Face Selectivity in the Reduction with Dideuteriodi-imide of Endoperoxides derived from the Singlet Oxygenation of Cycloalka-1,3-dienes

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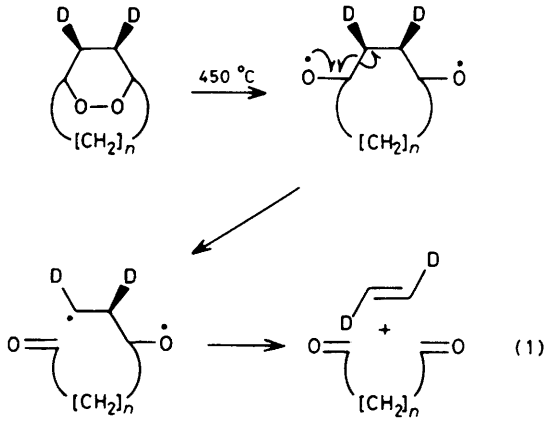
Four dioxabicyclo[*n*.2.2]alkenes (*n* = 1—4) have been reduced with dideuteriodi-imide. For each reduction, the ratio of the amount of product arising from *cis*-addition of two deuterium atoms to the face of the double bond *syn* to the dioxygen bridge to that arising from addition to the *anti* face has been determined by ^{1}H-decoupled ^{2}H n.m.r. spectroscopy, and the structures of the individual isomers have been determined by ^{1}H n.m.r. spectroscopy. The cyclopentadiene endoperoxide (*n* = 1) yields exclusively the *anti*-isomer, whereas the cyclohexadiene endoperoxide (*n* = 2) affords a mixture containing 66% of *syn* isomer, and the cycloheptadiene and cyclo-octadiene endoperoxides (*n* = 3 and 4) give only the *syn*-isomer. The results are consistent with the expected variation across the series in both electronic and steric effects.

The products obtained in the thermolysis [1] and photolysis [2] of a variety of saturated bicyclic peroxides can be accounted for in terms of preferred modes of β-scission in the cycloalkanedioxyl intermediates resulting from O–O homolysis. Further insight into the mechanistic details of these β-scissions could be gained by studying the decomposition of peroxides labelled with deuterium at specific sites. For example, one mode of decomposition of dioxabicyclo[*n*.2.2]alkanes (*n* = 2—4) involves fragmentation into ethene and α,ω-dialdehyde.[1] Thus, an investigation of this reaction using peroxides vicinally *cis*-dideuteriated in the two-carbon bridge should indicate whether the two β-scissions occur stepwise or in a concerted fashion, since the latter will afford only *cis*-1,2-dideuterioethene whereas the former [equation (1)] could lead to the *trans*-isomer.

Since unlabelled dioxabicyclo[*n*.2.2]alkanes are prepared by reducing the singlet-oxygen adducts of cycloalka-1,3-dienes with di-imide,[3] and since di-imide reduction of alkenes is generally accepted to involve *cis*-addition,[4] it was expected that reduction of the singlet oxygenates with dideuteriodi-imide would afford peroxides of the desired type. In carrying out these reactions we have confirmed that *cis*-addition takes place, but we have also found that the face of the double bond to which the deuterium atoms add is dependent upon the ring size of the starting cycloalkadiene. These results are of interest because they provide new information about a reaction, namely the di-imide reduction of endoperoxides, which has been much used in recent years,[5] and because they extend the range of bicyclic alkenes for which dideuteriodi-imide reduction has been studied since only bicyclo[2.2.1]heptene derivatives have previously been investigated.[6,7]



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Results and Discussion

Dioxabicyclo[*n*.2.2]alkenes (**1**), obtained by photo-oxygenation of the corresponding cycloalka-1,3-dienes,[5] were reduced with dideuteriodi-imide generated *in situ* from potassium azodicarboxylate and acetic [$^2H_1$]acid [equation (2)]. The reactions were carried out in methan[$^2H_1$]ol (CH_3OD) at room temperature for the endoperoxides (**1b—d**), and in dichloromethane at *ca.* −30 °C for the [2.2.1] endoperoxide (**1a**).

Extent of Deuteriation.—The extent of deuterium incorporation was determined by mass spectrometry. Table 1 shows the relative peak intensitives in the molecular ion region for each of the four products, together with the corresponding data for the fully protio compounds.

