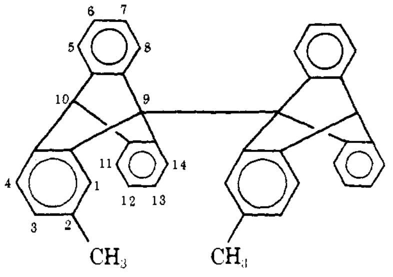
cyano-1-methylethyl)triptycene.[3] Previously, we reported the synthesis of 9,9′-bitriptycyl.[4] We report herein on 2,2′-dimethyl-9,9′-bitriptycyl (**1**), which exhibits an enormous rotational barrier between the central 9 and 9′ sp^3-hybridized carbon atoms, in excess of 54 kcal mol^{-1}.

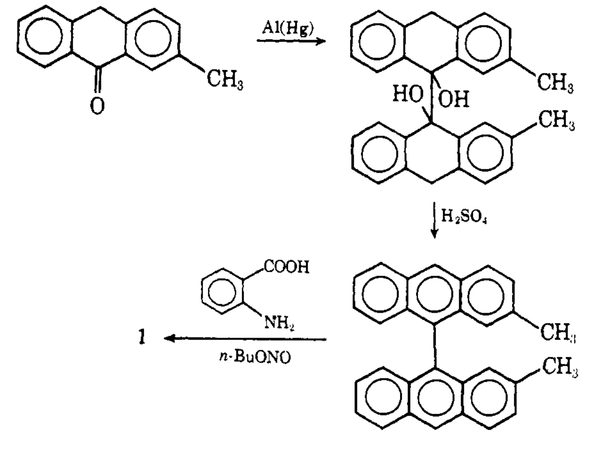


1

The synthesis of **1** is outlined in Scheme I.[5] The NMR spectrum, in $CDCl_3$, of the initially isolated material from column chromatography exhibited two closely spaced singlets at δ 1.83 and 1.81 ($ArCH_3$). In repetitive experiments, the higher field singlet was ~50–80% the height of the lower field singlet. The rest of the spectrum consisted of a singlet at δ 5.55 (H_{10} and $H_{10'}$) and a complex multiplet at 7.6–6.4 (ArH). IR, UV, and mass spectra were consistent with structure **1**. This material was separated into two samples, **1a** (mp 473–478 °C dec, more soluble) and **1b** (mp 505 °C dec, less soluble) by repeated crystallization from chloroform-acetone and combination of appropriate fractions. **1a** and **1b** exhibited virtually identical TLC, IR, UV, and mass spectral behavior, both to one another, as well as to the initially isolated material. Their NMR spectra differed from each other and from the initially isolated material only in the methyl region. Both showed δ 1.83 and 1.81 peaks. However, the δ 1.83/1.81 peak height ratios differed, 2.10 ± 0.04 for **1a** and 0.44 ± 0.02 for **1b**. We conclude, from these results, that **1a** and **1b** are both mixtures of differing amounts of noninterconverting skew and anti conformers of **1**. The δ 1.83 peak corresponds to one of the conformers and the δ 1.81 peak to the other.[6] On the basis of higher melting point and lower solubility, the δ 1.81 peak is, tentatively, assigned to the more symmetrical anti conformer.

In an attempt to measure the rotational barrier between the conformers, **1a** and **1b** were heated in a variety of solvents. However, we were unable to bring about a significant change in the ratio of the δ 1.83 and 1.81 peaks. Our most severe conditions involved heating in naphthalene solution, under a nitrogen atmosphere in a sealed glass vial, for 171 h at 300 ± 5 °C. Sublimation of the naphthalene resulted in quantitative recoveries of **1a** and **1b** with δ 1.83/1.81 ratios of 2.06 ± 0.05 and 0.42 ± 0.02, respectively. Assuming an arrhenius preexponential factor of $10^{13.7}$ and an error of 2.5% in the measurement of the δ 1.83/1.81 ratio, a minimum rotation barrier of 54 kcal mol^{-1} is calculated.[8] By comparison with the large rotation barriers previously observed for 9-alkyl substituted triptycenes,[2b,3] the enormity of the barrier in the 9,9′-bitriptycyl system is reasonable.

