by mixture melting point, 167–168.5°, and by infrared spectrum with an authentic sample prepared by sodium borohydride reduction of the ketone. The alkalinity of the aqueous amine solutions is sufficient to lead to the benzhydrol either by decomposition of the pinacol or by conversion of the semipinacol radicals to radical ions which may disproportionate directly, without forming the pinacol. Evidence that the reaction may take the latter course will be presented shortly.[6]

Since formation of one molecule of the benzhydrol involves the equivalent of two ketyl radicals, the reduction of the carboxy ketone to ketyl radicals by primary and tertiary amines in the aqueous systems has a high quantum yield, equal to that of benzophenone in the neat primary amine. The absence of effects due to D_2O indicates that the N–H bond of the primary amine is not broken in a rate-determining step. The equal reactivity of I and II in water indicates that the N–H bond is not required for the reactivity of primary amines in this medium. Photoreduction of the carboxy ketone by the tertiary amine II in benzene was slow and similar in rate to that of benzophenone, indicating no significant effect due to the carboxyl substituent.

Photoreduction of 4-benzoylbenzoic acid by triethylamine (III) was examined in more detail. Photoreduction of 0.1 M ketone by 0.5 M and 1.0 M III in H_2O showed zero-order kinetics, no light-absorbing transient was observed, and the benzhydrol was isolated in 82% yield. As in photoreduction by amine II, the rate was again half as fast as the standard, benzophenone in 2-butylamine (I), corresponding to an equal rate of formation of ketyl radicals. Photoreduction of 0.1 M ketone by 2 M triethylamine (III) in benzene did not show zero-order kinetics, and the ketone was converted largely to the pinacol. The reduction was rapid initially, 0.7 times the rate of the standard over the first 15% reaction, but it slowed down markedly as a light-absorbing intermediate built up, and the over-all rate at 40% reaction was only 0.4 times the rate of the standard.

The photoreduction of the carboxy ketone in aqueous triethylamine led to oxidative cleavage of the amine (eq 1). Acetaldehyde and diethylamine were formed in 77 and 85% yields, respectively, as indicated by vapor phase chromatography, based on amount of ketone reduced. The products were characterized as the 2,4-dinitrophenylhydrazone and p-toluenesulfonamide, respectively, which were identical with derivatives of authentic samples. Photoreduction by the tertiary amine II in water also led to oxidative cleavage and characterization of formaldehyde and N-methyl-2-butylamine as the 2,4-dinitrophenylhydrazone and N-methyl-N-2-butyl-N′-phenylthiourea, respectively. The photoreduction of the carboxy ketone by triethylamine in benzene also led to some acetaldehyde and diethylamine. This cleavage appeared due to traces of water in the system and is being studied further. A related cleavage of dimethylaniline[4] may also be due to traces of water.

We have previously proposed[3] that photoreduction by a tertiary amine in hydrocarbon medium may be initiated by movement of an electron from nitrogen to the excited ketone, leading to a charge-transfer complex and a pair of ions, as indicated in eq 2. This is

$$\mathrm{Ar,Ar'C{=}O^{*} + CH_3CH_2NR_2 \longrightarrow [Ar,Ar'\dot{C}O^{-}\ \ CH_3CH_2\overset{+}{\dot{N}}R_2]} \quad (2)$$

$$\mathrm{[Ar,Ar'\dot{C}O^{-}\ \ CH_3CH_2\overset{+}{\dot{N}}R_2] \longrightarrow Ar,Ar'\dot{C}OH + CH_3\dot{C}HNR_2} \quad (3)$$

followed by a proton transfer (eq 3). Such a process may well be enhanced in aqueous systems, leading to the observed increased reactivity.

The oxidative cleavage, the absence of mixed coupling products, and the high reactivity of primary and tertiary amines in aqueous systems indicate that a second reducing moiety may be transferred from tertiary amine derived radical to ground-state ketone, as has been proposed for photoreductions by 2-propanol[7] and by primary and secondary amines.[2] The second moiety may be an electron from N (eq 4) or H from β-C (eq 5).

$$\mathrm{Ar,Ar'C{=}O + CH_3\dot{C}HNR_2 \longrightarrow Ar,Ar'\dot{C}O^{-} + CH_3CH{=}\overset{+}{N}R_2} \quad (4)$$

$$\mathrm{Ar,Ar'C{=}O + CH_3\dot{C}HNR_2 \longrightarrow Ar,Ar'\dot{C}OH + CH_2{=}CHNR_2} \quad (5)$$

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[6] S. G. Cohen and N. Stein, unpublished results.

[7] J. N. Pitts, R. L. Letsinger, R. P. Taylor, J. M. Patterson, G. Recktenwald, and R. B. Martin, *J. Am. Chem. Soc.*, **81**, 1068 (1959).