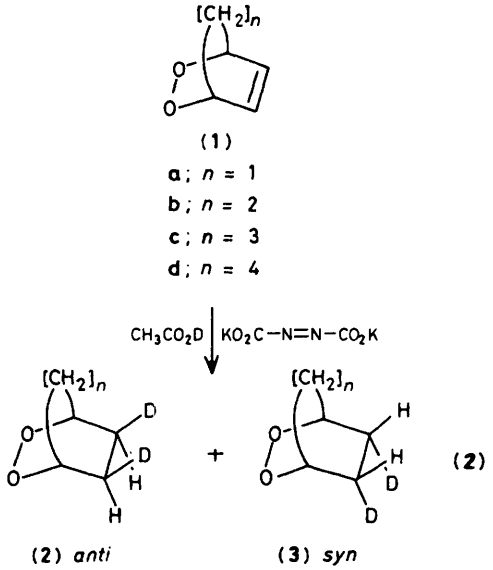
The results indicate that the major product is the desired dideuterio peroxide. Only 0.7—1.3% of the fully protio peroxide and 9—18% of the monodeuterio peroxide are formed in the reductions of the endoperoxides (**1b—d**), but rather more of these species (2.5 and 29% respectively) is obtained in the reduction of the [2.2.1] endoperoxide (**1a**). The most likely source of exchangeable protium is a contaminant of the potassium azodicarboxylate, which is prepared from azodicarbonamide and concentrated aqueous potassium hydroxide and is washed with methanol. That slightly larger amounts of monodeuterio peroxide were obtained from the endoperoxides (**1c**) and (**1d**) than from compound (**1b**) is consistent with this view, since the endoperoxides (**1c**) and (**1d**) are rather sluggish in reduction and larger quantities of potassium azodicarboxylate have to be used. The markedly lower uptake of deuterium in the reduction of the [2.2.1] endoperoxide (**1a**) is presumably due mainly to the fact that it is necessary to use a solvent that does not possess exchangeable deuterium and so the relative concentration of exchangeable protium in the system is much higher. The incomplete incorporation of deuterium does not affect the arguments that follow concerning stereoselectivity.

Stereoselectivity.—For each reduction, the isomer distribution in the product was determined from its proton-decoupled ^{2}H n.m.r. spectrum (Table 2). Endoperoxides (**1a**), (**1c**), and (**1d**)

Table 1. Molecular ion region of the mass spectra of products from reduction with di-imide and dideuteriodi-imide of dioxabicyclo[*n*.2.2]alkenes

Starting material	Reducing agent	Molecular formula of expected product	M_r of expected product[a]	Found *m/z* (Relative intensity)
(**1a**)	HNNH	$C_5H_8O_2$	100	101 (4.7), 100 (100), 99 (0.19)
(**1a**)	DNND	$C_5H_6D_2O_2$	102	103 (7.4), 102 (100), 101 (43.3),[b] 100 (3.7)
(**1b**)	HNNH	$C_6H_{10}O_2$	114	115 (3.2), 114 (100), *c*
(**1b**)	DNND	$C_6H_8D_2O_2$	116	117 (3.0), 116 (100), 115 (10.2),[b] 114 (0.95)
(**1c**)	HNNH	$C_7H_{12}O_2$	128	129 (4.1), 128 (100), *c*
(**1c**)	DNND	$C_7H_{10}D_2O_2$	130	131 (3.5), 130 (100), 129 (22.1),[b] 128 (0.85)
(**1d**)	HNNH	$C_8H_{14}O_2$	142	143 (3.7), 142 (100), 141 (0.20)
(**1d**)	DNND	$C_8H_{12}D_2O_2$	144	145 (4.7), 144 (100), 143 (16.5),[b] 142 (1.5)

[a] To the nearest whole number for the most abundant species. [b] Arising mainly from the product of reduction with HNND. [c] $(M - 1)^+$ peak had zero intensity.



each afforded a product for which only one signal could be detected.* This is consistent with the expected stereospecific *cis*-mode of addition, and renders highly unlikely the possible interpretation that the two signals observed for the product from endoperoxide (**1b**) arise through partial *trans*-addition. It is therefore concluded that only one of the two possible products of *cis*-addition [equation (2)] is obtained for the [2.2.1], [3.2.2], and [4.2.2] peroxides, whereas both are obtained for the [2.2.2] peroxide. This confirms the conclusion reached in an earlier study of the dideuteriodi-imide reduction of the [2.2.1] endoperoxide (**1a**),[7] but that was based on ^{1}H n.m.r. spectroscopy which is less sensitive than our technique for the detection of the second isomer.

