Stereochemistry of Mercuric Azide Addition to Cyclopropenes. A Synthesis of Cyclopropyl Azides[1]

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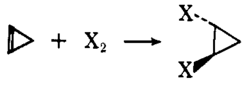
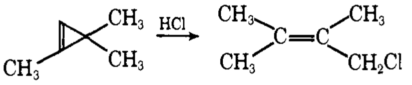
Abstract: Mercuric azide has been shown to add syn to cyclopropenes **3a–d** giving the *cis*-2-azidocyclopropylmercuric azide salts **4a–d**. Treatment of **4a–d** with HBr and NaBr produced the *cis*-2-azidocyclopropylmercuric bromide salts **5a–d** which were characterized. Reduction of **4a** and **4b** with $NaBH_4$ and of **5c** with sodium amalgam in H_2O gave the azidocyclopropanes **6a–d**. The use of sodium amalgam in D_2O in the reduction of **5a–c** led to stereospecific replacement of mercury and formation of *cis*-1-azido-2-deuteriocyclopropyl azides **7a–c**. Addition of hydrazoic acid to 3,3-dimethyl-1-phenylcyclopropene, **3b**, also proceeds in a syn manner leading to cyclopropyl azide **7b**. Nmr correlations as well as Hg-H coupling in these systems are discussed.

Despite numerous examples of syn stereoselectivity in electrophilic additions to strained olefins such as norbornene,[2] there have been few reported examples of syn additions to cyclopropenes. Cyclopropene itself adds bromine and iodine forming mostly the *trans*-dihalocyclopropanes (**1**) as indicated by their nmr spectra.[3] Diborane adds to methylcyclopropene in a syn manner; this is expected, however, since the normal mode of diborane additions is syn.[4a] Trimethylcyclopropene adds HCl with formation of the ring-opened product **2**.[4b]



1

X = Br, I



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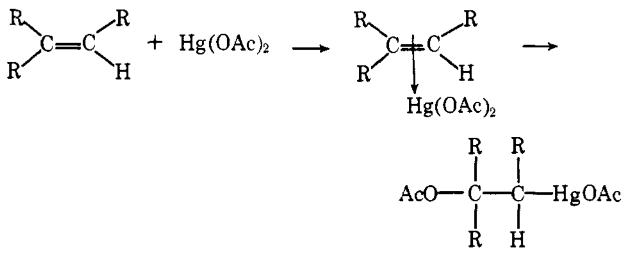
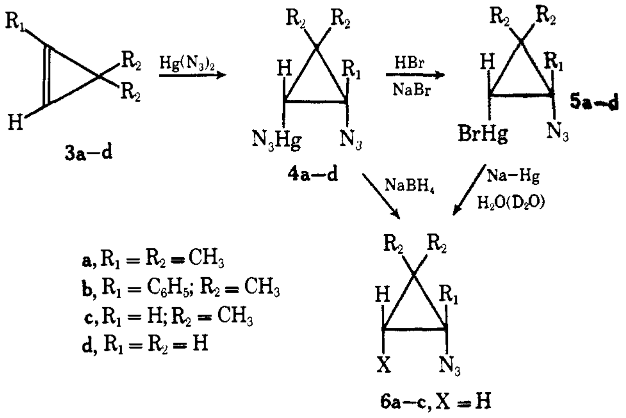
Generally mercuric acetate additions are believed to occur through initial complexation of the mercury, followed by collapse giving the β-acetoxyalkylmercuric acetates in a regioselective manner, with the acetate occupying the most substituted position as shown below. Traylor predicted that mercuric salts should add syn to cyclopropenes,[2] but so far such attempts with $Hg(OAc)_2$ have led only to ring-opened products.[2b] Recently mercuric azide has been added successfully to norbornene.[5] Since the reaction mechanism of this addition is expected to be similar to that of mercuric acetate, the reaction of $Hg(N_3)_2$ with cyclopropenes would be of great stereochemical as well as synthetic interest.



