π* transition but presumably should apply equally well to a π → π* transition except that in such a case the reverse effect would be observed on the long wavelength side.

Experimental Section[22]

Tlc was carried out on 0.25 mm silica gel plates from Brinkmann Instruments. Developing solutions varied from 5 to 40% ethyl acetate in hexane. Organic solutions were dried over anhydrous $MgSO_4$ and distillation of small quantities of oils was carried out on a Kugelrohr. CD data were obtained on a Cary 60 spectropolarimeter with CD attachment. Pertinent data are given in Table I.

TABLE I

Compd	Concn, mg/ml	Sensitivity	Cell width, mm	Solvent
XVI	1.29	0.1	0.1	Cyclohexane
XVII	1.13	0.1	0.1	Cyclohexane
XVI	1.14	0.1	0.1	Trifluoroethanol
XV	8.40	0.1 and 0.2	0.1	Cyclohexane
XIV	8.00	0.1 and 0.2	0.1	Cyclohexane
(*R*)-α-Phenylethylamine	4.96	0.1	0.5	Cyclohexane
(*R*)-α-Phenylethylamine	1.24	0.04	0.1	Cyclohexane

Urethans from α-Phenylethylamines.[24]—The literature procedure was followed using 6.4 ml (50 mmol) of (*R*)-α-phenylethylamine to get 6.5 g of crude product which was purified by passage over Davison 62 grade silica gel using 10% ethyl acetate in hexane as eluting solvent. The analytical sample was obtained by distillation at 100° under 80 μ pressure to get a colorless oil which solidified at room temperature: $[\alpha]^{25}\text{D}$ +82.5 ± 0.19° (*c* 1.032, MeOH); $\lambda_{\max}^{\text{MeOH}}$ 209 nm (ε 1600) and 257 (57); nmr (CCl_4) δ 1.18 (3 H, triplet, *J* = 7 Hz, $\text{-OCH}_2\text{CH}_3$), 1.45 (3 H, doublet, *J* = 7 Hz, α-CH_3), 4.08 (2 H, quartet, *J* = 7 Hz, $\text{-OCH}_2\text{CH}_3$), 4.88 (1 H, quartet, *J* = 7 Hz, benzylic proton), 5.03 (1 H, broad exchangeable signal, NH), and 7.30 (5 H, singlet, aromatic protons).

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.24; H, 7.85; N, 7.18.

The urethan from (*S*)-α-phenylethylamine had $[\alpha]^{25}\text{D}$ −82.0 ± 0.34° (*c* 0.587, MeOH).

Nitroso-α-phenylurethans.—The procedure of Moss[25] and White[26] was followed using 4.0 g (just under 21 mmol) of (*S*)-α-phenylethylurethan. The crude reaction product was partially purified by silica gel chromatography using 5% ethyl acetate in hexane as eluting solvent. About 500 mg of the partially purified product was subjected to partition chromatography over 200 g of acid-washed diatomaceous earth using the system heptane saturated with CH_3CN. The nitroso carbamate was recovered from the second holdback volume as a yellow oil which could be distilled at 75° under 70 μ pressure: $[\alpha]^{25}\text{D}$ −310 ± 0.18° (*c* 1.115, MeOH); nmr (CCl_4) δ 1.37 (3 H, triplet, *J* = 7 Hz, $\text{-OCH}_2\text{CH}_3$), 1.62 (3 H, doublet, *J* = 7 Hz, α-CH_3), 4.60 (2 H, quartet, *J* = 7 Hz, $\text{-OCH}_2\text{CH}_3$), 5.95 (1 H, quartet, *J* = 7 Hz, benzylic proton), and 7.12 (5 Hz, singlet, aromatic protons).

Anal. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.00. Found: C, 59.74; H, 6.30; N, 12.20.

