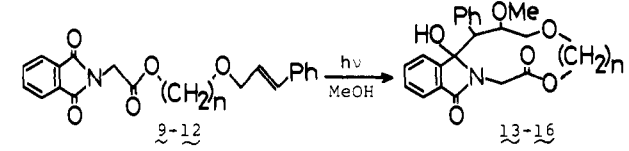


Table I. Photoproducts from *N*-Alkenylphthalimides 9-12


sub- strate	<i>n</i>	prod- uct ^a	yield, % ^b	mp, °C	ring size	rel efficiency ^c
9	2	13	68	184-186	11	1.0
10	4	14	55	144-147	13	0.4
11	5	15	65	187-190 ^{d,f} 197-200 ^{e,f}	14	0.2
12	6	16	35	oil	15	0.1

^a In methanol (2 mM) for 5-8 h at ambient temperature. ^b Based on the consumed imide. ^c Disappearance of imide with 9 as a standard. Using a Pyrex filter on a merry-go-round. ^d 15a. ^e 15b. ^f 15a:15b, 3:1.

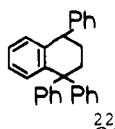
N-alkenyl group attached by β -styryl group at the end. Irradiation of 5 in methanol gave 6, mp 237-239 °C (64%). In this case, the primary product seems to be unstable and results in the formation of the dehydrated product 6. Photolysis of 7 in methanol afforded 8, mp 217-219 °C (55%). A series of examples is summarized in Table I.

Irradiation of a methanol solution of 17 possessing the α -styryl moiety in the *N*-alkenyl group gave product 18, mp 167-169 °C (68%). Photolysis of 19 having the 2-methyl-1-propenyl group instead of the α -styryl group afforded a mixture of the corresponding products 20a (mp 168-169 °C) and its isomer (20b) as a mixture (total 35%). In this case, a hydrogen-abstraction product 21 was also obtained.⁵ 21: mp 169-171 °C; ¹H NMR (CDCl₃) δ 1.17 (s, 3 H), 1.83 (s, 3 H), 3.2-3.5 (m, 1 H), 3.6-4.5 (m, 5 H), 4.7-5.1 (m, 2 H), 5.05 (br d, 1 H), 7.3-7.8 (m, 4 H) (the decoupling examination clearly demonstrated the presence of Me₂C=C(H)CH< unit); IR (KBr) 3285 (OH), 1748 (ester), 1694 (amide) cm⁻¹; *m/e* (rel intensity) (20 eV) 317 (M⁺, 7), 231 (100).

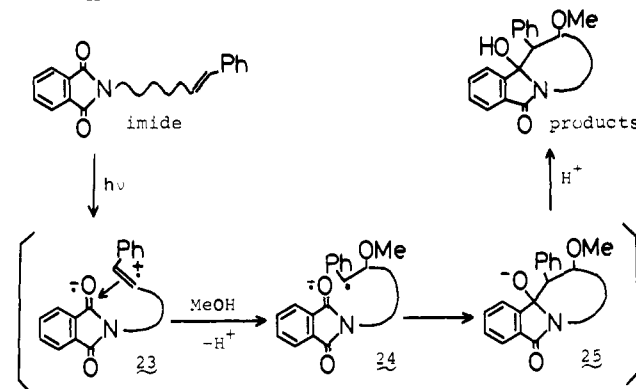
In recent years, radical ion pair formation in bimolecular photochemical reactions has been paid great interest.⁶⁻⁹ In some cases olefins behave as electron donors. Arnold and his co-workers reported anti-Markownikoff methanol addition to some aromatic olefins photosensitized by methyl *p*-cyano-benzoate.⁷ Similarly, photochemically induced methanol addition (substitution) reactions have been reported in the photoreaction of several cyanated aromatics with olefins,⁸ and in the photoreaction of phthalimides with olefins.^{4,9}

Photochemical intramolecular cyclomerization between two chromophoric units bridged by more than four bonds requires a certain interaction between the two remote chromophores in their excited state. Kanaoka and his co-workers reported the interesting "remote" photochemical hydrogen abstraction reaction of acceptor (phthalimide)-donor (S or N atom) systems, in which charge interaction in the excited state could play an important role to achieve the highly regioselective "remote" photoreaction.⁵ Thus, the present reaction may be regarded as an application of the photoinduced methanol addition between electron acceptor (phthalimide) and donor (olefin) to the synthesis of "remote" cyclomerization products.

