Complex Rearrangements of the Dimer of 3-Hydroxy-2,3-dimethylindolenine[1]

VINOD DAVE AND E. W. WARNHOFF
Department of Chemistry, University of Western Ontario, London, Ontario

Received November 3, 1970

In the presence of acid the dimer **1** of 3-hydroxy-2,3-dimethylindolenine rearranges to **4**, and then via **6** to **7***a* which is cleaved to 2,3-dimethylindole (**2**) and 2-formyl-3-methylindole (**3**). If peroxides and oxygen are not excluded, two other products, **13** and **30**, are also formed. A rationalization of these reactions is offered which takes into account subtle differences in migratory aptitudes.

Le dimère **1** de l'hydroxy-3 diméthyl-2,3 indolénine se réarrange, en milieu acide, en **4** puis en **7***a* via **6**; **7***a* est scindé dans ces conditions en diméthyl-2,3 indole (**2**) et formyl-2 méthyl-3 indole (**3**). Si des précautions pour exclure les peroxydes et l'oxygène ne sont pas prises, deux autres produits, **13** et **30** sont aussi formés. La rationalisation proposée pour ces réactions fait appel à des différences subtiles dans les aptitudes migratrices des groupes.

Canadian Journal of Chemistry, 49, 1921 (1971)

During the accumulation of evidence for the structure **1** of the dimer ($C_{20}H_{22}N_2O_2$) of 3-hydroxy-2,3-dimethylindolenine presented in the preceding paper (1), the dimer was treated with acid (2). With hot hydrochloric acid in an organic co-solvent or with phosphoric acid the major products were 2,3-dimethylindole (**2**) and 2-formyl-3-methylindole (**3**), as noted by Berti *et al.* (3), with varying amounts of another crystalline compound ($C_{20}H_{20}N_2O_2$, m.p. 217°) formed if oxygen and/or traces of organic peroxides were present (see later).[2] In peroxide-free co-solvent and the absence of oxygen, the yield of equimolar amounts of **2** and **3** was nearly quantitative (t.l.c.). However, with dilute hydrochloric acid at room temperature, t.l.c. (benzene–ether 50:50) revealed intermediates (2). After about 1 h the only product detectable, **A** (R_f 0.34), was more polar than the dimer **1** (R_f 0.62). After longer periods (~3 h) another less polar compound **B** (R_f 0.46) appeared as well as the ultimate products **2** (R_f 0.81) and **3** (R_f 0.71). Compounds **A** and **B** are probably intermediates on the reaction path from the dimer **1** to **2** and **3** because pure **A** was shown to be transformed into **B**, **2** and **3** without any noticeable amount of dimer being reformed. Furthermore **B** was converted into **2** and **3** without any dimer or **A** becoming evident on t.l.c.

The structure of **B** was determined to be **7***a* in the following way. Initially it was a liquid which was purified through the crystalline *O*-acetate **7***b*, m.p. 175°, to obtain crystals, m.p. 169°, whose u.v. absorption contained both indole and indoline chromophores (Fig. 1). The compound was a secondary alcohol (δ_{CHOH} 5.00 → δ_{CHOAc} 6.31) with an indoline NH and three unsplit methyl groups, one of which (δ 2.35) was attached to the indole heterocyclic ring (Fig. 2*b*), thus accounting for all of its non-aromatic hydrogen atoms. Moreover, the n.m.r. spectrum of this alcohol prepared from the hexadeuterio dimer (1) lacked two methyl peaks, one being the indolic methyl. With this information plus the dual requirements that the action of acid on the dimer monoacetate **8** give *N*-acetyl indole and the aldehyde **3** (Scheme 1), and that acid treatment of the alcohol **B** yield **2** and **3**, there were only two reasonable structural possibilities, **7***a* or **15**. These isomers were distinguishable through their desoxy derivatives. Alcohol **B** could be converted by two different routes (Scheme 2) into its desoxy derivative, m.p. 126°, whose formation is, therefore, unlikely to have involved rearrangement. Firstly, sodium – *t*-butyl alcohol hydrogenolysis of alcohol **B** yielded the desoxy compound (either **10***a* or **18**) directly. Secondly, alcohol **B** was oxidized by the chromic acid – pyridine reagent to a pale yellow ketone, subsequently found to be **11**, m.p. 194°, which on mild Wolff–Kishner reduction at 155° gave, as the only product, the same desoxy compound, m.p. 126°. By direct comparison this desoxy derivative was *not* identical with a sample

[1]Presented in part at the 52nd Conference of the Chemical Institute of Canada, Montreal, Quebec, May 25–28, 1969.

[2]A fourth compound was occasionally isolated if peroxides were not excluded, and it is also discussed later.

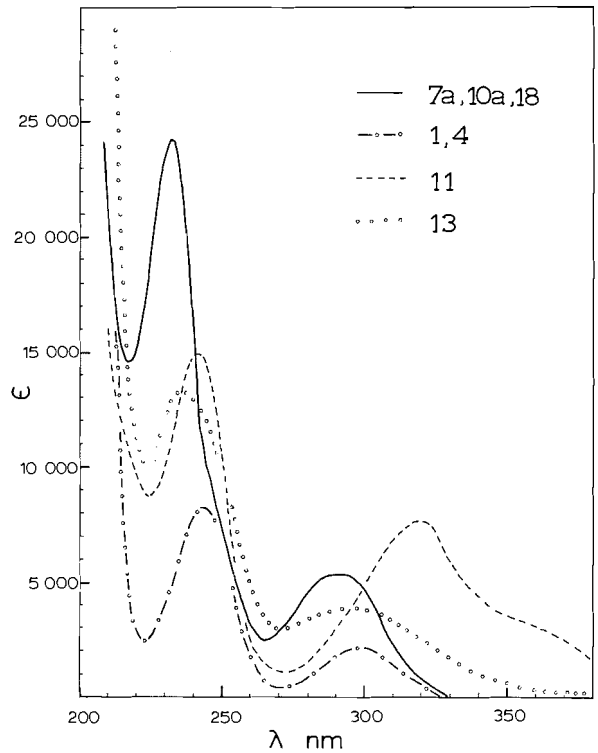
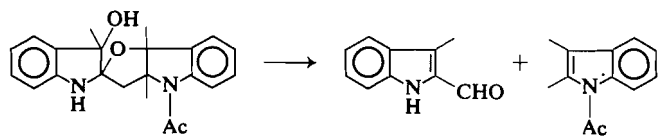


FIG. 1. The u.v. spectra of dimer **1** transformation products.