Saul G. Cohen, Nina Stein, Helen M. Chao
Department of Chemistry, Brandeis University
Waltham, Massachusetts 02154

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The Nuclear Overhauser Effect, a Unique Method of Defining the Relative Stereochemistry and Conformation of Taxane Derivatives

Sir:

The prediction of Anet and Bourn[1] that the so-called nuclear Overhauser effect (NOE) should be of considerable interest in stereochemical and conformational studies of organic molecules has been substantiated to some extent in our work on the ginkgolides;[2] a more striking demonstration of the utility of this effect is provided in the case of the taxane derivatives.

The nmr spectrum[3] of taxinine[4] (**1**) exhibits a number of NOE's which serve to define the relative configurations of at least five asymmetric centers with respect to C_1 in the molecule (*cf.* **1** and **5**), as well as providing an unambiguous assignment of the signals due to the C_{15}-methyls. Irradiation (saturation) of the 15α-Me causes increases of 10–20% in the areas of the C_2- and C_9-proton signals; irradiation of the 12-Me similarly effects the C_{21}- and C_{10}-proton signals and irradiation of C_7–H increases the area of the signal due to H_{10}. Of all the possible stereostructures for taxinine with a *planar* structure **1**, only that with the conformation and stereochemistry (with the possible exception of the C_5 stereochemistry) shown in **5** can reasonably account for the occurrence of *all* of these NOE's, as can be

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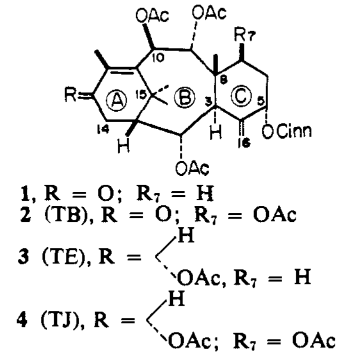
[1] F. A. L. Anet and A. J. R. Bourn, *J. Am. Chem. Soc.*, **87**, 5250 (1965).

[2] M. C. Woods, I. Miura, Y. Nakadaira, A. Terahara, M. Maruyama, and K. Nakanishi, *Tetrahedron Letters*, 321 (1967).

[3] M. C. Woods, K. Nakanishi, and N. S. Bhacca, *Tetrahedron*, **22**, 243 (1966). An incorrect stereochemistry was given in this paper, but the nmr assignments are valid.

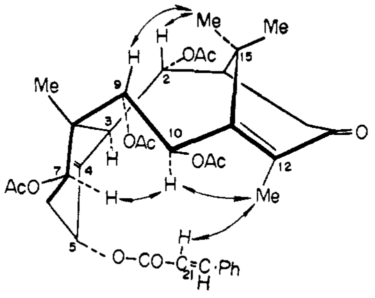
[4] The stereochemistry of taxinine has been established by an X-ray analysis and by chemical means; see M. Shiro, T. Sato, H. Koyama, Y. Maki, K. Nakanishi, and S. Uyeo, *Chem. Commun.*, 98 (1966), and D. H. Eyre, J. W. Harrison, and B. Lythgoe, *J. Chem. Soc., Sect. C*, 452 (1967), for leading references.



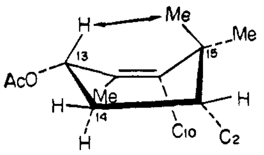
1, R = O; R_7 = H
2 (TB), R = O; R_7 = OAc
3 (TE), R = $\langle^{H}_{OAc}$, R_7 = H
4 (TJ), R = $\langle^{H}_{OAc}$; R_7 = OAc

verified by constructing the various stereoisomers from Dreiding models.

Application of this technique to the following three new diterpenoids,[5] TB (**2**) (mp 265–266°; $[\alpha]^{CHCl_3}{}_D$ $+93.8°$; $C_{37}H_{44}O_{11}$; ν^{max}_{KBr} 1665 cm^{-1}), TE (**3**), and TJ (**4**) (mp 249–251°; $C_{39}H_{48}O_{12}$), isolated in only very small amounts from the leaves of *Taxus cuspidata* Sieb. *et* Zucc., led to the establishment of the structures shown. In each case assignment of the 100-Mc spectrum was achieved with the aid of solvent changes to separate overlapping signals and confirmed by multiple resonance experiments which also revealed the NOE's indicated (by arrows) in **5** and **6**. Deduction of the planar structures was relatively straightforward since in many respects the spectra were similar to that of taxinine,[3] the differences being easily correlated with the structural modifications peculiar to each compound.



