Table I. Asymmetric Hydroboration of Representative Trans-Disubstituted Olefins with Isopinocampheylborane ($IpcBH_2$)[a] in 1:1 Ratio[b]

olefin	product alcohols				
	alcohol	yield, % (isolated)	$[\alpha]^{23}_D$, deg	% ee	config
trans-2-butene	2-butanol	73	+9.8 (neat)	73[c]	*S*
trans-3-hexene	3-hexanol	83	+5.3 (neat)	75[d]	*S*
trans-2,2,5,5-tetramethyl-3-hexene	2,2,5,5-tetramethyl-3-hexanol	61	+34.8 (*c* 5, EtOH)	92[e]	*R*[h,i]
trans-2-pentene	2-pentanol (47%), 3-pentanol (53%)	78	+12.95 (*c* 7.39, Et_2O)	70[f]	*S*
trans-β-methylstyrene	1-phenyl-1-propanol	72	+20.6 (neat)	75[g]	*R*[i]

[a] The reagent is prepared from (+)-α-pinene: $[\alpha]^{23}_D$ +48.3°; 94.4% ee. [b] The reactions were carried out on a 50-mmol scale. [c] Based on maximum rotation $[\alpha]^{25}_D$ -13.5° (neat): Leroux, P. J.; Lucas, H. J. *J. Am. Chem. Soc.* **1951**, *73*, 41. [d] Based on maximum rotation $[\alpha]^{18}_D$ -7.13° (neat): Kenyon, J.; Poplett, R. *J. Chem. Soc.* **1945**, 273. [e] As determined by 90-MHz NMR with the chiral lanthanide shift reagent tris[[(heptafluoroprop-1-yl)hydroxymethylene]-*d*-camphorato]-europium(III) [Eu(hfc)$_3$]. [f] Based on maximum rotation $[\alpha]^{20}_D$ +18.5° (*c* 7.39, Et_2O): Levene, P. A.; Mikeska, L. A. *J. Biol. Chem.* **1927**, *75*, 587. [g] Based on maximum rotation $[\alpha]^{17}_D$ -27.35° (neat): Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1911**, *99*, 45. [h] The absolute configuration of 2,2,5,5-tetramethyl-3-hexanol has not been established. We predict that the (+) isomer is probably *R*. [i] *R* notation arises for the related absolute configuration of the other products, designated *S*, because of a change in the priorities of the substituents attached to the chiral carbon atom.

Table II. Summary of the Asymmetric Hydroboration Results of Various Classes of Alkenes with Diisopinocampheylborane and Isopinocampheylborane

class of alkene	Ipc_2BH ee, %	$IpcBH_2$ ee, %
2-methyl-1-alkenes	5-30	1.5[a,b]
cis-alkenes	76-98.4	20-24
trans-alkenes	13[a,c]	70-92
trisubstituted alkenes	14-22	52-100

[a] Only one example. [b] 2-Methyl-1-butene. [c] *trans*-2-Butene.

free $IpcBH_2$ was then removed from the slurry of TMED·$2BF_3$ by filtration under nitrogen through a filter chamber.[11] The solid TMED·$2BF_3$ was washed with three 9-mL portions of THF. The solution of $IpcBH_2$ in THF thus obtained was found to be 0.8 M by hydride estimation. $IpcBH_2$ (62.5 mL, 50 mmol) in THF was cooled to -25 °C. The flask was then charged with 2.7 mL of THF (to make the solution of 0.7 M in $IpcBH_2$) followed by dropwise addition of 6.2 mL (50 mmol) of *trans*-3-hexene over a period of 5 min. The dialkylborane precipitates out of the solution after 10 min. The contents of the flask were further stirred at -25 °C for 9 h to ensure completion of the reaction. The reaction mixture was carefully (H_2 evolution!) treated with 4 mL (100 mmol) of methanol at -25 °C and slowly warmed up to 25 °C. It was then treated with 18.4 mL of 3 M NaOH followed by 15 mL of 30% aqueous hydrogen peroxide dropwise, with the temperature of the reaction mixture maintained below 40 °C. After an additional hour at 50 °C, the reaction mixture was cooled, and the alcohol products were extracted into ether and dried. Fractional distillation provided 4.25 g of (*S*)-(+)-3-hexanol: bp 130–133 °C (745 mm); 83% yield (>97% GLC pure). The alcohol was further purified by preparative GLC (10% Carbowax) to obtain >99.9% GLC-pure material: n^{20}_D 1.4145; $[\alpha]^{25}_D$ +5.3° (neat); 75% ee.

