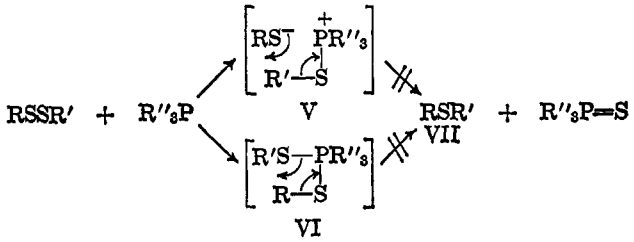
IV

concerted breakdown of a pentacovalent species, VI, are thus ruled out as primary product-determining reaction modes.



VI

R = $CH_2C_6H_4Br$
R′ = $CH_2C_6H_4C_6H_5$
R″ = NEt_2

If either transformation depicted by V or VI were exclusively operating, only sulfide VII would have been observed.[11] Preliminary observations on the kinetics of this reaction have indicated that the mechanism is, however, more complicated than originally anticipated. Work is continuing in this area.

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(12) Author to whom correspondence should be addressed.

David N. Harpp,[12] John G. Gleason
Department of Chemistry, McGill University
Montreal, Quebec, Canada

James P. Snyder
Department of Chemistry, Belfer Graduate School of Science
Yeshiva University, New York, New York 10037

Received April 17, 1968

Radical Reaction of Isocyanide with Organotin Hydride

Sir:

Recently we reported a novel insertion reaction of isocyanide into a silicon–hydrogen linkage by a copper catalyst, a new type of hydrosilation.[1]

$$R_3SiH + R'N{\equiv}C: \longrightarrow R_3SiCH{=}NR' \qquad (1)$$

Attempted copper-catalyzed insertion of isocyanide into the tin–hydrogen linkage of organotin hydrides proved unsuccessful. Instead, we found a new radical reaction of isocyanide with trialkyltin hydride in which trialkyltin (iso)cyanide[2] (I) and the hydrocarbon II were produced in fairly high yields.

$$R_3SnH + R'N{\equiv}C: \longrightarrow \underset{\text{I}}{R_3SnCN} + \underset{\text{II}}{R'H} \qquad (2)$$

Under a nitrogen atmosphere, a mixture of benzyl isocyanide (14.0 mmol), tri-*n*-butyltin hydride (14.0 mmol), and di-*t*-butyl peroxide (6 mol % for isocyanide) was stirred at 120–130° for 8 hr. The reaction mixture, which solidified on cooling at room temperature, was washed with cold ether. The insoluble crystalline solid on recrystallization from ether gave 3.63 g (11.5 mmol, 82%) of tri-*n*-butyltin (iso)cyanide (III), mp 88–89° (lit.[3] 88.5°). *Anal.* Calcd for $C_{13}H_{27}NSn$: C, 49.40; H, 8.61; N, 4.43. Found: C, 49.11; H, 8.80; N, 4.26. The ir spectrum and the glpc retention time of III were identical with those of an authentic sample prepared from tri-*n*-butyltin chloride and potassium cyanide.[4] The ether washings of the cooled reaction mixture were analyzed by glpc and contained 1.25 g (13.6 mmol, 97%) of toluene.

Similarly, the reaction of cyclohexyl isocyanide with tri-*n*-butyltin hydride induced by azobis(isobutyronitrile) in benzene produced III (52%) and cyclohexane (47%).

Reaction 2 requires a free-radical initiator. Heat treatment of a mixture of isocyanide and tri-*n*-butyltin hydride without a radical initiator under nitrogen gradually produced hexa-*n*-butyldistannane. Perhaps isocyanide played the role of a base catalyst for the coupling reaction of trialkyltin hydride.[5] In the radical-initiated reaction of isocyanide with trialkyltin hydride, distannane was formed only in small quantities.

Considering the necessity of a radical initiator and the generally known, high reactivity of organotin hydride toward free radicals,[5] the following scheme may outline the course of reaction.

$$R_3SnH \xrightarrow{\text{free radical}} R_3Sn\cdot$$

$$R_3Sn\cdot + R'N{=}C: \longrightarrow R'N{=}\dot{C}SnR_3 \xrightarrow{\beta\ \text{scission}} R'\cdot + R_3SnCN$$

$$R'\cdot + R_3SnH \longrightarrow R'H + R_3Sn\cdot$$

As to the nature of the radical R′· in the above scheme, the reaction of *t*-butyl isocyanide with tri-*n*-butyltin hydride with the aid of azobis(isobutyronitrile) was examined. In the reaction at the reflux temperature of benzene as solvent for 24 hr the products were isobutane (45% yield) and III (51% yield). Isobutylene was not detected here. This observation has an interesting bearing on the character of the radical reaction of isocyanide.

