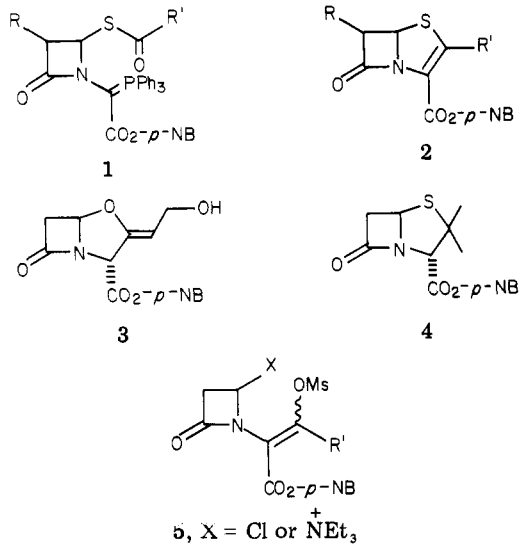
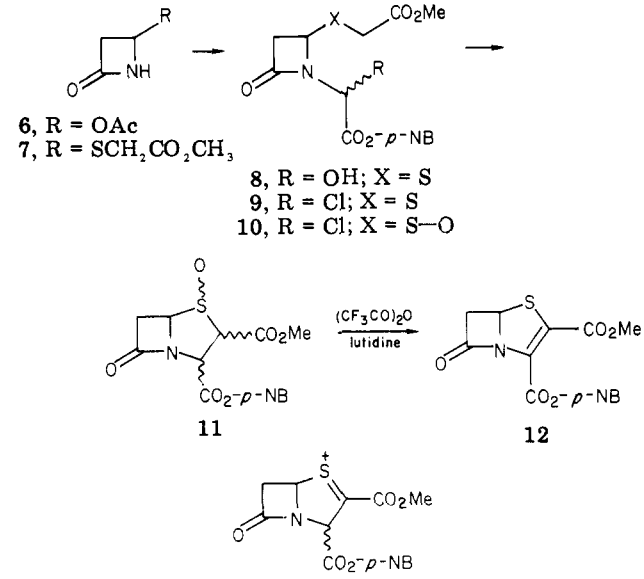
Chart I[a]



[a] p-NB = p-nitrobenzyl.

Scheme I



via the treatment of the intermediate **5** with hydrogen sulfide and triethylamine.

As part of a program aimed at the total synthesis of derivatives of compound **2**, we have investigated and developed a new penem synthesis via a Pummerer rearrangement of a penam sulfoxide **11**. The carbomethoxy group was chosen for the R′ of compound **2** because it was anticipated that it would enhance the acylating power of the β-lactam by conjugation through the penem double bond. Increased acylation power is felt to be associated with increased antibacterial potency in the case of β-lactam antibiotics (e.g., the cephalosporins[4]). The required penam sulfoxide **11** was obtained from the racemic azetidinone **6** by a five-step synthesis (Scheme I). Treatment of **6** with methyl thioglycolate gave the thioazetidinone **7**[5] in 87% yield. Condensation of **7** with *p*-nitrobenzyl glyoxylate[6] in refluxing benzene for 12 h gave the hydroxy compound **8** in 92% yield as a 1:1 diastereoisomeric mixture. Treatment of **8** with thionyl chloride–lutidine in methylene chloride at 0 °C produced the chloro compound **9** in a quantitative yield. Satisfactory generation of the sulfoxide **10** was achieved in 75% yield by exposure of **9** to *m*-chloroperbenzoic acid (1.1 equiv in CH_2Cl_2, O °C), followed by a fast silica gel column chromatography. Treatment of the sulfoxide **10** with lithium diisopropyl amide (1.1 equiv in THF, −78 °C) furnished the cyclized azetidinone **11** in 53% yield as an oily diastereoisomeric mixture.[7] A high IR β-lactam carbonyl frequency (1790 cm^{-1}) of **11** is in accord with the formation of the bicyclic azetidinone.[8] Although **11** existed as a complex diastereoisomeric mixture, the Pummerer rearrangement of **11** converted all isomers into a single product, **12**. Thus, exposure of **11** to $(CF_3CO)_2O$–lutidine at 25 °C overnight produced the penem **12** as a gum in 37% yield after silica gel column chromatography.[9]

