On the Absence of Lithium-6–Lithium-7 Spin–Spin Coupling in Alkyllithium Compounds[1]

Sir:

The results of the preceding communication by McKeever, Waack, Doran, and Baker[2] prompt us to report results relating to the absence of observable ^{6}Li–^{7}Li scalar coupling in alkyllithium compounds.

Methyllithium was prepared as previously described[3] from normal abundance lithium metal and from 96% ^{6}Li metal. An ether solution containing methyllithium with about 50% abundance ^{6}Li was prepared by mixing appropriate quantities of the two methyllithium solutions. The ^{7}Li spectrum of the resulting solution was examined in the temperature region corresponding to slow intermolecular exchange, below −60°. The ^{7}Li appeared as a single line with essentially the same width as reported previously[3] for a normal abundance ^{7}Li sample. This result indicates that scalar coupling between ^{6}Li and ^{7}Li must be on the order of perhaps 0.3 Hz or less.

A similar experiment involving about 38% abundance ^{6}Li was performed on *t*-butyllithium in cyclopentane solvent. Again, no evidence of ^{7}Li–^{6}Li scalar coupling was observed; the line width observed is essentially the same as for a sample containing 99.2% abundance ^{7}Li.

It should be emphasized that, since ^{7}Li, which has the larger quadrupole moment of the two nuclei, appears as a relatively sharp resonance, decoupling of the spins through a rapid relaxation of the Li spin states is not involved. The results indicate that the scalar coupling between lithium spins in the alkyllithium tetramers is very small.

It is difficult to estimate what the ^{6}Li–^{7}Li coupling might be for a pair of singly bonded lithium atoms, but a crude indication can be obtained[4,5] from a comparison of the quantity $J = \tau\gamma_{N}\gamma_{N'}[\phi_{N}(0)]^{4}/\Delta E$ for ^{6}Li–^{7}Li, as compared with H_2. The coupling in H_2 is evaluated as 278 Hz from the value observed in HD. Assuming that ΔE for the Li_2 system is about 0.25 that for H_2, and inserting the appropriate γ's, $J(^{6}\text{Li}–^{7}\text{Li})/J(H_2) \approx 0.25 \times [\phi_{Li}(0)]^{4}/[\phi_{H}(0)]^{4}$. The contact charge densities cannot be estimated with any reliability for the molecular case, even when reliable atomic wave-function data are available. Mixing of core (1s) orbitals of Li in the valence-shell molecular orbitals, in particular, would greatly increase $[\phi_{Li}(0)]^{2}$. Accordingly the ratio of coupling constants could be as small as 0.01, or as large as perhaps 0.25. An estimate of about 10 Hz for $J(^{6}\text{Li}–^{7}\text{Li})$ seems reasonable.[6] *The results indicate that the effective metal–metal bond order may be near zero, despite a close Li–Li distance*[7,8] *of 2.5–2.6 Å, as compared with 2.67 Å in* Li_2.[9] Presumably most of the bonding charge distribution in the alkyllithium tetramer lies in the region about the bridging alkyl carbon. There is apparently sufficient covalency, however, to give rise to a scalar ^{7}Li–^{13}C interaction, as reported in the previous communication.[2]

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[1] This research is sponsored by the National Science Foundation.

[2] L. D. McKeever, R. Waack, M. A. Doran, and E. B. Baker, *J. Am. Chem. Soc.*, **90**, 3244 (1968).

[3] L. M. Seitz and T. L. Brown, *ibid.*, **88**, 2174 (1966).

[4] H. M. McConnell, *J. Chem. Phys.*, **24**, 460 (1956).

[5] M. Barfield and D. M. Grant, *Advan. Magnetic Resonance*, **2**, 149 (1965).

[6] The appreciable value seen for the ^{7}Li–^{13}C coupling,[2] in a bond which is no doubt highly polar, is consistent with the magnitude of contact charge density from the valence orbitals which is implied in this estimate.

[7] H. Dietrich, *Acta Cryst.*, **16**, 681 (1963).

