tion with the composition data, is consistent with a structure in which all six of the amino groups from three molecules of I are octahedrally coordinated with sodium.

Finally, it is significant that the *meso* isomer of I does not precipitate sodium chloride. A coordination structure in which I acts as a bidentate requires that it be in an eclipsed conformation. The apparent inability of the *meso* isomer to coordinate may be due to the higher energy of its eclipsed conformer compared to that of the racemate.

We have also found that good yields of crystalline adducts are formed with sodium bromide, iodide, nitrate, and azide, but not with sodium carbonate, sulfate, sulfide, or acetate. Certain halides of potassium, rubidium, and cesium, but not calcium or barium, also form adducts with I and will be discussed elsewhere.

Acknowledgment. We wish to thank the Research Corporation for a Frederick Gardner Cottrell Grant in support of this work and Professor D. P. Miller for the X-ray examination.

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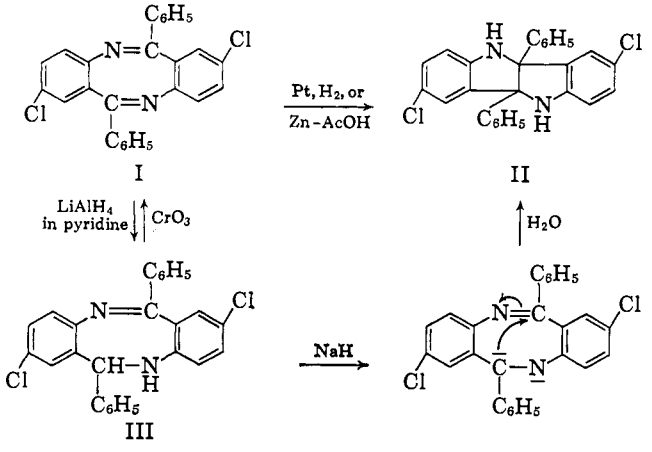
Transannular Reactions in the Dibenzodiazocine Series

Sir:

We wish to report the formation of compounds of the indoloindole type II from the dibenzodiazocine I. Compound I, mp 217–219° (*Anal.* Calcd for $C_{26}H_{16}Cl_2N_2$: C, 73.08; H, 3.77; N, 6.56; mol wt, 427.3. Found: C, 73.37; H, 3.86; N, 6.75; mol wt, 445, by thermoosmosis), λ_{max} (2-propanol) 260 (ϵ 38,000), shoulder at approximately 320 mμ (ϵ 6,000), was obtained from the corresponding *o*-aminobenzophenone in almost 90% yield on treatment with Lewis acids in inert solvents.[1]



When compound I was hydrogenated (Pt, 25°, 1 atm) in acetic acid containing hydrogen chloride, only 1 mole of hydrogen was consumed. A product (II), mp 228–230°, was isolated in 88% yield and was stable to further hydrogenation. The same product was obtained on reduction of I with zinc in acetic acid. Its nmr spectrum in THF-d_8[2] showed two exchangeable protons (δ = 6.23 ppm) but no indication of aliphatic protons. It is, therefore, proposed that this product was formed by a transannular ring closure and possesses structure II, λ_{max} (2-propanol) 248 (ϵ 25,000) and 315 mμ (ϵ 5500). *Anal.* Calcd for $C_{26}H_{18}Cl_2N_2$: C, 72.73; H, 4.22; Cl, 16.52. Found: C, 72.62; H, 4.37; Cl, 16.30. The relative position of the phenyl groups is assumed to be *cis* because of the steric requirements for the ring junctions. As expected, a diacetyl derivative, mp 299–301°, was formed with acetic anhydride and boron fluoride.

Reduction of I with lithium aluminum hydride in pyridine gave the isomeric dihydro derivative III in 78% yield; λ_{max} (2-propanol) 257 (ϵ 30,000) and 320 mμ (ϵ 5000). *Anal.* Found: C, 72.92; H, 4.42; Cl, 16.39. This compound formed a monoacetyl derivative. The structure of III was proved by reoxidation to the starting material I and by further reduction to a pair of diastereomeric tetrahydro derivatives of I which will be discussed in detail in a forthcoming publication.