Configurational Assignments.—The configurational assignments given in Table 2 are based mainly on a comparison of the 200 MHz ^{1}H n.m.r. spectra of the products with those of the fully protio compounds (**4**).

The assignment of the configuration for the [2.2.1] peroxide is made easy by the fact that in the fully protio compound (**4a**) there is **W**-plan coupling between the three protons *syn* to the dioxygen bridge (2 H_s and $H_{s'}$). Since this coupling is still observed in the dideuterio peroxide, the deuterium atoms must occupy the *anti*-positions on the two-carbon bridge, *i.e.* the compound has structure (**2**). The same conclusion was reached previously from a consideration of 100 MHz ^{1}H n.m.r. spectra of the peroxides in C_6D_6.[7] We used $CDCl_3$ as solvent, but our spectra are similar to the published ones[7] except that the chemical shifts and the sequence of signals are different. We observed multiplets at δ 1.6, 1.8, 2.1, and 2.2 corresponding to H_a, H_s, $H_{a'}$, and $H_{s'}$ respectively, whereas in C_6D_6 the data were δ 1.1 (H_a), 1.35 ($H_{a'}$), 1.6 (H_s), and 1.85 ($H_{s'}$).[7]

For the other [*n*.2.2]peroxides, the configurations were determined by first assigning signals in the spectrum of each fully protio compound (**4**) to the *syn*- and *anti*-protons on the two-carbon bridge (H_s and H_a respectively), and then observing which of these signals was absent from the spectrum of the corresponding dideuterio peroxide. An examination of Dreiding models of the peroxides suggests that in all three compounds the dihedral angle between the bridgehead protons (H_b) and H_a is in the range 80—100°, whereas that between H_b and H_s is in the range 20—40°. From the Karplus relationship it is therefore expected that there will be little or no coupling between H_b and H_a, but significant coupling between H_b and H_s. Thus the signal for H_a is expected to appear less complex than that for H_s, and decoupling of the bridgehead protons by double irradiation is expected to simplify the signal for H_s but to have little effect on that for H_a.

On this basis we assigned a multiplet at δ *ca.* 1.7 to H_a and a multiplet at δ *ca.* 2.2 to H_s for all three peroxides.† For the [3.2.2] and [4.2.2] compounds, the low-field multiplet was missing from the spectra of the dideuterio peroxides while the high-field

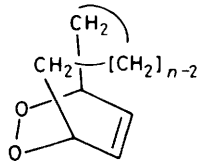
* It is reasonable to expect that signals for the monodeuterio peroxides (*vide supra*) will overlap with those of their dideuterio counterparts.

† The slight differences between these chemical shifts and those of the ^{2}H resonances in the dideuterio peroxides (Table 2) probably arise mainly from solvent effects, since the peroxides were dissolved in $CDCl_3$ for the ^{1}H n.m.r. spectra but in CCl_4 for the ^{2}H n.m.r. spectra. A comparison of the ^{1}H n.m.r. spectra of the fully protio and the corresponding dideuterio peroxides in $CDCl_3$ revealed a small isotope effect upon chemical shifts, a *gem*-deuterium causing an upfield shift of *ca.* 0.02 p.p.m.

Table 2. Isomer distribution and chemical shift data from proton-decoupled ^2H n.m.r. spectra of products from reduction of dioxabicyclo[*n*.2.2]alkenes with dideuteriodi-imide.

Starting material	Fraction of (2) (%)	Chem. shift of (2)[a]	Fraction of (3) (%)	Chem. shift of (3)[a]
(**1a**)	100	1.43	0	*b*
(**1b**)	34[c]	1.53	66[c]	2.02
(**1c**)	0	*b*	100	2.05
(**1d**)	0	*b*	100	2.10

[a] Solvent was CCl_4 with a few drops of $CDCl_3$ added to provide an internal reference; shifts are in p.p.m. from $(CD_3)_4Si$, assuming δ 7.27 for $CDCl_3$. The line width at half height was 0.96 ± 0.12 Hz. [b] No signal attributable to this product was detected. [c] Calculated from peak integrals.



