JOURNAL OF PHYSICAL ORGANIC CHEMISTRY, VOL. 6, 228–232 (1993)

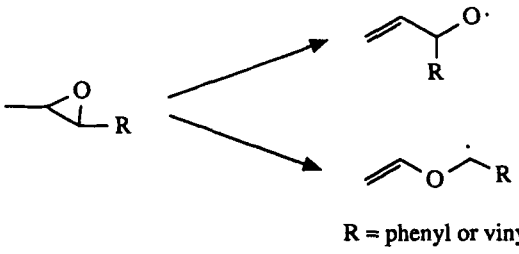
RADICAL REACTIONS OF EPOXIDES. 2.* INTRAMOLECULAR COMPETITION BETWEEN CYCLOPROPYLMETHYL AND OXIRANYLMETHYL RADICAL RING-OPENING REARRANGEMENTS†

KEVIN W. KROSLEY‡ AND GERALD JAY GLEICHER
Department of Chemistry, Oregon State University, Corvallis, Oregon 97331-4003, U.S.A.

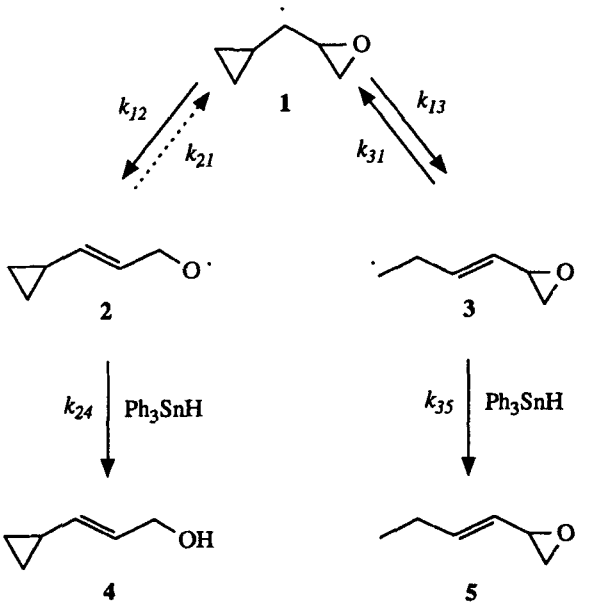
The *erythro*-thioimidazole precursor to the cyclopropyloxiranylmethyl radical has been prepared. Treatment with 7–19 equiv. of triphenyltin hydride at 70 °C gave only 3-cyclopropylprop-2-en-1-ol, the product of epoxide ring opening. No product in which the cyclopropyl ring had opened was observed. Kinetic analysis allowed the assignment of a lower limit for the rate of oxiranylcarbinyl radical rearrangements of 1×10^{10} s^{-1} at this temperature.

INTRODUCTION

Radicals in which the unpaired electron is adjacent to an epoxide ring will undergo ring-opening rearrangements[1,3–20] which are analogous to the well characterized rearrangements of cyclopropylcarbinyl radicals.[21,22] The regiochemical direction of epoxide ring opening has been shown to depend on substitution within the three-membered ring. Generally, ring opening proceeds with carbon–oxygen bond cleavage unless carbon–carbon bond cleavage generates a benzylic or allylic radical (Scheme 1).[17]



Scheme 1. Regiochemical behavior of epoxy radical ring opening rearrangements



Scheme 2. Overall kinetic scheme for formation of **4** and **5** from radical **1**

* For Part 1, see Ref. 1.
† Initial results presented at the 46th Northwest Regional Meeting of the American Chemical Society, LaGrande, OR, 1991. Taken from the Thesis of K. W. Krosley.[2]
‡ Present address: Department of Chemistry and Biochemistry, University of Texas at Austin, Austin, TX 78712, U.S.A.