It was found that compound III, by treatment with sodium hydride (2 equiv) in dimethylformamide and subsequent work-up, gave II in 88% yield. This transannular carbanion rearrangement constitutes an alternate route to compounds of type II and offers additional proof for the indoloindole structure. That this is a general reaction for the dihydrodibenzodiazocine ring was shown by the fact that the N-methyl derivative of III also gave the corresponding mono-N-methyl analog of II under the same conditions.

Acknowledgments. The authors wish to thank Professors G. Büchi and W. G. Dauben for valuable discussions.

(1) A. Sondheimer, *Chem. Ber.*, **29**, 1272 (1896), described the preparation of diphenyldibenzodiazocine by heating 2-aminobenzophenone hydrochloride. A general method for the preparation of I and various analogs in good yields will be published shortly.

(2) The nmr spectra were taken by Dr. E. Billeter using a Varian A-60 spectrometer at 60 Mc/sec.

(3) Originally submitted in this form on April 9, 1964.

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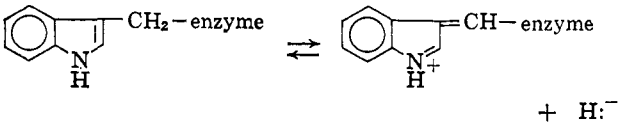
Reactions of an Indolenine Salt as a Possible Model for Dehydrogenase Enzymes[1]

Sir:

Studies of the mechanism of hydrogen transfer catalyzed by yeast alcohol dehydrogenase had led to the hypothesis that a tryptophan residue participated in the enzymatic reaction by means of a reversible dehydrogenation to an indolenine salt (3H-indolylidenemethane).



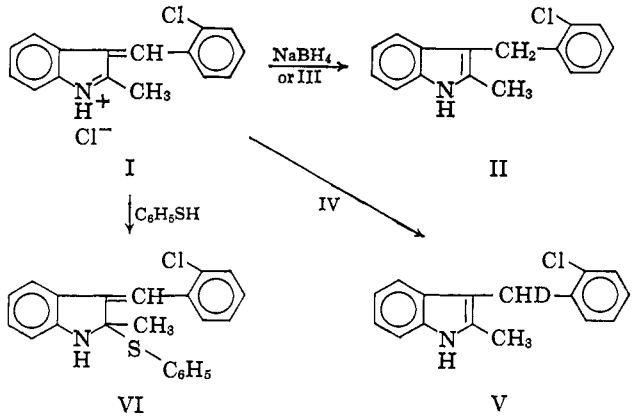
The evidence for this hypothesis consisted in the finding of tritium-labeled transferred hydrogen in the meth-

(1) Supported by Research Grant GM-11799 from the National Institutes of Health.

ylene group of tryptophan after appropriate interruption of the enzymatic reaction and hydrolysis of the protein.[2] Preliminary study of rabbit muscle lactate dehydrogenase has recently given an entirely similar result, suggesting a possible generality of the reaction.

We wish to report here (Scheme I) some reactions of an indolenine salt that might serve as a "model" for the

Scheme I



enzyme reactions. The indolenine salt I was readily reduced to the indole II by sodium borohydride or by 1-benzyl-1,4-dihydronicotinamide (III). Reduction of I by 1-benzyl-1,4-dideuterionicotinamide (IV) gave the indole V with deuterium in the methylene group, analogous to the enzymic tritium transfer[2] and to the direct transfer of hydrogen in other "model" reductions.[3-6] Mercaptobenzene added to the indolenine I to give the stable adduct VI. A corresponding addition of a cysteine sulfhydryl group to the tryptophan-derived indolenine in the native enzyme could stabilize the structure; such an adduct would presumably be dissociated to the reactive species by an alteration of protein conformation on binding of coenzyme and substrate to the enzyme.