Results

We have found that mercuric azide generated *in situ* from mercuric acetate in tetrahydrofuran–water adds to cyclopropenes **3a–d** forming the syn addition products **4a–d** in fair yield. Reductive demercuration with $NaBH_4$ gave rise to cyclopropyl azides **6a–b** in moderate yield (see Table I). Alternately, treatment of **4a–d** with HBr and NaBr gave the mercuric bromide salts **5a–d** which were characterized. Reduction of **5a–c** with sodium amalgam and D_2O replaces the mercury stereospecifically with deuterium leading to *cis*-1-azido-2-deuteriocyclopropanes **7a–c**.[6] This reduction also leads to significant amounts of cyclopropyl-



3a–d

4a–d

5a–d

a, $R_1 = R_2 = CH_3$
b, $R_1 = C_6H_5$; $R_2 = CH_3$
c, $R_1 = H$; $R_2 = CH_3$
d, $R_1 = R_2 = H$

6a–c, X = H
7a–c, X = D

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(1) Stereochemistry. LXVI. For paper LXV see A. Hassner and A. B. Levy, *J. Amer. Chem. Soc.*, **93**, 5469 (1971).

(2) (a) T. G. Traylor, *Accounts Chem. Res.*, **2**, 153 (1969); (b) *ibid.*, footnote 27e.

(3) (a) K. B. Wiberg and W. J. Bartley, *J. Amer. Chem. Soc.*, **82**, 6375 (1960); (b) N. Y. Den'yanov and M. N. Doyarenko, *Ber.*, **56**, 2200 (1923).

(4) (a) R. Köster, S. Arora, and P. Binger, *Angew. Chem., Int. Ed. Engl.*, **8**, 205 (1969); (b) G. L. Closs, *Advan. Alicyclic Chem.*, **1**, 93 (1966).

(5) C. H. Heathcock, *Angew. Chem., Int. Ed. Engl.*, **8**, 134, (1969). *Caution:* it is important to add the mercuric acetate to the solution of NaN_4 in THF–water and not vice versa. Nevertheless, at best one explosion occurred in the mercuric azide addition to norbornene (Professor C. H. Heathcock, private communication).

(6) (a) T. G. Traylor and W. A. Baker, *J. Amer. Chem. Soc.*, **85**, 2746 (1963); A. Factor and T. G. Traylor, *J. Org. Chem.*, **33**, 2607 (1968); F. G. Bordwell and M. L. Douglass, *J. Amer. Chem. Soc.*, **88**, 993 (1966). (b) In addition, S. J. Cristol and R. S. Beckley (private communication) report that 8 and other organomercurials are reduced stereospecifically with retention by sodium amalgam and D_2O.

Table I. Synthesis and Properties of Cyclopropyl Azides

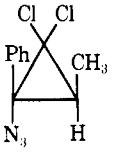
Compd	% yield (mp or bp, °C)^a	Anal, % calcd (found)	Nmr spectra, τ in CCl_4 or $CDCl_3$
5a	100 (68–69)	Hg, 49.59 (49.61)	8.40 (s, 3), 8.63 (s, 3), 8.79 (s, 3), 8.88 (s, 1)
5b	87 (71–73)	Hg, 43.0 (43.27)	2.65 (s, 5), 8.30 (s, 1), 8.48 (s, 3), 9.06 (s, 3)
5c	81 (45.5–46.5)	Hg, 51.37 (51.60)	6.83 (d, 1, J_{H-H} = 6.8, J_{Hg-H} = 80 Hz), 8.6 (d, 1, buried), 8.64 (s, 3), 8.82 (s, 3)
5d	96 (52–53)	C, 9.93 (9.74); H, 1.10 (0.94); Hg, 55.34 (55.57)	6.4–6.7 (m, 1, J_{H-H} = 6.5, 6.5, 3.5; J_{Hg-H} = 85 Hz), 8.3–9.1 (m, 3, J_{Hg-H} = 195, 305 Hz)
6a	26^d (58–60 at 90 mm)	C, 57.60 (57.46); H, 8.80 (8.91)	8.53 (s, 3), 8.81 (s, 3), 8.88 (s, 3), 9.38 (d, 1, J = 6.5 Hz), 9.67 (d, 1, J = 6.5 Hz)
7a	10^b		8.53 (s, 3), 8.81 (s, 3), 8.88 (s, 3), 9.67 (s, 1)
6b	25^d 60^c	C, 70.59 (70.72); H, 6.95 (6.86)	2.68 (s, 5), 8.90 (d, 1, J = 5.5 Hz), 9.10 (d, 1, J = 5.5 Hz), 8.65 (s, 3), 9.19 (s, 3)
7b	3^b 38^c		2.68 (s, 5), 8.65 (s, 3), 8.91 (s, 1), 9.19 (s, 3)
6c	5^d	C, 54.05 (54.30); H, 8.12 (8.29); N, 37.84 (37.60)	7.33 (dd, 1, J = 7, 4.5 Hz), 8.85 (s, 3), 8.95 (s, 3), 9.2–9.7 (m, 1)
7c	5^b		7.33 (d, 1, J = 7 Hz), 8.85 (s, 3), 8.95 (s, 3), 9.40 (d, 1, J = 7 Hz)