0894–3230/93/040228–05$07.50

Received 22 July 1992
Revised 9 October 1992

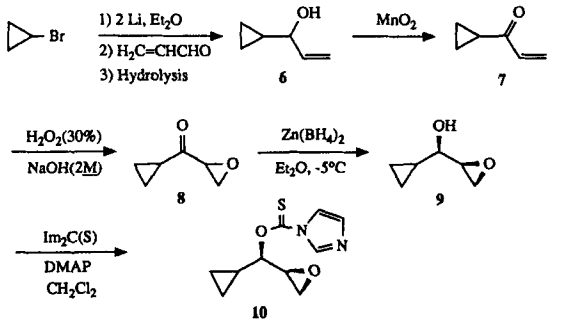
It is apparent from the literature that rearrangement of these epoxy radicals is rapid. In fact, no report of chemical trapping or spectroscopic observation of these species prior to rearrangement has appeared. One study attempted to determine the rate of epoxide radical rearrangement by intramolecular competition with hex-5-enyl radical cyclization.[11] In that case, the ring opening proved to be sufficiently faster than cyclization and no cyclization product was observed. A similar result has been reported for photogenerated biradicals in which a fused epoxide and a fused cyclopropane could compete.[18]

In an attempt to determine the rate of oxiranyl alkyl radical ring opening, we have generated the cyclopropyloxiranylmethyl radical **1**. Scheme 2 shows the possible fate of this radical in the presence of excess of triphenyltin hydride. The rate constants are labeled with respect to the corresponding reaction, e.g. k_{12} is the rate constant for radical **1** going to radical **2**.

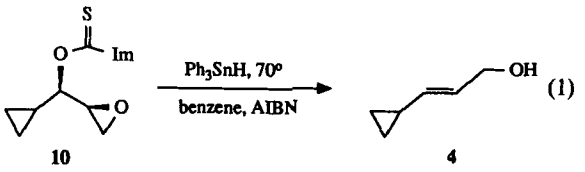
RESULTS

Scheme 3 shows the synthetic route used in preparation of the *erythro*-thioimidazole radical precursor **10**. In addition to the *erythro* isomer, a parallel synthesis of a 1:1 mixture of diastereomers was carried out. Results for the diastereomeric mixture were identical with those obtained with the single isomer. The *erythro* compound was chosen owing to its ease of preparation and in order to investigate one isomer at a time. Based on the results (see below), for both the mixture of diastereomers and for the *erythro* isomer, preparation of the *threo* isomer was not attempted.

Radical **2** was generated by treating **10** with 7–19 equiv. of triphenyltin hydrides in benzene-d_6.[12–14] Azobisisobutyronitrile (AIBN) (0·05 equiv.) was present as an initiator. The reaction mixture was divided into several ampoules and sealed under a reduced pressure of nitrogen after three freeze–thaw cycles. At 70 °C, the radical precursor was completely consumed within 30 min. Analysis of the crude reaction



Scheme 3. Synthesis of the *erythro*-thioimidazole ester precursor to cyclopropyloxiranylmethyl radical



(1)

mixture by proton NMR showed only 3-cyclopropylprop-2-en-1-ol [equation (1)]. Further, no evidence for the presence of any unrearranged epoxide groups or any ring-opened cyclopropyl groups was observed (as would be expected from the presence of compound **5**, Scheme 2). Based on the limitations of NMR integration, we estimate that the ratio of **4** to **5** is greater than 25 : 1.

DISCUSSION

The ratio of products **4** to **5** is represented by the equation

$$\frac{4}{5} = \frac{k_{12}}{k_{13}} \times \frac{k_{24}(k_{31} + k_{35}[\mathrm{Ph_3SnH}])}{k_{35}(k_{21} + k_{24}[\mathrm{Ph_3SnH}])} \qquad (2)$$

This equation is obtained by assuming steady-state concentrations for radicals **2** and **3**. The ratio of products will represent the ratio of rate constants, k_{12}/k_{13}, only under conditions for which the rearrangement reactions are irreversible.

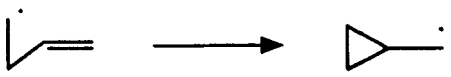
No report of allyloxyl radicals cyclizing to oxiranyl alkyl radicals has appeared. However, its importance can be assessed by considering the effect that reversibility of oxiranyl ring opening would have on the ratio of **4** to **5** and the ratio k_{12}/k_{13}. If the cyclization of **2** to **1** is occurring, it will increase the amount of product **5** which is formed and yield a value of k_{12}/k_{13} that is too low. Since only a lower limit of the ratio of rate constants can be obtained (because no formation of **5** was observed), the reaction of **2** going to **1** can be dismissed. Therefore, for the purpose of determining a lower limit for the ratio k_{12}/k_{13} it can be assumed that $k_{21} \ll k_{24}[\mathrm{Ph_3SnH}]$. This assumption yields a simplified expression:

$$\frac{4}{5} = \frac{k_{12}}{k_{13}}\left(\frac{k_{31}}{k_{35}[\mathrm{Ph_3SnH}]} + 1\right) \qquad (3)$$