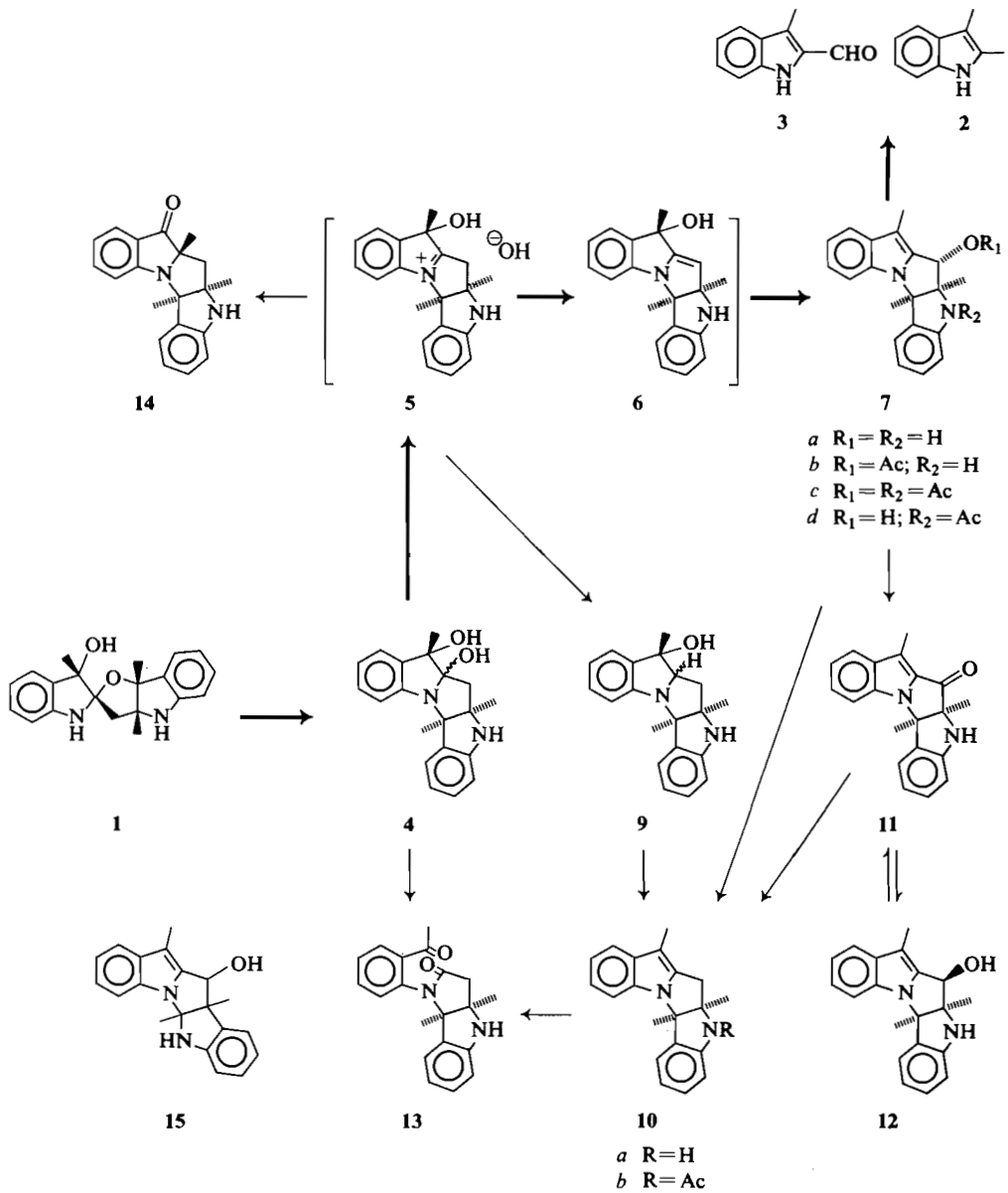
8 **3**

SCHEME 1

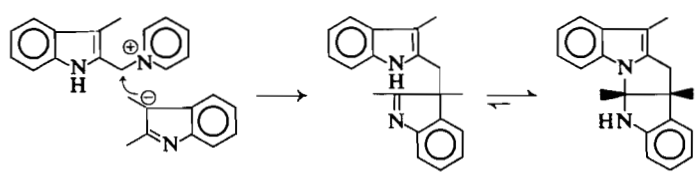
of **18**, m.p. 194°, prepared by the unambiguous synthesis of Berti *et al.* (4), which employs the Grignard reagent from 2,3-dimethylindole in a nucleophilic displacement of the pyridinium group of **16** (Scheme 3). (See Fig. 2*d* and *e* for the n.m.r. spectra of the two compounds.)

Although both **10***a* and **18** can exist as *cis* and *trans* racemates, the desoxy compound of m.p. 126° cannot differ from the synthetic compound **18** in stereochemistry alone. The formation of **18** occurs by closure of the central ring in a reversible reaction, amine addition to an imine, and results in the more stable, presumably *cis*, 5/5 ring fusion. If the alcohol precursor of the 126° desoxy compound, which alcohol is also formed by closure of the central ring, had had the structure **15**, it would also have been formed by the same reversible reaction and would necessarily have the same ring configuration as the synthetic desoxy compound **18**. Therefore, the 126° desoxy derivative must possess the other structure **10***a*. This assignment was confirmed by demonstrating that the 126° compound **10***a* did not undergo deuterium exchange under the same conditions that Berti's 194° compound **18** did incorporate deuterium into the methyl group (δ 1.79) adjacent to the potential imine (see **17**).

The initial, more polar compound **A** formed in acid is identical by direct comparison with the boron fluoride isomerization product of the dimer **1** reported by Berti *et al.* (3), whose procedure is the better preparative method. The u.v.



SCHEME 2



SCHEME 3

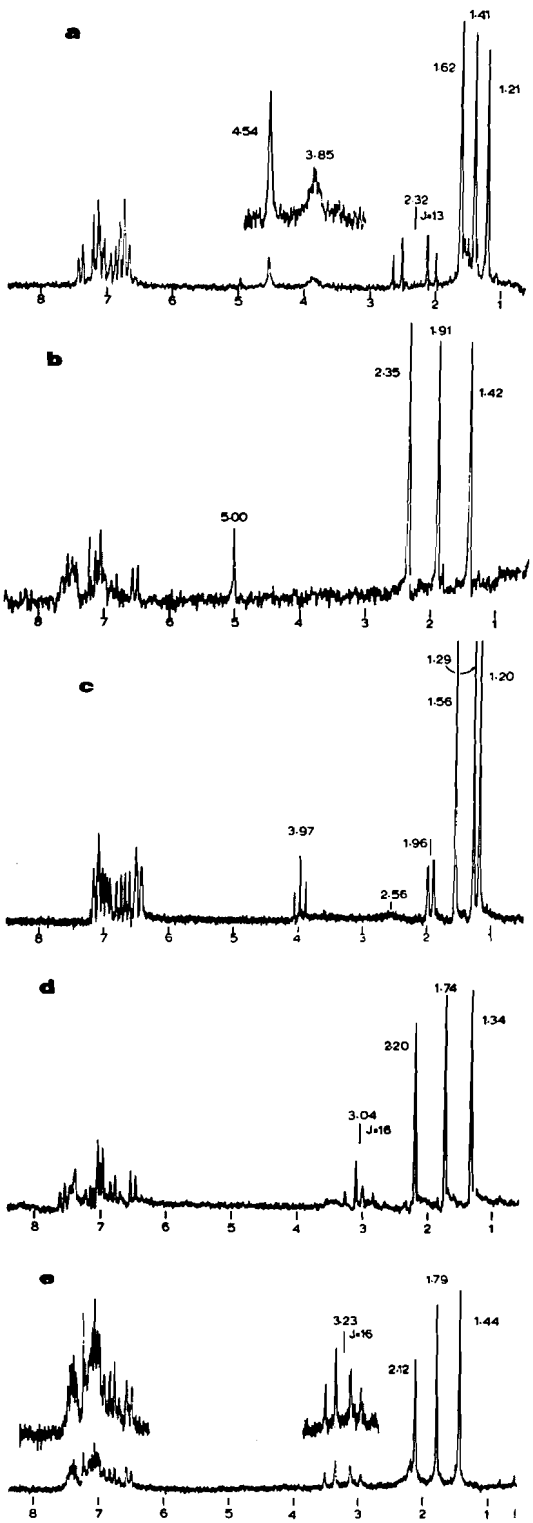
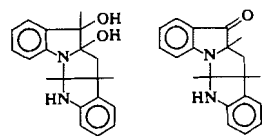


FIG. 2. The n.m.r. spectra ($CDCl_3$, 100 MHz) of diol **4** (*a*), alcohol **7***a* (*b*), sodium borohydride product **9** (*c*), 126° desoxy compound **10***a* (*d*), and Berti's 194° desoxy compound **18** (*e*).

spectrum (Fig. 1) contains two indoline chromophores while the n.m.r. spectrum (Fig. 2*a*) contains three unsplit methyl peaks and a methylene AB pattern. Intermediate **A** shows the properties of a carbinolamine in that it is readily reduced by sodium borohydride with loss of one oxygen atom. This borohydride product **9** (see Fig. 2*c* for the n.m.r. spectrum) is very sensitive to acid and readily loses a molecule of water to generate the 126° desoxy compound **10***a* encountered above. Acetylation of the borohydride product under mildly basic conditions also resulted in dehydration and formation of the *N*-acetyl derivative **10***b* of the 126° desoxy compound. It is unlikely that skeletal rearrangement occurred during the borohydride reduction or the acetylation,[3] and consequently the initial diol must be assigned structure **4** instead of the alternative **19** proposed by Berti *et al.* (3). It follows that the yellow indoxyl that is formed readily from diol **4** on heating or treatment with base must be **14** rather than **20** proposed by the same group (3).[4]



19 **20**

The vicinal relationship of the two hydroxyl groups in **4** was demonstrated by sodium periodate oxidation. Surprisingly, the same crystalline compound, $C_{20}H_{20}N_2O_2$, m.p. 217°, was obtained that was formed during acid treatment of the dimer in the presence of oxygen or peroxides (see above). Previously, the n.m.r. spectrum of this compound from the acid reaction had been very puzzling, but this second method of preparation provided the clue needed to realize that it must indeed be the ketone **13**. The i.r.