In our reaction initial one-electron transfer from the *N*-alkenyl double bond to the phthalimide moiety may be involved. Such an electron-transfer process is supported by the fact that photolysis of an acetonitrile solution containing *N*-methylphthalimide and 1,1-diphenylethylene gave 1,1,4-tri-



Scheme II



phenyl-1,2,3,4-tetrahydronaphthalene (22); 22 is known to be derived from the radical cation of 1,1-diphenylethylene.^{7a} Formation of the solvent-incorporated medium to macrocyclic products may be rationalized as shown in Scheme II.

The synthetic utility of this reaction has to be emphasized. Its scope, limitation, and mechanism are being studied.

References and Notes

- (1) J. A. Ors and R. Srinivasan, *J. Am. Chem. Soc.*, **100**, 315 (1978); (b) J. A. Ors and R. Srinivasan, *J. Chem. Soc., Chem. Commun.*, 400 (1978); (c) F. C. De Schryver, N. Boens, and J. Put, *Adv. Photochem.*, **10**, 359 (1977).
- (2) 1 was synthesized by the esterification reaction of phthaliminoacetyl chloride^{2a} and an alcohol which was derived from cinnamyl chloride and sodium salt of neopentyl glycol. Other *N*-alkenylphthalimides described in this paper prepared by the similar procedure. (a) S. Gabriel, *Chem. Ber.*, **40**, 2648 (1907).
- (3) All new compounds (imides and products) gave satisfactory analytical results as well as reasonable spectral properties (IR, NMR, and mass spectra). Especially, all products showed obvious molecular ion peaks (M⁺).
- (4) K. Maruyama, Y. Kubo, M. Machida, K. Oda, Y. Kanaoka, and K. Fukuyama, *J. Org. Chem.*, **43**, 2303 (1978).
- (5) (a) Y. Sato, H. Nakai, T. Mizoguchi, Y. Hatanaka, and Y. Kanaoka, *J. Am. Chem. Soc.*, **98**, 2349 (1976); (b) Y. Sato, H. Nakai, H. Ogiwara, T. Mizoguchi, and Y. Kanaoka, *Tetrahedron Lett.*, 1889 (1976); (c) M. Machida, T. Takeuchi, and Y. Kanaoka, *Heterocycles*, **7**, 273 (1977).
- (6) (a) D. R. Arnold and A. J. Maroullis, *J. Am. Chem. Soc.*, **98**, 5931 (1976); (b) D. R. Arnold and A. J. Maroullis, *ibid.*, **99**, 7355 (1977); (c) A. J. Maroullis, Y. Shigemitsu, and D. R. Arnold, *ibid.*, **100**, 535 (1978).
- (7) (a) R. A. Neunteufel and D. R. Arnold, *J. Am. Chem. Soc.*, **95**, 4080 (1973); (b) Y. Shigemitsu and D. R. Arnold, *J. Chem. Soc., Chem. Commun.*, 407 (1975).
- (8) (a) J. J. McCullough and W. S. Wu, *J. Chem. Soc., Chem. Commun.*, 1136 (1972); (b) K. Mizuno, C. Pac, and H. Sakurai, *J. Am. Chem. Soc.*, **96**, 2993 (1974); (c) S. Yamada, Y. Kimura, and M. Ohashi, *J. Chem. Soc., Chem. Commun.*, 667 (1977); (d) C. Pac, A. Nakasone, and H. Sakurai, *J. Am. Chem. Soc.*, **99**, 5806 (1977).
- (9) K. Maruyama and Y. Kubo, *Chem. Lett.*, 851 (1978).