5 (TB)



6 (TJ, TE)

The ring C structures in TB and TJ give rise to a similar series of signals which (for TB in $CDCl_3$) are assigned as follows: $\delta_{7\text{-H}}$ 5.43 (dd), $\delta_{6\alpha\text{-H}}$ $\sim$2.23 (m), $\delta_{6\beta\text{-H}}$ 1.74 (ddd), $\delta_{5\text{-H}}$ $\sim$5.38 ppm (m), $J_{7\alpha,6\alpha} = 5.5$, $J_{7\alpha,6\beta} = 11$, $J_{6\alpha,6\beta} = 14.5$, $J_{5\beta,6\alpha} = J_{5\beta,6\beta} = \sim 4$ cps (*cf.* **5**). The large $J_{7\alpha,6\beta}$ and the detection of a NOE involving $H_{7\alpha}$ and $H_{10\alpha}$ define the configuration at C_7; the stereochemistry at C_5 is similarly defined by the H_5 couplings. The presence of a C_{13}-acetoxyl grouping in TE and TJ (*cf.* **6**) is indicated by the absence of any strong infrared absorption in the 1650–1700-cm^{-1} region and by the appearance of the following nmr signals (assignment for TE in $CDCl_3$): $\delta_{12\text{-Me}}$ 2.30 (d), $\delta_{13\beta\text{-H}}$ 5.80 (ddq), $\delta_{14\alpha\text{-H}}$ 1.48 (br dd), $\delta_{14\beta\text{-H}}$ 2.64 ppm (ddd), $J_{13\beta,12\text{Me}} = 1.5$, $J_{13\beta,14\alpha} = 7$, $J_{13\beta,14\beta} = 10$, $J_{14\alpha,14\beta} = 15$, $J_{14\alpha,1} = \sim 1$, $J_{14\beta,1} = 9$ cps. The stereochemistry at C_{13} cannot be unequivocally assigned from the magnitudes of the couplings between $H_{13\beta}$ and the adjacent CH_2 protons. However, irradiation of the 15β-Me in either TE or TJ causes a 10–15% increase in the area of the signal due to the C_{13} proton which therefore must be assigned a β configuration (*cf.* **6**).

As can be seen from **5** and **6**, the observed NOE's define the relative configurations of *at least eight asymmetric centers* (*i.e.*, C_2, C_3, C_7, C_8, C_9, C_{10}, and C_{13} with respect to C_1) in TJ; in the cases of TB and TE seven centers are defined.

In the study of these NOE's by frequency-swept double-resonance techniques, care has been taken to distinguish between an increase in signal height due to the removal of an unresolved coupling (in which case the band width is reduced and the signal area remains unchanged) and the increase in signal height resulting from an NOE (in which case the signal area increases proportionately, but the band width remains essentially unchanged). If both an increase in signal area and a significant reduction in band width occurs then it may be assumed that both effects are operating. For example, irradiation of the 15α-methyl group in taxinine causes a $\sim$0.75-cps reduction in the band width at half-height of the 15β-methyl group, which indicates that there is a small, unresolved, long-range coupling of $\sim$0.25 cps between these two methyls; there also appears to be a small but consistent increase in the area of the 15β-methyl signal, indicative of an NOE, but it is difficult to be certain of the validity of this effect since the proximity of the C_{15}-methyl signals ($\sim$70-cps separation) leads to some distortion of the 15β signal when the 15α signal is irradiated.[6]

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[5] Satisfactory microanalyses were obtained for TB and TJ; TE was isolated as a mixture containing $\sim$15% of an as yet unidentified congener. The nmr spectrum of TE, however, provided adequate characterization. Infrared and nmr absorptions due to acyl groupings are present in the spectra of each compound but are omitted from the discussion.

[6] This work has been partially supported by the National Institutes of Health, Public Health Service Research Grant No. CA 08394.

M. C. Woods, H.-C. Chiang
Y. Nakadaira, K. Nakanishi
Department of Chemistry, Tohoku University
Sendai, Japan

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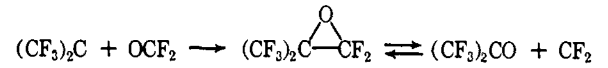
The Abstraction of Oxygen by Carbenes

Sir:

Reports have accrued on the abstraction of oxygen by carbenes from substrates such as carbon dioxide,[1] pyridine N-oxide,[2,3] and dimethyl sulfoxide.[2,4]

We wish to describe the interactions of fluorinated carbenes with OCF_2 and OPF_3 which reveal some details of this type of reaction and further illustrate the very strong reducing power of carbenes. OCF_2 and OPF_3 have not previously been reduced to CF_2 and PF_3, respectively, by any reagent under 600°.

The reaction of bis(trifluoromethyl)carbene (from bis(trifluoromethyl)diazirine[5]) with carbonyl fluoride at 180° for 4 hr in a sealed-glass tube gives a 40% yield of the adduct, perfluoroisobutylene oxide,[6] and a 10%



$$(CF_3)_2C + OCF_2 \longrightarrow (CF_3)_2\overset{O}{C{-}CF_2} \rightleftarrows (CF_3)_2CO + CF_2$$

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[2] E. E. Schweizer and G. J. O'Neill, *J. Org. Chem.*, **28**, 2460 (1963).

[3] E. E. Schweizer, G. J. O'Neill, and J. N. Wemple, *ibid.*, **29**, 1744 (1964).

[4] R. Oda, M. Meino, and Y. Hayashi, *Tetrahedron Letters*, 2363 (1967).

[5] D. M. Gale, W. J. Middleton, and C. G. Krespan, *J. Am. Chem. Soc.*, **88**, 3617 (1966).

[6] The synthesis of perfluoroisobutylene oxide from difluorocarbene