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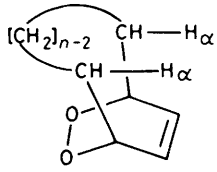

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signal now appeared as a broad singlet. It was therefore concluded that these compounds have structure (**3**), with the deuterium atoms *syn* to the dioxygen bridge. The relevant spectra for the [3.2.2] peroxides are reproduced in the Figure.

The conclusion from coupling data that the *syn*-protons on the two-carbon bridge resonate at lower field than their *anti*-counterparts for all four dioxabicyclo[*n*.2.2]alkanes (*n* = 1—4) is consistent with the known effect that protons are deshielded by oxygen atoms in close proximity.[8] Furthermore, it has been observed that the *syn*-protons on the one-carbon bridge of 2,3-dioxabicyclo[2.2.1]heptane (*vide supra*) and of 8,9-dioxabicyclo[5.2.1]decane[9] also resonate downfield of their *anti*-counterparts. Thus, the chemical shift data support the configurational assignments given in Table 2.

Steric and Electronic Effects on Face Selectivity.—Addition of hydrogen from di-imide usually occurs on the less hindered face of an unsymmetrical alkene,[10] but it has been shown that 7-oxy substituents in norbornadienes favour addition *syn* to themselves, presumably as a result of electrostatic stabilisation of the transition state.[6a] It is therefore conceivable that the dioxygen bridge in the endoperoxides (**1**) could exert a similar electronic effect and direct attack of di-imide to the *syn*-face.

Whereas *syn*-addition was observed exclusively for the [4.2.2] and [3.2.2] endoperoxides [(**1d**) and (**1c**)] and was favoured by a factor of 2:1 for the [2.2.2] endoperoxide (**1b**), exclusive *anti*-addition occurred in the dideuteriodi-imide reduction of the [2.2.1] endoperoxide (**1a**) (see Table 2). It has been proposed that the π-bond of bicyclo[2.2.1]heptene is unsymmetrical with greater electron density on the face *syn* to the one-carbon bridge.[11] A similar effect in the [2.2.1] endoperoxide could outweigh any electronic influence of the dioxygen bridge.

Thus, the results are consistent with possible electronic effects, but they can also be accounted for by steric factors. Steric hindrance to attack on the *syn*-face is provided by two of the lone pairs of electrons on the oxygen atoms. This is expected to remain fairly constant across the series of endoperoxides, since as one lone pair is tipped away from the double bond by the increase in the C–O–O–C dihedral angle which occurs as the

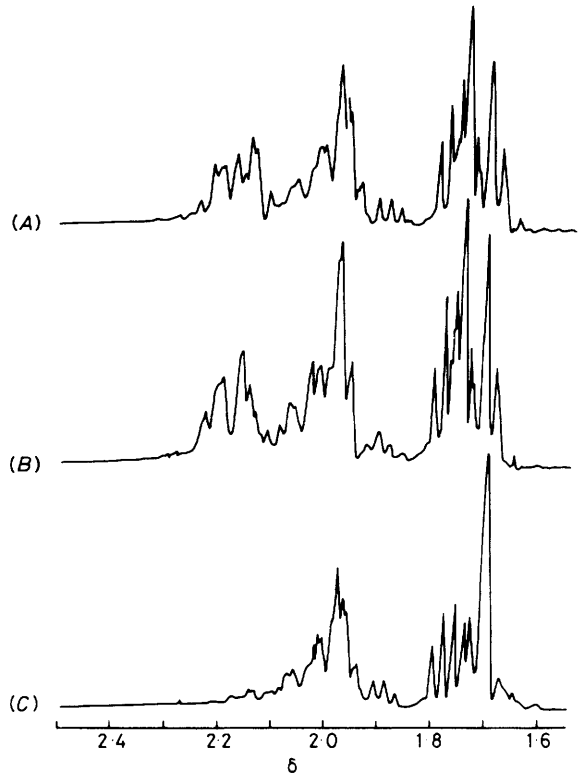

Figure. 200 MHz ^1H n.m.r. spectra of [3.2.2] peroxides in $CDCl_3$: (*A*) 6,7-Dioxabicyclo[3.2.2]nonane (**4c**); (*B*) (**4c**) with decoupling of H_b; (*C*) 8,9-dideuterio-6,7-dioxabicyclo[3.2.2]nonane (**3c**). The bridgehead protons (H_b) appear as a broad singlet at δ 4.4—4.5

