purified by chromatography on alumina in $C_6H_6$ and eluted with $C_6H_6$ with increasing proportions of EtOAc, when the product was obtained as an oil.

**2-(*N*-β-Hydroxyethyl-*N*-substituted)aminomethylquinoline (II) (R′ = $(CH_2)_2OH$).** T.—A mixture of 2-substituted aminomethylquinoline (II, R′ = H, 0.03 mol) and ethylene oxide (0.04 mol) in EtOH (50 ml) was stirred at 30° for 18 hr, solvent was evapd to dryness and the products were isolated as hydrochlorides.

**2-(3,4-Dihydroxyphenethyl)aminomethyl-1,2,3,4-tetrahydroquinoline (54).** U.—2-(3,4-Dimethoxyphenethyl)aminomethyl-1,2,3,4-tetrahydroquinoline (2.0 g) and HBr (20 ml of 48%) were refluxed 20 hr. Excess HBr was evapd *in vacuo* and the residue crystallized from EtOH–$Et_2O$ to give the HBr salt of the dihydroxy compound.

**2-Phenethylaminomethyldecahydroquinoline (IV) (63).**—2-Phenethylaminomethylquinoline (II, R′ = H, R = $(CH_2)_2C_6H_5$, 2.9 g) in AcOH (50 ml) and 5% Rh-C (1 g) at 70–80° were hydrogenated under 5 atm of $H_2$. The usual work-up gave the free base, which was purified by chromatography and obtained as an oil: yield, 2.7 g; nmr ($CCl_4$) showed only one singlet (2.8 δ, $C_6H_5$) in the aromatic region. *Anal.* ($C_{18}H_{22}N_2$), N.

**3-Phenethyl-1,2-dioxoperhydro-1(*H*)-pyrazino[1,2-*a*]quinoline (V) (64).**—IV was converted into V by the action of diethyl oxalate as described earlier: crystallized from EtOAc hexane, mp 210°; yield, 75%. *Anal.* ($C_{20}H_{26}N_2O_2$), N.

**3-Phenethylperhydro-1(*H*)-pyrazino[1,2-*a*]quinoline (VI) (65)** was obtained by LAH reduction of V as described earlier, and purified by chromatography: mp 55–60°, yield 70%; nmr ($CCl_4$) 2.85 (s, $C_6H_5$), 7–8.8 (m, 25 protons); VI·2HCl, crystallized from EtOH, mp 220°. *Anal.* ($C_{20}H_{30}N_2$) C, H.

**Acknowledgment.**—We wish to express our thanks to Dr. B. N. Dhawan for his interest in this work, to Mr. R. M. Saxena, G. Shanker, and P. S. Gupta for technical assistance, and to Riker Laboratories, Northridge, Calif., for a supply of chemicals. The assistance of Mr. B. B. P. Srivastava and Mr. J. Saran and his associates for nmr and microanalyses is gratefully acknowledged.

# Benzo[*g*]quinolines. II. Novel Synthesis and Pharmacological Evaluation of *cis*-1-Alkyl-1,2,3,4,4a,5,10,10a-octahydrobenzo[*g*]quinolines[1]

W. F. MICHNE AND N. F. ALBERTSON

*Sterling-Winthrop Research Institute, Rensselaer, New York*

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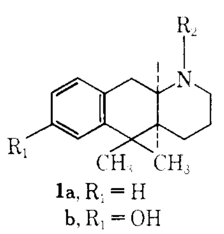
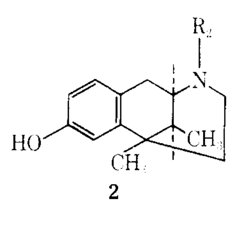
Cyclization of N derivatives of *trans*-2-(*p*-methoxybenzyl)-α,α-dimethyl-3-piperidinemethanol gives derivatives of mixtures of *cis*- and *trans*-1,2,3,4,4a,5,10,10a-octahydro-7-methoxy-5,5-dimethylbenzo[*g*]quinoline, the product ratios depending on the N substituent. Cyclization of the *cis* alcohols gives the *cis* products exclusively. A possible explanation involving olefinic intermediates is discussed, along with the application of this phenomenon to the synthesis of *cis*-1-alkyl-1,2,3,4,4a,5,10,10a-octahydrobenzo[*g*]quinolines and their evaluation as narcotic antagonists.

