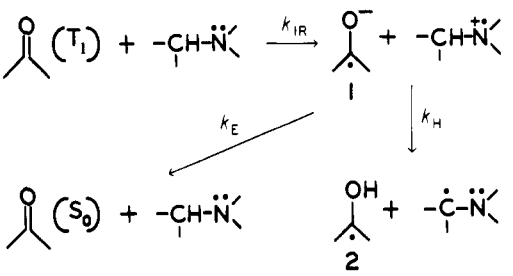
Picosecond Dynamics of the Photoreduction of Benzophenone by Triethylamine

Sir:

The mechanism for the photoreduction of benzophenone by triethylamine has been extensively investigated and reviewed.[1] It is generally accepted[2] that an electron is transferred from the amine to the triplet state of benzophenone, forming a charge-transfer complex. This complex is then quenched either by proton



transfer, generating the benzhydrol radical (**2**) and amine radical, or by spin inversion followed by back transfer of the electron, resulting in ground-state benzophenone and amine.

The approach for elucidating this mechanism has mainly relied upon phosphorescence quenching studies which are limited to concentration regions for ketone and amine in which the rate of electron transfer is dependent upon translational diffusion of the amine and triplet ketone. Thus the intrinsic rate for electron transfer, k_{IR}, has not been directly obtainable. Utilization of picosecond absorption spectroscopy has allowed the direct observation of the charge–transfer complex **1** in the photoreduction of benzophenone by triethylamine. The intrinsic rate of electron transfer, k_{IR}, as well as the rate of proton transfer, k_H, were directly measured.

The experimental apparatus employed in these experiments is similar to the one recently reported[3] except that a mode-locked ruby laser with a 10-ps time resultion[4] was utilized, and thus 347-nm wavelength light was used for sample excitation. In the absence of amine, the triplet state of benzophenone (λ_{max} 525 nm) is formed within 10 ps from excitation (Figure 1A). However, in the presence of 3 M triethylamine, the triplet state of benzophenone is quenched forming a new intermediate with a half-life of 10 ± 5 ps and a λ_{max} of 610 nm (Figure 1B). This intermediate then decays and another transient is formed with a half-life of 15 ± 5 ps and a λ_{max} at 545 nm (Figure 2B). This transient persists beyond 2 ns with no measurable decay of the absorption maximum. At 30 ps after excitation, the absorbance of the triplet of benzophenone in the absence of amine is 0.45 ± 0.05 OD (Figure 2A) while the absorbance of the intermediate with λ_{max} 545 nm resulting from the addition of amine is 0.20 ± 0.03 OD.

These experimental results are readily interpreted in light of our earlier findings,[3] where a charge-transfer complex (λ_{max} 655 nm) was observed to be formed within 20 ps of excitation of benzophenone in the presence of 1 M diazabicyclooctane. The intermediate with a λ_{max} of 610 nm observed in the benzophenone/triethylamine photolysis is identified as a charge-transfer complex **1**. It is noted that the absorption spectrum of the complex is similar to that found for the radical anion of benzophenone[5] produced electrochemically. The charge-transfer complex is subsequently quenched by a proton transfer, with a half-life of 15 ± 5 ps, generating the benzhydrol radical and amine radical

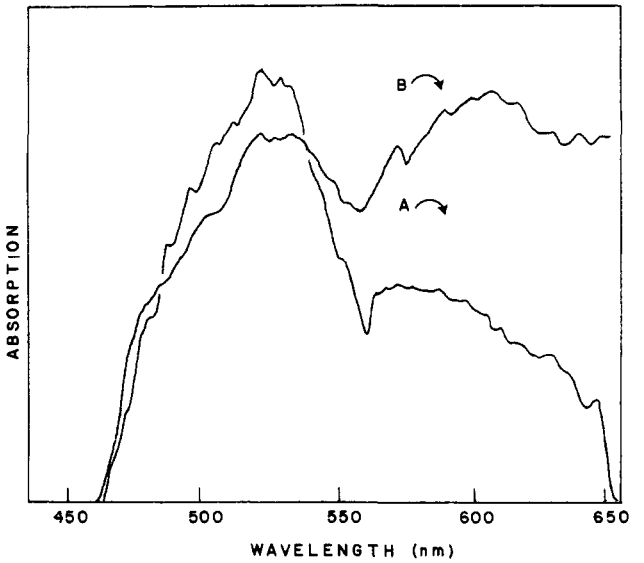


Figure 1. Transient adsorption spectrum of (a) 0.1 M benzophenone in acetonitrile at 10 ps; (b) 0.1 M benzophenone and 3 M triethylamine in acetonitrile at 10 ps.