***ONN*-1-Phenylazoxyethanes.**—About 2.6 g of *tert*-BuOK were stirred in 30 ml of ether and cooled to −30° under positive nitrogen pressure. About 2.8 g (13 mmol) of (*R*)-nitroso-α-phenylethylurethan was added through a septum using a syringe. The ether was evaporated off by increasing the nitrogen flow and then 50 ml of dry CH_2Cl_2 was added. About five or six 1-g aliquots of $(C_2H_5)_3OBF_4$ were added from an ether suspension (reagent is supplied by Baker as a solid under ether). Stirring was continued for 2 hr. The organic layer was extracted with H_2O, dried, and evaporated to 1.2 g of faintly yellow oil. Passage over silica gel and elution with 10% ethyl acetate in hexane gave 970 mg of nearly colorless oil. Further purification was effected by partition chromatography over 180 g of acid-washed diatomaceous earth using the heptane-CH_3CN system, yield 600 mg. For analytical and CD purposes, a small sample was distilled at 65° under 70 μ pressure to get a colorless, mobile liquid which spectral data showed to be (*R*)-*ONN*-1-phenylazoxyethane (VI): mass spectrum *m/e* 178; $[\alpha]^{25}\text{D}$ +139.5 ± 0.19° (*c* 1.049, MeOH); $\lambda_{\max}^{\text{MeOH}}$ 210 nm (ε 11,700); nmr (CCl_4) 1.48 (6 H, distorted triplet, *J* = 7 Hz, $\text{-N}(\rightarrow\text{O})\text{CH}_2\text{CH}_3$ and α-CH_3), 4.10 (2 H, quartet, *J* = 7 Hz, $\text{-N}(\rightarrow\text{O})\text{CH}_2\text{CH}_3$), 5.01 (1 H, quartet, *J* = 7 Hz, benzylic proton), and 7.17 (5 H, singlet, aromatic protons).

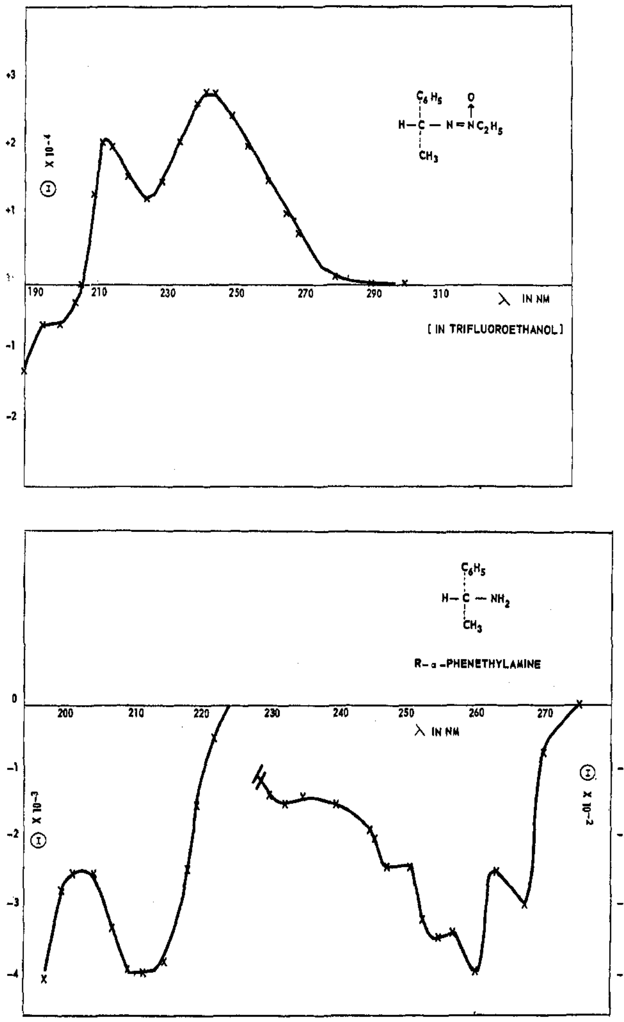

Figure 3.—CD curves of (*R*)-*ONN*-1-phenylazoxyethane (above) in trifluoroethanol and (*R*)-α-phenylethylamine (below) in cyclohexane.

Anal. Calcd for $C_{10}H_{14}N_2O$: C, 67.38; H, 7.92; N, 15.72. Found: C, 67.15; H, 8.13; N, 16.14.

The other isomer, (*S*)-*ONN*-1-phenylazoxyethane (V), had $[\alpha]^{25}\text{D}$ −141.4 ± 0.3° (*c* 0.654, MeOH).

