(10) For a review of propellane chemistry, see D. Ginsburg, *Int. Rev. Sci., Org. Chem., Ser. 2*, **5**, 369 (1976); D. Ginsburg, "Propellanes," Verlag-Chemie, New York, N.Y., 1975.
(11) D. Lloyd, "Carbocyclic Non-Benzenoid Aromatic Compounds," Elsevier, Amsterdam, 1966, p 132, and references cited therein.
(12) Diisopropylamine, the by-product of enolate formation, must be deprotonated again before the methylation step. Failure to do so leads to competitive formation of an ammonium ion which protonates the enolate, thus giving up to 60% recovered starting material (**10**).
(13) IUPAC name for compound **11**: 3-methoxybicyclo[5.3.1]undeca-1,3,5,7,9-pentaene.
(14) J. A. Elvidge and L. M. Jackman, *J. Chem. Soc.*, 859 (1961); L. M. Jackman, F. Sondheimer, Y. Amiel, D. A. Ben-Efraim, Y. Gaoni, R. Wolovsky, and A. A. Bothner-By, *J. Am. Chem. Soc.*, **84**, 4307 (1962); R. C. Haddon, *Tetrahedron*, **28**, 3635 (1972), and references cited therein.

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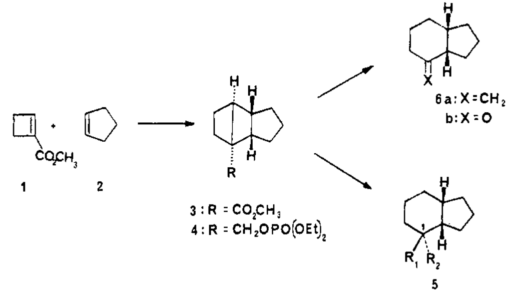
A Photochemically Mediated [4C + 2C] Annelation. Synthesis of (±)-10-Epijunenol

Sir:

We described in a previous communication[1a] a metathetical route to medium-sized carbocycles and a procedure for differentiated dialkenylation of olefins, methods pertinent to germacrane and elemane syntheses. More recently, our continuing studies on these and related annelation methods[2] have been extended to a further objective of general importance in synthesis design, the controlled synthesis of trans-[3] and cis-fused ring systems. The synthetic salience of a [4C + 2C] route to cis-fused [4.*n*.0] systems is described herein along with an application of this method to the synthesis of (±)-10-epijunenol (**18**).[4]

As illustrated for the annelation of cyclopentene (Scheme I), a [2 + 2] photocycloaddition[5] is utilized in the present method to effect a latent [4C + 2C] connection under mild thermal conditions (−78 °C to ambient temperature). The second step involving a σ-bond cleavage[6] facilitated by the strain[7] of the bicyclo[2.2.0]hexane subunit is readily performed by addition of the photoadduct (1 mol equiv in diethyl ether containing 5 mol equiv of *tert*-butyl alcohol) to a solution of lithium (10 g-atom equiv) in liquid ammonia (−33 °C). These reducing conditions (A), which provided the alcohols **5a–5a′** [8] in an isolated yield of 87% from photoadduct **3**, can be readily tailored to suit various synthetic objectives. For example, reduction of photoadduct **3** (1 mol equiv in tetrahydrofuran containing 0.8–0.9 mol equiv of aniline) with lithium (2.5 g-atom equiv) in liquid ammonia followed by addition of NH_4Cl (conditions B) provided esters **5b–5b′** [9] (79%, isolated), while quenching of the ester enolate intermediate with methyl iodide (conditions C) afforded the methylated esters **5c–5c′** (76%, isolated). Alternatively, the commonly occurring methylenecyclohexane subunit (vide infra) can be elaborated by metal–ammonia reduction of the phosphate ester[10] derived[11] from the photoadduct (e.g., **4** to **6a**).