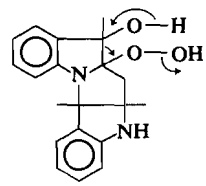
[3]However, acetylation of the diol **4**, which cannot be readily dehydrated to an indole, does proceed with rearrangement since the *O*,*N*-diacetate **7***c* of alcohol **B** was obtained.

[4]The structure of the indoxyl *N*-nitroso compound prepared by this group (3) must also be re-assigned; structure **14** with N–NO in place of NH would fit the reported n.m.r. effects on the methylene and (one) methyl groups.

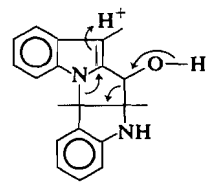
spectrum contained both carbonyl (1680 cm^{-1})[5] and amino (3390 cm^{-1}) absorption. In the u.v. spectrum (Fig. 1) there were indoline and *o*-acylaminobenzoyl chromophores. The non-aromatic region of the n.m.r. spectrum in deuteriochloroform contained two narrow unsplit quaternary methyl signals (δ 1.35 and 1.52), a methylene AB pattern (δ 2.70 and 2.87, J = 17 Hz), an indoline NH (δ 4.18), but instead of a sharp three-proton singlet for the acetyl methyl group there was only a broad three-proton lump centered at δ 2.25. The explanation for this remarkable observation lies in rotation of the acetyl and heterocyclic groups being substantially hindered by their *o*-relationship. At 37° the deuteriochloroform solution is coincidentally near the coalescence point for conformations of the acetyl methyl group which have appreciably different chemical shifts due to varying anisotropic effects, and the absorption for this group is a broad ill-defined pattern. This signal is absent in the spectrum of **13** prepared from the hexadeuterio dimer in which the acetyl methyl is now a CD_3 group. A variable temperature study, the effects of various solvents, and the results of additional chemical experiments all fully confirm this interpretation.[6] Ketone **13** is also formed by periodate oxidation of the desoxyindole **10***a* according to Dolby's procedure (6). This transformation completes a web of reactions inter-relating compounds **4**, **7**, **9**, and **10** and providing assurance that they all have the same C, H, N skeleton.

The origin of the same ketone **13** during the acid-catalyzed rearrangement of the dimer is understandable after the first stage of the reaction sequence. The carbinolamine **4** on loss of hydroxide ion could then undergo addition of any hydroperoxide present (or formed by air oxidation during reaction) to form **21**. Breakdown as indicated would yield the keto pyrrolidone **13** just as Witkop and Patrick (5) have found for the reaction of hydroxyindolenines with peracid. In fact, when precautions were taken to exclude both oxygen and peroxides in the solvent, no **13** was formed in the acid-catalyzed reaction.

The evidence presented above strongly supports the probable sequence of reactions (Scheme 2) for the acid-catalyzed reaction to be rearrangement of the dimer **1** to diol **4**, dehydration of the carbinolamine to the enamine **6** (postulated) via **5**, allylic rearrangement of the enamine to the indole alcohol **7***a* (well precedented by the work of Taylor (7)), and finally cleavage of the alcohol as indicated in **31** to 2,3-dimethylindole (**2**) and 2-formyl-3-methylindole (**3**). This mechanism is



21

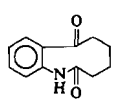


31

supported by the fact that rearrangement of the dimer in DCl–D_2O gives alcohol **7***a*-d_1 (see Scheme 4) with the deuterium atom on the carbon atom bearing the hydroxyl group, and this alcohol is further transformed by phosphoric acid into 2-formyl-3-methylindole-d_1 bearing the deuterium atom in the aldehyde function.

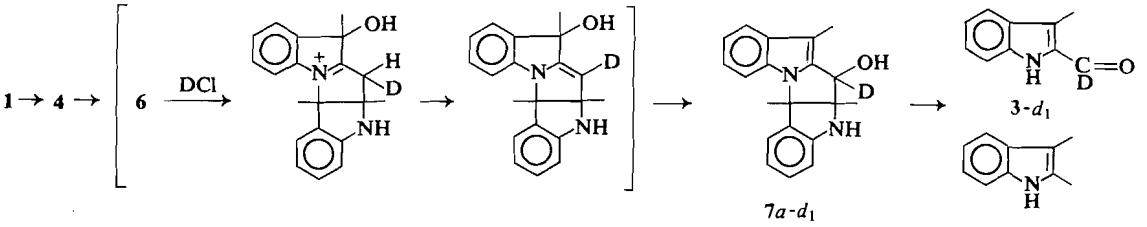
Although the overall driving force toward the cleavage products is the reformation of two stable indole systems from the dimer, it must be asked why, with such good grounds for divorce, the partners of this union choose this roundabout route (**1** → **4** → **5** → **6** → **7***a* → **2** + **3**) to sever relations when there is an apparently more direct way (**1** → **22** → **23** → **24** → **2** + **3**, Scheme 5) that does not involve formation of a new N–C bond. Part of the answer is that the carbinolamine ether ring is more reluctant to open and enolize than might be expected, perhaps due to the intramolecular hydrogen bonding of OH and NH groups (8). The dimer was not affected by sodium borohydride in refluxing methanol, although it was reduced to the dihydroderivative **26** by lithium aluminum hydride (3). The dimer slowly incorporates up to two *C*-deuterium atoms in refluxing methanol-*O*-d_1 containing sodium methoxide (~20% deuteration in 12 h, but with no rearrangement to indoxyl detectable by n.m.r.

[5]The carbonyl absorption of *N*-phenylpyrrolidone is at 1684 cm^{-1} and the ketone carbonyl absorption of *o*-acetamidoacetophenone is at 1650 cm^{-1}. The model compound **i** has a single carbonyl peak at *ca.* 1670 cm^{-1} (5).

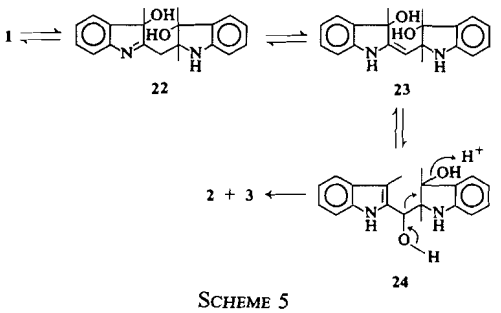


i

[6]Dave and Warnhoff, unpublished work to be submitted to Can. J. Chem.



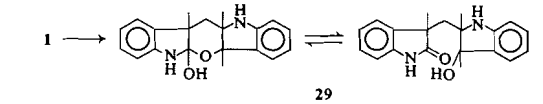
SCHEME 4



SCHEME 5

in this time).[7] In dilute deuteriochloric acid – acetone-d_6 solution when rearrangement was allowed to proceed part way, only 15% of the recovered dimer had incorporated *C*-deuterium atoms after ½ h at room temperature. The observed slow rates of the forward steps leading to **22** and **23** together with the fast back reactions (undetectable equilibrium concentration of **22** and **23** in n.m.r. solutions of **1**) and the slowness of the allylic rearrangement **23** → **24** (*cf.* the slow rate of **4** → **6** → **7***a*), all combine to allow the alternative rupture of one of the benzylic oxygen bonds to become a competitive process.