In our previous paper,[2] it was established that certain *N*-alkyl derivatives of *cis*-1,2,3,4,4a,5,10,10a-octahydro-5,5-dimethylbenzo[*g*]quinolin-7-ol (**1b**) possessed approximately 0.05 the narcotic antagonist activity (*vs.* meperidine) of the correspondingly *N*-substituted β isomer of 2′-hydroxy-5,9-dimethyl-6,7-benzomorphan (**2**). Our basic premise was that these alkyl derivatives of **1b** probably owe their activity to the fact that they can assume a conformation in which much of the



**1a**, $R_1$ = H
**b**, $R_1$ = OH



**2**

molecule is superimposable on the corresponding *N*-alkyl derivative of **2**. If such be the case, then one might conclude that the mechanisms of action of the two different types of molecules are the same, or at least very similar.[3] A necessary (but not sufficient) condition for the validity of this interpretation is that removal of the C7-OH function of **1b** to give **1a** should lead to decreased activity in this series, since the corresponding change in the series of **2** derivatives results in such a decrease.[4] With this idea in mind, synthetic approaches to the efficient production of **1a** ($R_2$ = H) were explored.

**Chemistry.**—The general synthesis of compounds in the **1b** series found only limited applicability to the preparation of **1a** ($R_2$ = H **9**) = (Scheme I). Acylation of diethyl 2-cyanoethylmalonate with phenylacetyl chloride using NaH afforded **3**. Catalytic reduction of this ketonitrile over Pt gave **4**. Carbobenzoxylation of **4** gave **5** which was saponified to half-acid ester **6**. Decarboxylation of **6** gave **7a** as a mixture of stereoisomers. However, unlike the mixture **7b** from which the *cis* isomer crystallized readily, mixture **7a** could not be separated. Treatment of mixture **7a** with MeMgI followed by hydrogenolysis of the carbobenzoxy group gave a mixture of **8a** isomers, also inseparable. Cyclization of mixture **8a** with hot 1:5 $H_2SO_4$–AcOH gave a mixture of approximately 60% **9** and 40% **10** as determined by nmr.[2,5] This mixture could be separated through the use of dry column chromatography[6] on alumina; however, only small quantities of the mixture could be separated at any one time.

The difficulties attending the separation of stereoisomers in Scheme I made it desirable to find an alternative route to the large scale preparation of **9**.

(1) Taken in part from the Ph.D. thesis of W. F. Michne, Rensselaer, Polytechnic Institute, Troy, New York, June, 1968.

(2) W. F. Michne and N. F. Albertson, *J. Med. Chem.*, **12**, 402 (1969).

(3) For a discussion of the implications of such a comparison, see P. S. Portoghese, *J. Pharm. Sci.*, **55**, 865 (1966).

(4) N. F. Albertson, unpublished results.

(5) Since the **8b** isomers cyclize without losing their configurations, it can be assumed that the **8a** isomers behave similarly. Hence, the composition of mixture **8a** is probably 60% *cis* and 40% *trans*.

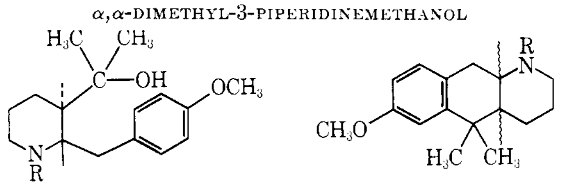
(6) B. Loev and M. M. Goodman, *Chem. Ind.*, 2026 (1967).

