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.

Acknowledgments. The authors thank Dr. John D. Douros, National Cancer Institute, for constant encouragement throughout this work. The authors are grateful to Dr. D. Rosenthal and Mr. F. Williams for mass spectral data (obtained from the Research Triangle Center for Mass Spectrometry, with support from the Bio-technology Resources Branch of the Division of Research Resources, NIH, Grant No. RR-330), Dr. B. Berrang for GLC of the triacetates of the unknown sugar and daunosamine, and Mr. J. B. Thompson and Ms. C. Shelnutt for expert technical assistance. The authors also thank Dr. W. T. Bradner, Bristol Laboratories, for supplying the crude antibiotic extract and Dr. D. W. Henry, Stanford Research Institute, for supplying a sample of daunosamine. One of us (K.O.) is indebted to the American Enka Company for the award of a Graduate Fellowship.

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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(8) (a) "Carminomycin" is a mixture of a number of carminomycin antibiotics which have been termed carminomycin I, II, III, etc.[6] Mild acidic treatment converts the carminomycins II and III to I. Dr. G. R. Pettit, and his colleagues, Arizona State University, have compared the properties of a sample of **3** from our laboratory with a purified sample ocarminomycin I from Russian sources and have informed us that the two substances and the corresponding aglycone **4** are identical.[8b] We wish to thank Dr. Pettit for giving us this information prior to publication of this data. (b) G. R. Pettit, *et al.*, *J. Am. Chem. Soc.*, in press.
(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.
(12) Satisfactory elemental analyses and/or high resolution mass spectra were obtained for all new compounds.
(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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Received May 19, 1975

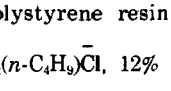
Triphase Catalysis[1]

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

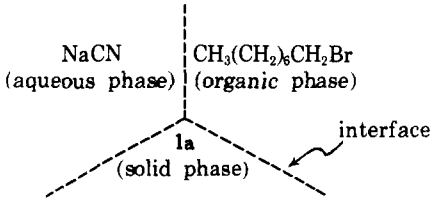
quaternary ammonium groups) was suspended in a heterogeneous mixture of 2 ml of 0.55 *M* 1-bromooctane in benzene and 3 ml of 8.0 *M* aqueous sodium cyanide, contained in an 8-ml vial (Scheme I).[5] The vial was sealed with a Teflon-lined screw-cap, placed in an oil bath maintained at 110° for 4 hr,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

Table I. Cyanide Displacement on 1-Bromo- and 1-Chlorooctane[a]

1-Halooctane	Catalyst	Time, hr	1-Cyanooctane,[b] %
1-Bromooctane		100	0
	1a	4	92
	1b	4	0
1-Chlorooctane		100	0
	1a	24	50[7]
	1b	24	0

[a] The temperature for all reactions was 110°. Product mixtures were analyzed by GLPC. [b] Yields are based on 1-halooctane.

Scheme I



of 1-cyanooctane plus 8% unreacted 1-bromooctane.[6] When the reaction was carried out using unfunctionalized polystyrene (**1b**) in place of **1a** as the catalyst or in the absence of any polymer matrix, 100% of the alkyl bromide remained unchanged. Similar results were obtained with 1-chlorooctane as the substrate (Table I).

In order to ensure that these displacement reactions were, in fact, being catalyzed by the solid phase, the reaction of cyanide ion with 1-bromooctane was repeated but stopped after 0.5 hr so that only a 43% yield of 1-cyanooctane was obtained. A portion of the aqueous phase (0.4 ml) and the organic phase (0.6 ml) was transferred to a second vial, which, along with the original vial, was heated for an additional 2 hr period at 110°. Analysis of the product mixture in the vial containing **1a** showed a 90% yield of 1-cyanooctane. In the absence of **1a**, the yield of 1-cyanooctane remained at 43%.

We have also found that **1a** catalyzes the generation of dichlorocarbene from chloroform solutions placed over aqueous sodium hydroxide. Thus, when α-methylstyrene (0.165 g, 1.4 mmol) dissolved in 2 ml of chloroform was added to 2 ml of a 50% aqueous sodium hydroxide solution containing **1a** (0.1 g) and the mixture was heated for 40 hr at 50°, 1,1-dichloro-2-methyl-2-phenylcyclopropane was produced in 99% yield.[6,8,9] Without **1a** present, a similar reaction afforded less than 0.1% of the dichlorocyclopropane derivative.[10]

A technique recently developed for accelerating aqueous phase–organic phase reactions (phase-transfer catalysis) has proven particularly useful in several synthetic transformations.[11] One practical limitation to this method, however, is that many phase-transfer agents promote stable emulsions which render work-up difficult. The major advantage that triphase catalysis has over phase-transfer catalysis is that the catalyst can be removed from the product mixture by simple filtration.

The detailed nature of the catalytic processes reported herein needs further clarification and we therefore wish to defer mechanistic comments until a later time. Work in progress is aimed at (1) defining resin activity in terms of concentration of ionic groups along the polymer backbone, type of ionic group employed, and degree of swelling of the polymer lattice, and (2) exploring the synthetic utility of this technique.

References and Notes

(1) Supported by the National Science Foundation, Grant No. MPS74-23925.

(2) Anion-exchange resins have previously been found to catalyze certain cyanide displacement reactions: H. B. Copelin and G. B. Crane, U.S. Patent 2779781 (1957). Although such systems bear a resemblance to the triphase catalyzed process reported herein, the fact that these reactions proceed at a significant rate in the absence of suitable resins makes their relationship to triphase catalysis questionable.

(3) Chloromethylated polystyrene was purchased from Bio-Rad Laboratories and was used without further purification.

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(5) For this system, the polystyrene beads reside at the interface of the organic and aqueous phases.

(6) An internal standard (*n*-dodecane) was added to the mixture prior to GLPC analysis. A 6-ft column packed with 5% Carbowax 20M on 80–100 mesh Chromasorb P was employed.

(7) The yield remained unchanged after heating for an additional 24 hr. When the aqueous phase was replaced by a fresh cyanide solution and the reaction mixture heated to 110° for 24 hr, the yield of 1-cyanooctane increased to 64%. It is presumed that the competing hydrolysis of sodium cyanide to sodium formate becomes significant with these longer reaction times.

(8) The yield reported is based on the starting α-methylstyrene.

(9) We are grateful to Professor Michael A. McKinney for his gift of authentic 1,1-dichloro-2-methyl-2-phenylcyclopropane.

(10) Analysis showed that >99% of the starting olefin remained unchanged.

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Received July 12, 1975

Stereospecific Conversion of Peptides into β-Lactams

Sir:

Evidence has accumulated which supports the hypothesis that the β-lactam antibiotics, penicillin (**1**) and cephalosporin C (**2**), are derived from the so-called Arnstein tripeptide (**3**).[1] In order to achieve this conversion in vitro we have investigated the oxidative chemistry of the cysteinylvaline