From this expression, it can be seen that the relationship between the ratio of the products formed and the ratio of the rate constants is governed by the relative rates of cyclization of **3** to **1** and trapping of **3** by triphenyltin hydride. Three possible situations should be considered. First, if trapping of radical **3** by triphenyltin hydride is much faster than ring closure of **3** to **1**, i.e. $k_{35}[\mathrm{Ph_3SnH}] \gg k_{31}$, then the ratio of products represents the ratio of ring-opening rates. Second, if the rates of cyclization and trapping are similar, then the ratio of products will be larger than the ratio of rate

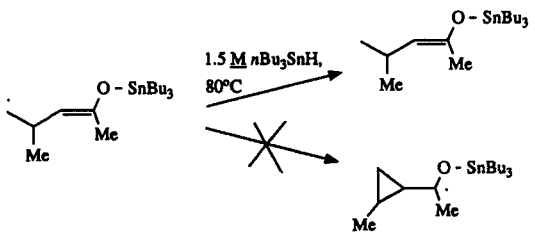
constants. For example, if the rates of cyclization and trapping were equal, then the ratio of products would actually represent twice the ratio of ring-opening rate constants. Third, if cyclization was much faster than trapping, then the ratio $k_{31}/k_{35}[Ph_3SnH]$ would become very large and the product ratio would not represent the ratio of ring-opening rates at all.

The rate of hydrogen atom transfer from triphenyltin hydride to various radicals has been studied. Carlsson and Ingold[23] found that the rate for hydrogen atom transfer from tin hydrides to *tert*-butyl radicals was dependent on the nature of the tin substituents. Similar results have been reported by Chatgilialoglu *et al.*[24] for hydrogen abstraction from tin hydrides by the more reactive *tert*-butoxyl radical. In this case, the rate of hydrogen transfer from triphenyltin hydride is twice as fast as it is for tri-*n*-butyltin hydride. Hydrogen atom transfer from tri-*n*-butyltin hydride to a primary radical has been measured over the temperature range -30 to 80 °C.[25] The rate constant is $3{\cdot}0 \times 10^6$ l mol^{-1} s^{-1} at 80 °C. Based on the relationship between triphenyltin hydride and tri-*n*-butyltin hydride (a factor of at least 2), and the use of a 2·3 M solution of triphenyltin hydrides, a reasonable estimate for $k_{35}[Ph_3SnH]$ is $1{\cdot}4 \times 10^7$ s^{-1}.



(4)

It is more difficult to arrive at estimates for the value of k_{31}. For the cyclization of unsubstituted but-3-enyl radicals [equation (4)], a rate constant of $8{\cdot}0 \times 10^3$ s^{-1} has been reported for reaction at 25 °C.[26,27] This is certainly much smaller than the rate for trapping with triphenyltin hydride; however, the cyclization of **3** to **1** forms a more stable secondary radical which should increase the rate of ring closure. For this reason, empirical evidence must be relied upon. Davies and coworkers[28] found that at 80 °C, a tri-*n*-butyltin hydride concentration of 1.5 M was sufficient to trap their substituted but-3-enyl radical prior to ring closure [equation (5)]. This radical should cyclize faster than radical **3**. Not only is the cyclized radical secondary, but it is also stabilized by the oxygen substituent at the radical center. In addition, it has been shown that methyl substitution in the ring accelerates the rate of



(5)

but-3-enyl radical cyclization.[27] It is reasonable to expect that the use of a larger concentration of a better hydrogen atom donor should be sufficient to trap a slower radical rearrangement (**3** to **1**).

Since the ratio of **4** to **5** is >25, the rate of oxiranylcarbinyl radical ring opening is at least 25 times faster than the rate of ring opening of cyclopropylcarbinyl radical.

Bowry *et al.*[22] have recently reported rate constants and Arrhenius parameters for a large number of cyclopropylcarbinyl rearrangements. Using their data for the rearrangement of 1-cyclopropylethyl radical, the rate constant for cyclopropyl ring opening in **1** at 70 °C can be estimated to be $4{\cdot}7 \times 10^8$ s^{-1}. Therefore, the rate constant for oxiranyl ring opening in **1** is greater than 1×10^{10} s^{-1}.

