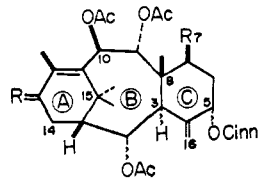
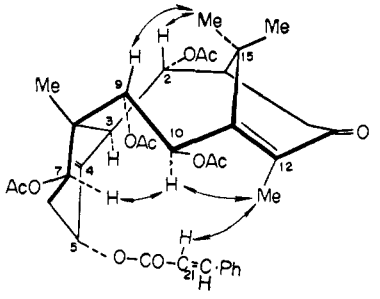


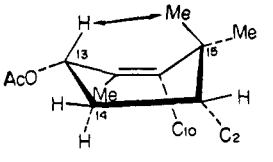
1, R = O; R_7 = H
2 (TB), R = O; R_7 = OAc
3 (TE), R = H, OAc, R_7 = H
4 (TJ), R = H, OAc; R_7 = OAc

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_{KBr}^{max} 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), $\delta_{6\alpha\text{-H}}$ ~2.23 (m), $\delta_{6\beta\text{-H}}$ 1.74 (ddd), $\delta_{5\text{-H}}$ ~5.38 ppm (m), $J_{7\alpha,6\alpha}$ = 5.5, $J_{7\alpha,6\beta}$ = 11, $J_{6\alpha,6\beta}$ = 14.5, $J_{5\beta,6\alpha}$ = $J_{5\beta,6\beta}$ = ~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), $J_{13\beta,12Me}$ = 1.5, $J_{13\beta,14\alpha}$ = 7, $J_{13\beta,14\beta}$ = 10, $J_{14\alpha,14\beta}$ = 15, $J_{14\alpha,1}$ = ~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 ~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 ~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 (~70-cps separation) leads to some distortion of the 15β signal when the 15α signal is irradiated.[6]

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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%

$$(CF_3)_2C + OCF_2 \longrightarrow (CF_3)_2C\overset{O}{\diagup\!\diagdown}CF_2 \rightleftharpoons (CF_3)_2CO + CF_2$$

(1) G. B. Kistiakowski and K. Sauer, *J. Am. Chem. Soc.*, **80**, 1066 (1958).
(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

(5) Satisfactory microanalyses were obtained for TB and TJ; TE was isolated as a mixture containing ~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.

yield of hexafluoroacetone. Perfluoroisobutylene oxide requires 320° for 24 hr for significant formation of hexafluoroacetone and difluorocarbene, suggesting that the displacement of difluorocarbene from carbonyl fluoride by bis(trifluoromethyl)carbene at 180° occurs by way of excited perfluoroisobutylene oxide.

Difluorocarbene reacts with OPF_3 in two ways: as a reducing agent and as a fluorinating agent (eq 1 and 2). These reactions are isokinetic at 60° At

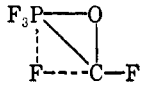
$$CF_2 + OPF_3 \longrightarrow OCF_2 + PF_3 \quad (1)$$

$$CF_2 + OPF_3 \longrightarrow CO + PF_5 \quad (2)$$

100°, reaction 1 accounts for 95% of the products and reaction 2 for 5%. At 25°, reaction 1 accounts for 5% and reaction 2 for 95%.[8] From the product ratios we estimate that reaction 1 has an enthalpy and entropy of activation 18 kcal mole^{-1} and 50 eu, respectively, greater than those of reaction 2. By analogy to the carbene–ketone adduct[6] we suggest that addition of CF_2 to the PO bond is the first step common to reactions 1 and 2. Reaction 1 then pro-

$$CF_2 + F_3PO \longrightarrow F_3P\overset{O}{\diagdown\diagup}CF_2$$

ceeds by breaking the PO bond, or the PC bond, or both. Reaction 2 proceeds by way of a fluorine shift from C to P *via* a very tight bicyclic transition state to



give $F_4PC(=O)F$ (not isolable at 25°) which shifts fluorine once more to give CO and PF_5.

Bis(trifluoromethyl)carbene (from bis(trifluoromethyl)diazomethane) reacts with OPF_3 at 160° or in sunlight at 25° to give hexafluoroacetone.