This development makes it possible to realize high optical purities in the hydroboration of three of the four major classes of alkenes. Only the less steric demanding group, the 2-methyl-1-alkenes, do not yield optically active products in the desirable range.

With increasing knowledge of the steric requirements of different chiral hydroborating agents, it may be possible to tailor-make reagents which will improve the already promising results.

Registry No. 2, 64065-15-2; *trans*-2-butene, 624-64-6; *trans*-3-hexene, 13269-52-8; *trans*-2,2,5,5-tetramethyl-3-hexene, 692-48-8; *trans*-2-pentene, 646-04-8; *trans*-β-methylstyrene, 873-66-5; (*S*)-2-butanol, 4221-99-2; (*S*)-3-hexanol, 6210-51-1; (*R*)-2,2,5,5-tetramethyl-3-hexanol, 79449-64-2; (*S*)-2-pentanol, 26184-62-3; (*S*)-3-pentanol, 79449-65-3; (*R*)-1-phenyl-1-propanol, 1565-74-8.

(11) For a description of the filtration chamber, see: Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M., Eds.; "Organic Syntheses via Organoboranes"; Wiley-Interscience: New York, 1975; p 191.

(12) Postdoctoral research associate on Grant 2 R01 GM 10937-19 from the National Institutes of Health.

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On the Mechanism of Graham's Reaction

Summary: The oxidative cyclization of amidines to 3-chloro-3-substituted diazirines with aqueous sodium hypochlorite proceeds through *N*-chloro- and *N,N'*-dichloroamidines; the latter are isolable in certain cases.

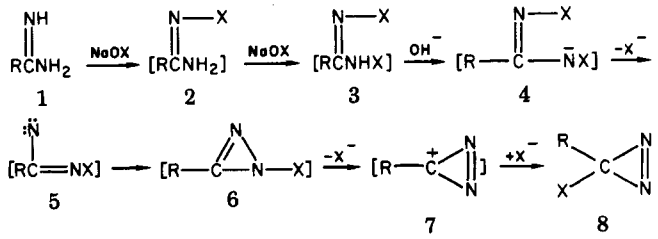
Sir: In 1965, Graham reported the direct preparation of (3-alkyl-, 3-aryl-, and 3-alkoxy-3-halodiazirines by the action of aqueous NaOCl (or NaOBr) on various alkyl- or arylamidines and isoureas in aqueous dimethyl sulfoxide (Me_2SO) solution.[2] Despite the importance of this conversion for the generation of numerous halocarbene precursors,[3,4] its mechanism remains obscure. Graham's original suggestions are summarized in Scheme I.[2]

Successive N-halogenations of amidine **1** produce *N*-haloamidine **2** and then *N,N'*-dihaloamidine **3**. The latter is converted to *N*-halodiazirine **6**, either by internal displacement of X^- within anion **4** or by cyclization of a subsequent iminonitrene, **5**. Intermediate **6** is finally converted to 3-halodiazirine **8** by an addition–elimination reaction with X^- or by ionization to diazirinium ion **7**,

(1) (a) Rutgers University. (b) Merck Institute.
(2) W. H. Graham, *J. Am. Chem. Soc.*, 87, 4396 (1965).
(3) "Science Citation Index" (Institute for Scientific Information, Philadelphia, PA) reveals 58 citations of ref 2 between 1965 and 1980.
(4) For a brief review, see K. MacKenzie in "The Chemistry of the Hydrazo, Azo, and Azoxy Groups", S. Patai, Ed., Wiley, New York, 1975, Part 1, pp 329 ff. see especially pp 333, 334, 342, 343.