Compound I was synthesized according to Burr and Gortner[7] in 63% yield, golden needles, mp 189–191° dec, lit.[7] 192°; infrared ν_{max}^{KBr} 2325, 1903, and 1627 cm^{-1}. *Anal.* Calcd for $C_{16}H_{13}Cl_2N$: C, 66.22; H, 4.51; N, 4.83; Cl, 24.44. Found: C, 66.19; H, 4.64; N, 4.76; Cl, 24.31. I was stable in absolute ethanol; after heating under various conditions no reduction to II was detectable by gas chromatography; ultraviolet λ_{max}^{EtOH} 278 (ϵ 7700) and 289 mμ (ϵ 6320). More concentrated solutions in ethanol showed in addition a concentration-dependent broad peak with λ_{max} at 382 mμ (ϵ 85 at 10 m*M*, ϵ 450 at 50 m*M*). I was reduced immediately to II on dissolving the solid in a solution of $NaBH_4$ in dimethylformamide at 0°. After ether extraction, alumina chromatography, and crystallization from ethanol, II was obtained in 85% yield as colorless needles, mp 78–81°; infrared ν_{max}^{KBr} 3450 (sharp), 1625 (weak), 1463, and 1445 cm^{-1}; ultraviolet λ_{max}^{EtOH} 275 (ϵ 6550), 279 (ϵ 6640), and 290 mμ (ϵ 5670); nmr ($CDCl_3$, $-\delta$, ppm from tetramethylsilane) 2.30 (singlet, 3 H), 4.10 (singlet, 2 H), 6.9–7.4 (multiplet, 8 H), and 7.70 (broad singlet, 1 H). No detectable impurities were found by gas chromatography. *Anal.* Calcd for $C_{16}H_{14}ClN$: C, 75.15; H, 5.48; N, 5.48; Cl, 13.89. Found: C, 75.09; H, 5.60; N, 5.68; Cl, 13.94. 1-Benzyldihydronicotinamide (III) was synthesized according to Mauzerall and Westheimer,[3] and 1-benzyldideuterionicotinamide (IV) was synthesized by a recently devised procedure published elsewhere.[8] I was reduced by III when equimolar solutions in absolute ethanol were allowed to react 5 min at room temperature. The product II was obtained in 88% yield and was identified by infrared and gas chromatography. Preliminary rate studies of this reduction are shown in Table I.

Table I. Indolenine Reduction by 1-Benzyl-1,4-dihydronicotinamide[a]

I, *M*	Other components, *M*	k_2, l./mole sec
0.002	...	26
0.001	...	20
0.0002	...	21
0.0001	...	23
0.001	Thioglycol, 0.0001	17
0.001	Ferric nitrate, 0.00002	18
None	VI, 0.002	0

[a] Reactions were carried out in absolute ethanol in thermostated cuvettes at 25.0°, with III at an initial concentration of 0.0002 *M*. The disappearance of III was measured by automatically recording the change in absorbance at 354 mμ with time. Measurements over 2–4 half-lives followed the rate law $v = k_2(I)(III)$. Gas chromatographic analysis of solutions after completion of the reaction indicated the presence of the theoretical amount of the product II.

It is seen that the reduction is quite rapid, that the reaction is first order in each reactant, and that the rate is unaffected by the addition of transition metal or mercaptan, which might be expected to modify the rate if it were a free-radical chain mechanism.[9] Corresponding reduction of I by IV gave the deuterated indole V. The infrared spectrum of V was similar to II except for slight changes in the fingerprint region and a very slight peak at 4.65 μ. Deuteration of the methylene group was demonstrated by the nmr spectrum, which showed only 1 H at δ 4.10; the nmr was otherwise identical with that of II. The thio ether VI was produced when I was allowed to react 5 min at room temperature with a fourfold excess of mercaptobenzene in ethanol. After ether extraction and recrystallization from ethanol–water, the yield of colorless needles, mp 143–145°, was 75%; infrared ν_{max}^{KBr} 3450 and 1587 cm^{-1}; nmr δ 2.20 (singlet, 3 H), 6.06 (singlet, 1 H), and 7.1–8.0 (three groups of peaks, 14 H). *Anal.* Calcd for $C_{22}H_{18}ClNS$: C, 72.61; H, 4.99; Cl, 9.74; N, 3.85; S, 8.81. Found: C, 72.29; H, 4.85; Cl, 9.92; N, 3.84; S, 8.96.