Detailed mechanistic investigation will be the subject of future studies.

(1) T. Saegusa, Y. Ito, S. Kobayashi, and K. Hirota, *J. Am. Chem. Soc.*, **89**, 2240 (1967).
(2) J. S. Thayer and R. West, *Advan. Organometal. Chem.*, **5**, 183 (1967).
(3) J. Lorberth, *Ber.*, **98**, 1201 (1965).
(4) J. G. A. Luijten and G. J. M. van der Kerk, *J. Appl. Chem.*, **6**, 49 (1956).
(5) Reviewed by H. G. Kuivila, *Advan. Organometal. Chem.*, **1**, 47 (1964).

Takeo Saegusa, Shiro Kobayashi
Yoshihiko Ito, Naohiko Yasuda
Department of Synthetic Chemistry, Faculty of Engineering
Kyoto University, Kyoto, Japan

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Mass Spectrometry of Nucleic Acid Components. Trimethylsilyl Derivatives of Nucleotides, Nucleosides, and Bases[1]

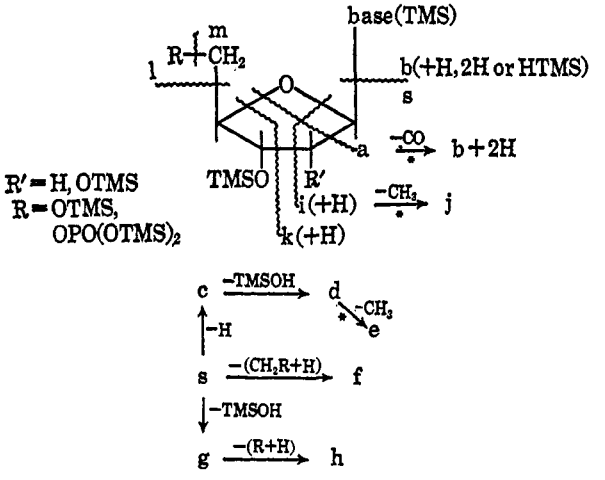
Sir:

Although the potential value of mass spectrometry in the structure elucidation of nucleosides and related

(1) This work was supported by the Robert A. Welch Foundation (Q-125) and the National Institutes of Health (GM 13901), and computer facilities were supported by the National Institutes of Health (FR 254, FR 259).

compounds has clearly been demonstrated,[2] the application of this technique to nucleotides and the more polar nucleosides (*e.g.*, guanosine, cytidine) has been precluded because of their low volatility. We have therefore examined the more volatile trimethylsilyl (TMS) derivatives[3] of these compounds,[4] which permits extension of the inherent structural specificity and sensitivity of mass spectrometry to include all nucleosides and provides the first mass spectra of mononucleotides (Figure 1).[7]

The molecular ion, M, and a characteristic M − 15 (CH_3)[8] are observed in all spectra except the pyrimidine deoxyribosides, where they are usually evident only in spectra recorded on a photographic plate. Structural relationships of the most significant fragment ions from



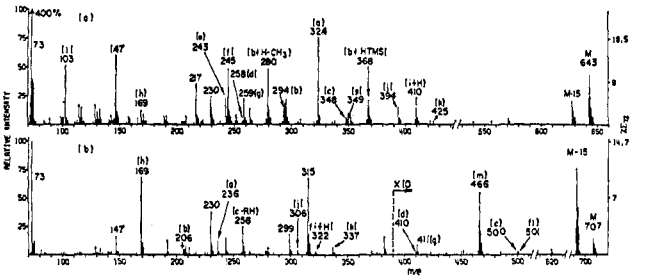


Figure 1. Mass spectra of (a) guanosine-(TMS)$_5$, (b) 5′-AMP-(TMS)$_5$.