One possibility was to convert mixture **8a** into some derivative mixture from which the *cis* isomer could be readily crystallized. Such a derivative could then either be converted back into *cis*-**8** and cyclized, or be cyclized and subsequently converted into **9**. When mixture **8a** was treated with TsCl in pyridine (Scheme II), there resulted a crystalline, easily purified N-Ts derivative **12** (30% yield). This derivative cyclized readily to give 95% pure **14** which in turn was converted into **9** by treatment with LAH. The *N*-methyl, -allyl, -propyl, and -cyclopropylmethyl derivatives of **9** were prepared by the usual procedures.

Having achieved our objective of a facile preparation of **9**, it was of interest to determine if **10** could be equally readily prepared by cyclization of the residue **13** from the crystallization of **12**. To our great surprise, cyclization of **13** did not produce any more than 20% **15**; the major portion of the product (approximately 80% of the crude material) was the *cis* product **14**. Now, since about half of the crude tosylation product was isolated as the crystalline *cis* isomer **12**, then the major portion of the residue **13** should be the *trans* isomer. If this is so, then the cyclization of the N-Ts derivatives of both *cis* and *trans* starting materials gives largely the *cis* product! Needless to say, this most unusual transformation was a bonus for our synthetic effort and certainly warranted further investigation.

The investigation of this cyclization reaction was carried out using as starting materials the pure *cis* and *trans* isomers of **8b** because of their availability. The *N*-methyl, -*p*-nitrophenyl, -acetyl, and -*p*-nitrobenzenesulfonyl derivatives of each isomer were prepared and cyclized, and the composition of the crude reaction mixture determined by nmr. All of the *cis* isomers cyclized to give >95% *cis* product. The results from the *trans* isomers are shown in Table I. That the

Table I
Product Distribution in the Cyclization of Derivatives of *trans*-2-(*p*-Methoxybenzyl)-$\alpha,\alpha$-dimethyl-3-piperidinemethanol

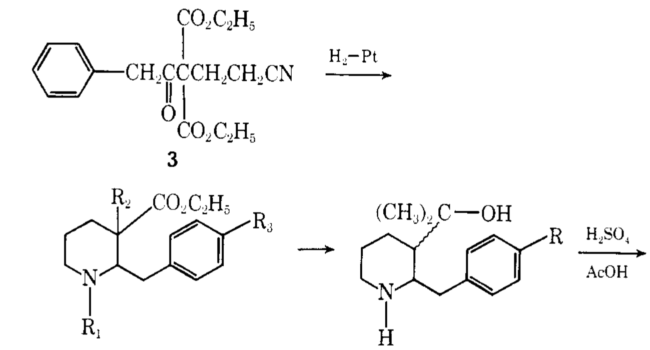


| R | % *trans* | % *cis* |
|---|---|---|
| H | >95 | <5 |
| $CH_3$ | 80 | 20 |
| *p*-$C_6H_4NO_2$ | 65 | 35 |
| $COCH_3$ | 40 | 60 |
| *p*-$SO_2C_6H_4NO_2$ | 20 | 80 |

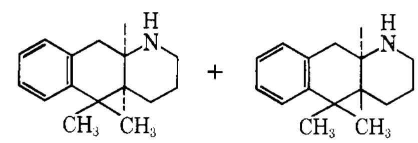
interchange does not take place after the cyclization reaction was shown by the fact that when *trans*-1,2,3,4,4a,5,10,10a-octahydro-7-methoxy-5,5-dimethyl-1-(*p*-nitrobenzenesulfonyl)benzo[*g*]quinoline is subjected to the reaction conditions, it is recovered unchanged. These results suggest that the extent of isomer interchange is in some way dependent on the basicity of the nitrogen.