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Selectivity Features of Polystyrene-Based Triphase Catalysts¹

Sir:

Triphase catalytic methods serve as a compliment to phase-transfer catalysis.²⁻⁶ Recently it occurred to us that triphase catalysts might possess inherent selectivity toward reactants. In particular, polystyrene resins are known to impose a modest size selectivity to attached catalysts and reagents in solid/liquid biphasic reactions.^{7,8} This effect has been attributed to the restriction in size of solvent channels by random cross-links in the polymer.⁷ We reasoned that, not only would similar selectivity be found with certain of the polystyrene-based triphase catalysts, but, in addition, for those polymers that function as cosolvents,⁶ a more pronounced degree of selectivity would be present owing to the relative solubility (ab-

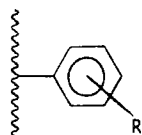
Table I. Relative Rates Using Triphase Catalysis (TC) and Phase-Transfer Catalysis (PTC)^a

organic halide	TC					PTC,
	1	2	3	4	5	6
1-bromobutane	1.40	2.07	5.29	62.00	64.00	1.06
1-bromopentane	1.41	1.50	1.80	19.25	40.00	0.96
1-bromohexane	1.17	1.44	1.75	5.09	6.89	1.02
1-bromoheptane	1.12	1.17	1.27	2.49	2.53	1.04
1-bromooctane	1.00	1.00	1.00	1.00	1.00	1.00

^a Procedures and reaction conditions used are described in the text.

sorption) of the reactants within the catalytically active regions of the resin. Since such a feature could significantly expand the scope of this technique we have examined this question.

We now report the results of an investigation into the selectivity of triphase catalytic reactions of phenoxide ion with a homologous series of primary alkyl bromides. Resins studied were of the ion exchange (**1**, **2**), cosolvent (**3**, **4**, **5**) type,⁹ and, for comparison, a phase-transfer catalyst, **6**.¹⁰ Data presented herein reveal selectivity which is (1) high for cosolvent-type resins, (2) modest for ion-exchange polymers, and (3) nondetectable using the phase-transfer catalyst.



functionalized polystyrene—1% divinylbenzene

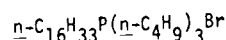
1, R = CH₂P(C₄H₉)₃Cl; percent ring substitution (prs) = 17

2, R = CH₂N(CH₃)₃Cl; prs = 17

3, R = CH₂NCH₃PO[N(CH₃)₂]₂; prs = 92

4, R = CH₂O(CH₂CH₂O)₁CH₃; prs = 17

5, R = CH₂O(CH₂CH₂O)₂CH₃; prs = 17



6

A standard triphase reaction was carried out as follows. An 8-mL culture tube (Corning No. 9826, 13 × 100 mm) equipped with a Teflon-lined screw cap was charged with 0.1 g of resin, 2.0 mL of an aqueous sodium phenoxide solution (0.25 M), and 2.5 mL of a toluene solution which contained 3 mmol each of 1-bromooctane (reference) and a competing organic halide. After purging the reaction mixture with nitrogen for 5 min, the tube was sealed and placed in an oil bath maintained at 105 ± 0.5 °C. All of the competition studies were carried out to ~7% completion based on the total organic halide present.¹¹ The ratios of ether products were determined by GLC using internal standard techniques. Additional competition experiments were carried out for 1-bromobutane vs. 1-bromohexane and 1-bromobutane vs. 1-bromoheptane to confirm the relative rate data. For the phase-transfer catalyzed reactions, 78 mg (0.15 mmol) of **6** was used in place of the insoluble catalyst. Table I summarizes the data obtained.¹²

For true phase-transfer catalysis, **6** is expected to "drag" phenoxide ion into the bulk organic phase where chemical reaction takes place. The fact that no detectable selectivity was found with this catalyst is consistent with such a mechanism. In contrast, under triphase catalytic conditions employing **3–5** (and to a lesser extent **1** and **2**), a distinct preference for the smaller organic halides was observed. This selectivity must arise from a difference in the effective concentration of the

Table II. Absorption of 1-Bromobutane and 1-Bromooctane into Triphase Catalysts^a

catalyst	1-bromobutane, % ^b	1-bromooctane, % ^b
1	4.5	5.2
2	3.8	4.7
3	2.0	0.7
4	8.6	0.7
5	7.2	1.1

^a Determined by equilibrating 2 mL of toluene containing 3 mmol of organic halide plus 1 mmol of *n*-dodecane (internal standard) with 2 mL of distilled water in the presence of 0.1 g of polymer at 25 °C.

