butanone and two different enolic species.

In conclusion, the use of carbon-13 CIDNP has revealed an important mechanistic aspect of alcohol oxidation by photolysis of *t*-BuOOH. Direct evidence for enolic species as transient intermediates was found. The possibility now exists to study the carbon-13 chemical shifts of this important class of organic intermediates. Furthermore, acid catalyzed studies may lead to a better kinetic understanding of these unstable species. We are currently exploring these possibilities as well as the synthetic utility of the photooxidation reaction.

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(4) This compound was prepared in situ by mixing equal portions of acetaldehyde and *t*-BuOOH. After a brief exothermic reaction new proton NMR signals, most notably a quartet at 4.13 ppm and new carbon-13 signals at 96.8 and 26.3 ppm, were observed. See also *Chem. Abstr.*, **63**, P17903d (1965).
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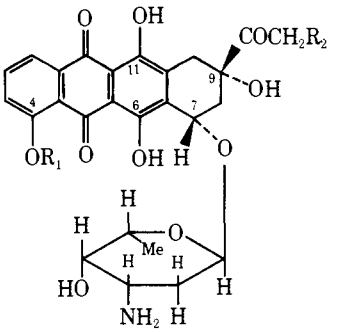
Antitumor Agents. XIII. Isolation and Absolute Configuration of Carminomycin I from *Streptosporangium sp.*[1,2]

Sir:

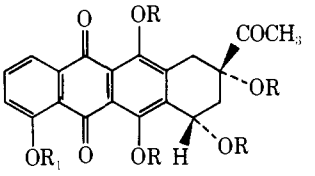
Recent reports on the promising antitumor activity of daunorubicin (**1**)[3,4] and adriamycin (**2**)[5] and carminomycin (**3**)[6,7] in a variety of animal and human cancers has aroused considerable interest in the chemical and biological properties of this group of anthracyclic compounds. Although the gross structure of **3** is known,[6] we now report for the first time the absolute stereochemistry of this important compound[8a] and its isolation from a new source, *Streptosporangium sp.*[9]

Chromatography of the crude extract (10 g) on silicic acid[10] utilizing in vitro and in vivo bioassay procedures to locate active fractions[11] gave 0.3 g of **3**: $C_{26}H_{27}NO_{10}\cdot H_2O\cdot HCl$;[12] mp 183–185° dec; $[\alpha]^{25}D$ +193° (*c* 0.18, MeOH; lit.[6] $[\alpha]^{20}D$ +289°];[13] λ_{max} (MeOH) 234 nm (ϵ 32200), 255 (19600), 292 (12000), 492 (8200), 526 (6000); ir (KBr) 1715 cm^{-1} (CO), 1600 (quinone and aromatic C=C).

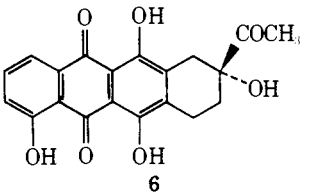
The uv and visible spectra of **3** were similar to those of daunorubicin[3] suggesting the presence of a 1,4,5-trihydroxyanthraquinone chromophore. Mild acid hydrolysis (0.1 *N* HCl, 100°, 0.5 hr) of **3** afforded a red aglycone carminomycinone (**4**) ($C_{20}H_{16}O_8$;[12] mp 233–235° (13% MeOH–$CHCl_3$–EtOAc; lit.[6] mp 224°); $[\alpha]^{28}D$ +171° (*c*, 0.14, dioxane; lit.[6] $[\alpha]^{20}D$ +272° (*c* 0.1, dioxane)];[13] NMR



1, R_1 = Me; R_2 = H
2, R_1 = Me; R_2 = OH
3, R_1 = R_2 = H



4, R = R_1 = H
5, R = R_1 = Ac



6

(CF_3CO_2D) δ 2.64 (s, 3, $COCH_3$), 3.30 (q, 2, C-10), 5.57 (br s, 1, C-7), 7.36–7.83 (m, 3, ArH)) and an amino sugar. The latter was identified as daunosamine[14] by direct comparison of the physical properties (GLC, TLC, mass spectrum) of its triacetate with those of daunosaminetriacetate. Acetylation of **4** gave the pentaacetate **5**: $C_{30}H_{26}O_{13}$;[12] mp 218–220° (CH_2Cl_2–hexane; lit.[6] mp 190°); $[\alpha]^{24}D$ −160° (*c* 0.10, $CHCl_3$; lit.[6] $[\alpha]^{20}D$ +40° (*c*, 0.11, $CHCl_3$));[13] ir ($CHCl_3$) 1740 cm^{-1} (aliphatic acetate), 1775 (phenolic acetate); NMR ($CDCl_3$) δ 2.02 (s, 6, C-7 and C-9 OAc), 2.22 (s, 3, $COCH_3$), 2.36 (s, 3, C-4 OAc), 2.40 (s, 3, C-11 OAc), 2.50 (s, 3, C-6 OAc), 6.36 (br s, 1, C-7), 7.34–8.12 (m, 3, ArH).

The attachment of the sugar moiety to the benzylic C-7 position was established by catalytic hydrogenolysis (5% Pd–$BaSO_4$, MeOH, 1 hr) of **3**. Under these conditions, there was obtained daunosamine and a new aglycone **6**: $C_{20}H_{16}O_7$;[12] mp 261–262° (13% MeOH–$CHCl_3$–EtOAc); $[\alpha]^{26}D$ −54° (*c* 0.13, dioxane).