It is tempting to speculate on the intermediacy of a tetrasubstituted olefin in this reaction.[7] The required olefin **23** (R = H) could not be synthesized directly by dehydration of the **8b** carbinols because of their facile cyclization. However, the olefin was isolated from a large scale preparation of **8b** isomers, and the same derivatives were prepared and cyclized. In all cases, the product mixture contained the *cis* and *trans* products in a ratio of 80:20, respectively. Hence the olefin could conceivably be an intermediate in the cyclization of the *trans* carbinols **8b**, with the amount of olefin formed being determined by the conformational preference of the starting alcohol in the cyclization medium, which in turn is influenced by the basicity of the nitrogen. Specifically, both isomers of the alcohols under consideration can exist in two conformations as shown in Scheme III. The *cis* isomers (**16** and **17**) can undergo cyclization in either conformation, since the distance between reacting centers is the same

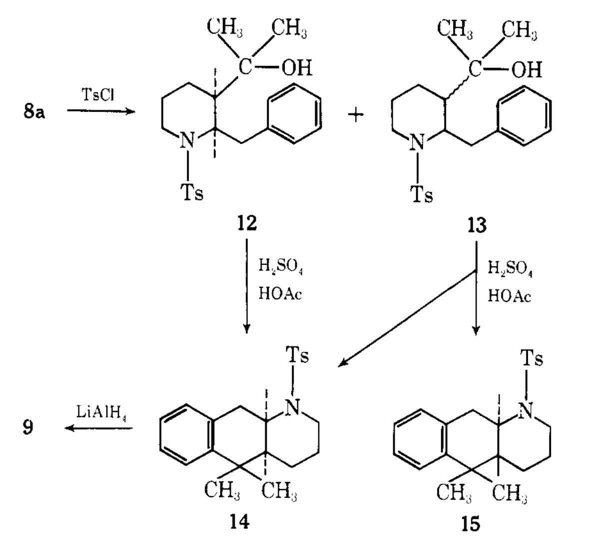
Scheme I



**4**, $R_1 = H; R_2 = CO_2C_2H_5; R_3 = H$
**5**, $R_1 = CbzO; R_2 = CO_2C_2H_5; R_3 = H$
**6**, $R_1 = CbzO; R_2 = COOH; R_3 = H$
**7a**, $R_1 = CbzO; R_2 = H; R_3 = H$
**b**, $R = CbzO; R_2 = H; R_3 = OCH_3$
**8a**, R = H
**b**, $R = OCH_3$



Scheme II

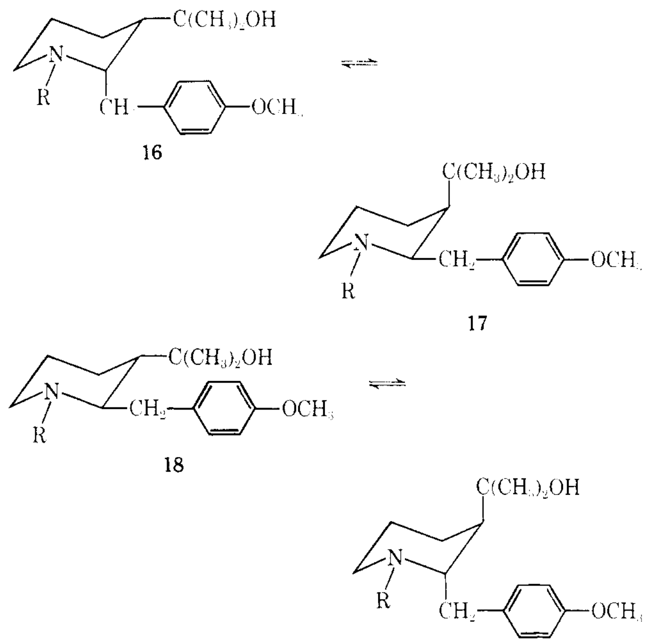


(7) A tetrasubstituted olefin should cyclize to give predominantly the *cis* product.[8,9]

(8) H. E. Zimmerman and T. W. Cutshall, *J. Amer. Chem. Soc.*, **80**, 2893 (1958).