Scheme I



References and Notes

- (1) Partial support from the National Science Foundation, the Research Corporation, and the General Faculty Research Committee of the City College of New York is gratefully acknowledged.
- (2) For leading references, see (a) J. E. Anderson, C. W. Doeke and D. I. Rawson, *Tetrahedron Lett.* 3531 (1975); (b) M. Oki, *Angew. Chem., Int. Ed. Engl.*, **15**, 87 (1976).
- (3) H. Iwamura, *J. Chem. Soc., Chem. Commun.*, 232 (1973).
- (4) C. Koukotas, S. P. Mehlman, and L. H. Schwartz, *J. Org. Chem.*, **31**, 1970 (1966).
- (5) All new compounds gave satisfactory elemental analyses and exhibited spectral properties (IR, NMR, mass, UV) consistent with their structures.
- (6) To eliminate the possibility that a major contaminant was present which caused one of the peaks in the δ 1.8 region, we synthesized, for comparison, a variety of compounds which could either be contaminants or would serve as models for possible contaminants. These included[5] 2-methylanthracene; 2,3-benzotriptycene; 2,2′-, 3,3′-, and 4,4′-dimethyl-9,9′-bianthryl; 1-, 2-, and 9-methyltriptycene; and 3,3′- and 4,4′-dimethyl-9,9′-bitriptycyl. The spectral properties of these compounds led to the conclusion that they could not be present to any significant degree in our sample of **1**.
- (7) For leading references, see ref 2b.
- (8) A change of one order of magnitude in the estimated Arrhenius preexponential factor results in a change of ~2.6 kcal mol^{-1}. If the error in measurement of the δ 1.83/1.81 ratio is taken to be ±5%, the calculated minimum rotational barrier is 53 kcal mol^{-1}.

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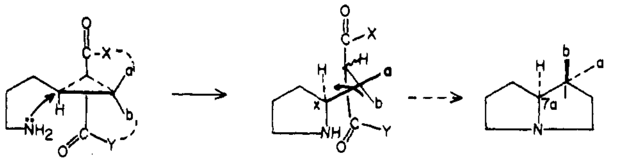
Stereospecific Total Synthesis of *dl*-Hastanecine and *dl*-Dihydroxyheliotridane

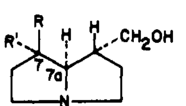
Sir:

Recently[1] we described a new method for achieving stereospecific control in the synthesis of the simple necine bases[2] trachelanthamidine (**3**) and isoretronecanol (**4**). The approach drew heavily on the notion of ring mutations[3,4] of activated cyclopropanes bearing intramolecular nucleophiles. At a crucial stage, systems such as **1**, of defined chirality, are unmasked. Ring mutation, through the spiro mode,[3] *with inversion of configuration*, leads to system **2** and thence to the final products.

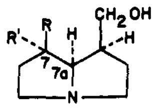


1 **2** **3** a = CH_2OH; b = H
4 a = H; b = CH_2OH

Below we describe the extension of this strategy to the synthesis of the more complex necine bases, bearing oxygen at C_7. Nature provides us with one representative enantiomer from each of the four diastereomeric families of these bases.[2] These are shown in formula **5–8**. Aside from the intellectual interest in learning how to systematically solve the stereochemical issues posed by these structures, the diverse,[5,7] and potentially useful,[8] biological properties of the senecio alkaloids (various acylated versions of the necine bases) provide additional synthetic incentives. In this paper, we report the stereospecific total synthesis of *dl*-hastanecine (**5**)[9] and *dl*-dihydroxyheliotridane (**6**).[10]

