(*R*,*S*)-BPPFA. See also: S. Tanimori, M. Kirihata, *Tetrahedron Lett.* **2000**, *41*, 6785.

[8] The formation of an olefin – L_nPd^0 complex after the reaction between an allylpalladium complex and sodium malonate has been demonstrated; see ref. [4b].

[9] Taking advantage of the different reactivity, selective monosubstitution of **1** has been reported when using $[Pd(PPh_3)_4]$: a) Y. Tanigawa, K. Nishimura, A. Kawasaki, S.-i. Murahashi, *Tetrahedron Lett.* **1982**, *23*, 5549; b) J. P. Genêt, M. Balabane, J. E. Bäckvall, J. E. Nyström, *Tetrahedron Lett.* **1983**, *24*, 2745; c) the slow oxidative addition of **5a** to L_nPd^0 was also utilized to introduce two kinds of nucleophiles onto **1** in a one-pot synthesis; see ref. [9a].

[10] P. Manaresi, A. Munari in *Comprehensive Polymer Science*, *Vol. 5* (Eds.: Sir G. Allen, J. C. Bevington), Pergamon, Oxford, **1989**, p. 21; average degree of polymerization using two monomers, A and B, $(DP) = (1+r)/(1-r)$; $r = [A]_0/[B]_0$, $r < 1$.

[11] Based on our mechanism, stoichiometric ratios should not affect DPs. The decreasing DPs might be caused by the lower selectivity in the presence of excess **1**, which accelerates the olefin – ligand exchange of **7**.

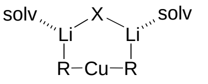
[12] a) W. Koch, W. Risse, W. Heitz, *Makromol. Chem. Suppl.* **1985**, *12*, 105; b) N. Kihara, S.-i. Komatsu, T. Takata, T. Endo, *Macromolecules* **1999**, *32*, 4776.

[13] For reviews on heterogeneous carbon–heteroatom bond-forming polycondensation out of stoichiometric control, see: a) V. Percec, *ACS Symp. Ser.* **1987**, *326*, 96; b) S. Boileau in *New Methods for Polymer Synthesis* (Ed.: W. J. Mijs), Plenum, New York, **1992**, p. 179.

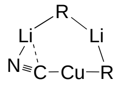
Kinetic Reactivity of “Higher Order Cuprates” in S_N2 Alkylation Reactions[**]

Eiichi Nakamura,* Masahiro Yamanaka,
Naohiko Yoshikai, and Seiji Mori

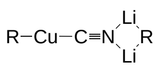
Among a variety of organocopper reagents,[1] “higher order” cyanocuprates have attracted much interest in the past years.[2] Lipshutz originally offered this reagent to the synthetic society as a highly reactive substitute for the classical Gilman reagent, **1a** (denoted hereafter as series **a** (R = Me) throughout the text).[3] The high reactivity was ascribed to a dianionic tricoordinated copper(I) structure,[4] but this structure was soon challenged by Bertz.[5] The structural debate ended recently and it was concluded that the Lipshutz reagent is not the tricoordinated species, but **1b** (denoted hereafter as series **b** throughout the text).[6–8] The latter structure is essentially the same as that of the classical Gilman reagent **1a** except that the bridging group (X) in the Lipshutz reagent is a cyanide group instead of the $[RCuR]^-$ group, with which the Gilman reagent forms a dimeric copper structure.[9] The Lipshutz reagent is therefore no more than a “lower order” cuprate, yet the fact still remains that it is often a more powerful nucleophile than a normal Gilman reagent. For instance, the Lipshutz reagent is the reagent of choice for S_N2 reactions, in which the Gilman and other lower order cuprates are far less reactive.[10] Furthermore, the Lipshutz reagent shows some unusual reactivity, which suggests that a minute amount of alkyllithium is generated in equilibrium with the major $[R_2Cu]^-$ species.[11] Thus the kinetic reactivity of the Lipshutz reagent is still an open question. We report herein density-functional studies on the S_N2 reaction of MeBr with the Lipshutz reagent **1b**, which suggest that **1b** could indeed be much more reactive than the Gilman reagent **1a**. The higher reactivity of **1b** has been ascribed both to the higher Lewis acidity of the $[LiCNLi]^+$ group, and to the energetically favorable structural change of the $[LiCNLi]^+$ moiety in the transition state (TS) of the reaction of **1b**. The studies also suggest that minor structural isomers of the Lipshutz reagent, **1c** and **1d**, might play a role in solution chemistry despite their low equilibrium concentration.[8]