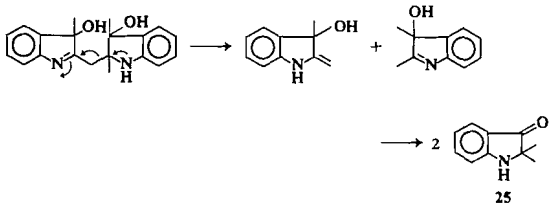
Loss of a protonated hydroxyl group from the dimer should lead by migration of the adjacent *trans*-situated methylene group to **29** (or a transformation product thereof) (Scheme 6), which was not found among the products of the acid treatment. However, in the absence of anchimeric



SCHEME 6

assistance the loss of this hydroxyl group might be slower than scission of the protonated benzylic ether bond because of the additional electronegative substituent in the β-position with respect to the hydroxyl group. Once the benzylic ether bond is broken, the subsequent attachment of nitrogen to form the five-membered ring of **4** is expected,[8] and the remainder of the route to **2** and **3** is thereby fixed. This ring closure takes place *without* migration of the methylene group from the 2- to the 3-position, probably because the migrating efficiency of the methylene group with an adjacent carbinolamine (or imine) function is reduced. Nevertheless, $C_2 \rightarrow C_3$ migration can occur when the methylene group has fewer electronegative groups nearby as in Berti's dihydrodimer **26** from lithium aluminum hydride reduction of **1**. On heating (3) or treatment with acid (see Experimental) this compound undergoes loss of water, rearrangement, and ring closure (**26** → **18**, Scheme 7). The migrating group is either the β-aminomethylene of **26** or, more likely, the methylene of **27** resulting from loss of the first molecule of water because this same indole **27** obtained in the sodium – *t*-butanol reduction of the dimer also undergoes dehydration with migration of the benzylic methylene group (**27** → **28** → **18**) on standing in chloroform solution (1).[9]

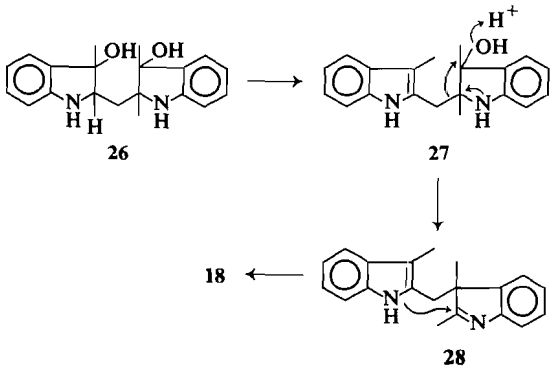
[7]However, heating the dimer to its melting point does result in rearrangement to a mixture of indoxyl **14** and the decomposition product 2,2-dimethylindoxyl (**25**) (1). The decomposition is presumably initiated by a retro Mannich reaction:



This behavior probably accounts for the dimer's wide and variable melting point.

[8]Ring formation cannot be a concerted S_N2 displacement of the protonated ether because inversion at the carbon atom undergoing displacement cannot occur so long as the carbinolamine ether is intact.

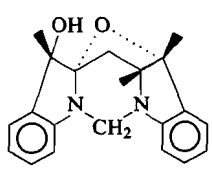
[9]Several of the compounds in the present work (**9**, **26**, **27**, and the most polar sodium – *t*-butanol reduction product from **1** (1)) were unstable in chloroform solution due to dehydration and rearrangement presumably catalyzed by hydrogen chloride formed either on exposure of these solutions to light or else from reaction of a basic nitrogen atom with the chloroform.



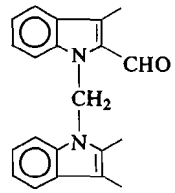
SCHEME 7

The relative stereochemistry of these compound can now be specified. When the dimer rearranges to **4**, only the *cis* stereochemistry of the fused pyrrolidine rings would be expected to result, and the all *cis* orientation of the methyl groups of **1** (8) would therefore become the *trans,trans,cis* arrangement shown in **4** after the required rotation of the right hand indoline moiety of **1**. For the two alcohol stereoisomers **7***a* and **12** which are epimeric only at the hydroxyl-bearing carbon atom, the stereochemistry depicted is assigned because formation of an alcohol by allylic rearrangement of **6** should occur by attack of water at the less hindered side of the carbon atom away from the fold of the molecule, while the hydroxyl group resulting from hydride reduction of ketone **11** should be in the more hindered position because hydride is donated to the less protected side.

The earlier mentioned second artifact found when peroxides were not excluded from the acid treatment of dimer in dioxane co-solvent proved to be **30**, a molecule of 2,3-dimethylindole and one of 2-formyl-3-methylindole joined at the nitrogen atoms by a methylene bridge presumably from formaldehyde or its precursor. Since treatment of these two indoles **2** and **3** with formaldehyde and acid gave no **30**, the two nitrogen atoms must have been joined earlier in the reaction sequence. When dimer **1** was treated with formaldehyde under the conditions for the acid-catalyzed rearrangement, it was changed completely into **30** within 15 min, much faster than the rearrangement sequence. However, under milder conditions (more dilute acid, shorter reaction time) the dimer was converted exclusively into the crystalline homo compound **32**. The formation of this product is not surprising in view of the stereochemistry of the dimer (8, 1). Acid treatment of **32** gave **30** quantitatively. Although the product is basically **2** + **3**, this latter rearrangement cannot take place by the path established for the dimer itself, and presumably occurs by some variation of it. The reaction was not investigated further.



32



30

Experimental[10]

Cleavage of Dimer 1 by Phosphoric Acid

To a solution of the dimer (200 mg) in warm 95% ethanol (5 ml) was added 85% H_3PO_4 (3.5 ml). The solution, which immediately became a cherry red to dark brown color, was stirred at room temperature for 2.5 h. The reaction mixture was diluted with water and extracted with ether. Evaporation of the water-washed and dried ethereal solution left 193 mg (~100%) of yellowish solid whose t.l.c. (benzene–ether, 1:1) had only two spots corresponding to **2** and **3**. The crude product was chromatographed on alumina (5 g). Petroleum ether eluted 65 mg of colorless crystalline **2,3-dimethylindole** (**2**). Petroleum ether – benzene (1:1) eluted 85 mg of **2-formyl-3-methylindole** (**3**), m.p. 137–140° (lit. (9) m.p. 139–140°) after two recrystallizations from chloroform – petroleum ether; ν_{max} 3550 (NH) and 1650 cm^{-1} (conj. C=O); λ_{max} 241 (4000) and 315 nm (6500).

Preparation of the Diol 4

(a) By the Action of Hydrochloric Acid on Dimer 1

To a stirred solution of the dimer (1.00 g) in acetone (25 ml) was added a solution of 0.1 *N* HCl (2 ml) and acetone (5 ml). After 1 h at room temperature the yellow solution was diluted with water and extracted with ether. The organic layer was dried and concentrated to leave 1.10 g of a pale yellow liquid whose t.l.c. had only two spots corresponding to **4** and **1**. Chromatography on four thick layer plates developed in benzene–ether (50:50) and ether extraction of the band at R_f 0.33 gave 220 mg of pale yellow oil. Further purification of this material on three thick-layer plates gave 85 mg (8.5%) of almost colorless oil which solidified. Recrystallization from ether – petroleum ether (b.p. 30–60°) gave colorless crystals of the **diol 4**, m.p. 115–125° (dec.).

Anal. Calcd. for $C_{20}H_{22}O_2N_2$ (322.4): C, 74.51; H, 6.88; N, 8.69. Found: C, 75.15; H, 7.14; N, 8.54.

The i.r., u.v., and n.m.r. spectra were identical with those of the compound prepared with boron trifluoride in section *b* below.

A yellow band (R_f 0.58) on some of the t.l.c. plates was found to contain the indoxyl **14**, m.p. 190–196° (lit. (3) m.p. 200–210°) after recrystallization from chloroform –

[10]For general experimental methods see the preceding paper (1). The n.m.r. data are given in Table 1.