5′-nucleotide and nucleoside[9] derivatives are shown below and indicated in Figure 1. Ions b, i, and k usually also occur with rearrangement of hydrogen, while ion a always includes hydrogen abstracted from the ribose skeleton. Ion m is found only in the nucleotide derivatives, which indicates the stability of the radical which is lost to be an influential factor. Ions f and l occur when R = OTMS. As in the free nucleosides,[2a] the considerable charge-stabilizing ability of purine bases results in the dominance of ions containing the base (a, i, k, etc.), while in the pyrimidines greater initial charge localization in the sugar moiety leads to increased prominence of ions f, s, and e. Ions of mass 73, 147, 217 are frequently observed in mass spectra of polysilylated compounds,[6,10] and their occurrence in the present case bears no structural significance. Mass 230 ($C_4H_4(OTMS)_2$) is abundant in most of the ribose derivatives.

Of unusual interest are *m/e* 315 ($C_9H_{23}O_4Si_3P$) and its daughter ion (from elimination of methane) *m/e* 299. The presence of such ions, arising from intramolecular rearrangement of intact TMS groups, underscores the unusual migratory aptitude of the TMS group[11] and becomes an important consideration in the interpretation of spectra of structural unknowns.

These mass spectra permit elucidation of the following basic structural features: (1) molecular weight or elemental composition (from exact mass measurement), determined from M and M − 15 or indirectly from various fragment ions; (2) identification of the base (ions a, b, i, k), including the nature and extent, but not always the position, of substitution; (3) confirmation of the sugar as ribose or 2′- or 3′-deoxyribose (*e.g.*, c, i, k). In addition, *m/e* 81 (h) is abundant in deoxyribose derivatives. Ions a, c, i, and k are structurally important since they permit location of substituents (*e.g.*, methyl groups) bound to either oxygen or carbon of ribose. With l or h they further permit differentiation of the four ribose oxygens, of considerable potential utility for the location and determination of biologically incorporated ^{18}O.

The mass spectrum of a 2′(3′)-AMP-(TMS)$_5$ mixture exhibits peaks i, j, and k, both at the same mass values shown in Figure 1b and shifted upward 152 mass units, the latter in agreement with the presence of a

(2) (a) K. Biemann and J. A. McCloskey, *J. Am. Chem. Soc.*, **84**, 2005 (1962); (b) S. H. Eggers, S. I. Biedron, and A. O. Hawtrey, *Tetrahedron Letters*, 3271 (1966); (c) S. Hanessian, D. C. DeJongh, and J. A. McCloskey, *Biochim. Biophys. Acta*, **117**, 480 (1966); (d) K. Biemann, S. Tsunakawa, J. Sonnenbichler, H. Feldmann, D. Dutting, and H. G. Zachau, *Angew. Chem. Intern. Ed. Engl.*, **5**, 590 (1966); (e) R. H. Hall, M. J. Robins, L. Stasiuk, and R. Thedford, *J. Am. Chem. Soc.*, **88**, 2614 (1966); (f) K. Biemann and P. V. Fennessey, *Chimia*, **21**, 226 (1967); (g) L. Baczynskyj, K. Biemann, and R. H. Hall, *Science*, **159**, 1481 (1968).

(3) (a) T. Hashizume and Y. Sasaki, *Anal. Biochem.*, **15**, 199 (1966); (b) R. L. Hancock, *J. Gas Chrom.*, 363 (1966); (c) Y. Sasaki and T. Hashizume, *Anal. Biochem.*, **16**, 1 (1966); (d) C. W. Gehrke, D. L. Stalling, and D. C. Ruyle, *Biochem. Biophys. Res. Commun.*, **28**, 869 (1967); (e) G. Krishna, *Federation Proc.*, 27, 649 (1968).

(4) Derivatives were prepared (*cf.* ref 3) by heating gently with bis-(trimethylsilyl)acetamide (BSA)[5] and trimethylchlorosilane (TMCS), or BSA-d_{18} and TMCS-d_9.[6] Traces of multiple derivatives were evident in some cases but were readily recognized and did not interfere with interpretation of the spectra. Compounds examined were the four major nucleosides and 5′-monophosphates of RNA and DNA, plus pseudouridine, xanthosine, inosine, 3′-deoxyadenosine, N^6-dimethyladenosine, 1-methyladenosine, 2′-deoxyuridine, 2′-deoxyinosine, cytosine arabinoside, 5-hydroxyuridine, dihydrouridine, 2′(3′)-adenosine monophosphate (2′(3′)-AMP), and 3′,5′-cyclic AMP. Amino groups, enolizable carbonyls, and sugar and phosphate hydroxyls were each monosilylated, except for thymidine, 2′-deoxyuridine, and 5′-cytidine monophosphate (CMP), in which silylation of the base occurred to only a small extent. CMP-(TMS)$_4$ decomposed in the gas chromatographic inlet system of the mass spectrometer but was introduced using the direct inlet probe.