0022-3263/81/1946-5048$01.25/0

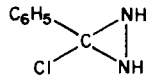
Scheme I[a]



[a] a, R = C_6H_5; b, R = i-C_3H_7; c, R = CH_3O; X = Cl for all specifically designated compounds, 2-8.

followed by recombination with X^-.

Recently, it was claimed[5] that oxidation of benzamidine (**1a**) by NaOCl under Graham's general conditions, but with the reaction temperature ≤20 °C, afforded 3-chloro-3-phenyldiaziridine (**9**) as an isolable, crystalline product



9

in 60% yield. Mechanisms were offered for the conversion of **1a** to **9**,[5] and it was suggested that **9** was the actual precursor of diazirine **8a**; i.e., under harsher Graham conditions (~35 °C), hypochlorite oxidation of **9** would afford **8a**.[5] Graham's mechanism[2] was thus considered incorrect.[5]

In this paper we show (a) that the compound described as **9** is actually the *N*-haloamidine **2a**, (b) that certain *N,N'*-dihaloamidines (**3**) are isolable and convertible to **8** under "nonoxidative" Graham conditions, and (c) that *free* diazirinium ions (**7**) are unlikely precursors to **8**.

Structure of "9". We were concerned that the reported IR spectrum of **9** (particularly the bands at 1580 and 1550 cm^{-1})[5] was more consistent with a C=N part structure, such as in **2a**, than with the diaziridine formulation, **9**. Accordingly, we prepared **2a** by direct halogenation[6] of benzamidine hydrochloride. Treatment of 10 mmol of **1a**·HCl in 5 mL of water with 1 equiv (6 mL of an 11% aqueous solution) of NaOCl at ≤10 °C afforded 77% of solid **2a**, which was dried and recrystallized from benzene to afford pure **2a**, mp 71–72.5 °C.[7] Our compound **2a** was *identical* with compound **9**[8] by IR, NMR (^1H and ^{13}C), melting point, TLC, and HPLC comparisons. The structure of **2a** (**9**) was secured as **2a** by X-ray analysis.

Crystals of **2a** (from CH_2Cl_2/heptane) formed as colorless prisms with symmetry $P2_1/c$. Preliminary diffraction experiments indicated cell constants of a = 12.146 (2) Å, b = 16.411 (1) Å, c = 16.135 (1) Å, and β = 109.45 (1)° for a calculated density of 1.35 g/cm^3 with Z = 16. The structure was solved with direct methods and refined to an unweighted R factor of 0.049 by using full-matrix least-squares techniques and minimizing $\sum w(|F_o| - |F_c|)^2$ with $w = 1/\sigma(F_o))^2$.[9] Intermolecular hydrogen bonds between the amino and imino functional groups and noncrystallographic symmetry are responsible for the four "independent" molecules in the asymmetric unit cell.

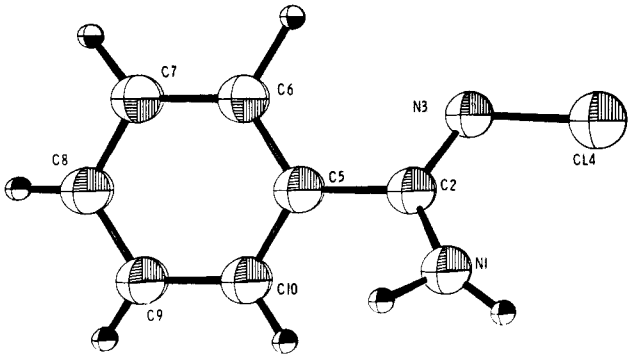


Figure 1. Computer-generated drawing of **2a** from the X-ray data.