[a] Melting points are those of analytical samples; yields are based on crude product. [b] *Via* sodium amalgam reduction in D_2O or H_2O. [c] *Via* HN_3 or DN_3 addition. [d] *Via* sodium borohydride reduction.

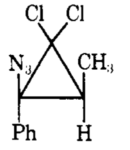
amines derived from over-reduction of the cyclopropyl azides. Since the crude mercury salts **5a–c** were used and no cyclopropyl azides were observed with the deuterium occupying the epimeric position (within the limits of nmr), the addition was completely stereospecific.

Stereochemistry

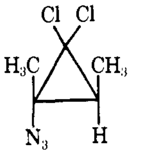
The stereochemistry of the addition was ascertained by comparison of chemical shifts in the nmr with those of analogous compounds as well as by evaluation of coupling constants. The related dichlorocyclopropyl azides **6e** and **6f** whose configuration is unambiguous from their method of synthesis[7] were used to determine the relative effect of a phenyl group geminal to an azide function on the chemical shifts of the cis and trans β hydrogens. The underlying assumption is that the two chlorine atoms in **6e** and **6f** only affect the absolute, but not the relative chemical shifts of these hydrogens. Thus a proton cis to a phenyl group and trans to an azide function is downfield in the nmr relative to its epimeric proton. Similarly, from the spectra of **6g** and **6h** one concludes that a proton cis to a methyl group and trans to an azide group occurs in the nmr upfield relative to its epimeric proton. This is also in agreement with nmr findings in substituted vinyl azides.[8] The nmr spectra of the deuterated cyclopropyl azides **7a** and **7b** indicate that the deuterium has entered the molecule cis to the azide group since the upfield proton has disappeared in going from **6b** to **7b** and the downfield proton in going from **6a** to **7a**.



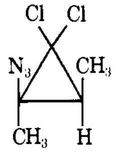
6e, τ 7.99



6f, τ 7.89

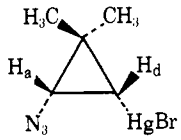


6g, τ 8.30

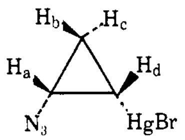


6h, τ 8.61

The stereochemistry of the cyclopropylmercuric compounds **5c** and **5d** can be assigned as being cis on the basis of the large geminal H–H coupling constants of 6.8 and 6.5 Hz. That this is valid is shown by the fact that azide **6c** has vicinal coupling constants of 7 and 4.5 Hz. The corresponding deuterated compound **7c** has a vicinal coupling constant of 7 Hz. Since in cyclopropanes $J_{cis} > J_{trans}$,[9] the deuterium must have been introduced cis to the azide and the corresponding mercury salts **4c** and **5c** must have been the cis adducts. Hydrogenolysis of alkylmercuric derivatives with sodium amalgam usually occurs with retention of configuration even in cases where $NaBH_4$ reduction is not entirely stereospecific.[6a,b]



5c



5d

$J_{ab} = J_{ad} = J_{bc} = 6.5 Hz$

$J_{bd} = 10$

$J_{ac} = 3.5$

$J_{cd} = 7.5$

The ^{199}Hg satellites of H_a in **5d** may also be used to assign the stereochemistry of the addition. They show a first-order spectrum of six lines which is consistent with coupling constants of about 6.5, 6.5, and 3.5 Hz (see Figure 1). The two 6.5-Hz coupling constants must be due to the two cis protons (H_b and H_d) and the 3.5-Hz coupling due to the trans proton (H_c). If **5d** had trans stereochemistry, then two small (trans) and one large (cis) coupling constants would be expected for the satellites of H_a. Examination of the ^{199}Hg satellites of H_b and H_c showed that these could also be interpreted in terms of first-order coupling constants as given (see Figure 1). J_{bd} (cis) and J_{cd} (trans) are larger than the other cis and trans couplings. The

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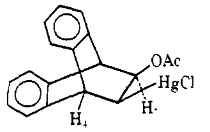
(7) A. B. Levy and A. Hassner, *J. Amer. Chem. Soc.*, **93**, 2051 (1971).