TABLE 1. The n.m.r. data exclusive of aromatic protons*

Compound	Absorption
Diol **4**	1.21 (s, 2-Me), 1.41 (s, 3-Me), 1.62 (s, 3-Me), 2.08 and 2.56 (AB of CH_2, J = 13), 3.85 (NH), 4.54 (OH)
Diol **4**-d_6	1.21 (s, 2-Me), 2.08 and 2.56 (AB of CH_2, J = 13) [spectrum too weak to see NH and OH]
$NaBH_4$ product **9**	1.20 (s, 2-Me), 1.29 (s, 3-Me), 1.56 (s, 3-Me), 1.96 (center of complex AB of CH_2), 2.56 (b, OH or NH), 3.65 (v.b, NH or OH), 3.97 (center of 1H 3-line pattern, 9Hz spacing)
Alcohol **7***a*	1.42 (s, 2-Me), 1.91 (s, 3-Me), 2.35 (s, indole Me), 5.00 (s, C*H*OH) [OH and NH too broadened to be noticeable]
Alcohol **7***a*-d_6	1.41 (s, 2-Me), 5.00 (s, C*H*OH)
Alcohol **7***a*-d_1	Same as spectrum of alcohol **7***a* except that the 1H peak at δ 5.00 missing
O-Acetate **7***b*	1.31 (s, 2-Me), 1.91 (s, 3-Me), 2.08 (s, OCOMe), 2.27 (s, indole Me), 4.00 (NH), 6.31 (s, C*H*OAc)
N-Acetate **7***d*	1.68 (s, 2-Me), 1.95 (s, 3-Me), 2.31 (s, indole Me), 2.42 (s, NCOMe) [spectrum too weak to locate C*H*OH]
O,*N*-Diacetate **7***c*	1.62 (s, 2-Me), 1.98 (s, 3-Me), 2.10 (s, OCOMe), 2.30 (s, indole Me or NCOMe), 2.35 (s, NCOMe or indole Me), [C*H*OAc indistinguishable among aromatic protons]
Alcohol **12**	1.35 (s, Me), 1.75 (s, Me), 2.33 (s, indole Me), 3.02 (2H, NH + OH), 5.00 (s, C*H*OH)
O-Acetate of **12**	1.47 (s, Me), 1.85 (s, Me), 2.05 (s, OCOMe), 2.23 (s, indole Me), 4.30 (NH), 6.12 (s, C*H*OAc)
Ketone **11**	1.49 (s, Me), 2.01 (s, Me), 2.54 (s, indole Me), 4.70 (NH)
126° Desoxy compound **10***a*	1.34 (s, 2-Me), 1.74 (s, 3-Me), 2.20 (s, indole Me), 2.96 and 3.12 (AB of CH_2, J = 16) [NH not observable]
N-Acetate of 126° compound **10***b*	1.62 (s, 2-Me), 1.75 (s, 3-Me), 2.18 (s, indole Me), 2.31 (s, NCOMe), 3.08 and 4.34 (AB of CH_2, J = 17)
194° Desoxy compound **18**	1.44 (s, 3-Me), 1.79 (s, 2-Me), 2.12 (s, indole Me), 3.06 and 3.42 (AB of CH_2, J = 16) [NH not observable]
Ketone **13**	1.35 (s, Me), 1.52 (s, Me), 2.25 (b.l. COMe), 2.70 and 2.87 (AB of CH_2, J = 17), 4.18 (NH)
Ketone **13**-d_6	1.35 (s, Me), 2.70 and 2.87 (AB of CH_2, J = 17), 4.18 (NH)
Indoxyl **14**	1.17 (s, Me), 1.41 (s, Me), 1.43 (s, Me), 2.02 and 2.16 (AB of CH_2, J = 13), 3.72 (b, NH)
Dihydrodimer **26** (Pyridine solution)	1.28 (s, Me), 1.41 (s, Me), 1.59 (s, Me), 2.16 and 2.74 (AB of CH_2, J = 13), 4.28 (1H, X of ABX, $J \sim 6$, ~ 6)
Homodimer **32**	1.21 (s, 2-Me), 1.50 (s, di-3-Me), 2.10 (s, CH_2), 3.30 (s, OH), 4.10 and 4.59 (AB of NCH_2N, J = 11)
The methylene bis indole **30**	2.13 (s, di Me), 2.61 (s, Me), 6.80 (s, NCH_2N) 10.00 (s, CHO)

*Chemical shifts are given in p.p.m. from tetramethylsilane (δ) and coupling constants in Hz; $CDCl_3$ solutions unless otherwise specified; 2-Me and 3-Me signify that the methyl group giving rise to the absorption originated from a 2- or 3-methyl group of 2,3-dimethylindole, respectively; s = singlet, d = doublet, b = broad absorption, l = lump.

petroleum ether. The i.r. and n.m.r. spectra were identical with those reported (3).

(b) By the Action of Boron Trifluoride on Dimer **1**

The procedure is that of Berti *et al.* (3), slightly modified. A solution of dimer (200 mg) in chloroform (20 ml) was chilled in an ice-salt bath and treated with a mixture of boron trifluoride etherate (0.2 ml) and chloroform (0.2 ml). After 5 min the yellow reaction mixture was diluted with 2 *N* Na_2CO_3 solution and extracted with ether. The pale yellow oil (185 mg) obtained after evaporation of the water-washed and dried organic layer was chromatographed on a thick plate developed with benzene–ether (50:50). Extraction of the band at R_f 0.32 gave 23 mg (11%) of almost colorless solid **4**. Recrystallization from ether – petroleum ether (b.p. 30–60°) gave colorless crystals, m.p. 114–125° (dec.) (lit. (3) m.p. 112–122° (dec.)); ν_{max} 3580, 3360, and 3340 (shoulder) cm^{-1} (NH and OH); λ_{max} 250 (8000) and 298 nm (3400).

(c) By the Action of Boron Trifluoride on Dimer **1**-d_6

The reaction was carried out on 54 mg of **1**-d_6 (1) as described in section *b*. There was obtained 53 mg of diol **4**-d_6 (90% pure by t.l.c.) whose n.m.r. spectrum was lacking the methyl peaks at δ 1.41 and 1.62 of the protio analog.

Borohydride Reduction of Diol **4**

A solution of the diol (35 mg), methanol (6 ml), and $NaBH_4$ (50 mg) was allowed to stand at room temperature for 4 h. The methanol was removed at reduced

pressure, and the residue was treated with water. Extraction with chloroform yielded 37 mg of colorless oily solid after evaporation of the water-washed and dried solution. The t.l.c. gave a single spot slightly more polar than **4**. Recrystallization from ether – petroleum ether (b.p. 30–60°) gave colorless crystals of **9**, m.p. 128–140°; ν_{max} 3575 (OH) and 3380 cm^{-1} (NH); λ_{max} 247 (8800) and 295 nm (5100).

Anal. Calcd. for $C_{20}H_{22}N_2O$ (306.4): C, 78.40; H, 7.24; N, 9.14. Found: C, 78.77; H, 7.31; N, 9.06.

When a chloroform solution of **9** was allowed to stand in an open vessel at room temperature for 3 days, it was found to have been dehydrated to **10***a*. The n.m.r. spectrum, m.p., mixed m.p., and t.l.c. behavior were identical with that of authentic **10***a*.

Acetylation of Borohydride Product **9**

A mixture of the borohydride reduction product (100 mg), sodium acetate (100 mg), and acetic anhydride (2.0 ml) was heated at 140° (bath temperature) for 12 h. The cooled mixture was added to 5% $NaHCO_3$ solution and extracted with chloroform. The organic layer was washed with water, dried, and evaporated to leave 104 mg (96%) of yellowish solid which was essentially pure (t.l.c.). Recrystallization from chloroform – petroleum ether gave colorless crystals of the **N-acetyl desoxy compound 10***b*, m.p. 273–275°; ν_{max} 1637 cm^{-1} (amide C=O); λ_{max} 232 (18 000), 285 (8900), and 290 nm (4400); *m/e* 330 (molecular ion).

Anal. Calcd. for $C_{22}H_{22}N_2O$ (330.4): C, 79.97; H, 6.71; N, 8.48. Found: C, 79.90; H, 6.31; N, 8.48.

Preparation of the Alcohol 7a

(a) From Dimer and Hydrochloric Acid

To a stirred (magnetic bar) solution of the dimer **1** (100 mg) in *p*-dioxane (2.5 ml Baker Analyzed freshly distilled from $LiAlH_4$) under a nitrogen atmosphere was added at room temperature a solution of 0.1 *N* HCl (0.2 ml) in the same dioxane (0.2 ml). The solution immediately became pale yellow changing successively to dark yellow, pale brown, and finally dark brown. After 5.5 h the reaction mixture was diluted with chloroform, washed once with water, dried, and concentrated at reduced pressure to leave 102 mg of brownish black viscous liquid. Chromatography on a thick plate developed with benzene–ether (75:25) gave a band (R_f 0.66) from which 15 mg of pale yellow oil was isolated. The n.m.r. spectrum of this fraction revealed it to be a mixture of the dimer **1**, 2-formyl-3-methylindole (**3**), and an unknown component. From a band with R_f 0.39 was extracted 51 mg (54%) of pure (t.l.c.) almost colorless liquid **alcohol 7***a*. Attempts to induce crystallization were unsuccessful. However, the crystalline compound was obtained by saponification of the crystalline *O*-acetate (see below) with sodium hydroxide in methanol at room temperature. The oily solid from the saponification was recrystallized from methanol to give colorless crystals of **7***a*, m.p. 162–169°; ν_{max} 3585 (OH) and 3380 cm^{-1} (NH); λ_{max} 232 (25 000) and 297 nm (6300); *m/e* 304 (molecular ion).