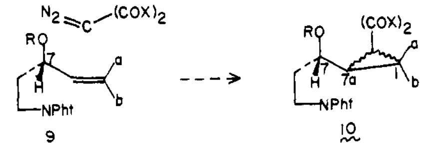


5 hastanecine R=H; R'=OH
7 turneforcidine R=OH; R'=H

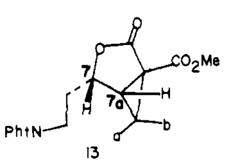


6 dihydroxyheliotridane R=H; R'=OH
8 platynecine R=OH; R'=H

The transformation, generalized as 9 → 10 would constitute a minimum perturbation of the route used for 3 and 4.[1] However, the conformational mobility of precursor 9 would tend to undermine the influence of C_7 in controlling the sense of cyclopropanation. A more promising possibility was envisioned in the transformation, 11 → 12 *wherein it was presumed that the transition state would arrange itself so that the bulky β-phthalimidoethyl group would emerge on the convex face of the cup-shaped bicyclo[3.1.0]oxahexanone system.*[11] By this postulate, 12 would predominate over 13 where the large function emerges on the concave surface.



9 10



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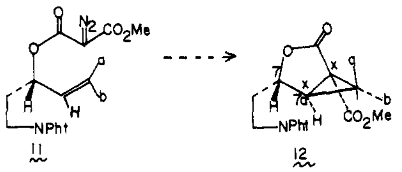
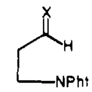
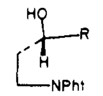


11 12

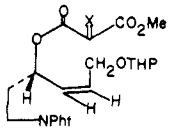
Ozonolysis of 14[3] (O_3, methylene chloride-methanol, −78 °C) afforded a 72% yield of aldehyde 15,[12] mp 107-109 °C. This was coupled to the magnesium salt of propargyl alcohol OTHP to provide a 54% yield of 16.[13,14] Semihydrogenation of 16[15] (H_2, Pd/$BaSO_4$-quinoline, MeOH) followed by chromatography on silica gel gave the pure Z isomer 17.[13,14] The alcohol was acylated with carbomethoxyacetyl chloride to give 18[13,14a] which was converted to the Z diazo ester, 19.[13,14a] Treatment of 19 with copper bronze at 110 °C afforded a 48% yield of a single cyclopropane. That this was indeed 20[13,14] was verified only through the subsequent steps, leading to hastanecine.



14 X = CH_2
15 X = O

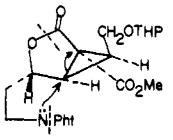


16 R = C≡C—CH_2OTHP
17 R = C(H)=C(H)CH_2OTHP

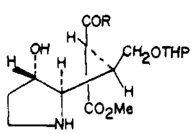


18 X = H_2
19 X = N_2

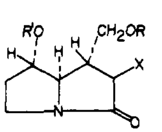
Compound 20 was converted (70%) to the diacetoxylactam 21d[14] by successive treatment with (i) 3 equiv of hydrazine in methanol (reflux 4 h), (ii) 10% aqueous HCl (reflux 12 h), (iii) sodium methoxide-methanol, and (iv) pyridine-acetic anhydride. In this sequence, we did not purify intermediates 21a–c. Treatment of 21d with lithium aluminum hydride gave an 81% yield of *dl*-hastanecine (5). The chromatographic mobility and infrared ($CHCl_3$), mass, and 250-MHz NMR spectra of synthetic *dl*-hastanecine were identical with those of the C_7 R enantiomer, kindly furnished by Professor C. C. J. Culvenor of Australia.



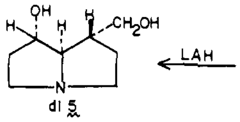
20



21a



21b R=OTHP; R'=H; X=$CONH_2H_3$
21c R=R'=X=H
21d R=R'=Ac; X=H



LAH

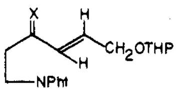
dl 5

It is seen again[1] that the ring opening of the cyclopropane has occurred with strict inversion of configuration. Any nonspecificity in this regard would have produced *dl*-platynecine (8) (the C_{7a} epimer of hastanecine). The TLC properties of platynecine (an authentic sample was also provided by Professor Culvenor) are sufficiently different from those of hastanecine, that it could easily have been detected were it present (vide infra).