(5) J. F. Klebe, H. Finkbeiner, and D. M. White, *J. Am. Chem. Soc.*, 88, 3390 (1966).

(6) J. A. McCloskey, R. N. Stillwell, and A. M. Lawson, *Anal. Chem.*, 40, 233 (1968).

(7) Mass spectra (70 eV) were obtained with an LKB 9000 gas chromatograph–mass spectrometer (1% SE-30 or 1% OV-17 stationary phases) and a CEC 21-110B high-resolution mass spectrometer using photographic recording and exact mass measurement of the entire mass spectrum.[2f] Interpretations of the spectra are supported by exact mass measurements and deuterium labeling in the TMS groups.[6]

(8) A. G. Sharkey, Jr., R. A. Friedel, and S. H. Langer, *Anal. Chem.*, 29, 770 (1957).

(9) Pseudouridine-(TMS)$_5$ exhibits generally different fragmentation behavior, most notably in the presence of *m/e* 357 (b + CHOTMS).

(10) O. S. Chizhov, N. V. Molodtsov, and N. K. Kochetkov, *Carbohyd. Res.*, 4, 273 (1967).

(11) See, for instance, (a) P. Capella and C. Zorzut, *Anal. Chem.*, 40, 1458 (1968); (b) G. H. Draffan, R. N. Stillwell, and J. A. McCloskey, Sixteenth Annual Conference on Mass Spectrometry and Allied Topics, Pittsburgh, Pa., May 1968.

derivatized phosphate group at C-2′. Ion 1 (*m/e* 103) is also observed, reflecting the absence of the phosphate group at C-5′. Similarly, in 3′,5′-cyclic AMP-(TMS)$_3$,[3e] i, j, and k are unshifted from Figure 1b, while m and l are absent. A peak having no counterpart in 5′-AMP is present at *m/e* 310, due to carbons C-2′ through C-5′ of the ribose skeleton, plus their substituents, including the cyclic phosphate trimethylsilyl ester.

Mass spectra of the TMS derivatives of the bases[3c,d] are simple, consisting mainly of M and M − 15,[12] reflecting the resistance of the aromatic nucleus toward fragmentation.[13] While of little use in a detailed structural sense, their spectra appear well suited for analytical applications.[14]

The uncommon elemental compositions of nucleotide, nucleoside, and base TMS derivatives make their high-resolution mass spectra amenable to computer-based identification techniques. We are currently exploring the direct analysis of nucleic acid hydrolysates in this manner,[15] based on the TMS derivatives described above.

(12) For example, % Σ values for M and M − 15: uracil-(TMS)$_2$, 9, 17; thymine-(TMS)$_2$, 8, 17; cytosine-(TMS)$_2$, 10, 12; adenine-(TMS)$_2$, 9, 30; guanine-(TMS)$_3$, 7, 18.

(13) See, for instance: (a) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, pp 585, 592; (b) J. M. Rice and G. O. Dudek, *J. Am. Chem. Soc.*, **89**, 2719 (1967).

(14) P. M. Krueger and J. A. McCloskey, unpublished experiments.

(15) D. M. Desiderio, N. R. Earle, P. M. Krueger, A. M. Lawson, L. C. Smith, R. N. Stillwell, K. Tsuboyama, J. Wijtvliet, and J. A. McCloskey, Sixteenth Annual Conference on Mass Spectrometry and Allied Topics, Pittsburgh, Pa., May 1968.

(16) Recipient of a Robert A. Welch Foundation Postdoctoral Fellowship.

(17) Postdoctoral fellowship support through the National Institutes of Health (Grant 5 TO1 HE 05703) is gratefully acknowledged.