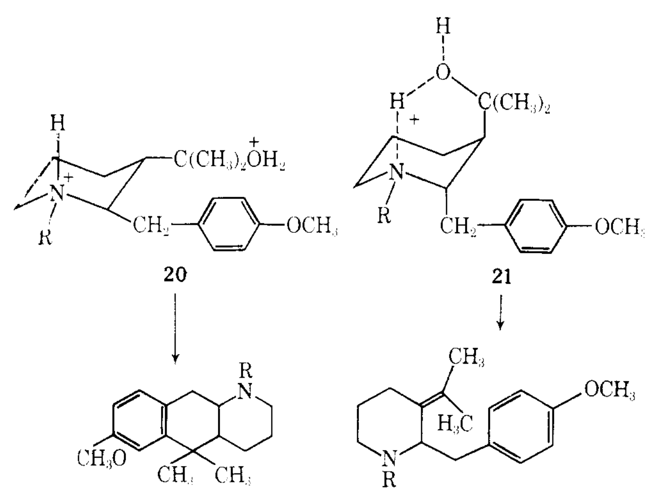
(9) F. Johnson and S. K. Malhotra, *ibid.*, **87**, 5492, 5493 (1965).

Scheme III



16 17 18 19

Scheme IV



20 21 22 23

in both conformations. In the *trans* isomers, only conformation **18** can cyclize readily; conformation **19** would prefer olefin formation over cyclization due to the prohibitive distance over which the cyclization would have to occur. In the cyclization medium, **20** (Scheme IV) would probably be preferred in the more basic derivatives since this would result in maximum separation of charge in the N,O-diprotonated species. With the less basic derivatives, **21** would probably be preferred due to an intramolecular stabilization of a monoprotonated species. This proposal presupposes that the *trans* carbinols can exist in the diaxial conformation **19**. Ir spectral studies of the *trans* carbinols have established that in $CCl_4$ when R = Me, **19** is the exclusive conformation; and that when R = *p*-nitrobenzenesulfonyl, a large percentage of the molecules exist as **19**.[10]

**Pharmacology.**—The *N*-methyl, -allyl, -propyl, and -cyclopropylmethyl derivatives of **9** were assayed for narcotic antagonist activity by the rat tail flick method[11] *vs.* meperidine. Using this method, low narcotic antagonist activity was indicated for these compounds, but no reliable $AD_{50}$ values were obtained. Thus, the 7-OH function enhances activity.

## Experimental Section

Melting points were determined by the capillary method and are uncorrected. Ir (Perkin-Elmer) and nmr (Varian Associates A-60) substantiated all structures.

Where analyses are indicated only by symbols of the elements, analytical results obtained for those elements are within ±0.4% of the theoretical values.

**Diethyl 2-Cyanoethylphenylacetylmalonate (3).**—This procedure has been described.[2] Using 21.9 g (0.55 mol, 60% dispersion) of NaH, 106 g (0.55 mol) of diethyl 2-cyanoethyl malonate, and 77.5 g (0.5 mol) of phenylacetyl chloride, there was obtained 152 g (92%) of crude **3**. A sample was twice distilled, bp 165–166° (0.02 mm), $n^{25}$ 1.4977. *Anal.* ($C_{18}H_{21}NO_5$) C, H, N.

**Diethyl 2-Benzyl-3,3-piperidinedicarboxylate Hydrochloride (4).**—This procedure has been described.[2] Using 91.8 g (0.28 mol) of crude **3**, there was obtained 57.4 g of crude **4**, mp 179°. Recrystallization from EtOH–$Et_2O$ gave pure **4**, mp 188°. *Anal.* ($C_{18}H_{26}ClNO_4$) C, H, N.

**Diethyl 2-Benzyl-1-benzyloxycarbonyl-3,3-piperidinedicarboxylate (5).**—This procedure has been described.[2] Using 68.7 g (0.19 mol) of **4**, 36 g (0.21 mol) of carbobenzoxy chloride, 280 ml of $CHCl_3$, and 43 g (0.42 mol) of $Et_3N$ there was obtained 89 g (102%). A sample was crystallized and recrystallized from hexane, mp 66–70°. *Anal.* ($C_{26}H_{31}NO_6$) C, H, N.