These reactions of an indolenine possibly mimic only part of the enzymatic reaction, since the indolenine is

(2) K. A. Schellenberg, *J. Biol. Chem.*, 240, 1165 (1965).
(3) D. Mauzerall and F. H. Westheimer, *J. Am. Chem. Soc.*, 77, 2261 (1955).
(4) B. E. Norcross, P. E. Klinedinst, Jr., and F. H. Westheimer, *ibid.*, 84, 797 (1962), and references cited therein.
(5) D. C. Dittmer and R. A. Fouty, *ibid.*, 86, 91 (1964).
(6) K. Wallenfels and D. Hofmann, *Tetrahedron Letters*, No. 15, 10 (1959).
(7) G. O. Burr and R. A. Gortner, *J. Am. Chem. Soc.*, 46, 1224 (1924).
(8) W. S. Caughey and K. A. Schellenberg, *J. Org. Chem.*, 31, in press.
(9) K. A. Schellenberg and F. H. Westheimer, *ibid.*, 30, 1859 (1965).

only reduced by the dihydropyridine coenzyme model and not by ethanol. Other as yet undefined groups in the enzyme must then be postulated to function in the activation of substrate and in the activation of indole to permit the reverse reaction. Further studies are in progress; in particular, the effect of substituents on the phenyl group of the indolenine on the rate of reduction will be investigated.

Acknowledgment. We wish to thank Dr. D. P. Hollis for his assistance in obtaining the nmr spectra.

(10) John and Mary R. Markle Foundation Scholar in Medical Science.

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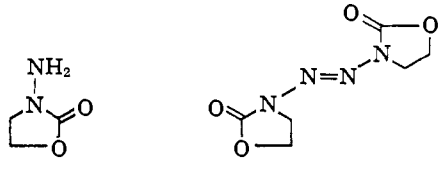
Received January 12, 1966

Stereospecific Oxidation of a 1,1-Disubstituted Hydrazine *via* Metal Ion Coordination. A New Approach to Isomeric Azo Compounds

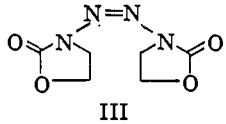
Sir:

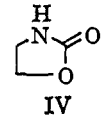
2-Tetrazenes, substituted amino derivatives of azo compounds, are capable of existing in the *cis* and *trans* forms, but to date only single isomeric products have been reported.[1-3]

We wish to report the first example of a tetrazene synthesis which affords both the *cis* and *trans* isomers. This has been accomplished by the stereospecific oxidation of the 1,1-disubstituted hydrazine, 3-amino-2-oxazolidinone (I), which results in the formation of either the *trans* (II) or *cis* (III) 3,3′-azobis(2-oxazolidinone), depending on the specific oxidizing agent used.


I

II


III


IV

Thus oxidation of I with bromine in aqueous solution, or with potassium iodate in concentrated nitric acid, or with potassium bromate in 6 *N* HCl at 5°, affords compound II, mp 298–299° (from acetonitrile), in 76, 82, and 86% yield, respectively. *Anal.* Calcd for $C_6H_8N_4O_4$: C, 36.01; H, 4.03; N, 27.97; mol wt, 200. Found: C, 36.31; H, 4.19; N, 28.06; mol wt,[4] 197.

Reaction of I with excess yellow mercuric oxide in either dry dioxane or tetrahydrofuran for several days at room temperature affords a new isomer, compound III, mp 170–171[5] (from dioxane), in 50% yield. Found: C, 36.11; H, 4.12; N, 27.91; mol wt, 199 (thermistor vapor pressure method in acetonitrile). In addition, compound II (10%) was also isolated by extraction of the mercuric oxide cake with hot acetonitrile.