^b Percent decrease in concentration of halide in the organic layer after the polymer is added to the liquid-liquid biphasic system.

reactants at the catalytically active sites. The concentration of organic halide in these polymers is defined by either (1) a concentration gradient and/or (2) a coefficient of absorption. Whether 1 or 2 is relevant depends on the diffusional barrier imposed by the matrix on the halide relative to the activation energy of the reaction. If concentration gradients are present they are expected to increase with decreasing swelling (greater diffusional resistance) and increasing catalyst activity, leading to greater selectivity. We find, to the contrary, that for phenoxide displacement those polymers which exhibited the greatest selectivity were less active¹² and swelled the most.¹³ In addition, absorption data reported in Table II reveal that, while **1** and **2** absorb both 1-bromooctane and 1-bromobutane to nearly the same extent, polymers **3–5** significantly favor the latter. Taken together, these results provide evidence for absorption-controlled selectivity¹⁴ for **3–5** and diffusion-controlled selectivity for catalysts **1** and **2**.

The magnitude of the selectivity observed is sufficiently large that it can be of potential practical importance. Moreover, it demonstrates a difference between phase-transfer and triphase catalytic processes which reflects the greater complexity of the latter.

These systems will require considerable detailed examination before their relationship to phase-transfer,¹⁵ micellar,¹⁶ and interfacial¹⁷ catalysis becomes clear.

References and Notes

- (1) Supported by the Division of Basic Energy Sciences of the Department of Energy (Contract EG-77-S-02-4446).
- (2) For a description of the triphase catalytic method, see S. L. Regen, *J. Am. Chem. Soc.*, **97**, 5956 (1975).
- (3) S. L. Regen, *J. Am. Chem. Soc.*, **98**, 6270 (1976); S. L. Regen, *J. Org. Chem.*, **42**, 875 (1977); S. L. Regen, "Catalysis in Organic Synthesis", Academic Press, New York, 1977, p. 119.
- (4) M. Cinouini, S. Colonna, H. Molinari, F. Montanari, and P. Tundo, *J. Chem. Soc., Chem. Commun.*, 394 (1976); H. Molinari, F. Montanari, and P. Tundo, *ibid.*, 639 (1977).
- (5) J. M. Brown and J. A. Jenkins, *J. Chem. Soc., Chem. Commun.*, 458 (1976); P. Tundo, *ibid.*, 641 (1977); P. Tundo, *Synthesis*, 315 (1978); M. Tomoi, T. Takubo, M. Ikeda, and H. Kakiuchi, *Chem. Lett.*, 473 (1976); F. Rolla and W. Roth, *Naturwissenschaften*, **64**, 377 (1977); S. Colonna, R. Fornasier, and U. Pfeifer, *J. Chem. Soc., Perkin Trans. 1*, 8 (1978); E. Chiellini and R. Solaro, *J. Chem. Soc., Chem. Commun.*, 231 (1977); H. K. Zadeh, H. J.-M. Dou, and J. Metzger, *J. Org. Chem.*, **43**, 156 (1978).
- (6) S. L. Regen and L. Dulak, *J. Am. Chem. Soc.*, **99**, 623 (1977); S. L. Regen, *ibid.*, **99**, 3838 (1977); S. L. Regen, A. Nigam, and J. J. Besse, *Tetrahedron Lett.*, in press; S. L. Regen, J. J. Besse, and J. McLick, unpublished work.
- (7) R. H. Grubbs and L. C. Kroll, *J. Am. Chem. Soc.*, **93**, 3062 (1971); R. H. Grubbs, L. C. Kroll, and E. M. Sweet, *J. Macromol. Sci. Chem.*, **7**, 1047 (1973); R. H. Grubbs, "Catalysis in Organic Synthesis", Academic Press, New York, 1976, p. 153.
- (8) S. L. Regen and D. P. Lee, *Isr. J. Chem.*, in press.
- (9) The preparation and characterization of these resins have been previously described; see ref 3, 4 and 6.
- (10) C. M. Starks, *J. Am. Chem. Soc.*, **93**, 195 (1971).
- (11) All catalyzed ether syntheses reported in this work proceed essentially to completion with respect to phenoxide ion.
- (12) Under the experimental conditions described, the time required for 50% conversion of phenoxide to *n*-butyl phenyl ether using catalysts **1**, **2**, **3**, **4**, **5**, and **6** were 0.25, 4.00, 5.83, 4.17, 4.33, and 0.50 h, respectively. In the absence of catalyst, <4% of the ether was formed after 6 h. It is interesting to note that the polymeric phosphonium salt **1** exhibits greater activity as well as greater selectivity compared to the soluble catalyst, **6**.