CONCLUSION

Intramolecular competition between cyclopropylcarbinyl and oxiranylcarbinyl radical rearrangements has allowed a lower limit for the rate of ring opening for β-epoxy radicals to be set at 1×10^{10} s^{-1} at 70 °C.

EXPERIMENTAL

Nuclear magnetic resonance spectra were obtained using a Bruker AM-400 or AC-300 instrument, with chloroform-d_1 or benzene-d_6 as solvent.

The purity of the reagents was determined by gas chromatography and was greater than 98% in all cases. In most cases, the purification methods were taken from *Purification of Laboratory Chemicals.*[29]

Preparation of 1-cyclopropylprop-2-en-1-ol. A solution of 20 g (0·164 mol) of cyclopropyl bromide in 20 ml of diethyl ether was added dropwise to 100 ml of diethyl ether at 0 °C, containing 5·0 g (4 equiv.) of lithium wire.[30] Addition was such that the temperature did not rise above 10 °C. After addition, the reaction mixture was stirred for another 2 h at 0 °C.

The cyclopropyllithium solution was then transferred into an addition funnel and added dropwise to 9·2 g (0·164 mol) of acrolein in 100 ml of diethyl ether at -78 °C (dry ice–acetone bath). The rate of addition was sufficiently slow that the temperature remained below -20 °C. Once addition was complete, the reaction mixture was allowed to warm slowly to room temperature. The reaction mixture was then poured over ice and the ether layer was washed twice with water and dried with magnesium sulfate. Solvent removal under vacuum and reduced pressure distillation gave 8·9 g (56%) of 1-cyclopropylprop-2-en-1-ol. ^{1}H NMR 300 MHz, $CDCl_3$): δ5·98 (1H, ddd, J = 17·3, 10·5 and 5·4 Hz), 5·25 (1H, d, J = 17·2 Hz), 5·11 (1H, d, J = 10·5 Hz), 3·49 (1H, dd, J = 5·4 and 7·4 Hz), 1·98 (1H, broad s, OH), 1·00 (1H, m), 0.55 (2H, m), 0·30

(2H, m). ^{13}C NMR (75·5 MHz, C_6D_6): δ140·6, 113·8, 76·3, 17·6, 2·9, 2·0.

Preparation of 1-cyclopropylprop-2-en-1-one. Oxidation of 1-cyclopropylprop-2-1-ol with 4–6 equiv. of manganese dioxide[31] in chloroform at room temperature gave 1-cyclopropylprop-2-en-1-one. The reaction was run for 4–6 days and followed by ^{1}H NMR. Filtration to remove inorganic material and solvent evaporation gave low isolated yields (typically 15–20%) of analytically pure ketone. ^{1}H NMR (300 MHz, $CDCl_3$): δ6·48 (1H, dd), 6·29 (1H, dd), 5·83 (1H, dd), 2·21 (1H, m), 1·12 (2H, m), 0·96 (2H, m). ^{13}C NMR (75·5 MHz, $CDCl_3$): δ200·5, 136·6, 127·5, 18·2, 11·2.

Preparation of 1-cyclopropyl-2,3-epoxypropan-1-one. A solution of 0·73 g (7·6 mmol) of 1-cyclopropylprop-2-en-1-one in 3·8 ml of methanol containing 2·2 ml of 30% hydrogen peroxide was prepared and cooled to 0 °C in an ice-bath.[32] To this was added dropwise 1·9 ml of aqueous 2·0 M sodium hydroxide over a 30 min period. Following this addition, the reaction was stirred for 1 h. Extraction of the reaction mixture with diethyl ether and solvent removal gave 0·69 g (80%) of 1-cyclopropyl-2,3-epoxypropan-1-one. ^{1}H NMR (300 MHz, $CDCl_3$): δ3·48 (1H, m), 3·03 (1H, m), 2·97 (1H, m), 2·02 (1H, m), 1·10 (2H, m), 0·093 (2H, m). ^{13}C NMR (75·5 MHz, $CDCl_3$): δ207·4, 53·6, 45·8, 14·6, 12·0, 11·4.