Figure 1 is a drawing of one of the molecules. The X-ray structure clearly shows that **2a** is an *N*-chloroamidine, both from the positions of the hydrogen atoms and from the average C–N bond lengths of 1.31 and 1.34 Å. The average angle between the plane of the benzene ring and the plane of the amidine group is 36°. Tables I–III which contain the fractional coordinates, temperature parameters, bond distances, and bond angles may be found in the supplementary material.

This demonstration of the identity of **2a** and **9** makes it clear that the initial step of the Graham reaction is indeed N-halogenation (Scheme I) and sets the stage for extended examination of the original mechanism.

***N,N'*-Dihaloamidines.** Further halogenation (1 equiv of NaOCl) of *N*-chlorobenzamidine (**2a**) did not afford the desired *N,N'*-dichloroamidine (**3a**); a mixture of **2a** and *N,N,N'*-trichlorobenzamidine was obtained instead, presumably from rapid disproportionation of **3a**. In other cases, however, it proved possible to prepare and isolate examples of **3**. By the N-chlorination procedure described above, HCl salts of **1b** and **1c** were converted to the corresponding *N*-haloamidines **2**.[10] Each of these compounds was reacted with 1 equiv of aqueous NaOCl solution at 0 °C. Thus, 10 mmol of **2** in 10 mL of CH_2Cl_2 was converted to the amidinium ion with 1 equiv of HCl in 6 mL of H_2O. Aqueous NaOCl (11%, 6 mL) was quickly added (with stirring), the phases were separated, and the dichloroamidines **3** were obtained from the CH_2Cl_2 solutions after drying and stripping. Amidine **3b** was purified[11] by silica gel chromatography (2:1 pentane/ether),[12] whereas the methoxy analogue **3c** was obtained by recrystallization of the crude product[13] from pentane.[14] The identities of **2b,c** and **3b,c** were substantiated by IR and NMR spectroscopy,[10,12,14] as well as mass spectroscopy or elemental analysis.

With representative *N,N'*-dihaloamidines in hand, we could separately test the **3** → **8** sequence of the Graham mechanism, Scheme I.[2] Indeed, addition of 5 mmol of **3b** or **3c** in 10 mL of triglyme to 20 mL of Me_2SO and 50 mL of 10% aqueous NaOH, saturated with NaCl and cooled in an ice bath ("nonoxidative Graham conditions"), afforded the anticipated 3-chlorodiazirines **8b** or **8c**. The

(5) H. Berneth and S. Hünig, *Chem. Ber.*, **113**, 2040 (1980).
(6) Cf. E. Haruki, T. Inaike, and E. Imoto, *Bull. Chem. Soc. Jpn.*, **41**, 1361 (1968), and references therein.
(7) Reference 5 reports a melting point of 71.5–72.5 °C for compound **9**.
(8) We thank Professor Hünig for a sample of **9**.
(9) The following crystallographic programs were used: MULTAN 78, University of York, York, Englend; Enraf-Nonius Structure Determination Package V17.0; ORTEP-II, Oak Ridge National Laboratory, Oak Ridge, TN.

(10) (a) **2b**: 78% from **1b**; IR (CH_2Cl_2) 3525, 3400, 1630, 1565 cm^{-1}; NMR (CCl_4) δ 1.27 (d, J = 7 Hz, 6 H, $CHMe_2$), 2.7 (m, 1 H, $CHMe_2$), 5.97 (br s, 2 H, NH_2). (b) **2c**: 69% from **1c**; mp 31–32 °C, IR (CCl_4) 3550, 3440, 1640, 1570 cm^{-1}; NMR ($CDCl_3$) δ 3.85 (s, 3 H, CH_3O), 5.3–4.1 (vbr, ~2 H, NH_2).
(11) The crude reaction product was a 1:2:1 mixture of mono-, di-, and trichloroamidines.
(12) **3b**: 49% from **2b**; mp 42 °C; IR (CH_2Cl_2) 3330, 1580 cm^{-1}; NMR (CCl_4) δ 1.30 (d, J = 7 Hz, 6 H, $CHMe_2$), 3.10 (septet, J = 7 Hz, 1 H, $CHMe_2$), 6.33 (br s, 1 H, NH).
(13) The crude product was a 30:70 monochloroamidine/dichloroamidine mixture.
(14) **3c**: 34% from **2c**; mp, 56–57 °C; IR (CCl_4) 3360, 1600 cm^{-1}; NMR ($CDCl_3$) δ 3.97 (s, 3 H, CH_3O), 5.83 (br s, 1 H, NH).