**2-Benzyl-1-benzyloxycarbonyl-3-carbethoxy-3-piperidinecarboxylic Acid (6).**—This procedure has been described.[2] Using 379 g (0.82 mol) of crude **5**, 54 g (0.82 mol) of KOH, 825 ml of EtOH, and 825 ml of $H_2O$, there was obtained 148 g of crude **6** along with 185 g of recovered **5**. A sample of crude **6** was recrystallized from EtOH, mp 182–184°. *Anal.* ($C_{24}H_{27}NO_6$) C, H, N.

*cis*- and *trans*-**1,2,3,4,4a,5,10,10a-Octahydro-5,5-dimethylbenzo[*g*]quinoline Hydrochloride (9 and 10). A. Using mixture 8a.** —These procedures have been described.[2] Using 300 g (0.70 mol) of crude **6**, there was obtained 216 g (80%) of crude mixture **7a**. When this mixture in 2000 ml of $Et_2O$ was treated with Grignard reagent from 41.3 g (1.7 mol) of Mg turnings, 242 g (1.7 mol) of MeI, and 500 ml of $Et_2O$, there was obtained 201 g of crude mixture. Hydrogenolysis in EtOH containing 1 equiv of HCl and 10 g of Pd–C gave 106 g of mixture **8a**. When 1.1 g (5 mmol) of this mixture was treated with 5.5 ml of AcOH and 1.1 ml of $H_2SO_4$, there was obtained a mixture (approximately 60:40 by nmr[12]) of **9** and **10**. This mixture was separated using dry column chromatography, on alumina, and developing with $CHCl_3$–5% MeOH. The bases were characterized as their hydrochlorides. The *cis* isomer **9** had mp 265–266°. *Anal.* ($C_{15}H_{22}ClN$) C, H, N. The *trans* isomer had mp 286–287°. *Anal.* ($C_{15}H_{22}ClN$) C, H, N.

**B.**—To a stirred suspension of 200 mg of LAH in 5 ml of THF was added 200 mg of **14** (*vide infra*) in 5 ml of THF. The reaction mixture was refluxed for 6 hr, quenched with 1 ml of $H_2O$, and filtered. The filtrate was evaporated, and the residue was partitioned between 1 *N* HCl and $Et_2O$. Basification of the acid layer with $NH_4OH$ followed by $Et_2O$ extraction, drying, and precipitation of the HCl salt gave **9** identical with that prepared according to procedure A.

**Derivatives for Pharmacological Evaluation.**—The *N*-Me, -cyclopropylmethyl, -allyl, and -Pr derivatives of **9** were prepared by the procedures referred to in ref 2, and had the following properties: N-Me, bp 75° (0.05 mm), *Anal.* ($C_{16}H_{23}N$) C, H, N; *N*-cyclopropylmethyl, bp 103–105° (0.05 mm), *Anal.* ($C_{19}H_{27}N$) C, H, N; *N*-allyl, bp 82–85° (0.05 mm), *Anal.* ($C_{18}H_{25}N$) C, H, N; N-Pr, bp 90–99° (0.05 mm), *Anal.* ($C_{18}H_{27}N$) C, H, N.

**2-Benzyl-α,α-dimethyl-1-(*p*-toluenesulfonyl)-3-piperidinemethanol (12 and 13).**—To a solution of 7.0 g (0.03 mol) of crude mixture **8a** in 35 ml of $C_5H_5N$ was added with stirring 5.7 g (0.03

(10) W. F. Michne, to be published.

(11) L. S. Harris and A. K. Pierson, *J. Pharmacol. Exp. Ther.*, **143**, 141 (1964).

(12) The Me signals for the *cis* isomer occurred at 78 and 73 Hz, while those for the *trans* isomer occurred at 78 and 66 Hz.

mol) of $p$-TosCl in 35 ml of pyridine. Stirring was continued for 0.5 hr after which the solvent was removed by distillation. The residue was partitioned between $H_2O$ and $Et_2O$. The $Et_2O$ layer crystallized to give 3.8 g of **12**. Evaporation of the mother liquor gave 3.5 g of mixture **13** which was not characterized. Two recrystallizations of **12** from EtOH afforded material which had mp 172–174°. *Anal.* ($C_{22}H_{29}NO_3S$) C, H, N.