n-carbon bridge gets bigger, the other approaches more closely. Steric hindrance to attack on the *anti*-face is provided by one C-7 hydrogen in the [2.2.1] endoperoxide but by C-7 and C-8 hydrogens in the [2.2.2] endoperoxide. The amount of steric hindrance in the [3.2.2] and [4.2.2] endoperoxides depends upon which of the two possible conformations is favoured, that with the central methylene groups of the *n*-carbon bridge lying over the C=C bond (**5**) or that with them over the O–O bond (**6**). As far as we are aware, there is no evidence concerning this question, but even in conformation (**6**), hydrogen atoms (H_α) on the carbon atoms α to the bridgehead atoms will provide steric hindrance which is probably greater than that in the [2.2.2] compound.

Thus, it is reasonable to conclude that steric hindrance to attack on the *anti*-face increases as the size of the *n*-carbon bridge increases and hence that *anti*-addition becomes increasingly disfavoured across the series.

Since the steric and electronic effects operate in parallel, it is not possible to assess the individual contribution that each makes to the observed results.

Experimental

Materials.—The fully protio dioxabicyclo[*n*.2.2]alkanes (**4b—d**) were prepared on a 20—40 mmol scale by a modified version of the procedure previously reported[7] for the [3.2.2] compound (**4c**). More methanol (100—200 cm^3 in total) and less potassium azodicarboxylate [5, 7.5, and 10 mmol for each mmol of (**4b**), (**4c**), and (**4d**) respectively] were used, and the acetic acid was added over a longer period (1.5—2 h). The methanol was removed from the reaction mixture using a rotary

evaporator and the residue was partitioned between water and dichloromethane. The dichloromethane layer was dried ($MgSO_4$) and the solvent evaporated off under reduced pressure to leave the crude peroxide (**4**) which was purified by column chromatography (SiO_2, CH_2Cl_2) or vacuum sublimation. The corresponding dideuteriodi-imide reductions of compounds (**1b**—**d**) were similarly carried out on a 4—5 mmol scale in CH_3OD (30—40 cm^3).

The published methods for preparing the fully protio[12] and dideuterio[7] [2.2.1] peroxides were also modified. Cyclopentadiene in dichloromethane was photo-oxygenated at −78 °C for 5 h[12] and then potassium azodicarboxylate (5 mmol per mmol of cyclopentadiene) was added, followed by CH_3CO_2H or CH_3CO_2D (1.9 mmol per mmol of azodicarboxylate) which was added dropwise over 5 min. The vigorously stirred mixture was allowed to warm up slowly and the reaction began to take place at *ca.* −30 °C. The mixture was kept at −30 to 0 °C for 1.5 h and was then filtered. The filtrate was concentrated under reduced pressure and the peroxide was isolated by low-temperature column chromatography.

Spectra.—Mass spectra were obtained using a VG 7070 F/H mass spectrometer plus Finnigan INCOS data system. A Varian XL200 spectrometer was used to record the ^1H and ^1H-decoupled ^2H n.m.r. spectra, and a Varian CFT20 instrument was used to record the ^1H-decoupled ^{13}C n.m.r. spectra.

The mass spectral data for the molecular ion region of each of the eight peroxides are given in Table 1. Details of the ^1H-decoupled ^2H n.m.r. spectra are presented in Table 2. The ^1H n.m.r. spectra of 6,7-dioxabicyclo[3.2.2]nonane (**4c**) and of the 8,9-dideuterio derivative (**3c**) are shown in the Figure, and the spectra of the [2.2.1] peroxides (**4a**) and (**2a**) have been discussed in the text above; the data for the [2.2.2] and [4.2.2] peroxides are given below.

Compound (**4b**): δ 1.74 (m resembling AB quartet) (H_a), 2.26 (dm) (H_s), and 4.11br (s) (H_b); irradiation at δ 4.11 caused the signal at δ 2.26 to assume an appearance similar to that at δ 1.74. Mixture of (**2b**) and (**3b**): δ 1.71br (s) [H_a *gem* to D in (**3b**)], and 2.24br (s) [H_s *gem* to D in (**2b**)] superimposed on spectrum of (**4b**). (**4d**): δ 1.64 (m) (includes H_a), 1.85 (m), 2.03 (m), 2.22 (m) (H_s), and 4.51br (s) (H_b). (**3d**): δ 1.6 (m), 1.66br (s) (H_a), 1.85 (m), 2.03 (m), and 4.51br (s) (H_b).