- (13) Swelling measurements made for 1-5 under triphase conditions and ambient temperature indicate the following degrees of swelling (volume of swelled resin/volume of dry resin): 1 (1.5); 2 (1.4); 3 (2.1); 4 (3.1), and 5 (3.2).
- (14) Analogous polar-selectivity features have been observed for certain polymer catalysts in solid/liquid biphasic reactions.⁷
- (15) W. P. Weber and G. W. Gokel, "Phase-Transfer Catalysis in Organic Synthesis", Springer-Verlag, New York, 1977; E. V. Dehmow, *Angew. Chem., Int. Ed. Engl.*, **16**, 493 (1977); A. Brändström, *Adv. Phys. Org. Chem.*, **15**, 267 (1977).
- (16) E. H. Cordes and R. B. Dunlap, *Acc. Chem. Res.*, **2**, 329 (1969); C. A. Bunton, *Prog. Solid State Chem.*, **8**, 239 (1973).
- (17) F. M. Menger, *J. Am. Chem. Soc.*, **92**, 5965 (1970).

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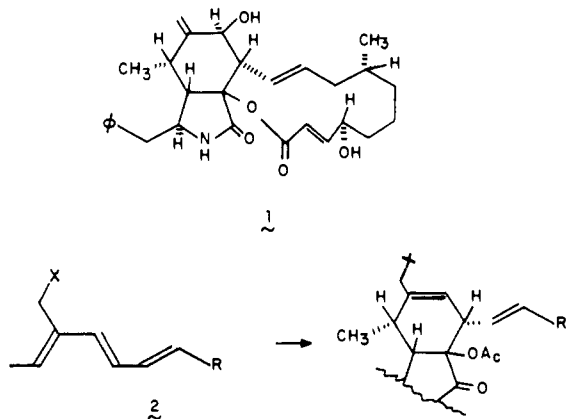
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Total Synthesis of Cytochalasin B

Sir:

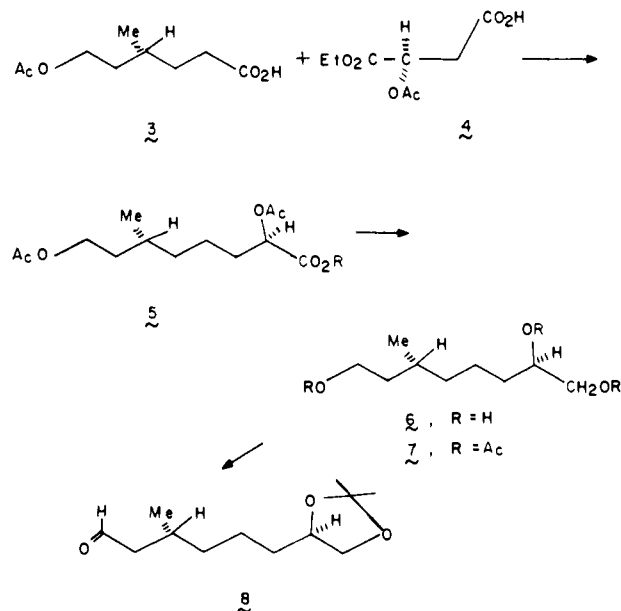
We report the total synthesis of cytochalasin B (**1**, phomin¹) a member of a class of natural cytostatic substances endowed with remarkable biological properties. The synthesis was designed on the assumption that a triene such as **2** should undergo regioselective [2 + 4] addition as indicated (for steric, as well as electronic reasons). We further expected that an acyloxy-



