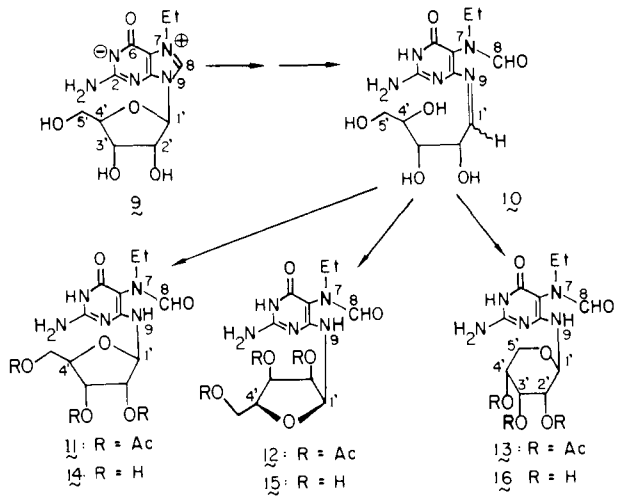

Figure 2. Products resulting from mild base treatment of 7-ethylguanosine (9).

changeable signals at 6.7–8.2 ppm corresponding to *N*-formyl, thus suggesting imidazole ring opening. Because 7-substituted purine nucleosides are also known to undergo an important but unclarified imidazole ring fission,[12,13] a model system was first investigated. Namely, 7-ethylguanosine (**9**)[14] was treated with 2N NH_4OH (room temperature, 2 lyophilized, lyophilized, and passed through Sephadex G-25. HPLC of the product gave an ill-resolved multiple peak pattern, the components of which also interconvert at room temperature. Since the UV resulting from subtraction of 2β,7-diamino-1α-hydroxymitosene from M–dG_I was almost identical with that of base-treated **9**, the latter was studied as a model for the M–dG_I constituents.

Thus the NH_4OH-treated 7-ethylguanosine (**9**) was acetylated and submitted to HPLC (IBM-ODS, MeCN/H_2O 15/85) to give triacetates (90% yield) **11**, **12**, and **13** (Figure 2) in 1:2:2 ratio: CI-MS *m/z* 456 (identical for **11–13**); UV (in CH_3CN) for all three with peaks at 211, 238 (sh), and 272 nm are typical for ring-opened 7-alkylguanosines. the ^1H NMR of **11**[15] and **12**[16] show them to be the C-1′ β- and α-anomers, respectively, of D-ribofuranose triacetate linked to N-9 of the imidazole-cleaved guanine moiety (Figure 2); similarly, **13**[16] is the β-anomer of ribopyranose triacetate linked to N-9. The C-1′ configurations of **11–13** were determined by NOE experiments. The furanoses and pyranose result from addition of 4′- and 5′-OH in **10** to the imine bond (Figure 2).[17]

The unacetylated mixture from **9** was separated by HPLC, (IBM-ODS, MeCN/H_2O 1.5/98.5) to yield pure **14**, **15**, and **16** upon collection at −78 °C; acetylation gave respective acetates **11**, **12**, and **13**.

We thus conclude that MdG_I also consists of interconverting ribosides **6–8** (Figure 1). Substitution of calf thymus DNA for d(GpC) (**3**) in the reaction with acid-activated MC was also found to yield M–guanines **4**/**5** and the MdG_I mixture.[18]

Although many carcinogens alkylate guanosine residues at N-7, the imidazolium fission products had to date not been adequately characterized. Apurination or rearrangement of the riboside moiety as shown in Figure 1 could lead to destruction of the secondary structure of DNA at the alkylation site. The nature of such ring-cleaved moieties resulting from interaction of MC with double-stranded DNA, as well as their relationship to excision–repair mechanisms, remains to be clarified.

Acknowledgment. We thank Min S. Lee, Columbia University, for the preparation of 7-ethylguanosine Dr. Reiji Takeda, Suntory Institute for Bioorganic Research, for discussions, Dr. Denise Frechet, Hunter College, CUNY, for NMR measurements, Dr. W. T. Bradner, Bristol Laboratories, Syracuse, NY, for the supply of MC, and NIH, Grants GM 34509 (to K.N.), CA 28681 (to M.T.), and PSC-CUNY Faculty Award (to M.T.).