The penem **12** had the following properties: IR ($CHCl_3$) 1805, 1740, 1725 cm^{-1}; UV (EtOH) λ_{max} 262 nm (ϵ 12 200), and 322 (5800); NMR ($CDCl_3$) δ 3.60 (1 H, dd, J = 2.5, 16.0 Hz, C-6H), 3.75 (3 H, s, OMe), 3.90 (1 H, dd, J = 3.0, 16.0 Hz, C-6H), 5.30 (2 H, s, OCH_2Ph-*p*-NO_2), 5.82 (1 H, dd, J = 2.5, 3.0 Hz, C-5H), 7.5 (2 H, J = 9.0 Hz, aromatic protons), 8.3 (2 H, J = 9.0 Hz, aromatic protons). A reasonable reaction pathway from **11** to **12** might involve a stepwise sequence through the intermediate **13**, followed by the migration of the double bond to furnish the penem **12**. In conclusion, it has been demonstrated that a highly activated penem system can be readily constructed via a Pummerer rearrangement process of a penam sulfoxide. The further application of this methodology for the synthesis of novel penems will be reported in due course.

Registry No. (±)-**6**, 64804-09-7; (±)-**7**, 79970-18-6; (±)-**8** (isomer 1), 79970-19-7; (±)-**8** (isomer 2), 79970-20-0; **9**, 79970-21-1; **10**, 79970-22-2; **11**, 79970-23-3; (±)-**12**, 79970-24-4; methyl thioglycolate, 2365-48-2; *p*-nitrobenzyl glyoxylate, 64370-35-0.

(9) Spectral properties of all new compounds were in accord with the proposed structure.

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A Stereospecific Synthesis of Trisubstituted Alkenes via Hydridation of Dialkylhaloboranes Followed by Hydroboration–Iodination of Internal Alkynes

Summary: Dialkylvinylboranes, prepared conveniently via the hydridation of dialkylhaloboranes in the presence of an internal alkyne, react with iodine under basic conditions to produce trisubstituted alkenes of established stereochemistry, providing a general synthesis of trisubstituted alkenes with unambiguous stereochemistry.

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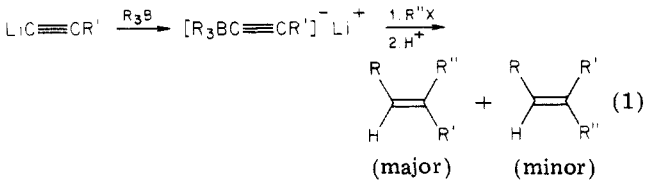
Table I. Syntheses of Trisubstituted Alkenes from Dialkylhaloboranes and Internal Alkynes[a]

alkene for R_2BX	X	alkyne	product[b]	% yield[c]	bp °C/mm	$n^{20}D$
ethylene	Br	2-butyne	(2Z)-3-methyl-2-pentene[d]	71[e]		
cyclopentene	Br	2-butyne	(2Z)-2-cyclopentyl-2-butene	71	83-85/90	1.4571
cyclopentene	Cl	4-octyne	(4Z)-4-cyclopentyl-4-octene	73	70-71/1	1.4645
cyclopentene	Br	5-decyne	(5Z)-5-cyclopentyl-5-decene	72	84-85/0.3	1.4641
cis-2-butene	Cl	5-decyne	(5Z)-5-(2-butyl)-5-decene	75	65-67/0.6	1.4432
1-octene	Cl	3-hexyne	(3Z)-4-ethyl-3-dodecene[d]	76	73-75/0.6	1.4393
1-hexene	Cl	2-butyne	(2Z)-3-methyl-2-nonene[d]	69	64-65/16	1.4263

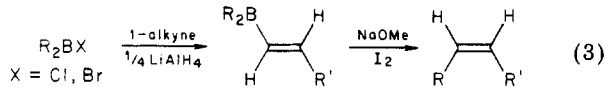
[a] All reactions were carried out on a 30-mmol scale. [b] Chemical purities of all products were >97% by GC analysis on a 6-ft SE-30 column; structures were confirmed by ^1H and ^{13}C NMR spectral data. [c] Yields of pure products, isolated by distillation, based on R_2BX or alkyne. [d] Distilled R_2BX was utilized. [e] GC yield determined using an internal standard, isomeric purity 100% by GC analysis on 12 ft × 0.25 in 20% TCP on firebrick.

Sir: The sterically defined synthesis of trisubstituted alkenes has attracted considerable attention of organic chemists in recent years because many biologically active compounds occurring in nature possess the structural skeleton of trisubstituted alkenes.[1] Application of organoboranes[2] for the stereospecific synthesis of cis[3] and trans[4] disubstituted alkenes has been well documented. However, only a limited number of methods are reported for the synthesis of trisubstituted alkenes via organoboranes.[5-7] These methods employ either trialkyl-1-alkynylborates[6] (eq 1) or trialkylvinylborates[7] (eq 2).