(8) F. W. Fowler, A. Hassner, and L. Levy, *ibid.*, **89**, 2077 (1967); A. Hassner and F. W. Fowler, *J. Org. Chem.*, **33**, 2686 (1968).

(9) K. L. Williamson, C. A. Lanford, and C. R. Nicholson, *J. Amer. Chem. Soc.*, **86**, 726 (1964).

Table II. Variation of Vicinal ^{199}Hg–^{1}H Coupling Constants with Dihedral Angle



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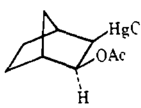

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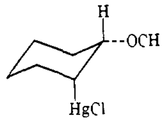

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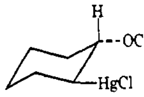

11

	8					5c	5d	5d	5d
	H_7	H_4	9	10	11	H_a	H_a	H_b	H_c
Approx dihedral angle	120°	60°	120°	180° (?)	60°	130°	130°	130°	0°
J, Hz	106	75[a]	93.2[b]	425[b]	99[b]	80	85	195	305

[a] Reference 6b. [b] Reference 10.

smaller electronegativity of the mercury *vs.* the azide function causes these couplings to be larger. Similar increases in coupling constants have been observed in trimethylsilylcyclopropanes.[9]

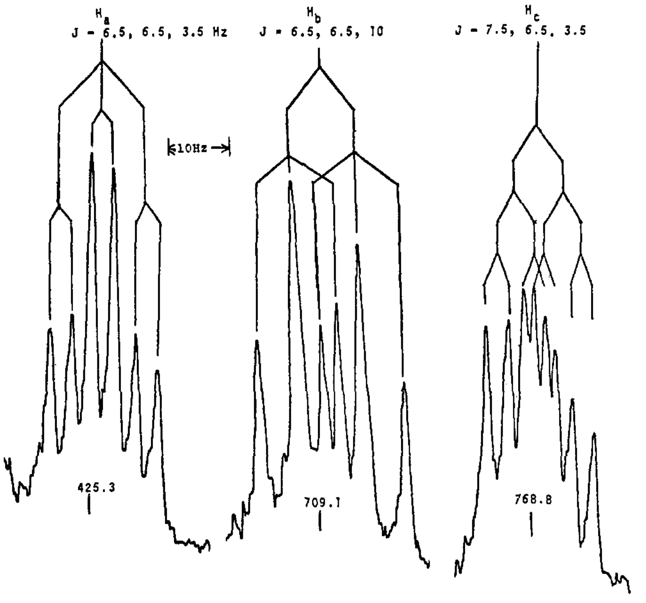

Figure 1. The 100-MHz nmr spectra of the upfield ^{199}Hg satellites of **5d**. The markers are the chemical shift in Hz upfield from a $CHCl_3$ internal lock signal.

It might be tempting to assign the stereochemistry on the basis of $J_{^{199}Hg-^{1}H}$ vicinal coupling constants since it has been implied that $J_{^{199}Hg-^{1}H} = 90$–100 Hz when the dihedral angle is smaller than 120°, whereas much higher J values are associated with angles between 120–180°.[10] However, this method seems to have severe limitations. Whereas **5c** and **5d** show mercury–hydrogen couplings for H_a of $J_{trans} = 80$ and 85 Hz, respectively, J_{trans} for H_b in **5d** appears to be 195 Hz. Yet, the dihedral angles Hg–H_a and Hg–H_b are most likely similar and close to 130°. It is unlikely that the 195-Hz coupling is due to geminal ^{199}Hg–^{1}H coupling (H_d) because attempts to find geminal coupling of this type in **5a**, **5b**, and **5c** were unsuccessful. Hence, the most tenable interpretation of the data is that in cyclopropane **5d** the 195-Hz value is due to trans coupling with H_b and that the 305-Hz value is due to cis coupling with H_c. It is to be expected that due to the geminal azide substituent the dihedral angle H_a–C–C–Hg is slightly different from that for H_b–C–C–Hg. The examples given in Table II indicate that the variations in $J_{^{199}Hg-^{1}H}$ that occur when the dihedral angle is in the range of 120°–130° are too large for diagnostic purposes. On the other hand, in the range of 60–120° the variations of the ^{199}Hg–^{1}H coupling constant are too minimal and equally difficult to predict. The only distinctly different J values (>300 Hz) are for dihedral angles in the immediate vicinity of 0 and 180°; *i.e.*, the system exhibits a rather flat Karplus curve.