Supplementary Material Available: Difference UV of MdG_I minus 2β,7-diamino-1α-hydroxymitosene, ^1H NMR of **11–16**, ^1H NMR of MdG_I mixture (downfield region), ^1H NMR of crude hydrolysis mixture from base treatment of 7-ethylguanosine, and ^1H NMR of M–guanine A (**4**) and M–guanine B (**5**) (11 pages). Ordering information is given on any current masthead page.

Multidentate Lewis Acids. Reduction of Thioketones in the Presence of Organomercury Trifluoroacetates

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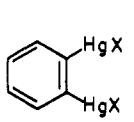
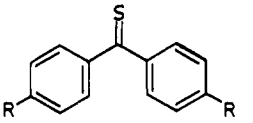
Recently we described the unusual coordination chemistry of three bidentate Lewis acids, the 1,2-phenylenedimercury dihalides **1–3**.[1] Unlike simple monodentate organomercuric halides, bi-





1 (X = Cl)
2 (X = Br)
3 (X = I)
4 (X = $OOCCF_3$)

5 (R = OCH_3)
6 (R = $N(CH_3)_2$)
7 (R = H)

dentate acids **1** and **2** form isolable complexes with added halides. We have now discovered that related bidentate Lewis acids bind and activate thioketones, facilitating their reduction by formal donors of hydride.

Deep blue solutions of bis(4-methoxyphenyl)methanethione (**5**)[2] in CH_3CN turned yellow-green when equimolar amounts of bis(trifluoroacetato)-1,2-phenylenedimercury (**4**)[3,4] were added. At the same time, singlets at δ −1595 (CD_3CN)[5a] in the ^{199}Hg

(12) Haines, J. A.; Reese, C. B.; Lord Todd, *J. Chem. Soc.* **1962**, 5281.
(13) Lawley, P. D. In "Progress in Nucleic Acid Research and Molecular Biology"; Davidson, J. N., Cohn, W. E., Eds.; Academic Press: New York, 1966; Vol. 5, p 81.
(14) Cf. 7-methylguanosine: Jones, J. W.; Robins, R. K. *J. Am. Chem. Soc.* **1963**, *85*, 193.
(15) **11–16** are each present as a set of inseparable rotameric formyl isomers; thus, many protons give rise to more than one signal. ^1H NMR of **11** (Me_2SO-d_6) δ 10.78 (br s, exchangeable, N^1–H); 8.11/7.71 (s, 8-CHO), 7.38/7.23 (d, exchangeable, N^9–H), 6.77/6.65 (br s, exchangeable, 2-NH_2), 5.93/5.82 (dd, 1′-H), 5.42/5.34 (dd, 2′-H), 5.25/5.20 (dd, 3′-H), 4.30–3.95 (m, 4′-H/5′-H), 3.52–3.12 (m, 7-CH_2), 0.96/0.92 (t, 7-CH_2CH_3).
(16) Supplementary material.
(17) Cf.: Lönnberg, H.; Lehikoinen, P. *J. Org. Chem.* **1984**, *49*, 4964.
(18) Tomasz, M.; Lipman, R.; Verdine, G.; Nakanishi, K., manuscript in preparation.

(1) Wuest, J. D.; Zacharie, B. *Organometallics* **1985**, *4*, 410–411. Beauchamp, A. L.; Olivier, M. J.; Wuest, J. D.; Zacharie, B. *J. Am. Chem. Soc.*, accepted for publication.
(2) Scheeren, J. W.; Ooms, P. H. J.; Nivard, R. J. F. *Synthesis* **1973**, 149–151.
(3) Prepared in 87% yield from chloride **1** by treatment with aqueous NaOH, followed by neutralization with CF_3COOH.
(4) The structure assigned to this new compound is consistent with its elemental analysis and its IR, NMR, and mass spectra. These data are included in the supplementary material.
(5) (a) All δ (^{199}Hg) are reported in parts per million relative to external neat dimethylmercury. Negative values indicate upfield shifts. (b) The direction of this shift is persuasive evidence of additional coordination to mercury. Kidd, R. G.; Goodfellow, R. J. In "NMR and the Periodic Table"; Harris, R. K., Mann, B. E., Eds.; Academic Press: London, 1978; pp 195–278. (c) Small upfield shifts in the ^{13}C NMR spectra of complexed thioketones are also reported by: Bret, J.-M.; Castan, P.; Commenges, G.; Laurent, J.-P.; Muller, D. *J. Chem. Soc., Chem. Commun.* **1983**, 1273–1275. Burman, S.; Sathyanarayana, D. N. *J. Inorg. Nucl. Chem.* **1981**, *43*, 1189–1192. Olah, G. A.; Nakajima, T.; Prakash, G. K. S. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 811–812.