Preparation of erythro-*1-cyclopropyl-2,3-epoxypropan-1-ol.* A solution of 90 mg (0·80 mmol) of 1-cyclopropyl-2,3-epoxypropan-1-one in 5·0 ml of diethyl ether was treated with 3·0 ml of zinc borohydride (prepared by a standard procedure)[33] in diethyl ether at −5 °C (ice–acetone bath) for 1 h. The reaction was then quenched with 2 ml of water and stirred for an additional 30 min at room temperature. Extraction with diethyl ether and solvent removal gave 54 mg (60%) of 1-cyclopropyl-2,3-epoxypropan-1-ol with an *erythro* : *threo* ratio of 97 : 3 by ^{13}C NMR line heights. The assignment of the *erythro* stereochemistry is based on analogy with the literature.[34] ^{1}H NMR (300 MHz, $CDCl_3$): δ3·09 (2H, m), 2·81 (1H, dd), 2·71 (1H, dd), 0·85 (1H, m), 0·51 (2H, m), 0·30 (2H, m7. ^{13}C NMR (75·5 MHz, $CDCl_3$): δ73·2, 54·0, 43·4, 13·2, 2·2, 1·6.

Preparation of thioimidazolide from erythro-*1-cyclopropyl-2,3-epoxypropan-1-ol.* A mixture of 54 mg (0·47 mmol) of *erythro*-1-cyclopropyl-2,3-epoxypropan-1-ol, 90 mg (0·50 mmol) of thiocarbonyldiimidazole and 6 mg (0·05 mmol) of 4-dimethylaminopyridine (DMAP) in 3·0 ml of chloroform was stirred for 12 h at room temperature.[14] The reaction mixture was washed twice with sodium hydrogencarbonate solution and twice with water. The organic layer was dried with magnesium sulfate and the solvent was removed under vacuum, leaving 73 mg (70%) of >98% pure thioimidazolide. ^{H} NMR (300 MHz, C_6D_6): δ8·30 (1H, s), 7·36 (1H, s), 6·88 (1H, s), 4·97 (1H, dd, J = 9.4 and 3·6 Hz), 2·79 (1H, m), 2·32 (1H, m), 2·18 (1H, m), 0·83 (1H, m), 0·23 (2H, m), 0·16 (2H, m). ^{13}C NMR (75·5 MHz, C_6D_6): δ184·5, 136·9, 131·5, 118·3, 87·0, 51·1, 44·2, 10·4, 3·3, 2·6.

Preparation of a diastereomeric mixture of 1-cyclopropyl-2,3-expoxypropan-1-ol and a diastereomeric mixture of thiomidazolids. A solution of 1-cyclopropyprop-2-en-1-ol in refluxing dichloromethane was treated with 1·2 equiv. of *m*-chloroperbenzoic acid (*m*-CPBA) for 2 h. This reaction yielded a 1 : 1 mixture of diastereomeric alcohols which were converted into a 1 : 1 mixture of thioimidazolides as above.

Reactions of thioimidazolide with triphenyltin hydride. Reaction mixtures contained the thioimidazolide, triphenyltin hydride, AIBN and benzene-d_6 in an approximate molar ratio of 1 : 7–19 : 0·05 : 10. The reaction mixture was divided among several ampoules which were sealed under a reduced pressure of nitrogen after three freeze–thaw cycles. In each case, one of the ampoules was withheld for analysis of starting material concentrations. The remaining ampoules were wrapped in foil and placed in a 70 ± 0·5 °C oil-bath. In each run, the reaction was found to be complete within 30 min. The only observed product was determined to be 3-cyclopropylprop-2-1-ol by ^{1}H NMR (300 MHz, C_6D_6): δ5·62 (1H, dt, J = 15·2 and 7·4 Hz), 5·05 (1H, dd, J = 15·2 and 5·9 Hz), 3·95 (2H, d, J = 7·4 Hz), 1·22 (1H, m), 0·53 (2H, m), 0·26 (2H, m). Decoupling experiments demonstrated connectivity between the signal at δ1·22 and those at δ5·05, 0·53, and 0·26.

ACKNOWLEDGMENT

We thank J. Eric Carlson for his extensive aid in the preparation of the manuscript.