Anal. Calcd. for $C_{20}H_{20}N_2O$ (304.4): C, 78.92; H, 6.62; N, 9.20. Found: C, 78.77; H, 7.03; N, 9.09.

The n.m.r. and i.r. spectra as well as the t.l.c. behavior of the crystalline material were identical with those of the liquid alcohol obtained from the reaction with HCl.

Essentially the same results were obtained when acetone was used in place of dioxane as the organic cosolvent. If reagent grade *p*-dioxane was used without purification for the reaction, varying amounts of two other compounds were formed in addition to the alcohol **7***a* when the reaction was conducted under a nitrogen atmosphere. One of these appeared in the least polar t.l.c. band (R_f 0.85) whose extraction yielded a pale yellow solid which was recrystallized from petroleum ether to give very pale yellow clusters of needles of **30**, m.p. 146–147.5°; ν_{max} 1650 cm^{-1} (conj. C=O), NH absorption absent; λ_{max} 230 (25 000) and 315 nm (13 000); *m/e* 316 (molecular ion).

Anal. Calcd. for $C_{21}H_{20}N_2O$ (316.4): C, 79.72; H, 6.37; N, 8.85. Found: C, 79.15; H, 6.40; N, 8.69.

A second artifact, the ketone **13**, is described later.

(b) From Diol **4**

To a stirred (magnetic bar) solution of the diol (~90% pure by t.l.c.) (35 mg) in acetone (1.5 ml) was added a solution of 0.1 *N* HCl (0.2 ml) in acetone (0.5 ml). After 4 h at room temperature during which the color of the solution changed from yellow to pink to brown to almost black, most of the solvent was removed at reduced pressure on the rotary evaporator. A chloroform solution of the residue was washed with water, dried, and evaporated to leave 27 mg of clear amber liquid whose i.r. and n.m.r. spectra as well as t.l.c. behavior were identical with those of **alcohol 7***a* prepared in section *a* above.

(c) From Dimer **1** *and Deuteriochloric Acid*

To a stirred (magnetic bar) solution of the dimer **1** (80 mg) in dioxane (1 ml, freshly distilled from $LiAlH_4$) was added a solution of 0.1 *N* DCl in D_2O (0.25 ml). The solution was kept at room temperature for 3 h, then diluted with chloroform, washed with water, dried, and evaporated. The 72 mg of residual brown oil was chromatographed on a thick plate developed in benzene – petroleum ether (75:25). Extraction of the band at R_f 0.34 gave 18 mg (24%) of the liquid **alcohol 7***a*-d_1 whose n.m.r. spectrum lacked the carbinyl proton (< 5%) present at δ 5.00 in the protio compound. The crystalline acetate, m.p. 173–177° was prepared for mass spectroscopy; *m/e* 347 (molecular ion corresponding to monodeuteration).

Phosphoric Acid Cleavage of Alcohol 7a-d_1

To a stirred (magnetic bar) solution of monodeuterio alcohol **7***a*-d_1 (140 mg) in 95% ethanol (2 ml) was added 85% H_3PO_4 (1 ml), and the reaction mixture was kept at room temperature for 3 h. The solution was diluted with ether, washed twice with water, dried, and concentrated to 118 mg of brown oily solid. The t.l.c. in benzene–ether (50:50) gave only two spots which corresponded to **2** and **3** in about equal amounts. Chromatography on alumina (5 g) gave 20 mg of colorless 2,3-dimethylindole (**2**) from the petroleum ether eluates. Elution with petroleum ether – benzene (50:50) gave 52 mg (70%) of pale yellow solid 2-deuterioformyl-3-methylindole (**3**-d_1). Recrystallization gave colorless plates, m.p. 137–140°; *m/e* 160 (molecular ion corresponding to monodeuteration), whose n.m.r. spectrum lacked the formyl proton.

Elution with chloroform yielded 42 mg of brown oily solid whose t.l.c. behavior and n.m.r. spectrum showed it to be the dimer **1**, presumably formed by air oxidation of the 2,3-dimethylindole.

*Reaction of Dimer Monoacetate **8** with Acid*

A solution of **8** (200 mg), acetone (4 ml), and HCl (0.8 ml of 0.1 *N* aqueous HCl) was refluxed for 2 h. Evaporation of the acetone and partition of the residue between chloroform and water gave 180 mg of crude product which was chromatographed on two thick plates developed with benzene–ether (88:12). The band at R_f 0.71 yielded 15 mg of colorless crystalline *N*-acetyl-2,3-dimethylindole identical with an authentic specimen. The band at R_f 0.53 yielded 7 mg of colorless crystalline 2-formyl-3-methylindole (**3**) identical with an authentic specimen. More polar products (48 mg) on the base line had a complex n.m.r. spectrum and were not investigated further.

O-Acetate of Alcohol 7a

A solution of the liquid alcohol (55 mg), pyridine (0.5 ml), and acetic anhydride (0.5 ml) was allowed to stand at room temperature for 5 h. After the addition of chloroform, the reaction mixture was washed with water, dried, and concentrated to leave 72 mg of a brown viscous oil. Chromatography on alumina (3 g) gave a white solid on elution with petroleum ether – benzene (80:20). Recrystallization from methanol – petroleum ether gave 23 mg (38%) of colorless crystals of 7*b*, m.p. 172–175°; ν_{max} 3371 (NH), and 1732 cm^{-1} (*O*-acetate C=O); λ_{max} 230 (26 000) and 295 nm (7000); *m/e* 346 (molecular ion).

Anal. Calcd. for $C_{22}H_{22}N_2O_2$ (346.4): C, 76.28; H, 6.40; N, 8.09; O, 9.24. Found: C, 76.81; H, 6.26; N, 8.29; O, 9.22.

N-Acetate of Alcohol 7a

To a solution of the *O,N*-diacetate 7*c* (180 mg) in a mixture of methanol (3 ml) and dioxane (3 ml) was added sodium hydroxide (3 pellets) with stirring at room temperature. Within 15 min solid began to precipitate. After 30 min water was added, and the mass was extracted with chloroform. The organic layer was washed with water, dried, and concentrated to leave 135 mg of pale yellowish solid. Recrystallization from chloroform–methanol gave colorless crystals of pure 7*d*, m.p. 268–280°; ν_{max} (Nujol) 3280 (OH) and 1625 cm^{-1} (amide C=O); *m/e* 346 (molecular ion).

Anal. Calcd. for $C_{22}H_{22}N_2O_2$ (346.4): C, 76.28; H, 6.40; N, 8.09. Found: C, 76.53; H, 6.32; N, 7.89.

O,N-Diacetate of Alcohol 7a

*(a) From Diol **4***

A mixture of the diol (320 mg), pyridine (5 ml), sodium acetate (320 mg), and acetic anhydride (2 ml) was heated at 120° for 17 h. The cooled reaction mixture was added to 5% aqueous $NaHCO_3$ and extracted with chloroform. The organic layer was washed with water, dried, and evaporated to give 327 mg of a brown solid. Recrystallization from chloroform–methanol gave 78 mg of colorless crystals of the *O,N*-diacetate 7*c*, m.p. 245–252° (capillary sealed under vacuum); ν_{max} 1735 (*O*-acetate C=O) and 1650 cm^{-1} (amide C=O); *m/e* 388 (molecular ion).

Anal. Calcd. for $C_{24}H_{24}N_2O_3$ (388.5): C, 74.21; H, 6.23; N, 7.21. Found: C, 74.42; H, 6.33; N, 7.10.

(b) From Alcohol 7a

A mixture of alcohol (70 mg), pyridine (1 ml), sodium acetate (70 mg), and acetic anhydride (0.5 ml) was heated at 120° for 17 h. Work-up as in section *a* gave 68 mg of viscous brown oil which was chromatographed on a thick plate developed with benzene–ether (50:50). The band at R_f 0.60 yielded 31 mg (47%) of colorless solid. On recrystallization from chloroform – petroleum ether there was obtained 18 mg of colorless crystals of 7*c*, m.p. 245–250° (capillary sealed under vacuum), undepressed on admixture with the sample prepared from the diol **4** in section *a*. The two samples had identical i.r., n.m.r., and t.l.c. data.