1a: X = $[RCuR]^-$
1b: X = CN^-

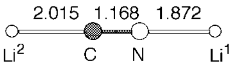


1c

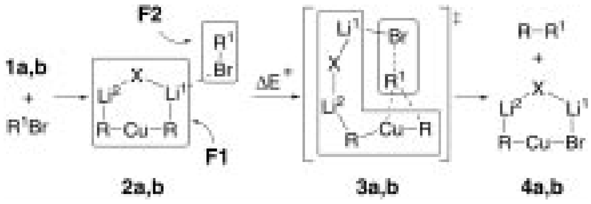


1d

(solv = none or Me_2O)



Previous studies have shown that the rate-determining step of the S_N2 reaction of the lithium organocuprate with MeBr is the C–Br bond cleavage stage (**3a**, **b**, Scheme 1), from which the potential surface goes steeply downhill to the alkylation product.[12, 13] The energy profile of the bromide displacement in series **a** and **b**, and the 3D structures of the stationary points are shown in Figures 1 and 2.[14a] As shown in Figure 1, the activation energy from the initial coordination complex (CP, **2b**) to the displacement TS (**3b**) for the major species of the Lipshutz reagent **1b** is 3.8 kcal mol⁻¹ smaller than that for the Gilman dimer **1a**.[15, 16]



Scheme 1. Substitution reaction between $R_2CuLi \cdot LiX$ (R = Me, series **a**: X = RCuR, series **b**: X = CN) and R^1Br (R^1 = Me).

Where is the origin of this small but finite difference in the activation energies between series **a** and **b**? The answer to this question was probed by fragment energy analysis[17] (Scheme 1 and Table 1) through the dissection of the CPs

---

[*] Prof. Dr. E. Nakamura, Dr. M. Yamanaka, N. Yoshikai, Dr. S. Mori[+]
Department of Chemistry, The University of Tokyo
Bunkyo-ku, Tokyo 113-0033 (Japan)
Fax: (+81) 3-5800-6889
E-mail: nakamura@chem.s.u-tokyo.ac.jp

[+] Present address:
Department of Environmental Sciences, Ibaraki University
Mito 310-8512 (Japan)

[**] We thank Prof. A. Alexakis and Prof. B. Breit for providing unpublished results.[11] Generous allotment of computer time from the Institute of Molecular Science and the Intelligent Modeling Laboratories, the University of Tokyo, is gratefully acknowledged.

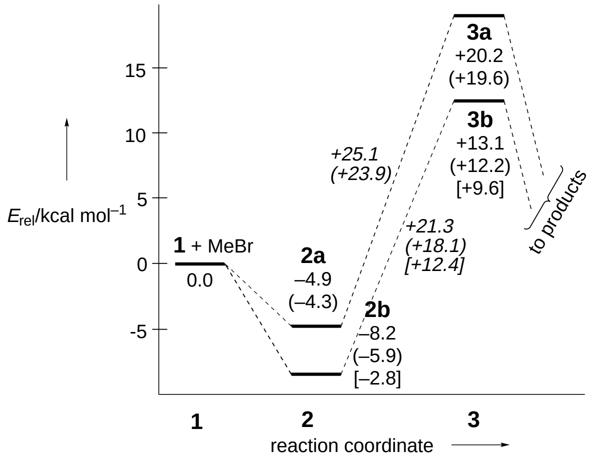


Figure 1. Energy profile of the S_N2 reaction of MeBr with the Gilman reagent (series **a**) or the Lipshutz reagent (series **b**). The potential energies of **1**+MeBr in series **a** and **b** are set to zero. The italicized numbers are the activation energies, in parentheses are the results of single point energy calculations with the self-consistent reaction field (SCRF) method based on the polarized continuum model (PCM, $\varepsilon = 4.335$ for Et_2O) at the gas-phase geometries, and in brackets are the energies for the model species **1b** bearing a Me_2O molecule on each lithium atom.