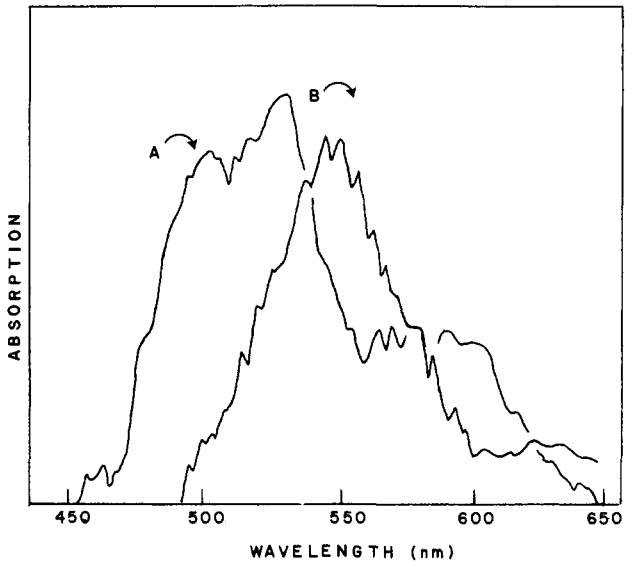


Figure 2. Transient absorption spectrum of (a) 0.1 M benzophenone in acetonitrile at 30 ps; (b) 0.1 M benzophenone and 3 M triethylamine in acetonitrile at 30 ps.

(**2**) with a λ_{max} at 545 nm. This radical has previously been observed in flash photolysis studies of benzophenone in ethanol.[6,7] The quantum yield for reduction of the triplet state of benzophenone by triethylamine can be determined from the ratio of the absorption maxima of triplet benzophenone and the benzhydrol radical determined in these experiments compared with the ratio of the known coefficients of triplet benzophenone (7630 M^{-1} cm^{-1}) and the radical (3220 M^{-1} cm^{-1}).[8] If the quantum yield for production of **2** were 1.0, then the expected ratio of the absorption maxima would be 2.37, which is in good agreement with out observations (2.25 ± 0.18). Thus the rate constant for back electron, k_E, is at most 5% that of proton transfer, k_H. This is consistent with our earlier findings[3] in which the triplet charge-transfer complex of benzophenone/diazabicyclooctane is stable on the picosecond time scale.

In summary, our picosecond absorption experiments on the mechanism of the photoreduction of benzophenone by triethylamine firmly establish the existence of the charge-transfer complex

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in the reduction process and the quantum yield for net hydrogen transfer is one.

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Synthesis of (±)-Illudol

Sir:

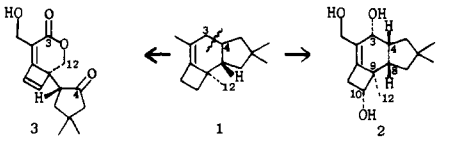
Among natural sesquiterpene alcohols, those possessing the Δ^6-protoilludane skeleton (**1**) have attracted attention as synthesis targets because of the unique methylene–cyclobutane structural feature.[1] Illudol (**2**), a member of this class, has recently been obtained by total synthesis.[2] Fomannosin (**3**) has been shown to arise through protoilludane precursors in nature[3] and has not yet been successfully synthesized.[4] The relation between illudol (**2**) and fomannosin (**3**) is indicated by the bond cleavage at C-3/C-4 (in **1**, and Scheme I) and reconnection at C-3/C-12 and provides an important suggestion for a strategy for the synthesis of fomannosin, currently under way in our laboratory.[5] The two carbons joining the four-membered and five-membered rings have the same configuration in both illudol and fomannosin. An appropriately functionalized protoilludane derivative provides a rigid skeletal framework for a stereocontrolled synthesis of fomannosin and illudol. We report here a short synthesis of the appropriate intermediate (**4**) and its conversion to illudol (**2**).

Illudol (**2**) has five contiguous chiral centers: two of them (C-3, C-10) bear hydroxyl groups where selective carbonyl reduction will control the configuration, one (C-4) is adjacent to a potential carbonyl group (C-3) and therefore easily epimerized, and the C-8/C-9 pair are to be controlled in the central carbon–carbon bond-forming step. This central operation is the Diels–Alder reaction of a cyclobutene (i.e., **5**) and a 1,3-diene (i.e., **6**). The ester substituent in **5** was expected to provide sufficient reactivity for cycloaddition, to provide the oxygen substituent required at C-12 in fomannosin (**3**), and to allow secondary orbital overlap leading to the required endo addition product (**4**).

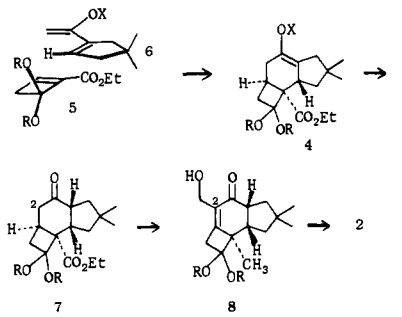
Scheme II presents the strategy for illudol, focusing on three critical stages: (a) cycloaddition to give **4**, (b) hydrolysis of the enol unit to give **7**, and (c) introduction of the hydroxymethyl group and double bond at C-2 to give **8**.