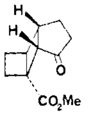
Scheme I

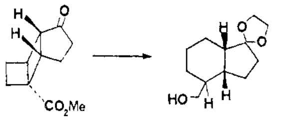


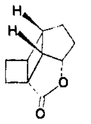
a: R_1=H, R_2=CH_2OH; a′: R_1=CH_2OH, R_2=H
b: R_1=H R_2=CO_2Me; b′: R_1=CO_2Me, R_2=H
c: R_1=Me R_2=CO_2Me; c′: R_1=CO_2Me, R_2=Me
d: R_1=H R_2=CO_2H; d′: R_1=CO_2H, R_2=H

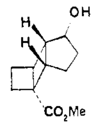
In accordance with a syn mode of photocycloaddition the *ring juncture stereochemistry* developed in this sequence was determined to be exclusively cis by the following correlations. Thus, saponification of esters **5b–5b′**, which were demonstrated to be related as C-1 epimers (NaOMe, MeOH) and which share a common ring juncture stereochemistry with **5a–5a′** and **5c–5c′**, gave the corresponding acid mixture from which the known acid **5d** (mp 77 °C, lit.[12] mp 77 °C) was easily isolated. Esterification (CH_2N_2) of **5d** afforded **5b**, the major product obtained from the initial cleavage reaction. Finally, acids **5d–5d′** were readily converted[12] to the known cis-fused indanone **6b.**[13]

As expected from previous studies,[14] the overall *regioselectivity* of the annelation is governed, in part, by steric and polar effects associated with the photocycloaddition step. While studies on how these effects can be utilized to control orientation are in progress, it is of interest to note at this point that the head-to-tail preference (1:2.5 = **7a:7b**, CH_2Cl_2, 50% yield) observed in the photoaddition of cyclopent-2-en-1-one to ester **1** is similar to that found in the related photodimerization of cyclopentenone.[15,16] The head-to-head and head-to-tail relationship between these adducts was unequivocally established by conversion of the **7a–7b** mixture (1:2 = **7a:7b**) to lactone **9** and ester **10** (1:2 = **9:10**, combined yield 90%);[17] independent transformation of **9** and **10** to adducts **7a** and **7b**, respectively; and comparison of the products obtained from pyrolysis of the original mixture and pure ester **7b.**[8] Finally, ketalization of **7b** followed by reduction (method A) furnished the annelated product **8**[8] (89%, isolated).

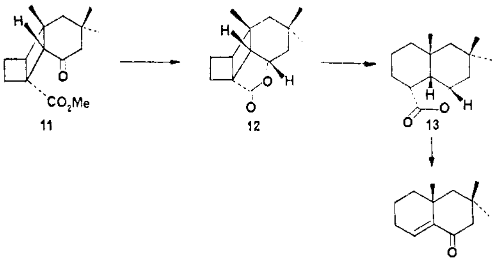

7a


7b
8


9


10

In contrast to cyclopentenone, irradiation of isophorone in the presence of ester **1** provided substantially, if not exclusively, adduct **11** (85%, isolated) which was assigned the cis-anti-cis, head-to-head structure on the basis of its conversion (K-selectride, H_3O^+; 76%) to lactone **12.**[1a] Reduction (method A) of **12** provided a single lactol (mp 127–128 °C) which on oxidation gave lactone **13** (92% overall, isolated). The further conversion[18] of this lactone (**13**) to enone **14** represents a potentially general extension of the annelation to the preparation of octalones.


11
12
13
14

As demonstrated in the following synthesis of (±)-10-epijunenol, the structural features of the photoadducts and derivatives can be effectively utilized in elaborating stereocenters in the preformed ring. Thus, photoadduct **15** (obtained in 62%

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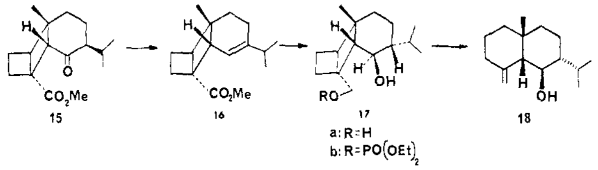
yield (distilled, mp 61-62 °C) from irradiation of piperitone in the presence of ester **1**) was converted to the corresponding tosylhydrazone (65%, mp 149.5-150.5 °C dec) which reacted with sodium hydride in toluene (ambient temperature for 5 min, 110 °C for 2 h)[19] to provide alkene **16** (64%, isolated).