Table 1. Deformation (DEF) and interaction energies (INT) which compose the activation energy ($\Delta E^{\neq}$). See Scheme 1 for definition of **F1** and **F2**.

	Series **a**	Series **b**
INT_{CP}	– 6.9	– 9.2
INT_{TS}	– 34.2	– 37.6
DEF_{F1}	38.4	34.2
DEF_{F2}	13.9	15.5
INT_{total}[a]	– 27.3	– 28.4
DEF_{total}[b]	52.3	49.7
$\Delta E^{\neq}$[c]	25.1	21.3

[a] $INT_{total} = INT_{TS} - INT_{CP}$. [b] $DEF_{total} = DEF_{F1} + DEF_{F2}$. [c] $\Delta E^{\neq} = INT_{total} + DEF_{total}$.

and the TSs into two fragments (with a fixed geometry at the original stationary points), **F1** (lithium cuprate cluster) and **F2** (MeBr). The origin of the smaller activation energy in series **b** than in series **a** has been traced back to the higher Lewis acidity of the Li^1 atom and the preference of the $[LiCNLi]^+$ moiety to be linear as is the case in **3b**.

Thus, in the initial coordination complexes (**2a** and **2b**), the cuprate cluster fragment (**F1**) and the MeBr fragment (**F2**) interact more strongly in series **b** ($INT_{CP} = -9.2$ kcal mol^{-1}) than in series **a** (-6.9 kcal mol^{-1}), which is corroborated by the shorter Li^1–Br distance (2.73 vs 2.77 Å, Figure 2). The stronger interaction of **F1** and **F2** in **2b** can be attributed to the larger positive charge of Li^1 atom ($+0.80$) than that in **2a** ($+0.76$). Similarly, the interaction energy between **F1** and **F2** (INT_{TS}) is larger in **3b** (-37.6 kcal mol^{-1}) than in **3a** (-34.2 kcal mol^{-1}) owing to larger electrostatic interactions between the Li^1 atom ($+0.86$) and the Br atom (-0.41) in **3b**. The natural charges of these atoms[18] in **3a** are much smaller ($+0.81$ and -0.38, respectively). The positive charges of the lithium atom in series **b** are larger than those in series **a** both for the CP and the TS because of the attachment of the Li^1 atom to the electronegative CN^- group instead of the $[MeCuMe]^-$ group.

The propensity of the $[LiCNLi]^+$ moiety for the near-linear geometry in **3b** rather than for the bent geometry in **2b** is another factor that contributes to the lower activation energy in series **b**. The deformation of **F1** upon going from **2b** to **3b** ($DEF_{F1} = 34.2$ kcal mol^{-1}) is much easier than that from **2a** to **3a** ($DEF_{F1} = 38.4$ kcal mol^{-1}). Further dissection of **F1** into $[MeCuMe]^-$ and $[LiXLi]^+$ fragments (data not shown) revealed that this difference is mainly a result of the energy gained from stretching the bent $[LiCNLi]^+$ moiety in **2b** to the near linear geometry in **3b** (14.3 kcal mol^{-1} gain; the $[MeCuMe]^-$ fragments in series **a** and **b** are essentially identical to each other, and hence do not contribute