Discussion

The results of $Hg(N_3)_2$ additions may be rationalized in terms of the twist–strain theory of electrophilic additions in which olefins which are rigid and cannot twist to a staggered conformation prefer to add electrophiles in a cis manner. Furthermore, the cis addition of mercuric salts as contrasted to the partial trans addition of bromine to norbornene[2] is similar to the stereochemical behavior of these reagents to cyclopropenes.

The fact that mercuric azide unlike mercuric acetate gave unrearranged products with cyclopropenes[2b] is perhaps explicable in terms of the greater nucleophilicity of the azide ion as compared to the acetate ion. This decreases the positive nature of the mercury atom and is expected to cause less positive charge buildup on the cyclopropane ring in the intermediate mercurium ion, resulting in less rearrangement. The excess azide ion present in this study probably also influenced the reaction pathway since excess acetate ion is known to increase the amount of cis product formed in mercuric acetate additions.[11]

These results suggest that other electrophilic reagents might give unrearranged products if a good trapping nucleophile is present. Indeed, when 3,3-dimethyl-1-phenylcyclopropene (**3b**) was treated with excess hydrazoic acid, azide **6b** was isolated in 60% yield. The

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(10) M. M. Kreevoy and J. F. Schaefer, *J. Organometal. Chem.*, **6**, 589 (1966).

(11) T. G. Traylor, *J. Amer. Chem. Soc.*, **86**, 244 (1964).

use of DN_3 gave the cis adduct **7b** indicating a syn stereochemistry in the addition.

Experimental Section

Nmr spectra were taken on a Varian A-60-A spectrometer at 1–10% concentration in CCl_4 or $CDCl_3$ (TMS internal standard). For determination of mercury satellites a nearly saturated solution of the salts **5a–d** in $CDCl_3$ and a Varian HA-100 spectrometer ($CHCl_3$ lock signal) were used. All compounds made had characteristic azide absorptions in the ir at near 2100 cm^{-1}. The cyclopropenes were made by previously published methods.[12-14]

Mercuric Azide Addition. The mercuric azide was formed by adding 0.10 mol of mercuric acetate to 0.30 mol of sodium azide in a stirred two-phase solution of 200 ml of 50% THF–H_2O at 0°.[5] After 20 min of stirring, the cyclopropene (0.10 mol) in 10–25 ml of THF was added in one portion in the cases of **3a**, **3b**, and **3c**, or bubbled in excess from an external generator in the case of **3d**. The solution was stirred for 15–25 hr while warming to room temperature to produce a two-phase solution of **4a**, **4b**, **4c**, or **4d**.

Sodium Borohybride Reduction of 4a and 4b. To the solution of **4a** or **4b** above was added rapidly at 0° 100 ml of 15% KOH followed by 2 g of $NaBH_4$ in 100 ml of 15% KOH as previously published.[6] The solution was poured into water, extracted with the minimum amount of pentane, and washed several times with water. The organic layer was dried ($MgSO_4$), the solvent removed *in vacuo* and the product purified as indicated.

1-Azido-1,3,3-trimethylcyclopropane (**6a**) was separated from nonvolatile material by distillation into a Dry Ice trap at 0.1 mm (bath temperature 30°). (*Caution:* direct distillation at higher pressures resulted in an explosion.) Distillation gave a 26% yield of **6a**, bp 58–68° (90 mm). The analytical sample was prepared by preparative vpc using the conditions given for **7a**.