***cis*-1,2,3,4,4a,5,10,10a-Octahydro-5,5-dimethyl-1-(*p*-toluenesulfonyl)benzo[*g*]quinoline (14).** **A.**—Compound **12** (2.8 g, 0.07 mol) was cyclized according to the procedure given above for the preparation of **9** and **10**. Crystallization of the crude residue from EtOH gave 2.2 g of **14**. Recrystallization from EtOH gave material, mp 143–145°. *Anal.* ($C_{22}H_{27}NO_2S$) C, H, N.

**B.**—Residue **13** (0.54 g, 0.0014 mol) was cyclized according to the above procedure to give 0.36 g of **14** identical with that prepared above.

**Carbinols for Cyclization Studies.**—These derivatives were prepared from the pure isomeric amino alcohols **8b**.[2] Reductive methylation with $CH_2O$ and $H_2$ over Pd–C gave the NMe derivatives: *cis* isomer m p94–96°, *Anal.* ($C_{17}H_{27}NO$) C, H, N; *trans* isomer mp 78–79°, *Anal.* ($C_{17}H_{27}NO$) C, H, N. Acylation with AcCl or $p$-$O_2NC_6H_4SO_2Cl$ in $CHCl_3$ in the presence of $Et_3N$ gave the corresponding amide: *cis-N*-acetyl, mp 138–141°, *Anal.* ($C_{18}H_{27}NO_3$) C, H, N; *trans-N*-acetyl, mp 111–113°, *Anal.* ($C_{18}H_{27}NO_3$) C, H, N; *cis-N-p*-$O_2SC_6H_4NO_2$, mp 182–186°, *Anal.* ($C_{22}H_{28}N_2O_6S$) C, H, N; *trans-p*-$O_2SC_6H_4NO_2$, mp 132–134°, *Anal.* ($C_{22}H_{28}N_2O_6S$) C, H, N. The $p$-$C_6H_4NO_2$ derivatives were prepared according to the procedure of Badar, et al.[13] These compounds could not be obtained crystalline, and were characterized only by their ir spectra.

**3-Isopropylidene-2-*p*-methoxybenzylpiperidine and Derivatives.**—The neutral fraction from the decarbobenzoxylation of 1-benzyloxycarbonyl-2-($p$-methoxybenzyl)-$\alpha$,$\alpha$-dimethyl-3-piperidinemethanol was allowed to stand for 3 months. A 21.7-g sample of this residue was diluted to 200 ml total volume with EtOH and hydrogenated over Pd–C at room temperature and 4 atm. Uptake ceased after 3 hr withthe consumption of approximately 1 molar equiv of $H_2$. The basic fraction was dissolved in dil HCl and cooled to give, after filtration and drying, 9.1 g of crude **23**·HCl. Recrystallization from EtOH–$Et_2O$ gave pure **23**, mp 255–257°, nmr ($CDCl_3$, TMS) 413 ($A_2B_2$,4) 223 (s, 3), 95 (s, 3), 64 Hz (s, 3). *Anal.* ($C_{16}H_{24}ClNO$) C, H, N.

The NMe and $p$-$SO_2C_6H_4NO_2$ derivatives were prepared by the procedures indicated in the previous section and had the following properties: NMe·HCl, mp 179–183°, *Anal.* ($C_{17}H_{26}ClNO$) C, H, N; *N-p*-$SO_2C_6H_4NO_2$, mp 114–116°, *Anal.* ($C_{22}H_{26}N_2O_5S$) C, H, N.