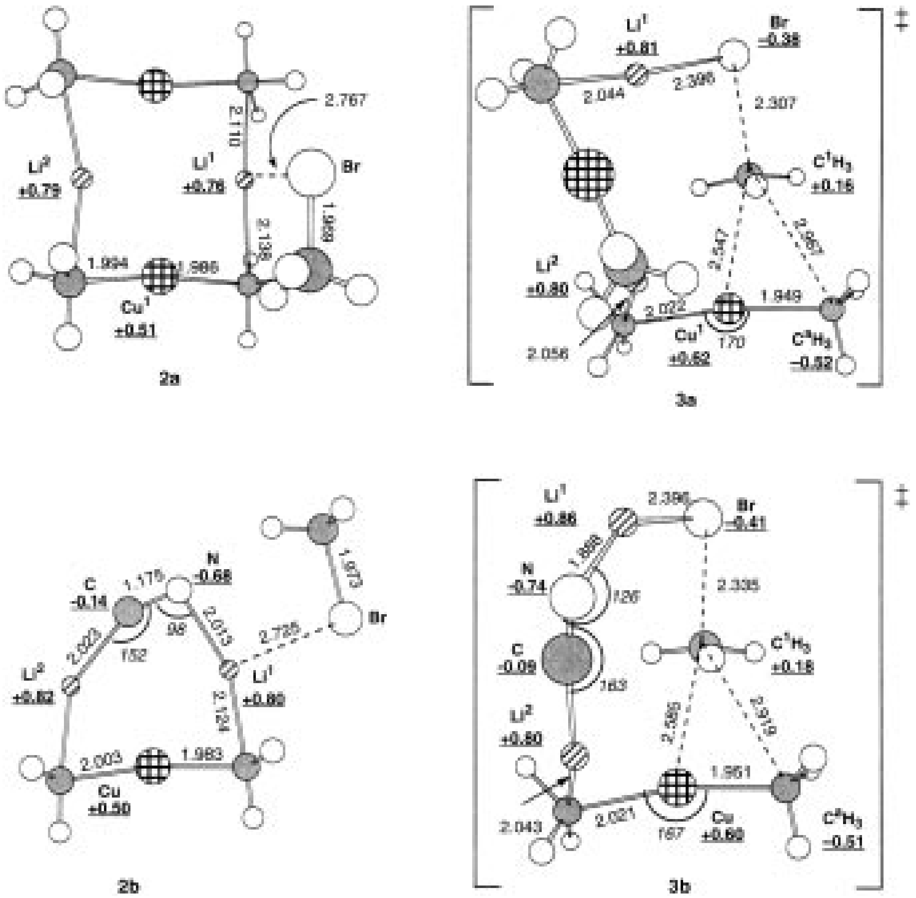


Figure 2. The 3D structures of CP and TS in series **a** and **b**, optimized at the B3LYP/631A level, with the bond lengths in Å, bond angles (italics) in degrees, and natural charges (underlined and bold). The imaginary frequencies of **3a** and **3b** are 224.0i cm^{-1} and 220.6i cm^{-1}, respectively.

much to DEF_{F1}).[19] Thus, the overall sum of the deformation energies (DEF_{total}) becomes 2.6 kcal mol^{-1} smaller in series **b** (49.7 kcal mol^{-1}) than in series **a** (52.3 kcal mol^{-1}), contributing to the smaller activation energy in series **b**.

The minor isomers of the Lipshutz reagent seem to play a role in synthetic reactions (see above).[11] Although isomer **1c** has been calculated to be much less stable than **1b** (hence not experimentally observable),[8] a model study of S_N2 reaction (Figure 3) suggests that there is a possibility that **1c** may take part in the C–C bond forming reactions of the Lipshutz reagent. The activation energy of **1c** (14.6 kcal mol^{-1}) is far smaller than that of **1b** (21.3 kcal mol^{-1}),[14b, 20] and thus **3c** is quite close in energy to **3b**.

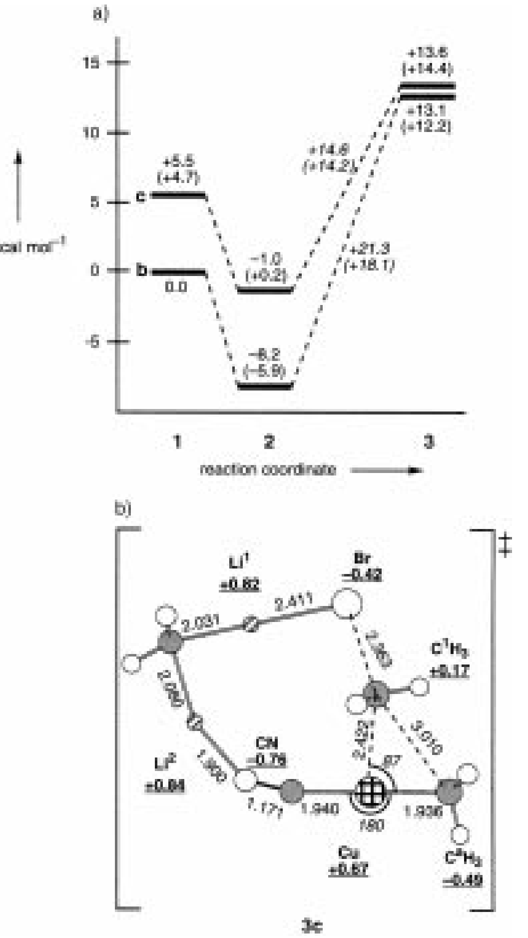
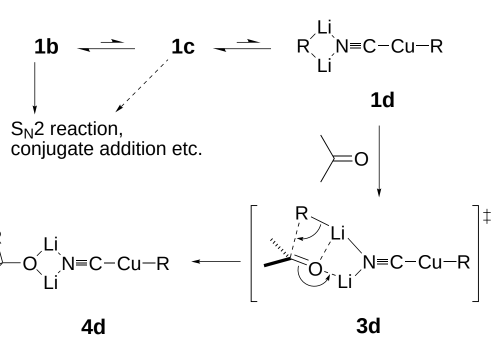