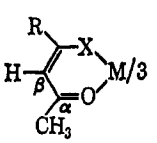
James A. McCloskey, A. M. Lawson[16]
K. Tsuboyama, P. M. Krueger,[17] R. N. Stillwell
Institute for Lipid Research and Department of Biochemistry
Baylor University College of Medicine, Houston, Texas 77025
Received April 19, 1968

Comparative Stereochemical Effects of Sulfur and Oxygen Donor Atoms in Four- and Six-Coordinate Metal Complexes

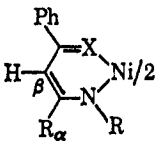
Sir:

In complexes of potentially variable stereochemistry, observations from a rapidly growing body of evidence indicate that unsaturated, sulfur-containing, chelating ligands may induce preferential stability of structures which are either unusual or of widespread occurrence. Pertinent examples include the planar structures of bis-dithiolene complexes with a variety of metal ions and the trigonal prismatic structures of certain trisdithiolenes.[1] Particular stereochemical consequences of sulfur donor atoms are most clearly recognized and assessed by structural comparisons with complexes identical in constitution except for the donor atom sets. Here are presented two structural comparisons: one of a qualitative nature for six-coordinate complexes (**1**), and the other quantitative for four-coordinate complexes (**2**), which reveal the relative stereochemical effects of sulfur *vs.* oxygen donor atoms.

(1) A. L. Balch, I. G. Dance, and R. H. Holm, *J. Am. Chem. Soc.*, 90, 1139 (1968), and references therein; J. A. McCleverty, *Progr. Inorg. Chem.*, in press.



1, M = Co, V; X = O, S



2, Ni(RPhHR$_\alpha$)$_2$; X = O
Ni(RSPhHR$_\alpha$)$_2$; X = S

cis (facial) and *trans* (meridianal) isomers are possible for complexes **1** with X = O, R ≠ CH$_3$,[2,3] or X = S. Equilibrium constants for the *trans* ⇌ *cis* reaction of tris(β-diketonato)metal(III) complexes are considerably less than statistical,[2] indicating preferential stability of the *trans* form. In sharp contrast, pmr studies of tris(β-thioketonato)cobalt(III) complexes ($CDCl_3$, ~30°) reveal *exclusive population of the cis isomer* for species with R = CH$_3$,[4] Ph, *i*-Pr, *t*-Bu; one α-CH$_3$ or β-H signal is observed consistent with C_3 (or C_{3v}) symmetry. Similarly, only the *cis* isomer was detectable in an analogous series of V(III) complexes (R = CH$_3$, Ph, *i*-Pr) whose lability ensures equilibrium isomer distributions and whose large contact shifts minimize the possibility of accidental chemical shift degeneracy and an incorrect structural assignment.[3,5] Chemical shift data for a typical pair of tris(β-thioketonates) (R = Ph) are the following: α-CH$_3$, −141, −4193; β-H, −395, −3507 cps (Co(III), V(III), TMS reference). Heating the thio V(III) complex with R = *i*-Pr in $CDCl_3$ for 24 hr at 118° produced no *trans* rearrangement. Preferential *cis* stability may arise in part from nonbonded S···S interactions in the S_3 unit, similar to those which may assist stabilization of trigonal prismatic coordination.[6]

The dynamic planar ⇌ tetrahedral equilibrium has been demonstrated for Ni(R–PhHR$_\alpha$)$_2$ (R$_\alpha$ = H, CH$_3$) in noncoordinating solvents and thermodynamic data derived from analysis of the temperature dependence of the contact shifts.[7-9] Analogous thio complexes (R$_\alpha$ = H), an unexplored group of compounds,[10] were prepared by nonaqueous chelation[7] employing β-aminothiones obtained by the reaction[11] of 3-phenyl-1,2-dithiolium perchlorate[12] with primary amines. For Ni(*t*-Bu–SPhHH)$_2$ close correspondence of solution (3.18 BM, $CHCl_3$) and solid-phase (3.20 BM) magnetic moments indicates that, like Ni(*t*-Bu–PhHH)$_2$,[9] the mole fraction of tetrahedral form (N_t) is equal to 1 in solution. For both, $-\Delta F^{300°} > 2.8$ kcal/mole and no sterochemical differences are observable. However, for the pairs Ni(R–SPhHH)$_2$–Ni(R–PhHH)$_2$, R = Amp (CH_3CHCH_2Ph), *sec*-Bu, the equilibrium positions in carbon tetrachloride or chloroform solution are such that detectable amounts of both stereoisomers of all

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(3) F. Röhrscheid, R. E. Ernst, and R. H. Holm, *Inorg. Chem.*, **6**, 1315 (1967).

(4) See also A. Yokoyama, S. Kawanishi, M. Chikuma, and H. Tanaka, *Chem. Pharm. Bull.* (Tokyo), **15**, 540 (1967).

(5) F. Röhrscheid, R. E. Ernst, and R. H. Holm, *Inorg. Chem.*, **6**, 1607 (1967); *J. Am. Chem. Soc.*, **89**, 6472 (1967).

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