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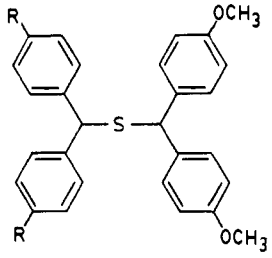
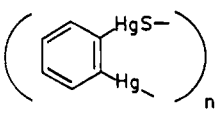
NMR spectrum of trifluoroacetate **4** and at δ 235.1 (CD_3CN) in the ^{13}C NMR spectrum of thioketone **5**[6] shifted to δ −1089[5b] and 228.8.[5c] Other thioketones behaved similarly. We attribute these changes to the formation of complexes containing mercury–sulfur bonds.

The bound thioketones are activated toward nucleophilic attack. For example, when *bidentate* trifluoroacetate **4** (*0.50 equiv*) was stirred with 1-benzyl-1,4-dihydronicotinamide (2.0 equiv)[7] and thioketone **5** (1.0 equiv) in CH_3CN (15 min, 25 °C), *reductive desulfurization occurred*,[8] and bis(4-methoxyphenyl)methane could be isolated in 41% yield. Small amounts (17%) of sulfide **8**[4,9] were also produced, and unreacted thioketone **5** could be



8 (R=OCH_3)

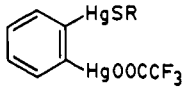
9 (R=H)



10

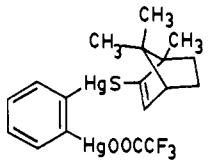
recovered in 26% yield in the form of the corresponding ketone. In addition, an insoluble yellow solid assigned oligomeric structure **10**[12] could be separated by filtration. In sharp contrast, an analogous reduction of thioketone **5** in the presence of *monodentate* phenylmercuric trifluoroacetate (*1.0 equiv*)[13] produced mainly sulfide **8** (71%) and minor amounts (17%) of bis(4-methoxyphenyl)methane. Only in the presence of larger amounts (≥2.0 equiv) of the monodentate acid was thioketone **5** efficiently reduced to the corresponding diarylmethane. Furthermore, no reduction occurred under these conditions when the organomercury trifluoroacetates were absent.[14]

Similar reactions of thioketone **6**[2] and thioxanthone[2] in the presence of equimolar amounts of bidentate acid **4** also led to reductive desulfurization in 66% and 73% yields. However, reductions of other thioketones stopped at the stage of mercuric thiolates. For example, diphenylmethanethione (**7**)[14c,15] and 2-adamantanethione[16a] were reduced to thiolates **11**[4,17a] and **12**[4,17b]



11 (R = $CHPh_2$)

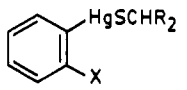
12 (R = 2-adamantyl)



13

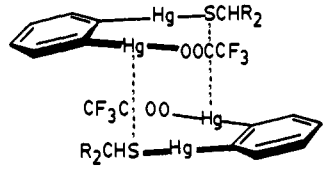
in 75% and 73% yields. Enolizable thioketones were not reduced. For example, (−)-thiocamphor[19] was converted into thiolate **13**[4,17c,20] in 74% yield.

Isolation of mercuric thiolates **11** and **12** suggests that similar compounds, represented by the general structures **14** and **15**, are



14 (X = $HgOOCCF_3$)

15 (X = H)



16

intermediates in the reductive desulfurizations. When the carbon–sulfur bond is sufficiently weak, further reduction to the hydrocarbon R_2CH_2 may occur, or reaction with thiolate may produce the sulfide $R_2CHSCHR_2$. Our observations indicate that intermediate **14** favors reduction, while intermediate **15** favors formation of sulfide. The following experiment shows that this striking difference between the bidentate and monodentate systems is not a consequence of steric factors alone. Reduction of thioketone **5** in the presence of compound **11** (1.0 equiv), which is effectively monodentate but sterically similar to bidentate acid **4**, gave mainly sulfides **8** and **9**[21] and little (21%) bis(4-methoxyphenyl)methane.