Figure 3. a) The S_N2 reaction energy profile of the minor Lipshutz reagent **1c**. The energy of **1b**+MeBr is taken as the reference. The italicized numbers are the activation energies, and results of single point energy calculations (in parentheses) were obtained by using the same method as noted in Figure 1. b) 3D structure of **3c** optimized at the B3LYP/631A level. The imaginary frequency of **3c** is 238.3*i* cm^{-1}.

The positive Gilman test of the Lipshutz reagent strongly suggests that RLi species are generated in solution.[11] Whereas the species that reacts with Michler's ketone could be **1c**, it would more likely be **1d**,[21] which would easily form from **1c** through the reorganization of the ionic bonds around the lithium atoms. Isomer **1d** is ideally disposed to undergo addition to a ketone through a six-centered TS typical for an alkyllithium reagent.[22] Scheme 2 summarizes possible pathways for the major and the minor reactions that the Lipshutz reagents undergo in synthetic applications.



Scheme 2. Alkylcopper(I)-like and alkyllithium-like reaction pathways of the Lipshutz reagent (solvent molecules on the lithium atoms are omitted).

In summary, the higher reactivity of the Lipshutz reagent than the Gilman reagent in the S_N2 alkylation has been ascribed to the structural and electronic effects of the bridging cyanide moiety coordinated to the two lithium cations. The present study provides an additional example of the important role of the $[LiXLi]^+$ bridging moiety in the chemistry of lithium organocuprates. This bridging moiety has recently identified in various reactions of such cuprates.[23] Furthermore, the studies provide a heuristic example of the kinetic importance of minor species in the reactions of organometallic clusters.[2b, 7a, 24]

Received: December 6, 2000 [Z16233]

---

[1] a) E. Nakamura, S. Mori, *Angew. Chem.* **2000**, *112*, 3902–3924; *Angew. Chem. Int. Ed.* **2000**, *39*, 3750–3771; b) B. H. Lipshutz, S. Sengupta, *Org. React.* **1992**, *41*, 135–631; c) *Organocopper Reagents* (Ed.: R. J. K. Taylor), Oxford University Press, Oxford, **1994**; d) B. H. Lipshutz in *Comprehensive Organometallic Chemistry II, Vol. 12* (Eds.: E. W. Abel, F. G. A. Stone, G. Wilkinson), Pergamon, Oxford, **1995**, pp. 59–130; e) N. Krause, A. Gerold, *Angew. Chem.* **1997**, *109*, 194–213; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 186–204; f) Y. Ibuka, Y. Yamamoto, *Synlett* **1992**, 769–777.

[2] a) B. H. Lipshutz, *Synlett* **1990**, 119–128; b) N. Krause, *Angew. Chem.* **1999**, *111*, 83–85; *Angew. Chem. Int. Ed.* **1999**, *38*, 79–81, and references therein.

[3] B. H. Lipshutz, R. S. Wilhelm, D. M. Floyd, *J. Am. Chem. Soc.* **1981**, *103*, 7672–7674.

[4] For a true higher order cuprate structure, see: M. M. Olmstead, P. P. Power, *J. Am. Chem. Soc.* **1989**, *111*, 4135–4136.

[5] S. H. Bertz, *J. Am. Chem. Soc.* **1990**, *112*, 4031–4032.