15 16 17 18

a: R = H
b: R = $PO(OEt)_2$

Reaction of alkene **16** with diborane occurred with addition to the sterically less encumbered olefin face and concomitant ester reduction to afford exclusively diol **17a**[8] (85%, mp 69.5-70.5 °C). Finally, selective esterification (1.1 equiv of BuLi; $(EtO)_2POCl$) of diol **17a** gave **17b** (99%) which upon reduction with lithium naphthalide[20] (THF, 0 °C) provided (±)-10-epijunenol (**18**, 70%, isolated).[4,21]

In addition to the above features, it is noteworthy that ester **1** and various substituted cyclobutene esters utilized as 4C components in the present annelation are readily available[22] in preparative quantities (e.g., ester **1**, 60% overall yield from commercially available[23] ethyl 1-bromocyclobutanecarboxylate; 170-mmol scale) and can be stored in methylene chloride solution (−15 °C) for periods in excess of 8 months. We have also found that cyclobutenecarboxylic acid can be used in the photocycloaddition and expect that this method would be readily extended to other cyclobutene derivatives. Further studies are in progress.

Acknowledgment. We thank the National Institutes of Health for support of this work (Public Health Service Research Grant CA21136-01), Mr. Sam Znaimer for assistance during the early stages of this research, and Dr. Alan F. Thomas (Firmenich) for a sample and spectra of authentic 10-epijunenol.

Supplementary Material Available: Structure assignments for **7a** and **7b** as determined from pyrolysis experiments, spectroscopic data on compounds **8**, **13**, and **14**, and a structure correlation which serves to independently confirm the relative stereochemistry previously assigned to 10-epijunenol (2 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) P. A. Wender and J. C. Lechleiter, *J. Am. Chem. Soc.*, **99**, 267 (1977). (b) For a study on the use of dimethyl cyclobutene-1,2-dicarboxylate in the preparation of cyclodecadienes, see G. L. Lange, M.-A. Huggins, and E. Neidert, *Tetrahedron Lett.*, 4409 (1976).
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(5) Photochemical experiments were performed using a 450-W immersion lamp and quartz apparatus (with Pyrex filtering in the case of enone excitations) and were monitored by the disappearance of ester **1**.
(6) For examples of reductive cleavage of σ bonds, see R. V. Volkenburgh, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Am. Chem. Soc.*, **71**, 3595 (1949); J. J. Bloomfield, R. G. Todd, and L. T. Takahashi, *J. Org. Chem.*, **28**, 1474 (1963); E. Bertele, H. Boos, J. D. Dunitz, F. Elsinger, A. Eschenmoser, I. Felner, H. P. Bribi, H. Gschwend, E. F. Meyer, M. Pesaro, and R. Scheffold, *Angew. Chem.*, **76**, 281 (1964); W. G. Dauben and R. E. Wolf, *J. Org. Chem.*, **35**, 2361 (1970); J. J. Bloomfield, R. A. Martin, and J. M. Nelke, *J. Chem. Soc., Chem. Commun.*, 96 (1972); P. G. Gassman and X. Creary, *ibid.*, 1214 (1972); and references cited therein.
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(8) Satisfactory spectroscopic data and elemental or exact mass analyses were obtained for all new compounds. Additional information on key assignments can be found in the supplementary material.
(9) H. O. House and T. H. Cronin, *J. Org. Chem.*, **30**, 1061 (1965).
(10) R. E. Ireland, D. C. Muchmore, and U. Hengartner, *J. Am. Chem. Soc.*, **94**, 5098 (1972).
(11) Phosphate ester **4** was prepared by lithium aluminum hydride reduction of ester **3** and reaction of the resulting alcohol with *n*-butyllithium followed by diethyl chlorophosphate.
(12) F. LeGoffic, *Bull. Soc. Chim. Fr.*, 2250 (1965).
(13) C. S. Foote, Ph.D. Thesis, Harvard University, 1961.
(14) For reviews related to [2 + 2] photocycloadditions, see P. E. Eaton, *Acc. Chem. Res.*, **1**, 50 (1968); P. de Mayo, *ibid.*, **4**, 41 (1971); and W. C. Herndon, *Top. Curr. Chem.*, **46**, 141 (1974).
(15) P. E. Eaton, *J. Am. Chem. Soc.*, **84**, 2344 (1962).
(16) The details concerning the regioselectivity obtained with ester **1** need not necessarily follow those invoked in the photodimerization in view of the differences between the two systems (e.g., ester **1** is relatively planar and can adopt both *s-cis* and *s-trans* conformations).
(17) These results in conjunction with the pyrolysis experiment[8] lead to unique assignments of orientation.
(18) The first step (NaOH, MeOH; $RuO_2 \cdot H_2O$, $NaIO_4$) in this transformation was based on the report of H. Gopal, T. Adams, and R. M. Moriarty (*Tetrahedron*, **28**, 4259 (1972)) while the second step ($Pb(OAc)_4$, $Cu(OAc)_2$) was modeled after the method of J. E. McMurry and L. C. Blaszczak (*J. Org. Chem.*, **39**, 2217 (1974)).
(19) R. H. Shapiro, *Org. React.*, **23**, 405 (1976); J.-F. Biellman and J.-P. Péte, *Bull. Soc. Chim. Fr.*, 675 (1967).
(20) H. E. Zieger, I. Angres, and D. Mathisen, *J. Am. Chem. Soc.*, **98**, 2580 (1976); S. J. Shafer, W. O. Closson, J. M. F. vanDijk, O. Piepers, and H. M. Buck, *ibid.*, **99**, 5118 (1977).
(21) The IR, NMR, and mass spectroscopic data and chromatographic properties of synthetic 10-epijunenol were identical in all respects with authentic material kindly provided by Dr. Alan F. Thomas.
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(23) Aldrich Chemical Co., Cat. No. 19,729-7.
(24) National Science Foundation Fellow, 1975-1978.