The absolute configuration of **3** was determined by direct single-crystal X-ray crystallographic analysis. Carminomycin I hydrochloride monohydrate (**3**), $C_{26}H_{28}ClNO_{10}\cdot H_2O$, M = 566.97, crystallizes in the monoclinic system, space group $P2_1$, with a = 19.98 (1) Å, b = 5.50 (1) Å, c = 11.86 (1) Å, β = 93.7 (1) Å, U = 1301 Å^3, d_m (flotation) = 1.43 g cm^{-3}, Z = 2, d_c = 1.447 g cm^{-3}. The crystal structure was solved by a combination of Patterson and direct phase-determining methods involving the "magic integer" approach[15] in conjunction with the MULTAN[16] series of programs. Refinement of the non-hydrogen atom positional and anisotropic thermal parameters by full-matrix least-squares calculations has reduced R to 0.109 over 1324 independent reflections with $I > 2.0\sigma(I)$ from 2649 measurements on an Enraf-nonius CAD 3 automated diffractometer using Ni-filtered Cu Kα (λ 1.542 Å) radiation and operating in the θ–2θ scanning mode. The absolute configuration was established by incorporation of the chlorine anomalous dispersion corrections[17] into the structure-factor calculations. For the configuration depicted by **3**, R was 0.109 in contrast to the significantly higher value[18] of 0.111 for the mirror image, thereby confirming that **3** correctly represents the absolute stereochemistry.[19] Thus the structure of carminomycin I is in complete accord at all asymmetric

centers with the stereochemistries derived earlier for daunomycin[20] (daunorubicin) and differs only in the presence of an -OH group at C_4 in place of an -OMe group in daunomycin.

Carminomycin I shows potent antitumor activity in P-388 mouse leukemia, preliminary activity in the B-16 mouse melanocarcinoma, and inhibition of 9KB cell culture;[11,21] if the observed inhibition of *B. subtilis* is noted with other microorganisms, **3** may also be a potent antibiotic.

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Supplementary Material Available. A listing of atomic coordinates and anisotropic thermal parameters will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Business Office, Books and Journals Division, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.00 for photocopy or $2.50 for microfiche, referring to code number JACS-75-5955.

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(9) The entire *Streptosporangium sp.* culture was extracted with methyl isobutyl ketone at pH 3.0–3.5, concentrated, and precipitated from solution as a crude solid with skellysolve B.
(10) The crude fermentation solids (10.0 g) were chromatographed on 2.0 kg of silicic acid (200 mesh, Mallinckrodt, 3 in. diameter column) using a gradient eluent of 4:1 chloroform:acetone containing 5% MeOH with increasing gradients of MeOH up to 50%. A sample for analysis and X-ray crystallography was obtained by crystallization from $CHCl_3$–acetone–MeOH (4:1:2).
(11) Our sample of **3** markedly inhibited *B. subtilis* (zone inhibition) on agar plate and 9KB cell culture. It also exhibited in vivo activity in P-388 mouse leukemia. The latter two procedures were carried out under the auspices of the National Cancer Institute by procedures described by R. I. Geran, N. H. Greenberg, M. M. McDonald, A. M. Schumacher, and B. J. Abbott, *Cancer Chemother. Rep., Part 3*, **3**, 1 (1971). All three procedures gave excellent correlation. In consequence the simpler and more rapid in vitro methods were used extensively.
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(13) The $[\alpha]_D$ values reported were determined using the same solvent and concentration as reported in the literature.[6] In spite of these precautions large differences in the $[\alpha]_D$ values for **3** and the corresponding aglycone and aglycone pentaacetate were observed. This discrepancy may be due to any one or a combination of the following factors: (a) highly colored nature of these compounds, (b) poor solubility in common organic solvents, (c) large rotations, and (d) possible impurities.
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(21) When tested against P388 lymphocytic leukemia in the mouse according to standard NCI protocols[11] **3** prolonged the survival time of tumor bearing animals by 100–150% beyond that of untreated controls at doses of 0.05–0.2 mg/kg. Because of sample size limitations the toxic and no-effect dose limits of **3** have not been determined. In the KB cell cytoxicity assay ED_{50} values on the order of 1×10^{-2} μg/ml are observed.

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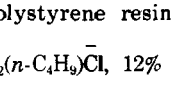
Triphase Catalysis[1]

Sir:

We wish to introduce a new concept in heterogeneous catalysis which we term, "triphase catalysis".[2] The underlying feature which distinguishes this from other forms of heterogeneous catalysis is that both the catalyst and each one of a pair of reactants are located in separate phases.

We have successfully applied this principle to certain *aqueous phase–organic phase* reactions employing a *solid phase* catalyst and now wish to report our observations for (1) the displacement of cyanide ion on 1-bromooctane and 1-chlorooctane and (2) the generation of dichlorocarbene from chloroform.

Chloromethylated polystyrene (1.0 mmol of chlorine/g of polymer, 200–400 mesh)[3] cross-linked with 2% divinylbenzene was transformed into **1a** using a procedure similar to that described elsewhere.[4] Resin **1a** (0.15 g, 0.14 mmol of



polystyrene resin

1a, R = $CH_2\overset{+}{N}(CH_3)_2(n\text{-}C_4H_9)\overset{-}{Cl}$, 12% ring substitution
b, R = H

quaternary ammonium groups) was suspended in a heterogeneous mixture of 2 ml of 0.55 *M* 1-bromooctane in benzene and 3 ml of 8.0 *M* aqueous sodium cyanide, contained in an 8-ml vial (Scheme I).[5] The vial was sealed with a Teflon-lined screw-cap, placed in an oil bath maintained at 110° for 4 hr, withdrawn, and cooled to room temperature. Analysis of the organic phase by GLPC showed a 92% yield