[6] a) S. H. Bertz, K. Nilsson, Ö. Davidsson, J. P. Snyder, *Angew. Chem.* **1998**, *110*, 327–331; *Angew. Chem. Int. Ed.* **1998**, *37*, 314–317; T. A. Mobley, F. Müller, S. Berger, *J. Am. Chem. Soc.* **1998**, *120*, 1333–1334; b) G. Boche, F. Bosold, M. Marsch, K. Harms, *Angew. Chem.* **1998**, *110*, 1779–1781; *Angew. Chem. Int. Ed.* **1998**, *37*, 1684–1686; C. M. P. Kronenburg, J. T. B. H. Jastrzebski, A. L. Spek, G. van Koten, *J. Am. Chem. Soc.* **1998**, *120*, 9688–9689.

[7] a) A. Gerold, J. T. B. H. Jastrzebski, C. M. P. Kronenburg, N. Krause, G. van Koten, *Angew. Chem.* **1997**, *109*, 778–780; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 755–757; b) H. Huang, C. H. Liang, J. E. Penner-Hahn, *Angew. Chem.* **1998**, *110*, 1628–1630; *Angew. Chem. Int. Ed.* **1998**, *37*, 1564–1566.

[8] Energetically disfavored **1c** may exist, but have not yet been experimentally identified; T. L. Stemmler, T. M. Barnhart, J. E. Penner-Hahn, C. E. Tucker, P. Knochel, M. Böhme, G. Frenking, *J. Am. Chem. Soc.* **1995**, *117*, 12489–12497.

[9] Cf. R. M. Gschwind, P. R. Rajamohanan, M. John, G. Boche, *Organometallics* **2000**, *19*, 2868–2873.

[10] Cf. C. M. P. Kronenburg, J. T. B. H. Jastrzebski, G. van Koten, *Polyhedron* **2000**, *19*, 553–555.

[11] The Lipshutz reagent gives a positive result in the Gilman test (i.e., reactive toward a diaryl ketone), is basic enough to deprotonate acetylenic protons (results by Alexakis and co-workers), and tends to undergo a 1,2-addition to the carbonyl group of α,β-unsaturated esters, whereas normal Gilman reagents undergo a smooth 1,4-addition (results by Breit and co-workers). We thank Prof. Alexakis and Prof. Breit for the unpublished data.

[12] a) E. Nakamura, S. Mori, K. Morokuma, *J. Am. Chem. Soc.* **1998**, *120*, 8273–8274; b) S. Mori, E. Nakamura, K. Morokuma, *J. Am. Chem. Soc.* **2000**, *122*, 7294–7307.

[13] Computational studies were performed in the same manner as described in ref. [12] by using a Gaussian 98 package: Gaussian 98, Revision A.7, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Lui, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh, PA, **1998**. All structures were optimized at the B3LYP/631A level (see ref. [12]) without symmetry assumption, and adequately characterized by normal coordinate analysis.

[14] a) Two different pathways, one of which proceeds by means of Li^1–R cleavage and the other by means of Li^2–R cleavage, are possible for **1b**. Only the former pathway is discussed here, since the energy profile of the latter was found to be essentially the same as that of the former. b) An isomer of **1c**, in which the CN group is oriented in the opposite direction, was also considered and was found to be energetically less favorable.

[15] The activation energies in series **a** and **b** calculated at the MP2/631A//B3LYP/631A level are 34.5 kcal mol^{-1} for series **a** and 30.9 kcal mol^{-1} for series **b**. Hence, the difference is 3.6 kcal mol^{-1}.

[16] This trend also holds when the solvent polarity and explicit solvent molecules (one Me_2O on each Li atom) are considered (Figure 1). The solvation of the Cu atom only takes place after the TS of the bromide displacement in which copper(I) becomes copper(III), and hence was not considered in the present discussion (see ref. [12a]).

[17] E. Nakamura, M. Nakamura, Y. Miyachi, N. Koga, K. Morokuma, *J. Am. Chem. Soc.* **1993**, *115*, 99–106.

[18] A. E. Reed, L. A. Curtiss, F. Weinhold, *Chem. Rev.* **1988**, *88*, 899–926.

[19] A full optimization of the $[LiCNLi]^+$ moiety in **1b** afforded the structure below, with an energy gain of 22.6 kcal mol^{-1}. Such a linear geometry is found in many crystal structures of lithium cyanide compounds (see ref. [6b]).