1-Azido-1-phenyl-3,3-dimethylcyclopropane (**6b**), crude, was passed over 50 g of basic alumina (pentane) and further purified by bulb-to-bulb distillation at 85° (0.1 mm) giving pure **6b** in 25% yield. Two further bulb-to-bulb distillations gave the analytical sample.

Conversion of 4a–d to 5a–d. To the solution of **4a**, **4b**, **4c**, or **4d** above were added at 0° 5 equiv of 48% HBr and 3 equiv of a saturated solution of NaBr. The THF and hydrazoic acid were removed *in vacuo* at room temperature, and the residue was extracted with three 200-ml portions of methylene chloride. The methylene chloride solution was washed with water until neutral, dried over NaBr, and concentrated *in vacuo* giving the crude product **5**. If the product was an oil, crystallization was induced by the addition of methanol and the methanol removed *in vacuo*. The yields given in Table I are for the crude material thus obtained. **5a** and **5b** had about 15% impurities by nmr integration, which were not taken into account in calculating the yield. Two recrystallizations from methanol gave the analytical samples with the melting points recorded in Table I. These compounds are sensitive to heat and light and are best stored in a freezing compartment where they have a shelf life of several weeks to several months.

Sodium Amalgam Reductions of 5a–c. To a suspension of 3 g of the crude product **5a**, **5b**, or **5c** in 10 ml of D_2O or H_2O was added 2 equiv of 2% sodium amalgam. The solution was stirred vigorously for 3 hr and purified as given.

***cis*-1-Azido-2-deuterio-1,3,3-trimethylcyclopropane** (**7a**) was steam distilled from the reaction mixture. Nmr analysis of the distillate showed the product to be a 1:1 mixture of **7a** and the over-reduction product *cis*-2-deuterio-1,3,3-trimethylcyclopropylamine. The products were separated by preparative vpc on a 3 ft × 0.25 in. 20% SE-30 on Chromosorb W column at 70° and 60 cc/min of helium. Under these conditions the retention times of **7a** and the amine were 7 and 3 min, respectively. Nmr of the amine showed τ 8.73 (s, 3), 8.85 (s, 3), 8.98 (s, 3), and 9.90 (s, 1). No attempt was made to further characterize the amine.

***cis*-1-Azido-2-deuterio-1-phenyl-3,3-dimethylcyclopropane** (**7b**) was extracted from the reaction mixture with pentane and purified as for **6b** giving a 5% yield.

1-Azido-3,3-dimethylcyclopropane (**6c**) and ***cis*-1-azido-2-deuterio-3,3-dimethylcyclopropane** (**7c**) were purified as for **7a** giving a 5% yield. No attempt was made to characterize the amine products. An analytical sample of **6c** was obtained by preparative vpc.

Addition of HN_3 and DN_3 to 3b. To a solution of HN_3 in dry ether[15] (from 30 g of NaN_3) was added 1.61 g of **3b**. After 7 days of reflux, the solvent and excess HN_3 were removed *in vacuo*. Two bulb-to-bulb distillations (85°, 0.1 mm) gave 1.27 g of product (61%), identical by nmr and ir with cyclopropyl azide **6b** prepared from **4b**. A solution of DN_3 in dry ether was obtained from 13 g of NaN_3 by substituting D_2O and D_2SO_4 for H_2O and H_2SO_4 used in the preparation of HN_3.[15] From 0.800 g of **3b** there was obtained 0.403 g of **7b** (38%). A nmr sample was further purified by preparative layer chromatography (silica gel, hexane), the band with R_f ~0.3 being collected. Nmr (CCl_4) showed the product to be the cis addition product **7b** contaminated by some HN_3 addition product **6b**. Within the limits of nmr there was no trans DN_3 addition product present.

Acknowledgment. Support of this research by a grant from the National Science Foundation and PRF Grant 5899-AC1,4 from the American Chemical Society is gratefully acknowledged.

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[12] G. L. Closs, W. A. Böll, H. Heyn, and V. Dev, *J. Amer. Chem. Soc.*, **90**, 173 (1968).

[13] G. L. Closs, L. E. Closs, and W. A. Böll, *ibid.*, **85**, 3796 (1963).

[14] C. L. Closs and K. D. Krantz, *J. Org. Chem.*, **31**, 638 (1966).

[15] L. F. Audrieth and C. F. Gibbs, *Inorg. Syn.*, **1**, 78 (1939).