(c) Saponification

A solution of the *O,N*-diacetate 7*c* (30 mg), NaOH (2 pellets), methanol (2 ml), and dioxane (2 ml) was refluxed for 4 days. After evaporation of solvent and addition of water, the product was extracted with chloroform. The organic solution was washed with water, dried, and evaporated to leave 24 mg of pale yellow oily alcohol 7*a*, whose t.l.c. behavior and n.m.r. spectrum were identical with those of authentic alcohol 7*a*.

*Ketone **11***

(a) From Liquid Alcohol 7a

To a stirred solution of the liquid alcohol 7*a* (200 mg, 0.66 mmol) in pyridine (2 ml) at room temperature was added CrO_3 (200 mg, 2.00 mmol) during 5 min. After the mixture was stirred at room temperature for 24 h, it was partitioned between water and chloroform. The organic layer was washed with water, dried, and evaporated to leave 183 mg of a violet oil which was chromatographed on alumina (3 g). Elution with petroleum ether – benzene (80:20) afforded 48 mg (25%) of yellow solid **ketone 11**. Recrystallization from methanol gave 17 mg of pale yellow crystals, m.p. 192–194°; ν_{max} 3370 (NH) and 1690 cm^{-1} (conj. ketone); λ_{max} 242 (15 000) and 322 nm (8500); *m/e* 302 (molecular ion).

Anal. Calcd. for $C_{20}H_{18}N_2O$ (302.4): C, 79.44; H, 6.00; N, 9.26. Found: C, 78.76; H, 5.81; N, 9.53.

*(b) From $LiAlH_4$ Alcohol **12***

A solution of alcohol **12** (150 mg, 0.49 mmol) in pyridine (3 ml) was oxidized at room temperature by addition of CrO_3 (150 mg, 1.5 mmol) in the same procedure used in section *a* above. There was obtained 12 mg of pale yellow ketone **11**, m.p. 188–194°, identical (i.r., t.l.c., n.m.r., mixed m.p.) with the ketone prepared by oxidation of 7*a*.

*Desoxy Compound **10a***

*(a) By Wolff–Kishner Reduction of Ketone **11***

A mixture of ketone **11** (45 mg), hydrazine hydrate (0.7 ml), and diethylene glycol (1 ml) was heated at 155° (bath temperature) for 2.5 h. Then NaOH (2 pellets) was added, and heating was continued for 1.5 h more. The reaction mixture was partitioned between water and ether. The organic layer was washed with water, dried, and evaporated to leave 40 mg of a colorless oil whose t.l.c. showed a single spot less polar than ketone **11**. Further purification on a thick layer plate gave 36 mg of an oil which crystallized on trituration with petroleum ether. Recrystallization from petroleum ether gave colorless rosettes of **10***a*, m.p. 125–126°, ν_{max} 3470 cm^{-1} (NH); λ_{max} 232 (24 000) and 295 nm (4600); *m/e* 288 (molecular ion).

Anal. Calcd. for $C_{20}H_{20}N_2$ (288.4): C, 83.30; H, 6.99. Found: C, 83.56; H, 7.08.

When the above reaction was carried out at 220°, the only product isolated was 2,3-dimethylindole (**2**).

(b) By Hydrogenolysis of Alcohol 7a

To a refluxing solution of alcohol **7***a* (160 mg) in *t*-butyl alcohol was added sodium metal (1 g). The mixture was refluxed for 9.5 h and then partitioned between water and ether. The ethereal extract was dried and concentrated to a brown oil (130 mg) which was chromatographed on a thick plate developed in benzene–ether (95:5). The band on the base line yielded 33 mg of recovered liquid alcohol **7***a*. Extraction of the band at R_f 0.55 gave 48 mg (32%) of almost colorless **desoxy compound 10***a*, m.p. 118–122° after recrystallization from ether – petroleum ether (b.p. 30–60°). The mixed m.p. with the specimen from the Wolff–Kishner reduction was 120–123°, undepressed. The i.r., n.m.r. and t.l.c. data were the same for both samples.

(c) By Saponification of the N-acetate 10b

A solution of the *N*-acetyl desoxy compound **10***b* (35 mg) and NaOH (2 pellets) in methanol (2 ml) – dioxane (2 ml) was refluxed for 12 h. After evaporation of the solvents, water was added and organic material was extracted with chloroform. The water-washed and dried organic solution was concentrated to leave 32 mg of a brown oil whose i.r. and n.m.r. spectra as well as t.l.c. behavior were identical with those of the desoxy compound **10***a*.

Deuteration of Desoxy Compounds

(a) Berti's 194° Desoxy Compound 18

A mixture of **18** (30 mg), methanol-*O*-d_1 (1.8 ml), and sodium methoxide (50 mg) protected from atmospheric moisture was refluxed for 10 h. The methanol was evaporated at reduced pressure and the residue was partitioned between chloroform and water to yield 30 mg of recovered **18** which was purified by recrystallization from chloroform – petroleum ether. In the n.m.r. spectrum the methyl peak at δ 1.79 had almost completely disappeared. Deuterium analysis by mass spectroscopy gave 2% d_0, 4% d_1, 15% d_2, 74% d_3, and 5% d_4.

(b) 126° Desoxy Compound 10a

The above reaction was carried out on 30 mg of **10***a* for 10 h. The crude product was recrystallized from ether – petroleum ether (b.p. 30–60°) to yield 18 mg of pure **10***a* whose n.m.r. spectrum showed no diminution of any peak. Deuterium analysis by mass spectroscopy gave 100% d_0, and no d_1 or d_2 species.

Epimeric Alcohol 12

A mixture of ketone **11** (50 mg), dry tetrahydrofuran (2 ml), and lithium aluminum hydride (50 mg) was stirred (magnetic bar) at room temperature for 5 h. Water was added and the reaction mixture was extracted with ether. The organic layer was washed with water, dried, and evaporated to leave 47 mg of colorless liquid epimeric alcohol **12** which crystallized on trituration with petroleum ether. Recrystallization from methanol and from chloroform – petroleum ether gave glistening granules, m.p. 189–193°; ν_{max} 3530 (OH) and 3360 cm^{-1} (NH); *m/e* 304 (molecular ion), whose R_f on t.l.c. was greater than that of alcohol **7***a*.

Anal. Calcd. for $C_{20}H_{20}N_2O$ (304.4): C, 78.92; H, 6.62; N, 9.20. Found: C, 78.39; H, 6.97; N, 9.07.

The ***O*-acetate** was prepared by treatment of **12** with acetic anhydride and pyridine at room temperature. Recrystallization from chloroform gave colorless crystals, m.p. 153–160°; ν_{max} 3395 (NH) and 1728 cm^{-1} (ester C=O); *m/e* 346 (molecular ion).

Anal. Calcd. for $C_{22}H_{22}N_2O_2$ (346.4): C, 76.28; H, 6.40. Found: C, 76.83; H, 6.51.

Preparation of Ketone 13

(a) During Treatment of Dimer 1 with Hydrochloric Acid

Treatment of the dimer with 0.1 *N* HCl in undistilled, unpurified Fisher *p*-dioxane (the n.m.r. spectrum showed only the *p*-dioxane peak) in a stoppered flask gave the liquid alcohol **7***a* (R_f 0.77, ether) in ~30% yield and in addition ~10% of a more polar (R_f 0.19, ether) compound which was separated by chromatography.[11] Recrystallization from chloroform – petroleum ether gave colorless crystals of the **ketone 13**, m.p. 214–217°, ν_{max} 3390 (NH) and 1680 cm^{-1} (Ar—C=O and pyrrolidone C=O); λ_{max} 235 (13 000) and 300 nm (3800); *m/e* 320 (molecular ion). The compound was identical with that prepared in section *b* below.

(b) By Periodate Oxidation of Diol 4

To a solution of the diol **4** (30 mg, 0.094 mmol) in methanol (3 ml) under a nitrogen atmosphere was added with stirring (magnetic bar) a solution of $NaIO_4$ (30 mg, 0.14 mmol) in water (1 ml) and methanol (0.5 ml). Within 5 min a white solid ($NaIO_3$) had precipitated. After 15 min water was added and the mixture was extracted with chloroform. The organic layer was washed with water, dried, and evaporated to leave 30 mg (100%) of an oily solid whose t.l.c. (chloroform–methanol, 87:13) showed the absence of starting material **4** and the presence of a single more polar spot of the same R_f as the ketone from section *a* above. Recrystallization from chloroform – petroleum ether gave colorless crystals of ketone **13**, m.p. 214–216°, undepressed on admixture with the compound from section *a* above. The n.m.r. and i.r. spectra of the two samples were identical.