The highly functionalized cyclobutene **5** is of a type which has recently been prepared by Lewis acid catalyzed [2 + 2] cycloaddition of propiolic esters with electron-rich alkenes.[6] After initial studies using various Lewis acids, we found that a simple uncatalyzed thermal reaction (CH_2Cl_2, reflux, 29 h) of ethyl propiolate with 1,1-diethoxyethylene produced **5** in 65% yield.[7] The acetylcyclopentene **9**[7,8] served as precursor of the general diene, **6**. It was prepared in 80% overall yield from 4,4-dimethylcyclohexanone via addition of methylmagnesium bromide, dehydration, and ozonolysis to give 3,3-dimethyl-6-oxoheptanal which underwent acid-catalyzed aldol condensation and dehydration to give **9**; a small amount of the alternative aldol product was separated by distillation. Treatment of **9** with lithium diisopropylamide produced the enolate anion **6a** which was trapped in separate experiments with methyl *p*-toluenesulfonate (to give **6b**), chlorotrimethylsilane (to give **6c**),[7] and *tert*-butylchlorodimethylsilane (to give **6d**).[7] Extensive studies on the reaction of

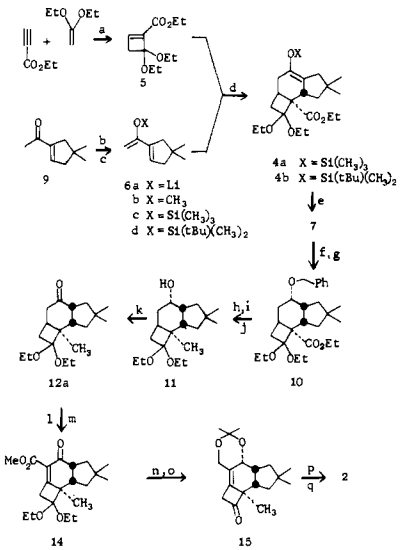
Scheme I. Biosynthesis Connection



Scheme II. Strategy for Illudol



Scheme III. Synthesis of Illudol[a]



[a] (a) 29 h, CH_2Cl_2, reflux, 65%; (b) $LiNR_2$, −78 °C; (c) CH_3OTs, $ClSi(CH_3)_3$, or $ClSi(t\text{-}Bu)(CH_3)_2$; (d) 48 °C, 10 days (sealed flask), 72%; (e) 3-Å molecular sieves, CH_3OH, 25 °C, 4.5 h, 96%; (f) $LiEt_3BH$, 0 °C, 3 min, 99%; (g) $PhCH_2Br$, NaH, 70 °C, 5 h, 92%; (h) $LiAlH_4$, 96%; (i) *n*-BuLi, THF, 25 °C, 5 min, followed by $ClPO(N(CH_3)_2)_2$, 25 °C, 5 h, 82%; (j) Li, $EtNH_2$, THF, *t*-BuOH, 0 °C, 0.5 h, 94%; (k) CrO_3, pyridine, CH_2Cl_2, 87%; (l) $LiNR_2$, THF, −78 °C, followed by CO_2 (gas, excess), followed by neutralization and CH_2N_2; (m) $LiNR_2$, THF, −78 °C, followed by H_2O_2, 25 °C, 0.5 h, 38% overall; (n) $NaAl(OR)_2H_2$, C_6H_6, 25 °C, 14 h (ref 2); (o) $C_7H_6SO_3H$, acetone, 25 °C (ref 2); (p) $NaAl(OR)_2H_2$, C_6H_6, 25 °C (ref 2), (q) HCl–THF.

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(3) D. E. Cane and R. S. Nachbar, *J. Am. Chem. Soc.* **100** 3208 (1978).
(4) Two syntheses of dihydrofomannosin derivatives (cyclobut*ane*) have been reported: (a) K. Miyano, F. Ohfune, S. Azuma, and T. Matsumota, *Tetrahedron Lett.*, 1545 (1974); (b) H. Kosugi and H. Uda, *Bull. Chem. Soc. Jpn.* **53**, 160 (1980).
(5) The biogenetic relationship between illudol and fomannosin was proposed to us by Professor D. Arigoni (ETH, Zurich) during seminar discussions at Cornell in 1974 and led to the strategy developed here.
(6) For examples, see: (a) B. B. Snider, D. J. Rodini, R. S. E. Conn, and S. Sealfon, *J. Am. Chem. Soc.*, **101**, 5283 (1979); (b) R. D. Clark and K. G. Untch, *J. Org. Chem.*, **44**, 248 (1979). Simple thermal [2 + 2] cycloaddition of enamines with propiolate esters also produces cyclobutene-2-carboxylates: (c) C. F. Huebner, L. Dorfman, M. M. Robison, E. Donoghue, W. G. Pierson, and P. Strachan, *ibid.* **28**, 3134 (1963); (d) K. C. Braunnock, R. D. Burpitt, V. W. Goodlett, and J. G. Thweatt, *ibid.*, **29**, 818 (1964).
(7) Characterization data for this compound are included in the supplementary material.
(8) K. Von Auwers and E. Lange, *Liebigs Ann. Chem.*, **409**, 149 (1915).

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