REFERENCES

1. K. W. Krosley, G. J. Gleicher and G. E. Clapp, *J. Org. Chem.* **57**, 840 (1992).
2. K. W. Krosley, PhD Thesis, Oregon, State University (1992).
3. A. G. Davies and B. J. Muggleton, *J. Chem. Soc., Perkin Trans. 2* 502 (1976).
4. A. G. Davies and M. W. Tse, *J. Orgaomet. Chem.* **155**, 25, (1978).
5. A. G. Davies, J. A. A. Hawari, B. Muggleton and M. W. Tse, *J. Chem. Soc., Perkin Trans. 2* 1132 (1981).
6. E. S. Huyser and L. R. Munson, *J. Org. Chem.* **30**, 1436 (1965).
7. E. L. Stogryn and M. H. Gianni, *Tetrahedron Lett.* **34**, 3025 (1970).

8. K. S. Feldman and T. E. Fisher, *Tetrahedron* **45**, 2969 (1989).
9. R. C. Gash, F. MacCorquodale and J. C. Walton, *Tetrahedron* **45**, 5531 (1989).
10. J. A. Murphy, C. W. Patterson and N. F. Wooster, *J. Chem. Soc., Chem. Commun.* 294 (1988).
11. A. Johns, J. A. Murphy, C. W. Patterson and N. F. Wooster, *J. Chem. Soc., Chem. Commun.* 1238 (1987).
12. D. H. R. Barton, R. S. H. Motherwell and W. B. Motherwell, *J. Chem. Soc., Perkin Trans. 1* 2363 (1981).
13. A. Johns and J. A. Murphy, *Tetrahedron Lett.* **29**, 837 (1988).
14. V. H. Rawal, R. C. Newton and V. Krishnamurthy, *J. Org. Chem.* **55**, 5181 (1990).
15. R. G. Carlson, J. H.-A. Huber and D. E. Henton, *J. Chem. Soc., Chem. Commun.* 223 (1973).
16. S. Ayral-Kaloustian, S. Wolff and W. C. Agosta, *J. Org. Chem.* **43**, 3314 (1978).
17. S. Ayral-Kaloustian and W. C. Agosta, *J. Am. Chem. Soc.* **102**, 314 (1980).
18. S. Ayral-Kaloustian and W. C. Agosta, *J. Org. Chem.* **48**, 1718 (1983).
19. E. Hasegawa, K. Ishiyama, T. Horaguchi and T. Shimizu, *J. Chem. Soc., Chem. Commun.* 550 (1990).
20. H. G. Kuivila, *Acc. Chem. Res.* **1**, 299 (1968).
21. D. Griller and K. U. Ingold *Acc. Chem. Res.* **13**, 317 (1980).
22. V. W. Bowry, J. Lusztyk and K. U. Ingold, *J. Am. Chem. Soc.* **113**, 5687 (1991).
23. D. J. Carlsson and K. U. Ingold, *J. Am. Chem. Soc.* **90**, 7047 (1968).
24. C. Chatgilialoglu, K. U. Ingold, J. Lusztyk, A. S. Nazran and J. C. Scaiano, *Organometalics* **2**, 1332 (1983).
25. L. J. Johnston, J. Lusztyk, D. M. Wagner, A. M. Abewickreyma, A. L. J. Beckwith, J. C. Scaiano and K. U. Ingold, *J. Am. Chem. Soc.* **107**, 4594 (1985).
26. A. Effio, D. Griller, K. U. Ingold, A. L. J. Beckwith and A. K. Serelis, *J. Am. Chem. Soc.* **102**, 1734 (1980).
27. M. Newcomb, A. G. Glenn and W. G. Williams, *J. Org. Chem.* **54**, 2675 (1989).
28. (a) A. G. Davies, J.-Y. Godet, B. Muddleton and M. Peryre, *J. Chem. Soc., Chem. Commun.* 813 (1976); (b) P. Blum, A. G. Davies, M. Pereyre and M. Ratier, *J. Chem. Soc., Chem. Commun.* 814 (1976).
29. D. D. Perrin, W. L. F. Armarego and D. R. Perrin, *Purification of Laboratory Chemicals.* Pergamon Press, New York (1984).
30. D. Seyferth and H. M. Cohen, *J. Organomet. Chem.* **1**, 15 (1963).
31. J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen and T. Walker, *J. Chem. Soc.* 1094 (1952).
32. K. Antczak, J. F. Kingston and A. G. Fallis, *Can. J. Chem.* **62**, 2451 (1984).
33. W. J. Gensler, F. A. Johnson and A. D. B. Sloan, *J. Am. Chem. Soc.* **82**, 6074 (1960).
34. T. Nakata, T. Tanaka and T. Oishi, *Tetrahedron Lett.* **22**, 4723 (1981).