[8] E. Weiss and E. A. C. Lucken, *J. Organometal. Chem.* (Amsterdam), **2**, 197 (1964).

[9] Although the Li–Li distance observed in the solid may be different in the tetrameric solution species, a slight increase in this quantity would not seriously alter the coupling constant.

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Total Synthesis of Prostaglandins. Synthesis of the Pure *dl*-E_1, -$F_{1\alpha}$, -$F_{1\beta}$, -A_1, and -B_1 Hormones

Sir:

The isolation and structural characterization of the naturally occurring C_{20} carboxylic acids of the prostaglandin family coupled with the discovery of their profound and diverse biological effects has opened a new chapter of hormone research,[1] the fundamental and practical significance of which already seems assured. Even at nanomolar concentrations the prostaglandins elicit widespread physiological responses, for example, in the cardiovascular, nervous, reproductive, renal, and gastric systems. Further, the individual prostaglandins often manifest qualitatively different activities despite the commonality of carbon skeleton. The lack of a satisfactory natural source of any of the prostaglandins and their biological importance have prompted the investigations of chemical synthesis which are reported in this and the following note.[2] Pure, crystalline synthetic prostaglandins have been obtained for the first time, and as a result of this work, the chemical synthesis of prostaglandins on a substantial scale becomes feasible.

The diene **1** was synthesized from 2-bromomethyl-1,3-butadiene[3] and 2-lithio-2-*n*-amyl-1,3-dithiane[4] in tetrahydrofuran–pentane at −25° (65–70%);[5,6,7b] [molecular ion found at *m/e* 256.1346 (theory 256.1320), $\lambda_{max}^{CH_3CN}$ 225 nm (ϵ 10,200), sh 256 nm (ϵ 1670)]. The dienophile **2**[6,7a,b] (*Anal.* Found: C, 59.52; H, 8.01; N, 15.02) was obtained from 7-cyanoheptanal[8] in ~60% yield

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[1] For recent reviews of the field including the pioneering work of the Bergström school, see (a) S. Bergström, *Science*, **157**, 382 (1967); (b) "Prostaglandins," Nobel Symposium 2, S. Bergström and B. Samuelsson, Ed., Interscience Publishers Inc., New York, N. Y., 1967.

[2] For other approaches to the synthesis of E_1 and F_1 hormones, see (a) G. Just and C. Simonovitch, *Tetrahedron Letters*, 2093 (1967); (b) D. Nugteren, H. Vonkeman, and D. A. van Dorp, *Rec. Trav. Chim.*, **86**, 1237 (1967); also (c) the conflicting report of K. G. Holden, B. Hwang, K. R. Williams, J. Weinstock, M. Harman, and J. A. Weisbach, *Tetrahedron Letters*, 1569 (1968), relative to the results reported in ref 2a.

[3] R. C. Krug and T. F. Yen, *J. Org. Chem.*, **21**, 1082 (1956). An improved procedure used in this work involved bromination of 3-methyl-2,5-dihydrothiophene 1,1-dioxide using N-bromosuccinimide in methylene chloride to give the corresponding bromomethyl sulfone (66%) followed by thermolysis at low pressure (~1 mm and 170–190°) to form the bromomethyldiene (60–75%).

[4] E. J. Corey and D. Seebach, *Angew. Chem. Intern. Ed. Engl.*, **4**, 1075, 1077 (1965).

[5] High-resolution mass spectral determinations were performed with an AEI-MS-9 double focusing spectrometer.

[6] The infrared and nuclear magnetic resonance spectra of this substance were in excellent agreement with the assigned structure.

[7] (a) Purified by adsorption chromatography using silica gel; (b) purified by vacuum distillation; (c) unless otherwise indicated, purified reaction products were obtained as colorless liquids; in several cases these could not be distilled without appreciable decomposition.

[8] (a) M. Ohno, N. Naruse, S. Torimitsu, and M. Okamoto, *Bull. Chem. Soc. Japan*, **39**, 1119 (1966); (b) M. Ohno, N. Naruse, S. Tori-