Anal. Calcd. for $C_{20}H_{20}N_2O_2$ (320.4): C, 74.98; H, 6.29; N, 8.74; O, 9.99. Found: C, 74.51; H, 6.11; N, 8.72; O, 9.96.

(c) By Periodate Oxidation of Desoxy Compound 10a

A modification of Dolby's procedure (6) was used. To a solution of **10***a* (25 mg, 87 μmol) in methanol (2 ml) was added with stirring (magnetic bar) at room temperature a solution of $NaIO_4$ (60 mg, 280 μmol) in water (0.5 ml). Within 15 min solid had begun to precipitate. The mixture was stirred for 12 h, then diluted with water and extracted with chloroform. Evaporation of the washed and dried chloroform solution left 24 mg of light brown oily solid. Recrystallization from chloroform – petroleum ether gave 18 mg of buff colored solid, m.p. 208–217°. Sublimation (190° at 0.1 mm Hg) gave colorless crystalline **13**, m.p. 213–217°, undepressed on admixture with the sample from section *b* above. Their i.r. and n.m.r. spectra and t.l.c. behavior were also identical.

(d) By Periodate Oxidation of Diol 4-d_6

The reaction was carried out with 50 mg of **4**-d_6 and 36 mg of $NaIO_4$ according to the procedure described in section *b* above. The n.m.r. spectrum of the 50 mg of

[11]When oxygen was deliberately bubbled into the reaction mixture, the yield of ketone **13** increased markedly.

13-d_6 obtained was lacking the methyl peak at δ 1.52 and the three proton lump centered at δ 2.25. Recrystallization from chloroform – petroleum ether gave material of m.p. 214–216° whose t.l.c. behavior was identical with that of **13**; *m/e* 326 (molecular ion corresponding to hexadeuteration).

*194° Desoxy Compound **18***

(*a*) The procedure of Berti *et al.* (3) was used. The pyridinium salt **16** was prepared from 2,3-dimethylindole (1.0 g), *N*-bromosuccinimide (1.23 g), and pyridine (0.6 g). The crude salt obtained was treated with the Grignard reagent prepared from 2,3-dimethylindole (2.0 g). There was obtained 3.1 g of crude product which after two chromatograms and recrystallization from chloroform – petroleum ether yielded 28 mg of **18**, m.p. 178–183° (lit. (4) 186–194°).

(*b*) The low yields of **18** from section *a* and the difficulty of obtaining reproducible yields of **18** by thermal dehydration (3) of the dihydrodimer **26** led to the development of the following procedure.

A solution of **26** (480 mg) from $LiAlH_4$ reduction of **1** (3) in chloroform (35 ml) was refluxed for 36 h. The t.l.c. (benzene:ether, 50:50) showed the absence of starting material and the presence of a less polar product. Evaporation of the chloroform and recrystallization from ether – petroleum ether (b.p. 30–60°) gave 66 mg of colorless crystals of **18**. The residue from evaporation of the mother liquors was chromatographed on four thick plates developed with benzene – petroleum ether (63:37). The bands at R_f 0.36 yielded 70 mg more of **18** which after recrystallization amounted to 31 mg of **18** to bring the total yield of pure material to 97 mg (23%), m.p. 175–188°, identical with the compound prepared by the other two methods.

*Deuteration of Dimer **1***

(a) In Methanol-O-d_1 with Sodium Methoxide

A mixture of dimer (100 mg), sodium methoxide (100 mg), and methanol-*O*-d_1 (2 ml) was refluxed for 12 h with exclusion of atmospheric moisture. Evaporation of the methanol and partition between water and chloroform yielded 93 mg of recovered dimer which was recrystallized from methanol – petroleum ether. The 60 mg of **1** obtained was identical in melting point and t.l.c. behavior with starting material. Deuterium analysis by mass spectroscopy gave 78% d_0, 20% d_1, and 2% d_2 species.

(b) In Acetone-d_6 with DCl

To a solution of dimer **1** (100 mg) in acetone-d_6 (2 ml) was added a solution of 0.1 *N* DCl in D_2O (0.2 ml). The yellow solution was stirred at room temperature for 0.5 h and was then diluted with chloroform. Extraction with water, drying, and evaporation of chloroform left 105 mg of colorless oil. The t.l.c. showed the presence of **4** and **7***a* in addition to **1**. Separation on a thick plate developed in benzene–ether (75:25) gave 43 mg of recovered dimer which after recrystallization from methanol – petroleum ether was identical in melting point and t.l.c. behavior with **1**. Deuterium analysis by mass spectroscopy gave 85% d_0, 6% d_1, and 9% d_2.

*Homodimer **32***

To a stirred (magnetic bar) mixture of dimer **1** (400 mg), acetone (8 ml), and formaldehyde (1.6 ml of 37% aqueous solution) at room temperature was added a mixture of aqueous HCl (0.8 ml of 0.01 *N*) and acetone (0.5 ml). At the end of 5 min the pale yellow solution was added to ether, washed with water, dried, and concentrated to leave an amber oil. The t.l.c. in benzene–ether (50:50) showed the absence of **1** and the presence of a spot slightly more polar than **1** with considerable tailing. Chromatography on two thick plates developed in benzene–ether (75:25) yielded 280 mg (67%) of colorless crystalline solid from a band at R_f 0.43. Two recrystallizations from methanol – petroleum ether gave pure homodimer of m.p. 155–170° unchanged by further recrystallization; ν_{max} 3505 cm^{-1} (OH); λ_{max} 252 (6700) and 290 nm (1400); *m/e* 334 (molecular ion). This material was pure from its n.m.r. spectrum, and the wide melting point is due to decomposition to **30** during melting as demonstrated by t.l.c.

Anal. Calcd. for $C_{21}H_{22}N_2O_2$ (334.4): C, 75.42; H, 6.63; N, 8.38. Found: C, 75.11; H, 6.39; N, 8.49.

Treatment of the dimer with formaldehyde under the same conditions of concentration and acidity that allowed isolation of **4** gave only **30** and no **32**. Thus, from dimer (100 mg), acetone (2 ml), formaldehyde (0.5 ml of 37% aqueous solution), and aqueous HCl (0.2 ml of 0.1 *N*) after 15 min at room temperature there was obtained 103 mg (97%) of crude **30**. Thick layer chromatography and recrystallization from chloroform – petroleum ether gave 62 mg of pale yellow needles of 30, m.p. 146–147.5°, identical with the compound obtained from treatment of **1** with acid in dioxane.

*Rearrangement of Homodimer **32***

To a stirred (magnetic bar) solution of **32** (100 mg) in acetone (2 ml) at room temperature was added a solution of aqueous HCl (0.2 ml of 0.1 *N*) in a few drops of acetone. After 10 min the pale yellow solution was poured into ether, washed with water, dried, and concentrated to leave 93 mg (98%) of yellow solid. Two recrystallizations from chloroform – petroleum ether gave colorless **30**, m.p. 146–149°, identical with the artifact obtained by the action of acid on dimer **1** in dioxane.

We gratefully acknowledge the financial support of the National Research Council of Canada.

1. V. Dave and E. W. Warnhoff. Can. J. Chem. This issue.
2. V. Dave and E. W. Warnhoff. Chem. Commun. 919 (1970).
3. G. Berti, A. Da Settimo, G. Di Colo, and E. Nannipieri. J. Chem. Soc. 2703 (1969).
4. G. Berti, A. Da Settimo, and E. Nannipieri. J. Chem. Soc. 2145 (1968).
5. B. Witkop and J. B. Patrick. J. Am. Chem. Soc. **73**, 2196 (1951).
6. L. J. Dolby and D. L. Booth. J. Am. Chem. Soc. **88**, 1049 (1966).
7. W. I. Taylor. Proc. Chem. Soc. 247 (1962).
8. S. McLean, E. K. Strøm-Gundersen, K. S. Dichman, J. K. Fawcett, and S. C. Nyburg. Tetrahedron Lett. 2645 (1970).
9. W. I. Taylor. Helv. Chim. Acta, **33**, 164 (1950).