Reduction of α-Phenylethylamines.—Some methods recommended for the reduction of the aromatic ring in compounds of this type in our hands gave only partial reduction.[27,28] A slight modification of Leithe's procedure gave the best results. About 12.8 ml of (*R*)-α-phenylethylamine in 50 ml of acetic

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[22] The optically active amines were purchased from Aldrich. Isomer *l*(−)-α-methylbenzylamine, which we call (*S*)-α-phenylethylamine, had $[\alpha]^{25}\text{D}$ −39.65 ±0.002° (neat). The other isomer, *d*(+)-α-methylbenzylamine, had $[\alpha]^{25}\text{D}$ +38.7 ±0.002° (neat) [lit.[23] $[\alpha]^{25}\text{D}$ +40.7° (neat)].

[23] W. Leithe, *Ber.*, **65**, 660 (1932).

[24] A. H. Blatt, Ed., "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1963, p 278.

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acid together with 2.5 g of PtO_2 catalyst were hydrogenated in a Parr shaker for 12 hr to get about 98% of theoretical hydrogen uptake. The acetic acid filtrate was diluted with ether and then with 4 *N* NaOH until the system was alkaline. The ether phase was recovered, dried, and evaporated to 12.0 g of faintly yellow oil. On exposure of this oil for any length of time in the laboratory, fine white crystals began to form on the surface of the container. An oxalate of the material prepared as described by Leithe[23] gave white crystals, mp 136° (lit.[23] 132°). A sample of the oxalate was added to water–ether (50:50) and 4 *N* NaOH was added until the system was strongly basic. The ether layer was processed to give a colorless oil. About 0.5 g of this oil was added to 20 ml of 5% NaOH solution and 2 ml of benzoyl chloride were added wtih stirring. The precipitate was recovered, taken up in ethyl acetate, dried, and worked up to give 500 mg of crystals: mp 158.5° (lit.[23] 162°); $[\alpha]^{25}\mathrm{D}$ $-21.3 \pm 0.06°$ (*c* 3.49, MeOH) (lit.[23] 19.2° for the other isomer).

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.92; H, 9.09; N, 5.92.

(*S*)-α-Cyclohexylethylamine was obtained in the same way. The *N*-benzoyl derivative melted at 159° and had $[\alpha]^{25}\mathrm{D}$ $+20.9 \pm 0.07°$ (*c* 2.57, MeOH).

α-Cyclohexylethylurethans.—These materials were prepared in the same fashion as the α-phenylethylurethans. The following physical data were obtained on the material (*R*)-α-cyclohexylethylurethan: mp 49–50°; $[\alpha]^{25}\mathrm{D}$ $+13.8 \pm 0.2°$ (*c* 1.043, MeOH); nmr (CCl_4) δ 1.09 (3 H, doublet, *J* = 7 Hz, α-CH_3), 1.23 (3 H, triplet, *J* = 7 Hz, -OCH_2CH_3) (the doublet and triplet appear as five lines on a broad base signal which integrates for 12 protons, that is, two CH_3 and six axial protons), 1.75 (5 H, broad signal for equatorial protons), 3.53 (1 H, broad signal for α-H), 4.08 (2 H, quartet, *J* = 7 Hz, -OCH_2CH_3), and 4.53 (1 H, broad exchangeable signal for NH).

Anal. Calcd for $C_{11}H_{21}NO_2$: C, 66.29; H, 7.03; N, 10.62. Found: C, 66.47; H, 7.07; N, 10.85.

The (*S*)-α-cyclohexylurethan had mp 51–52° and $[\alpha]^{25}\mathrm{D}$ $-14.32 \pm 0.09°$ (*c* 2.192, MeOH).

Nitroso-α-cyclohexylethylurethans.—The methods described for the syntheses of nitroso-α-phenylurethans were used. The corresponding cyclohexyl compounds could be passed over silica gel to get golden oils which appeared as single spots by tlc using 10% ethyl acetate in hexane developer. At this stage data on (*R*)-nitroso-α-cyclohexylethylurethan were as follows: $[\alpha]^{25}\mathrm{D}$ $+51.0 \pm 0.35°$ (*c* 0.56, MeOH); nmr (CCl_4) δ 1.00 (3 H, doublet, *J* = 7 Hz, α-CH_3), 1.45 (3 H, triplet, *J* = 7 Hz, -OCH_2CH_3) (these five lines appeared on broad base signals integrating for 21 protons which includes the axial and equatorial protons plus impurity), 4.18 (1 H, multiplet, α-H) and 4.47 (2 H, quartet, *J* = 7 Hz, -OCH_2CH_3).