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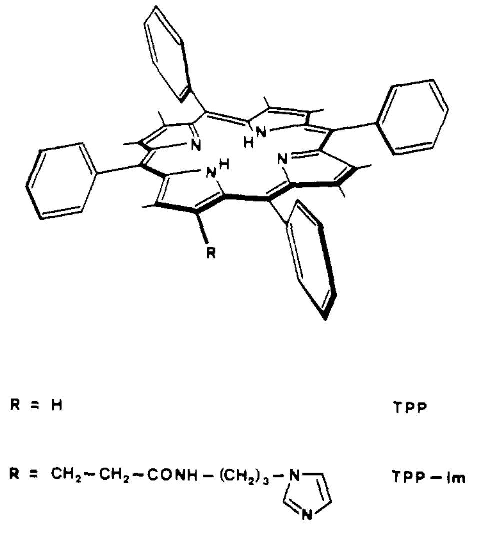
Photodissociation of Nitrogenous Bases from Hemochromes and Kinetics of Recombination of Axial Bases

Sir:

The photodissociation of low-spin iron(II) hexacoordinate complexes of biological importance, such as carboxymyoglobin, carboxyhemoglobin, oxyhemoglobin, or of synthetic carboxyhemochromes containing porphyrin, carbon monoxide, and an additional base as ligands is well known.[1-4] Photodissociation of other axial ligands (cyanide, isocyanide, nitric oxide) involving heterolytic bond cleavage from various d^6 complexes has also been reported.[5-8] We wish to present preliminary results on the photodissociation of low-spin hexacoordinate complexes of iron(II) porphyrins and nitrogenous bases as ligands (hemochromes) and on the kinetics of ligand recombination.



R = H TPP

R = $CH_2-CH_2-CONH-(CH_2)_3-N$ TPP − Im

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