The increasing importance of trisubstituted alkenes as valuable structural units in various natural products requires a simple, efficient, and stereospecific method for the preparation of such structures. In continuation of our recent interest in the stereospecific syntheses of alkenes,[3,4] we undertook to extend the Zweifel synthesis of cis alkenes[3a] to the preparation of trisubstituted alkenes of definite stereochemistry.

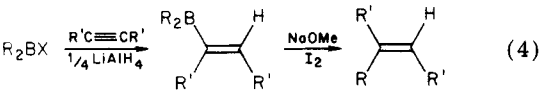
Recently we reported that representative dialkylboranes, obtained via hydridation of dialkylhaloboranes, hydroborate terminal alkynes to provide the corresponding dialkylvinylboranes (1), generalizing the synthesis of such intermediates.[8] Iodination of 1 in the presence of a base provides cis disubstituted alkenes in high isomeric purity[3b] (eq 3).



1

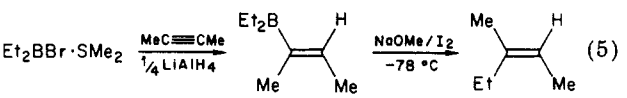
Consequently, it appeared to us that vinylboranes derived from internal alkynes should, in principle, provide trisubstituted alkenes with predictable stereochemistry. Accordingly, we examined the reaction with iodine of representative vinylborane derivatives from internal alkynes as a potential route for the synthesis of sterically defined trisubstituted alkenes.

We recently established that monohydroboration of internal alkynes with representative dialkylboranes proceeds cleanly to the corresponding dialkylvinylborane (2).[8] Iodination of 2 in the presence of NaOMe at −78 °C provided the expected trisubstituted alkene[9] (3, eq 4). A repre-



2

sentative group of trisubstituted alkenes was prepared following this reaction sequence (Table I). The cleanness of the stereochemistry was established by the synthesis of a simple trisubstituted alkene, (2Z)-3-methyl-2-pentene (eq 5). Fortunately, Z and E isomers of 3-methyl-2-



pentene are known[10a] and available.[10b] They separate nicely on a 12 ft × 0.25 in. column packed with 20% tricresyl phosphate on firebrick (60–80 mesh). The product obtained via the reaction in eq 5 was identical with the Z isomer, with no detectable presence of the E isomer.

The ^{13}C NMR spectra of (Z)- and (E)-3-methyl-2-pentene are distinctly different. In the case of the higher trisubstituted alkenes synthesized, we found that they were neither separated on the tricresyl phosphate column nor did they indicate the presence of more than one isomer in the ^{13}C spectrum. Consequently, we conclude that the reaction must proceed in accordance with the general equation (eq 4) to give sterically defined trisubstituted alkenes (3).

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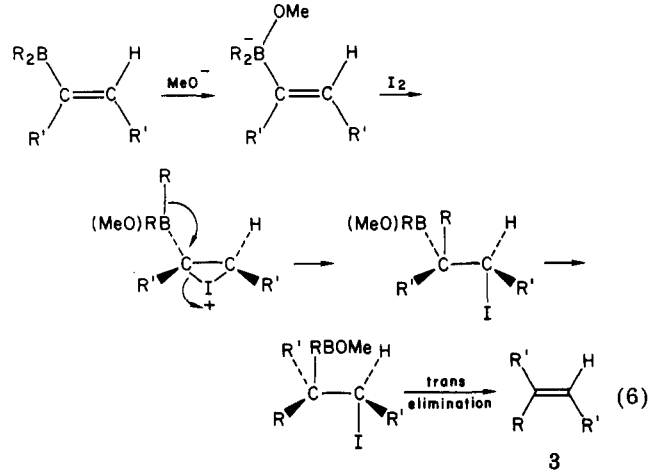
(9) Under these conditions, the formation of RI, which is a problem, especially when R = primary alkyl group, was minimized.

(10) (a) Prepared and characterized: Cornforth, J. W.; Cornforth, R. H.; Mathew, K. K. *J. Chem. Soc.* **1959**, 112. (b) Available from Farchan Division Albany International Chemicals.

These results indicate that a mechanism analogous to that involved in the formation of cis disubstituted alkenes[3a] is operative. Apparently the reaction proceeds via trans addition, followed by trans elimination, resulting in the trans stereochemistry of the two alkyl groups from the internal alkyne (eq 6).