The ^1H-decoupled ^{13}C n.m.r. spectra of the fully protio peroxides (**4**) have been reported previously,[3,7] and the data for the dideuterio compounds in $CDCl_3$ are given below.

Compound (**2a**): δ 78.53 (C-1 and C-4), 43.78 (C-7), and 28.71 p.p.m. [t, $J(^{13}C-^2H)$ 19.9 Hz, C-5 and C-6]. An additional line at δ 29.03 p.p.m. was assigned to C-6 of the 5-monodeuterio peroxide [δ 29.15 p.p.m. in (**4a**)[3]]. Mixture of (**2b**) and (**3b**): δ 71.61 (C-1 and C-4), 24.26 (C-7 and C-8), and 23.83 p.p.m. [t, $J(^{13}C-^2H)$ 20.1 Hz, C-5 and C-6]. (**3c**): δ 76.76 (C-1 and C-5), 34.94 (C-2 and C-4), 19.95 [t, $J(^{13}C-^2H)$ 20.1 Hz, C-8 and C-9], and 19.91 p.p.m. (C-3). An additional weak line at δ 20.29 p.p.m. was assigned to C-9 of the 8-monodeuterio peroxide [δ 20.43 p.p.m. in (**4c**)[7]]. (**3d**): δ 76.12 (C-1 and C-6), 34.69 (C-2 and C-5), 24.55 (C-3 and C-4), and 20.33 p.p.m. [t, $J(^{13}C-^2H)$ 20.0 Hz, C-9 and C-10]. An additional weak line at δ 20.66 p.p.m. was assigned to C-10 of the 9-monodeuterio peroxide [δ 20.68 p.p.m. in (**4d**);[3] *n.b.* the assignments for C-9/C-10 and C-3/C-4 in (**4d**) are incorrect in ref. 3].

The results revealed a small and consistent isotope effect on the ^{13}C n.m.r. chemical shifts. Replacement of one H by D in a CH_2 group led to an upfield shift of 0.33 ± 0.01 p.p.m. The isotopic substitution also led to shielding of the β-carbon by about 0.12 ± 0.04 p.p.m.

Acknowledgements

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References

1 A. J. Bloodworth, D. S. Baker, and H. J. Eggelte, *J. Chem. Soc., Chem. Commun.*, 1982, 1034.
2 A. J. Bloodworth and H. J. Eggelte, *Tetrahedron Lett.*, 1984, **25**, 1525.
3 W. Adam and A. J. Bloodworth, *Top. Curr. Chem.*, 1981, **97**, 121.
4 H. O. House, 'Modern Synthetic Reactions,' 2nd edn., Benjamin, New York, 1972, p. 248.
5 A. J. Bloodworth and H. J. Eggelte in 'Singlet Oxygen,' ed. A. A. Frimer, C.R.C. Press Inc., Boca Raton, 1984, in the press.
6 (*a*) W. C. Baird, B. Franzus, and J. H. Surridge, *J. Am. Chem. Soc.*, 1967, **89**, 410; (*b*) N. H. Werstiuk, *Can. J. Chem.*, 1975, **53**, 26; (*c*) J. W. Wilt and V. P. Narutis, *J. Org. Chem.*, 1979, **44**, 4899; (*d*) J.-P. Hagenbuch, B. Stampfli, and P. Vogel, *J. Am. Chem. Soc.*, 1981, **103**, 3934.
7 D. J. Coughlin, R. S. Brown, and R. G. Salomon, *J. Am. Chem. Soc.*, 1979, **101**, 1533.
8 L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd edn., Pergamon, Oxford, 1969, p. 81.
9 A. J. Bloodworth and J. A. Khan, *Tetrahedron Lett.*, 1978, 3075.
10 E. E. van Tamelen and R. J. Timmons, *J. Am. Chem. Soc.*, 1962, **84**, 1067.
11 S. Inagaki, H. Fujimoto, and K. Fukui, *J. Am. Chem. Soc.*, 1976, **98**, 4054; W. K. Chwang, V. J. Nowlan, and T. T. Tidwell, *ibid.*, 1977, **99**, 7233.
12 W. Adam and H. J. Eggelte, *J. Org. Chem.*, 1977, **42**, 3987.

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