**Benzo[*g*]quinoline Derivatives as Nmr References.**—The corresponding derivatives of *cis*- and *trans*-1,2,3,4,4a,5,10,10a-octahydro-5,5-dimethyl-7-methoxy-benzo[*g*]quinoline were prepared by the same procedures and the nmr spectra recorded. The compounds not previously reported had the following physical properties (the numbers in parentheses following the melting point are the chemical shifts in Hz of the *gem*-$Me_2$ groups in the 60 MHz nmr spectra): *cis*-N-$p$-$C_6H_4NO_2$, glass (80,79), *Anal.* ($C_{22}H_{16}N_2O_3$) C, calcd, H, 6.89, N, 7.67; found, H, 7.41, N, 8.60; *trans*-N-$p$-$C_6H_4NO_2$, mp 164–166° (83,70), *Anal.* ($C_{22}H_{26}N_2O_3$) C, H, calcd, N, 7.67; found, 9.04; *cis-N*-acetyl, mp 81–85° (80,78), *Anal.* ($C_{18}H_{25}NO_2$) C, H, calcd, N, 4.87; found 5.33; *trans-N*-acetyl, mp 157–159° (80,68), *Anal.* ($C_{18}H_{25}NO_2$) C, H, N; *cis*-N-$p$-$SO_2C_6H_4NO_2$, mp 159–161° (81,79), *Anal.* ($C_{22}H_{26}N_2O_5S$) C, H, N, *trans*-N-$p$-$SO_2C_6H_4NO_2$, mp 204–205° (79,59), *Anal.* ($C_{22}H_{26}N_2O_5S$) C, H, N.

**Cyclization Procedure.**—A solution of 100 ml of AcOH and 20 ml of $H_2SO_4$ was used for all cyclizations. A 125-mg sample of the carbinol and 1.0 ml of the acid were heated on a steam bath for 5 min, diluted with 25 ml of $H_2O$, made slightly basic with $NH_4OH$, and extracted with 25 ml of $CHCl_3$. The extract was dried, filtered, and concentrated and the entire residue used for nmr. The resulting spectrum was compared with that of the two pure products, and the relative amounts of each determined.

**Acknowledgments.**—The authors wish to thank Mr. K. D. Fleischer for elemental analyses, Dr. R. K. Kullnig for spectral data, and Mr. A. K. Pierson for pharmacological results.

(13) H. Bader, A. R. Hansen, and F. J. McCarty, *J. Org. Chem.*, **31**, 2319 (1966).

# Novel Analgetics and Molecular Rearrangements in the Morphine–Thebaine Group. XVIII.[1] 3-Deoxy-6,14-*endo*-etheno-6,7,8,14-tetrahydrooripavines

JOHN W. LEWIS AND MICHAEL J. READHEAD

*Pharmaceutical Research Laboratories, Reckitt & Sons, Hull, England*

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7-Substituted 3-deoxy-6,14-*endo*-etheno-6,7,8,14-tetrahydrooripavines have been prepared by hydrogenolysis of the oripavine diethylphosphatyl esters. In some cases partial reduction of the etheno bridge also occurs. The deoxy compounds show analgetic potency intermediate between the oripavine and thebaine analogs.

The nature of the $C_3$ substituent is very important in determining analgetic potency in the morphine series (**1**).[2] Thus heroin (**1c**) is more potent than morphine (**1a**) which is itself considerably more potent than codeine (**1b**). In the related series of analgetics (**3b–6b**) derived from 6,14-*endo*-ethenotetrahydrooripavine the effect of removing the phenolic hydroxyl group by hydrogenolysis with Na in liquid $NH_3$ of the diethyl phosphate derivatives (**2**)[3] has now been investigated.

The phosphates were prepared by reaction of the oripavine derivatives with diethyl phosphite and $CCl_4$ and were dissolved in $Et_2O$ for the Na–liquid $NH_3$ reaction. In most cases the hydrogenolysis reaction went to completion but purification of the products was not always easy. In the case of the 7-dimethylcarbinol (**3c**) a by-product having similar chemical and physical properties was isolated by preparative tlc. This was shown to be identical with the 3-deoxy compound (**8c**) derived from the 6,14-*endo*-ethanooripavine (**8b**). Hydrogenation of the olefinic bond by Na in liquid $NH_3$ was surprising in view of the fact that **3a** is catalytically hydrogenated only with difficulty,[4] and reduction of disubstituted olefins by metal–amine systems occurs only with the powerful Li–alkylamine reagents.[5] The

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