(6)

3

The following procedure for the synthesis of (3Z)-4-ethyl-3-dodecene is representative. To 8.16 g (30 mmol) of $(n\text{-}C_8H_{17})_2BCl$[11] were added 40 mL of THF and 3.4 mL of 3-hexyne (30 mmol) at 0 °C followed by a slow addition of $LiAlH_4$ in THF (7.5 mmol) with stirring. The reaction was allowed to proceed for 2.5 h at 0 °C, followed by 0.5 h at room temperature. Then the reaction flask was cooled to −78 °C and a solution of NaOMe in MeOH (120 mmol) and 7.7 g (30 mmol) of I_2 in 30 mL of THF were added, respectively, with vigorous stirring. After 3 h, the excess iodine was decolorized by adding an aqueous solution of $Na_2S_2O_3$ and the reaction mixture was allowed to warm up to room temperature. The reaction mixture was extracted with 3 × 40 mL of pentane, and the organic layer was washed with 3 N NaOH solution (30 mL) and water and dried over anhydrous K_2CO_3. The solvents were removed under reduced pressure and distillation furnished 4.46 g (76%) of (3Z)-4-ethyl-3-dodecene bp 73–75 °C (0.6 mm), n^{20}_D 1.4393. GC analysis showed >97% chemical purity.

For the assignment of stereochemistry, (2Z)-3-methyl-2-pentene was prepared from $Et_2BBr{\cdot}SMe_2$[12] and 2-butyne by following this procedure. The authentic samples[10] of (2Z)- and (2E)-3-methyl-2-pentene could be separated on a 12 ft × 0.25 in. column packed with 20% tricresyl phosphate on firebrick (60–80 mesh). The reaction product contained pure 2Z isomer (in 71% GC yield) as confirmed by coinjection with the authentic sample.

This reaction sequence represents a very convenient stereospecific synthesis of trisubstituted alkenes under mild conditions. We are presently exploring the possibilities of extending this procedure for the synthesis of more complex molecules.

Registry No. 2-Butyne, 503-17-3; 4-octyne, 1942-45-6; 5-decyne, 1942-46-7; 3-hexyne, 928-49-4; (z)-3-methyl-2-pentene, 922-62-3; (z)-2-cyclopentyl-2-butene, 79970-43-7; (z)-4-cyclopentyl-4-octene, 79970-44-8; (z)-5-cyclopentyl-5-decene, 79970-45-9; (z)-5-(2-butyl)-5-decene, 79970-46-0; (z)-4-ethyl-3-dodecene, 79970-47-1; (z)-3-methyl-2-nonene, 79970-48-2.

(11) Brown, H. C.; Ravindran, N.; Kulkarni, S. U. *J. Org. Chem.* **1979**, *44*, 2417.

(12) Prepared via the hydroboration of ethylene with $BH_2Br{\cdot}SMe_2$ in CH_2Cl_2 [bp 70–72 °C (75 mm)].

(13) (a) Postdoctoral research associate on Grant GM 10937-19 from the National Institutes of Health. (b) Postdoctoral research associate, Purdue University.

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Stable Peroxides from Chlorine-Photosensitized Oxidation of Perchlorinated Olefins

Summary: Chlorine-photosensitized oxidation of several perchlorinated olefins as neat liquids or adsorbed on silica gel leads to stable perchlorinated peroxides with α-chlorine atoms; these were identified by spectroscopic and X-ray crystallographic methods.

Sir: No perchlorinated peroxides with α-chlorine atoms appear to be described in the literature. Such compounds have been postulated as intermediates in order to explain the "aftereffect" sometimes observed in chlorine-photosensitized oxidations,[1] and indirect chemical[1a] evidence has been adduced for them. Highly-explosive α-chlorinated peroxides have been isolated from the reactions of ozone with 2,3-dichlorobutene[2] and of oxygen with vinylidene chloride,[3] but the product from reaction of oxygen with vinyl chloride is described as rather stable,[4] as are a series of α-chlorinated peroxides resulting from reaction of HCl with the corresponding α-hydroxy compounds.[5]

We have observed the formation of perchlorinated peroxides in the chlorine-sensitized oxidation of hexachlorocyclopentadiene (1), bis(pentachlorocyclopenta-2,4-dien-1-yl) (2), hexachlorobutadiene (3), tetrachloroethylene (4), and hexachloropropylene (5). The peroxide from 5 decomposes within 0.5 h at room temperature; the peroxides from 1–4, however, survive chromatography and are stable for many months at 5 °C.

The peroxides described here are most readily produced when the chlorinated olefins, adsorbed on silica gel under an atmosphere of oxygen and chlorine, are irradiated with visible light. While peroxides were also shown to result from irradiation of 1 and 3 as neat liquids, under these conditions the reaction is slower. Only trace amounts of peroxide resulted from irradiation of 1 in CCl_4 solution. We have not determined whether the higher rate in the adsorbed state is due to greater exposure of the chlorinated olefin to the chlorine and oxygen or to greater susceptibility of the double bonds to attack by chlorine radicals. It was shown for 1 and 3 that chlorine need not be present ini-

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