We therefore attribute the special reactivity of bound thiolate in intermediate **14** to the presence of an adjacent site of Lewis acidity. This may facilitate binding of the reducing agent, it may favor heterolysis of the carbon–sulfur bond, or it may lead to the formation of aggregates like dimer **16**[22] in which the carbon–sulfur bonds may be selectively activated toward reduction.

These results and other recent work[1,23,24] draw attention to interesting and potentially useful differences between multidentate and monodentate Lewis acids. Our next goal is to develop multidentate thiophiles that can be used catalytically or asymmetrically to activate carbon–sulfur bonds.

Acknowledgment. This work was financially supported by Research Corporation, the Natural Sciences and Engineering

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(9) (a) Bis[bis(4-methoxyphenyl)methyl] sulfide. (b) Independently synthesized from bis[bis(4-methoxyphenyl)methyl] disulfide[14a] by the method of: Harpp, D. N.; Smith, R. A. *Org. Synth.* **1978**, *58*, 138–143. Harpp, D. N.; Gleason, J. G. *J. Am. Chem. Soc.* **1971**, *93*, 2437–2445; or from 4,4′-dimethoxybenzhydryl chloride[10] and 4-methoxy-α-(4-methoxyphenyl)benzenemethanethiol[11] by the method of: Schönberg, A.; Schütz, O.; Nickel, S. *Chem. Ber.* **1928**, *61*, 2175–2177.

(10) Bethell, D.; Gold, V.; Satchell, D. P. N. *J. Chem. Soc.* **1958**, 1918–1926.

(11) (a) Prepared from 4,4-dimethoxybenzhydryl chloride[10] by the general method of: Klenk, M. M.; Suter, C. M.; Archer, S. *J. Am. Chem. Soc.* **1948**, *70*, 3846–3850. (b) For other syntheses, see: Alper, H.; Chan, A. S. K. *J. Am. Chem. Soc.* **1973**, *95*, 4905–4913. Walter, W.; Krohn, J. *Chem. Ber.* **1969**, *102*, 3786–3794.

(12) This material was identical by IR with the product of the reaction of trifluoroacetate **4** with Na_2S.

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(14) Under other conditions, diaryl thioketones are reduced by dihydropyridines to the corresponding disulfides or thiols. (a) Yasui, S.; Nakamura, K.; Ohno, A.; Oka, S. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 196–199. (b) Ohno, A.; Yasui, S.; Nakamura, K.; Oka, S. *Ibid.* **1978**, *51*, 290–293. (c) Abeles, R. H.; Hutton, R. F.; Westheimer, F. H. *J. Am. Chem. Soc.* **1957**, *79*, 712–716.

(15) Gofton, B. F.; Braude, E. A. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. IV, pp 927–928.

(16) (a) Greidanus, J. W. *Can. J. Chem.* **1970**, *48*, 3530–3536. (b) Greidanus, J. W. *Ibid.* **1970**, *48*, 3593–3597.

(17) Independently synthesized by the reaction of trifluoroacetate **4** with equimolar amounts of (a) α-phenylbenzenemethanethiol,[18] (b) 2-adamantanethiol,[16b] or (c) (−)-thiocamphor[19] in CH_2Cl_2.

(18) Klenk, M. M.; Suter, C. M.; Archer, S. *J. Am. Chem. Soc.* **1948**, *70*, 3846–3850.

(19) Prepared by the general method of: Pedersen, B. S.; Scheibye, S.; Nilsson, N. H.; Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 223–228.

(20) For related observations, see: Alper, H.; Marchand, B.; Tanaka, M. *Can. J. Chem.* **1979**, *57*, 598–600.

(21) Independently synthesized from 4,4′-dimethoxybenzhydryl chloride[10] and α-phenylbenzenemethanethiol[18] by the method of: Schönberg, A.; Schütz, O.; Nickel, S. *Chem. Ber.* **1928**, *61*, 2175–2177.

(22) Related structures have been described by: Biscarini, P.; Fusina, L.; Nivellini, G. *Spectrochim. Acta, Part A* **1980**, *36A*, 593–600. Canty, A. J.; Raston, C. L.; White, A. H. *Aust. J. Chem.* **1979**, *32*, 311–320, 1165–1166. Canty, A. J.; Raston, C. L.; White, A. H. *Ibid.* **1978**, *31*, 677–684.