Anal. Calcd for $C_{11}H_{20}N_2O_3$: C, 57.89; H, 8.77; N, 12.28. Found: C, 59.58; H, 9.24; N, 11.40.

These nitroso compounds could not be purified by partition chromatography since, because of their low polarity, they moved at the solvent front. Attempts to purify them by glc resulted in decomposition; consequently no analytically pure samples were obtained.

***ONN*-1-cyclohexylazoxyethanes.**—These materials were prepared as described for the corresponding phenyl compounds. Some purification was effected by silica gel chromatography but the ir spectrum of the material off the silica gel column had a carbonyl peak at 1730 cm^{-1} in addition to a strong azoxy peak at 1495 cm^{-1}. Glc using a 10-in. 10% SF-96 column gave the pure isomers.

For the material (*R*)-*ONN*-1-cyclohexylazoxyethane (III) the following physical data were obtained: mass spectrum *m/e* 184; $[\alpha]^{25}\mathrm{D}$ $-38.24 \pm 0.19°$ (*c* 1.025, MeOH); λ_{max}^{MeOH} 223 nm (ε 8200); nmr (CCl_4) δ 0.97 (3 H, doublet *J* = 7 Hz, α-CH_3) (this doublet appeared as two lines on a broad base signal accounting for the six axial protons), 1.47 (3 H, triplet, *J* = 7 Hz, $-N(\rightarrow O)CH_2CH_3$) (this triplet appeared as three lines on a broad base signal accounting for five equatorial protons), 3.80 (1 H, broad multiplet, α-H), and 4.08 (2 H, quartet, *J* = 7 Hz, $-N(\rightarrow O)CH_2CH_3$).

Anal. Calcd for $C_{10}H_{20}N_2O$: C, 65.17; H, 10.94; N, 15.20. Found: C, 64.81; H, 10.94; N, 14.77.

The material (*S*)-*ONN*-1-cyclohexylazoxyethane had *m/e* 184 in the mass spectrum and $[\alpha]^{25}\mathrm{D}$ $+36.00 \pm 0.55°$ (*c* 0.358, MeOH).

Registry No.—I, 24397-77-1; II, 23315-05-1; III, 33290-09-4; V, 33325-77-8; VI, 33290-10-7; urethan of (*R*)-α-phenylethylamine, 14185-43-4; urethan of (*S*)-α-phenylethylamine, 33290-12-9; nitroso-α-phenylurethans, 33290-13-0; (*S*)-α-cyclohexylethylamine *N*-benzoyl derivative, 33325-78-9; (*R*)-α-cyclohexylethylurethan, 33290-14-1; (*S*)-α-cyclohexylethylurethan, 33290-15-2; (*R*)-nitroso-α-cyclohexylethylurethan, 33364-43-1; (*S*)-*ONN*-1-cyclohexylazoxyethane, 33290-16-3.

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Woodhousin, a New Germacranolide from *Bahia woodhousei* (Gray) Gray[1]

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The isolation and structure determination of a new complex germacranolide, woodhousin (1), from *Bahia woodhousei* (Gray) Gray is reported. Jaceidin (4′,5,7-trihydroxy-3,3′,6-trimethoxyflavone) was also found. No homogeneous lactone component could be isolated from *Bahia dissecta* (Gray) Britton.

Earlier investigations of representatives of the genus *Bahia* (tribe Helenieae, Compositae) resulted in the isolation of several closely related guaianolides.[2,3] We now report isolation and structure determination of a new relatively complex germacranolide woodhousin from *Bahia woodhousei* (Gray) Gray,[4] which also contains the flavone jaceidin (4′,5,7-trihydroxy-3,3′,6-trimethoxyflavone).[5–7]

Woodhousin, $C_{21}H_{28}O_8$, mp 183–184.5°, $[\alpha]\mathrm{D}$ $-206.3°$, was a conjugated γ-lactone (ir bands at 1765 and 1662 cm^{-1}; strong uv end absorption). The nmr spectrum (Table I) exhibited the typical two doublets of H_a and H_b in partial structure A. Spin decoupling experiments involving H_a and H_b established the loca-

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