enone system would preferentially lead to the desired vicinal arrangement of the vinyl and acyloxy groups.² These expectations were rewarded.

We begin by describing the preparation of the required diene. We found it convenient to generate the chiral secondary methyl and hydroxyl groups of the side chain (the eventual substituents on the lactone ring of **1**) from (+)-citronellol and malic acid, respectively.

The acetate of pure citronellol,³ $[\alpha]_D^{20} +5.12^\circ$ (*c* 5.86), was converted (O_3 , CH_2Cl_2 , Zn dust/acetic acid; Jones oxidation of the crude aldehyde) to the acetate of 4(*R*)-methyl-6-hydroxyhexanoic acid (**3**): 81%, bp 112 °C (0.07 mm); $[\alpha]_D^{20} +3.1^\circ$ (*c* 5.7).⁴ Kolbe coupling of **3** (1 g) with the acetate of the 1-ethyl ester of (+)-malic acid (**4**)⁵ (4.6 g; 80 mL of 0.2% ethanolic sodium ethoxide, ~1.5 A, 45-50 °C, 75 min; solvent removal and reacylation of the crude mixture) gave, after elution of the coupling product from **3** (24%, *m/e* 287 (*M* + 1)), the desired cross-coupling product, the diacetate of ethyl 2-(*R*),8-dihydroxy-6(*R*)-methyloctanoate (**5**), in 42% yield ($[\alpha]_D^{20} +14.5^\circ$ (*c* 13.8); ¹³C NMR showed the required 15 peaks). Reduction of **5** with $LiAlH_4$ in ether gave 6(*R*)-methyl-2(*R*)-1,2,8-octanetriol (**6**). Its triacetate **7** (silica gel, 4:1 hexane-ethyl acetate, bp (Kugelrohr) 150 °C (0.1 mm)) had $[\alpha]_D^{20} +2.5^\circ$ (*c* 5.0), reported⁶ $[\alpha]_D +2.3 \pm 1^\circ$. The secondary hydroxyl and methyl groups are now established with their proper chirality in the triol **6**, which was prepared



for further elaboration to the required triene system by acetone formation (acetone, *p*-TsOH, room temperature, 3 h), followed by Collins oxidation (1 h, room temperature) to the aldehyde **8**.

Condensation of glycidaldehyde with carbethoxymethylene triphenylphosphorane (30% excess in benzene, 1.5-h reflux) gave the unsaturated ester **9** in 87% yield (bp 96-98 °C (15 mm)). Conversion to the glycol **10** (formic acid, 30 min; concentration under vacuum; aqueous saturated bicarbonate overnight, hexane washing and ethyl acetate extraction; 76% yield) was followed by protection of the primary alcohol as the *tert*-butyl dimethylsilyl ether and, after separation from some disilylated compound, by oxidation ($CrO_3 \cdot 2pyr$) to the unsaturated keto ester **11** (78% from **10**; homogeneous by TLC; $HC=CH$, two 1 H d at δ 6.80 and 7.43 ($J = 16$ Hz)). Condensation of **11** with ethylidene triphenylphosphorane (THF, -78 °C, 45 min) gave (74% yield) a 5.7:1 ratio of the desired *trans,trans*-dienic ester **12** and its more easily eluted (3% ethyl acetate in hexane) *trans,cis* isomer. Reduction with sodium bis(methoxyethoxy)aluminum hydride (toluene; ice-methanol cooling, 45 min) gave the corresponding alcohol **13** (89% yield) which was transformed into the phosphonate **14**, required for