(23) For related work on bifunctional catalysis, see: Hine, J.; Linden, S.-M.; Kanagasabapathy, V. M. *J. Am. Chem. Soc.* **1985**, *107*, 1082–1083.

(24) For references, see: Katz, H. E. *J. Am. Chem. Soc.* **1985**, *107*, 1420–1421.

Research Council of Canada, and le Ministère de l'Éducation du Québec. We are indebted to Robert Mayer and Sylvie Bilodeau for recording our ^{199}Hg and ^{13}C NMR spectra, to Michael J. Evans and Christine Johnson for recording our mass spectra, and to Howard E. Katz for useful suggestions.

Supplementary Material Available: Spectroscopic and analytical data for compounds **4**, **8**, and **11–13** (1 page). Ordering information is given on any current masthead page.

Palladium-Mediated Vicinal Cleavage of Allyl Epoxides with Retention of Stereochemistry: A Cis Hydroxylation Equivalent

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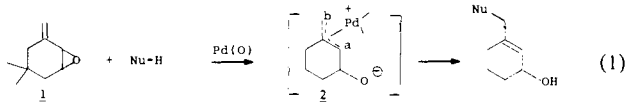
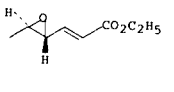
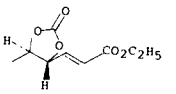
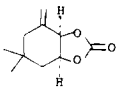
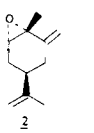
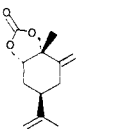
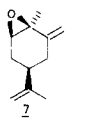
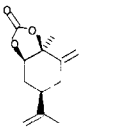
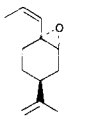
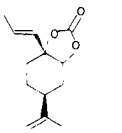
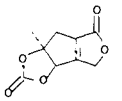
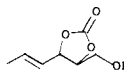
The value of epoxides as synthetic intermediates in complex synthesis has increased dramatically as a result of the ability to control stereochemistry in both a relative and absolute sense.[1] Subsequent transformations rely on the ease of opening epoxides which, of necessity, proceeds with inversion and thus corresponds to a trans addition to the olefin. If epoxides could be opened with retention of configuration to give an equivalent of a cis addition, a practical broadening of the application of these intermediates in synthesis would result. In the case of vinyl epoxides, such as **1**, such a possibility could derive from a metal-promoted opening via **2** (eq 1). However, there is a strong bias in such systems



(1)

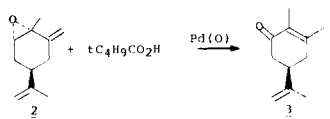
resulting from the presence of the oxygen substituent for a nucleophile to attack distal to that substituent (i.e., at C_b in **2**).[2] The net result is a clean 1,4-addition even in allyl systems of equal substitution or ones in which substitution might be thought to favor proximal attack (corresponding to C_a in **2**) even with carboxylic acids as the reacting partners. Considering oxygen nucleophiles, we are confronted with an additional problem, the product is also an excellent substrate for metal-catalyzed reactions.[3] In this paper we wish to report a practical solution to both of these problems involving carbon dioxide as a carboxylating agent in metal-catalyzed reactions.[4,5] The current great emphasis on diastereoselective methods to form polyol systems makes such a development highly timely.

Table I. Carbonate Synthesis from Vinyl Epoxides[a]

entry	vinyl epoxide	carbonate[b]	yield[c]
1			84%
2			85%
3			92%
4			95%
5			57%
6			82%
7			71%

[a] All reactions were performed according to the general procedure. [b] All new compounds have been fully characterized spectrally and elemental composition established by high-resolution mass spectroscopy or combustion analysis. [c] Yields are for isolated pure products.

The notion to resolve the regioselectivity problem revolves around the question of anchoring a pro-nucleophile to the oxygen of **2** such that the nucleophile would be delivered in an intramolecular fashion to favor proximal attack. Such a capture of the oxygen must be faster than the known hydrogen migrations



(2)

in Pd-mediated reactions.[6] For example, in the case of **2**, using pivalic acid as a pro-nucleophile led only to rearrangement product **3** and no trapping.[7] We envisioned the possibility that a cumulative unsaturated species (carbon dioxide, carbon disulfide, isocyanate, etc.) might be a sufficiently reactive electrophile to capture the alkoxide in **2** and the resulting carboxylate or related

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