diazirines were removed under vacuum as they formed and sequentially passed through a drying trap containing NaOH pellets and a second trap cooled to -30 °C. They were collected in a third trap (-78 °C) containing 2 mL of solvent. The chloroisopropyldiazirine **8b**, obtained in 49% yield from **3b**, was identical (IR and NMR) with the authentic material[15] obtained by standard Graham oxidation[2] of **1b**. The methoxychlorodiazirine **8c**, obtained from **3c**, was trapped in isobutene and permitted to decompose at 25 °C (sealed tube) to afford the known[16] isobutene adduct of methoxychlorocarbene in 43% overall yield.

These results indicate that the dichloroamidines **3** are likely precursors of the diazirines **8**, as suggested by Graham.[2] Moreover, control experiments with *N*-chloro- and *N,N,N'*-trichloroamidines (series **a** and **b**) show that none of these amidine derivatives afford **8** under nonoxidative Graham conditions. Preliminary experiments indicate that **3b** and **3c** can be converted to 3-azido-3-isopropyldiazirine and 3-bromo-3-methoxydiazirine, respectively, upon treatment with aqueous NaOH saturated with NaN_3 or NaBr. The new diazirines are formed as mixtures, however, with the appropriate 3-chlorodiazirine present and *dominant* in each case.

Diazirinium Ions. The final stage of Graham's mechanism remains unclear. On the assumption that **3** does afford **6** (in analogy[2] to the Neber rearrangement), how is **6** converted to **8**? Intervention of a free diazirinium ion (**7**), for which recent ab initio calculations indicate thermodynamic instability,[17] seems quite unlikely. Moreover, we have failed to obtain evidence for the ionization of **8** to **7**, despite the suggestion that diazirinium ion "formation under solvolytic conditions is not unreasonable".[2] Thus, treatment of **8c** (or methoxybromodiazirine) with $AgNO_3$, $AlBr_3$, SbF_5/SO_2, H_2SO_4, $AlCl_3$, AgF, or FSO_3H at various temperatures and with several methods of spectroscopic or chemical monitoring failed to provide evidence for diazirinium ions as spectroscopic entities or as chemical intermediates. Several related experiments failed with methylchlorodiazirine (our work) and with phenylhalodiazirines.[18]

The suggestion[2] that **6** affords **8** by an addition-elimination reaction with X^- is also difficult to accept. If this were so, we would expect nearly complete interception of **6** by added "foreign" anions. However, our experience with the conversion of **3** to **8** is that N_3^- or Br^-, although supplied in ~20-fold excess, compete poorly with the chloride initially present in **3**.

Our current working hypothesis is that **6** is a high-energy species which, in aqueous solution, is exothermically converted to **8** via an *intimate ion pair* (**7**, X^-) in which return of the "original" anion is favored over capture of a "foreign" anion. There is a clear analogy here to the interconversion of isomeric 3-chloro-1-azirines, which may well proceed via azirinium cation-chloride anion pairs.[19] We are vigorously exploring numerous mechanistic and synthetic ramifications of the present work.

Acknowledgment. We are grateful to the National Science Foundation for financial support, to Professor S. Hünig for helpful correspondence, to Professor K. Krogh-Jespersen for helpful discussions, to Professor H. Schugar for preliminary X-ray studies of **2a**, and to Dr. Dorothy Z. Denney for several NMR spectra of **2a**.