The infrared spectra of compounds II and III were as expected (*e.g.*, carbonyl bands at 1765 and 1770 cm^{-1}, respectively), while the Raman spectra[6] showed –N=N– stretching frequencies at 1479 and 1474 cm^{-1}, respectively. The ultraviolet spectrum[7] of II, devoid of fine structure, contained bands at 272 mμ (ε 17,880) and a shoulder at 252 mμ (ε 9960); compound III gave bands at 290 mμ (ε 3840) and 217 mμ (ε 5980). Examination of the nmr spectrum[8] [hot $(CD_3)_2SO$] of each compound showed a pair of triplets, as would be expected on the basis of their structures. Compound II showed absorption centered at τ 3.99 ($-OCH_2-$) and at 4.58 ($-N-CH_2-$), while III absorbed at τ 3.85 ($-O-CH_2-$) and 4.50 ($-N-CH_2-$). The slight difference in chemical shift tends to confirm that these two compounds are isomeric in nature and not crystal modifications of each other.

The mass spectrometric fragmentation behavior of II and III were essentially identical. A change was observed in the position of the mass peaks during the analysis. Neither compound showed any parent ion when heated to 250°; however, peaks with *m/e* up to 390 were noted. The peak present at *m/e* 87 (assigned a relative abundance of 100%) was used to determine the relative concentration of the observed peaks; thus, for compounds II and III, respectively, *m/e* 85 (5, 26); *m/e* 59 (68, 66); *m/e* 44 (92, 99). The compounds decomposed mainly to carbon dioxide, nitrogen, and ethylene.

The densities of II and III were determined using density gradient columns and found to be 1.64 ± 0.01 and 1.159 ± 0.001, respectively, indicating a higher packing order for II due to greater symmetry. The higher order of symmetry for II was also indicated by the relative simplicity of its infrared spectrum.

Hydrogenolysis[9] of III with platinum oxide catalyst at 50° in absolute ethanol resulted in the formation of 2-oxazolidinone (IV) in 75% yield. Compound II yielded only starting material under essentially similar reaction conditions, probably due to its generally poor solubility characteristics in the solvents tested.

Convincing evidence of the isomeric nature of the two compounds was obtained by the ultraviolet light catalyzed transformation of III to II in the crystal state. The isomerization proceeded to about 40% conversion in 8 hr and the product isolated (from acetonitrile) was identical in every way with II.

(1) H. Wieland, "Die Hydrazine," Verlog von Ferdinand Enke, Stuttgart, 1913, pp 32–39.
(2) C. G. Overberger and B. S. Marks, *J. Am. Chem. Soc.*, 77, 4104 (1955); C. G. Overberger, *Record Chem. Progr.*, 21, 21 (1960).
(3) W. R. McBride and H. W. Kruse, *J. Am. Chem. Soc.*, 79, 572 (1957).
(4) An X-ray molecular weight was obtained because of the poor solubility of this compound in the usual solvents used for molecular weight determinations.
(5) Extreme care should be exercised in handling this cmpound as it explodes violently, especially at its melting point.
(6) Determination of the Raman spectrum of tetramethyl-2-tetrazene showed –N=N– absorption at 1480 cm^{-1}.
(7) Ultraviolet spectra were all determined in acetonitrile. Tetramethyl-2-tetrazene in ethanol gave bands at 277 mμ (ε 8828) and 250 mμ (ε 4849); see W. E. Bull, J. A. Seaton, and L. F. Audrieth, *J. Am. Chem. Soc.*, 80, 2516 (1958).
(8) Chemical shifts are recorded in τ values: G. V. D. Tiers, *J. Phys. Chem.*, 82, 1151 (1958); internal standard $(CH_3)_4Si$.
(9) See, for example, C. Paal and W. N. Yao, *Ber.*, 63, 57 (1930). They report the hydrogenolysis of tetraphenyltetrazene with palladium catalyst to diphenylamine.