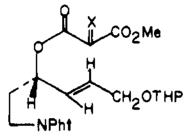
Our route to dihydroxyheliotridane was simplified by the finding that Corey oxidation[16] of Z alcohol 17 affords, quite cleanly, the E enone[14] 22. Sodium borohydride reduction of 22 thus afforded a simple route to E alcohol 23.[13,14] Compound 23 was converted ((i) carbomethoxyacetyl chloride-pyridine, (ii) tosyl azide-triethylamine) into 24[13,14a] and thence 25.[13,14a]

Compound 25 was heated at 110 °C in the presence of copper bronze to afford a 44% yield of a cyclopropane. The total cyclopropane material, formulated as 26,[13,14] was subjected to the same four-step sequence ((i) hydrazinolysis, (ii) decarboxylation, (iii) acetylation, (iv) lithium aluminum hydride reduction) to afford a 41% yield of *dl*-dihydroxyheliotridane. The TLC mobility and infrared, mass, and 250-MHz NMR spectra of the synthetic material were identical with those of an authentic sample of the optically active compound, obtained by catalytic reduction of a sample of heliotridine, kindly furnished by Professor Culvenor.

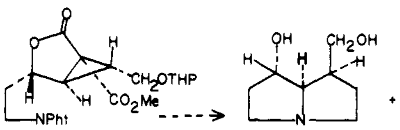
There was also detected from this sequence a trace amount (~2%) of platynecine (8) which was isolated by preparative TLC. We have not yet established the precise degree of correspondence of the ratio of the final necine bases to the ratio of the epimeric cyclopropanes derived from 25. However, it is clear that there is a heavy preponderance in favor of the exo precursor of 6.



17 ⟶ 22 X = O
23 X = H, OH



24 X = O
25 X = N_2



+ dl 8 (trace)

26 (+ trace of α-cyclopropane)

dl 6

In summary, it is clear that the presumption of exo cycloproponation (11 → 12 ≫ 13) has been sustained in practice. This coupled to the principle of spiro mode opening of activated cyclopropanes by intramolecular nucleophiles (in the ring size options at issue) can serve as the basis for a new and effective strategy for solving relative chirality problems in the synthesis of five-membered rings.[17-19]

Acknowledgments. This research was supported by PHS Grant CA-12107-12. NMR facilities were supported by RR 00292-08. Additional valuable support was provided by the Merck and CIBA-GEIGY Companies. We also wish to thank Professor C. C. J. Culvenor for providing us with authentic samples of hastanecine, platynecine, and heliotridine which were invaluable in verifying our synthetics.

References and Notes

(1) S. Danishefsky, R. McKee, and R. K. Singh, *J. Am. Chem. Soc.*, **99**, 4783 (1977).

(2) For a review of the chemistry of the necine bases, see (a) N. J. Leonard, "The Alkaloids", Vol. VI, R. H. F. Mauske, Ed., Academic Press, New York, London, 1960, Chapter 3; (b) F. L. Warren, "The Alkaloids", Vol. XII, R. H. F. Mauske, Ed., Academic Press, New York, London, 1970, Chapter 4; (c) "The Alkaloids", Vol. I–V, Chemical Society Specialist Reports, Periodical Reports, London, 1969–1975.

(3) S. Danishefsky, J. Dynak, W. Hatch, and M. Yamamoto, *J. Am. Chem. Soc.*, **96**, 1256 (1974).

(4) S. Danishefsky and J. Dynak, *J. Org. Chem.*, **39**, 1979 (1974).

(5) The senecio alkaloids[2] are composed of necine bases esterified with necic acids. For the toxological and/or antimitotic properties of the senecio alkaloids, see ref 6–8.