Registry No. **1a**·HCl, 1670-14-0; **1b**·HCl, 22007-68-7; **1c**·HCl, 5329-33-9; **2a**, 40078-03-3; **2b**, 79499-48-2; **2c**, 19224-53-4; **3b**, 79499-49-3; **3c**, 79499-50-6; **8b**, 29648-80-4; **8c**, 4222-27-9.

Supplementary Material Available: Tables I-III containing the fractional coordinates, temperature parameters, bond distances, and bond angles of **2a** from the X-ray experiments (5 pages). Ordering information is given on any current masthead.

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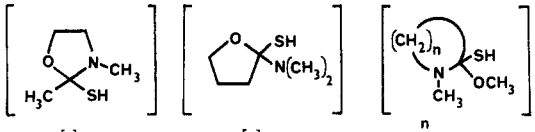
Breakdown of Hemiorthothioamide Tetrahedral Intermediates Derived from *O,N*-Dimethyllactamium Tetrafluoroborates[1,2]

Summary: The sulfhydrolytic cleavage of *O,N*-dimethylbutyrolactamium and *O,N*-dimethylvalerolactamium tetrafluoroborates involves C-N scission under kinetic control (61 °C, NaSH, Ac_2O, $CHCl_3$) but C-O cleavage under thermodynamic control (27 °C, NaSH, acetone).

Sir: We recently reported that hemiorthothioamide intermediates [**1**] and [**2**] derived from *anti*- and *syn*-imidates, respectively, undergo preferential cleavage of the C-N bond (rather than the C-O bond), under kinetic control (-78 °C, NaSH, acetone).[3] We hereby report on the breakdown of hemiorthothioamide tetrahedral intermediates [**3**] and [**4**], generated in aprotic solvents acetone and chloroform from NaSH and *O*-methyl derivatives of lactams **5** and **6**, respectively, at temperatures between -78 and 61 °C. The sulfhydrolytic breakdown for [**3**] and [**4**]



is presented in Scheme I and the results are summarized in Table I.

The reaction of **5** with NaSH in acetone at room temperature (75 min), gave thiolactam **11** exclusively (% C-N cleavage/% C-O cleavage = 7/11 = 0:100; Table I, entry 1).[4] Even at -78 °C, the sulfhydrolysis in acetone followed

(15) R. A. Moss and R. C. Munjal, *J. Chem. Soc., Chem. Commun.*, 775 (1978).
(16) R. A. Moss and W.-C. Shieh, *Tetrahedron Lett.*, 1935 (1978).
(17) K. Krogh-Jespersen, *Tetrahedron Lett.*, 4553 (1980).
(18) B. B. Wright and M. S. Platz, Central and Great Lakes Regional American Chemical Society Meeting, Dayton, OH, May 20, 1981, Abstract 247.
(19) J. Ciabattoni and M. Cabell, Jr., *J. Am. Chem. Soc.*, **93**, 1482 (1971); A. Padwa, T. J. Blacklock, P. H. J. Carlsen, and M. Pulwer, *J. Org. Chem.*, **44**, 3281 (1979).

(1) The Chemistry of Tetrahedral Intermediates. 7. For part 6, see: Kaloustian, M. K.; Khouri, F. *Tetrahedron Lett.* **1981**, *22*, 413-416; part 5, Kaloustian, M. K.; Khouri, F. *J. Am. Chem. Soc.* **1980**, *102*, 7579-7581.
(2) (a) Presented at the Second Chemical Congress of the North American Continent, Las Vegas, NV, Aug 25, 1980; ORG 76. (b) Taken in part from the Ph.D. Dissertation of R. B. Nader, Fordham University, 1980.
(3) Kaloustian, M. K.; Aguilar-Laurents de Gutierrez, M. I.; Nader, R. B. *J. Org. Chem.* **1979**, *44*, 666-668.

0022-3263/81/1946-5050$01.25/0