We are applying the reduction of OPF_3 as a probe for carbenes in more complex systems. For example, pentafluoroethyltetrafluorophosphorane, $CF_3CF_2PF_4$, decomposes at 240° in platinum with a half-life of 12 hr to give tetrafluoroethylene and pentafluorophosphorane. Trifluoromethylfluorocarbene is revealed as an intermediate because trifluoroacetyl fluoride is obtained in 80% yield with a threefold excess of OPF_3.

$$CF_3CF_2PF_4 \longrightarrow CF_3CF + PF_5$$

$$CF_3CF \longrightarrow F_2C{=}CF_2$$

$$OPF_3 + CF_3CF \longrightarrow PF_3 + CF_3\overset{O}{\overset{\|}{C}}F$$

Similarly, *n*-perfluoropropyltetrafluorophosphorane decomposes at 240° predominantly *via* an α-fluorine shift.

and hexafluoroacetone has been demonstrated by Moore.[7] The boiling point is 2°; infrared absorption is at 1500, 1335, 1280, 1255, 1225, 1090, 1025, 985, 725, 718, and 712 cm^{-1}. ^{19}F nmr resonances are at 72 ppm for CF_3 and 112 ppm for CF_2 from $FCCl_3$.

(7) Reported by D. P. Carlson and A. S. Milian, Fourth International Symposium on Fluorine Chemistry, Estes Park, Colo., 1967.

(8) The 25° source of CF_2 used was $(CF_3)_2PF_3 \rightarrow CF_2 + CF_3PF_4$ (half-life 3 days). $(CF_3)_3PF_2 \rightarrow 3CF_2 + PF_5$ served for the experiments at 60° (half-life 6 months) and 100° (half-life 12 hr). Experiments were run in sealed-glass or platinum tubes for at least two half-lives. The product ratios are independent of pressure. Reaction 1 was also observed using perfluorocyclopropane as CF_2 source[9] at 220° or perfluoro(methylcyclopropane) at 190°. The latter extrudes CF_2 exclusively, with no indication of CF_3CF.

(9) B. Atkinson and D. McKeagan, *Chem. Commun.*, 189 (1966).

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Pyrrolo[2,3-*d*]pyrimidine Nucleoside Antibiotics. Total Synthesis and Structure of Toyocamycin, Unamycin B, Vengicide, Antibiotic E-212, and Sangivamycin (BA-90912)[1]

Sir:

The antibiotic toyocamycin was first isolated from *Streptomyces toyocaensis* by Nishimura and coworkers[2] and later by Ohkuma[3] from *Streptomyces* strain 1922. Recently antibiotic 1037[4] has been shown[5] to be identical with toyocamycin. The unusual biological properties of toyocamycin[2,3] and its antitumor activity[6,7] have stimulated considerable interest in this antibiotic. Preliminary degradation studies[3,8] resulted in a tentative structure assignment for toyocamycin as 4-amino-5-cyano-7-(β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidine. Sangivamycin has been isolated from an unidentified species of *Streptomyces*[9] and was at that time referred to as BA-90912. Sangivamycin was reported to possess cytotoxicity against HeLa cells grown in cell cultures and to exhibit significant activity against Leukemia 1210 in mice. Sangivamycin has produced no evidence of toxicity in humans at maximally tolerated doses and is presently undergoing human clinical trial against leukemia.[10] It has been noted[11] that sangivamycin is structurally similar to toyocamycin. However, a recent review[12] points to the fact that the actual site of glycosidation, anomeric configuration, and structure of the sugar moiety for sangivamycin and toyocamycin have not been unequivocally established.

We now wish to report a total synthesis of toyocamycin (VIa) and sangivamycin (VIb) and the unequivocal assignment of their structures.

Ring closure of 2-amino-5-bromo-3,4-dicyanopyrrole[13] with formamidine acetate in 2-ethoxyethanol at reflux temperature furnished a 65% yield of 4-amino-6-bromo-5-cyanopyrrolo[2,3-*d*]pyrimidine (I): mp 300°, λ_{max}^{EtOH} 284 (ε 13,800) and 250 mμ (ε 7800). A mixture of I, acetic anhydride, and xylene was heated at reflux temperature for 18 hr to afford the monoacetylated product, 4-acetamido-6-bromo-5-cyanopyrrolo[2,3-*d*]pyrimidine (II, 94%), mp 265° dec.

A mixture of II and 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose was heated at 175° in the presence of a catalytic amount of bis(*p*-nitrophenyl) phosphate[14] for

(1) This work was supported in part by Research Contract No. PH 43-65-1041, Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service.

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