(6) L. B. Bull, C. C. J. Culvenor, and A. T. Dick, "The Pyrrolizidine Alkaloids", North Holland Publishers, Amsterdam, 1968.

(7) (a) L. B. Bull and A. T. Dick, *J. Pathol. Bacteriol.*, **78**, 483 (1959); (b) K. K. Cheu, P. N. Harris, and C. L. Rose, *J. Pharmacol. Exp. Ther.*, **68**, 130 (1940); (c) W. H. Butler, A. R. Mattocks, and J. M. Barnes, *J. Pathol.*, **100**, 169 (1970); (d) A. R. Mattocks and I. N. H. White, *Nature New Biol.*, **231**, 114 (1971).

(8) For the promising antitumor properties of indecine *N*-oxide (N.S.C. No. 132319), see V. K. Rao and T. J. McBride (Pfizer Inc), U.S. Patert 3 717 710; *Chem. Abstr.*, **78**, 140, 417b (1973).

(9) A. J. Aasen, C. C. J. Culvenor, and L. W. Smith, *J. Org. Chem.*, **34**, 4137 (1969). The structure of hastanecine was first established by K. G. Untch and D. J. Martin, *Ann. Rept. Mellon Inst., 52nd*, 11 (1965).

(10) R. Adams and B. L. van Duuren, *J. Am. Chem. Soc.*, **76**, 6379 (1954).

(11) The same result can be formulated by examination of the preferred conformation of the starting olefin, **11**. If it be assumed that the group CH═C(a)b is s-trans relative to the β-phthalimidoethyl function in the pre-insertion conformer, it is readily seen that the vinylic hydrogen, which becomes C_{7aH}, will be trans to the methine hydrogen which emerges at C_7 of the necine bases.

(12) The preparation of **15** by phase-transfer Gabriel reaction,[1] followed by ozonolysis, is more straightforward than direct Michael addition of potassium phthalimide to acrolein; see O. A. Moe and D. T. Warner, *J. Am. Chem. Soc.*, **71**, 1251 (1949).

(13) This is undoubtedly a diastereomeric mixture owing to the additional chirality in the tetrahydropyranyloxy function. At the level of chromatographic properties or spectral analysis this diastereomerism was not manifested and the two diastereomers are treated as a single entity.

(14) The structure assigned to this compound is in accord with (a) its infrared, NMR and mass spectra and (b) its C, H, and N combustion analysis within 0.4% of theory.

(15) Small amounts, ~5%, of *E* isomer were produced from the reaction and removed by silica gel chromatography; cf. E. N. Marvell and T. Li, *Synthesis*, 457 (1973).

(16) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1973).

(17) For the combination of stereospecific intramolecular carbene insertions and stereospecific inversion in the acid-catalyzed opening of an activated cyclopropane, see G. Stork and M. Marx, *J. Am. Chem. Soc.*, **1**, 2371 (1969).

(18) For a recent case where intermolecular inversion of configuration of an activated cyclopropane was used for purposes of achieving stereochemical control of a pendant center relative to a ring center, see B. M. Trost, D. F. Taber, and J. B. Alper, *Tetrahedron Lett.*, 3857 (1976).

(19) Two recent and very elegant contributions to the stereospecific synthesis of prostagsandins use the principle of inversion of configuration in the reactions of nucleophiles with activated vinylcyclopropanes. See (a) D. F. Taber, *J. Am. Chem. Soc.*, **99**, 3513 (1977); (b) K. Kondo, T. Umemoto, Y. Katahatake, and D. Tunemoto, *Tetrahedron Lett.*, 113 (1977).

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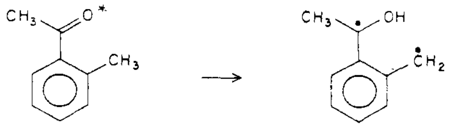
Role of Biradical Intermediates in the Photochemistry of *o*-Methylacetophenone

Sir:

The literature on the photoenolization of *o*-alkyl-substituted acetophenones and benzophenones is as abundant as it is confusing.[1] The process involves hydrogen abstraction from the γ position, i.e., as shown in eq 1.