[20] As in series **b**, the very small activation energy can be ascribed to the near-linear geometry of Li–NC moiety in **3c** (Figure 3b).

[21] A structure related to **1d** has been determined in crystals: C.-S. Hwang, P. P. Power, *J. Am. Chem. Soc.* **1998**, *120*, 6409–6410.

[22] M. Nakamura, E. Nakamura, N. Koga, K. Morokuma, *J. Am. Chem. Soc.* **1993**, *115*, 11016–11017.

[23] E. Nakamura, M. Yamanaka, *J. Am. Chem. Soc.* **1999**, *121*, 8941–8942; E. Nakamura, M. Yamanaka, S. Mori, *J. Am. Chem. Soc.* **2000**, *122*, 1826–1827.

[24] E. Nakamura, A. Hirai, M. Nakamura, *J. Am. Chem. Soc.* **1998**, *120*, 5844–5845.

Ionization of O_3 in Excess N_2: A New Route to N_2O via Intermediate $N_2O_3^+$ Complexes[**]

Fulvio Cacace, Giulia de Petris,[*] Marzio Rosi, and Anna Troiani

The environmental impact of N_2O, the major source of stratospheric NO_x oxides responsible for ozone depletion, and a harmful greenhouse gas,[1–3] accounts for the active search of formation processes[4, 5] other than microbiological soil denitrification.[6] Inspired by the increasing recognition of the role played by ionic processes in the atmosphere[7] and by the ability of O_3^+ to transfer oxygen atoms to simple molecules,[8–10] we focused this study on the ionization of O_3 diluted in N_2 as a new route to atmospheric N_2O. Experiments based on Fourier-transform ion cyclotron resonance (FT-ICR) mass spectrometry were performed, utilizing an instrument equipped with an external chemical ionization (CI) ion source, fed with an O_3/O_2 mixture. The ions formed were driven into the resonance cell, maintained at 300 K, where the $^{16}O_3^+$ ions, m/z 47.9847, were isolated by removing all other ions by "soft" RF pulses, and allowed to react with N_2, continuously admitted into the cell to reach stationary pressures ranging from 10^{-8} to 10^{-7} Torr. The results positively demonstrated the formation of N_2O^+ and O_2^+ as the primary reaction products [Eqs. (1) and (2)], through processes exothermic by 4.2 and 22.9 kcal mol^{-1}, respectively.[11]

$$O_3^+ + N_2 \rightarrow N_2O^+ + O_2 \quad (1)$$

$$O_3^+ + N_2 \rightarrow N_2O + O_2^+ \quad (2)$$

Although the nature of the experiments prevented accurate kinetic measurements,[12] we could roughly estimate $k_1 \sim 1.4 \times 10^{-11}$ and $k_2 \sim 1.6 \times 10^{-10}$ cm^{3}s^{-1}. In any case, accurate kinetic measurements were outside the scope of the experiments, whose primary goal was to exploit the unique ability of FT-ICR spectrometry to establish a parent–daughter relationship between charged species, and hence to ascertain the reaction(s) responsible for the formation of the product of interest, N_2O^+. Next, CI experiments of N_2/O_3 mixtures, of composition adjusted to obtain the maximum reaction extent (roughly 5 mol% O_3), were performed at 373 K, 0.01–0.1 Torr. All experiments were carried out in duplicate, utilizing either $^{14}N_2$ or $^{15}N_2$ as a convenient way to simplify

---

[*] Prof. Dr. G. de Petris, Prof. Dr. F. Cacace, Dr. A. Troiani
Dipartimento di Studi di Chimica e Tecnologia delle Sostanze Biologicamente Attive
Università di Roma "La Sapienza"
P. le Aldo Moro, 5, 00185 Roma (Italy)
Fax: (+39) 6-4991-3602
E-mail: giulia.depetris@uniroma1.it

Prof. Dr. M. Rosi
CSCISM, Dipartimento di Chimica
Università di Perugia
Via Elce di Sotto, 8, 06123 Perugia (Italy)

[**] This work was supported by the University of Rome "La Sapienza", the University of Perugia, the Italian National Research Council (CNR), and the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST). The authors are grateful for the skilled help of F. Angelelli and A. Di Marzio.