(1)

It has been reported that reaction 1 occurs from two different excited states.[2,3] Lindqvist et al.[2] have suggested that the reaction takes place from both singlet and triplet states, while Wagner and Chen[3] have proposed that the two species involved are the syn and anti conformers of the triplet state of the ketone (**1** and **2**). The triplet state of **1** decays with a rate constant of $5 \times 10^9\ s^{-1}$. The decay of triplet **2** is controlled by bond rotation and has a rate constant of $3 \times 10^7\ s^{-1}$ in benzene.[3]

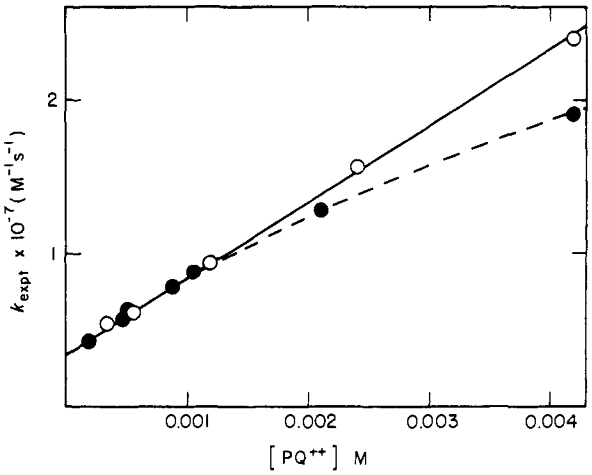
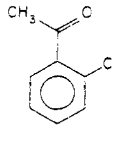
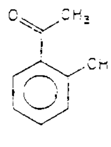


Figure 1. Plot of k_{expt} vs. $[PQ^{2+}]$ for *o*-methylacetophenone (○) in methanol containing 0.1 M *cis*-1,3-pentadiene and (●) containing no diene.



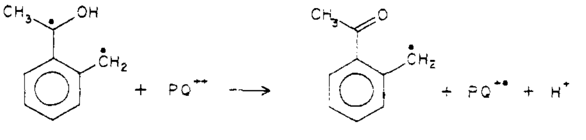
1



2

In this study we use a laser flash photolysis technique to examine the behavior of the biradical intermediate.[4] A nitrogen laser (400 kW, 337.1 nm, ~8-ns pulse duration) was used for excitation and the techniques employed are the same which we have recently developed for the study of the biradicals involved in the Norrish type II reaction.[6] We attempt to answer the following questions. (i) What is the lifetime of the biradical? (ii) Does the behavior of the biradical of reaction 1 resemble that of the biradicals produced in the Norrish type II reaction? (iii) Do we produce only one kind of biradicals as required by Wagner's mechanism,[3] or two, as apparently required[7] by Lindqvist's? (iv) What is the nature and rate constant of the interaction of oxygen with the biradicals?[5]

When biradicals having ketyl radical sites react with 1,1′-dimethyl-4,4′-bipyridilium dications (paraquat, PQ^{2+}) they produce the stable paraquat radical ion, $PQ^{+\cdot}$.[6,8] Reaction 2 illustrates the behavior in the case of the biradical form *o*-methylacetophenone.



(2)

The formation of $PQ^{+\cdot}$ follows pseudo-first-order kinetics, with a rate constant k_{expt}, which corresponds to[6b]

$$k_{expt} = \tau_B^{-1} + k_2[PQ^{2+}] \qquad (3)$$

where τ_B is the lifetime of the biradical intermediate. Figure 1 shows the results for a series of experiments in methanol. The experiments in the presence of 0.1 M *cis*-1,3-pentadiene were carried out to eliminate the reaction from the long-lived triplet state.[3] The addition of diene does not affect the intercept or the initial slope; therefore, the quenchable and nonquenchable