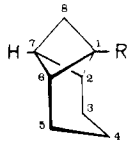
Whereas the reduction of **5f** by sodium in triglyme at 100 °C or by sodium–potassium alloy in boiling ether did not lead to a C_8H_{10} hydrocarbon fraction, the reaction of **5f** with *tert*-butyllithium (*t*-BuLi) was more successful. When 2.2 equiv of *t*-BuLi was added to a solution of **5f** in pentane/ether (3:2) at −35 °C, aqueous workup after 30 min afforded a 35% yield of 1-*tert*-butyltricyclo[4.2.0.$0^{2,7}$]octane (**6a**). The structure of **6a** is based



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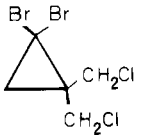
a: R = $C(CH_3)_3$

b: R = SC_6H_5



7

on its spectroscopic data: ^{1}H NMR ($CDCl_3$) δ 0.85 (s, 9 H, CH_3), 1.25 (s, 2 H, 8-H_2), 1.45–1.80 (m, 6 H, 3-H_2, 4-H_2, 5-H_2), 2.25 and 2.27 (s on top of broadened s, 3 H, 7-H, 2-H, 6-H); ^{13}C NMR ($CDCl_3$) δ 17.8 (t, C-4), 22.0 (t, C-3, C-5), 27.7 (q, CH_3), 28.5 (d, C-7), 32.2 (s, CMe_3), 42.7 (t, C-8), 53.5 (s, C-1), 54.8 (d, C-2, C-6); MS (70 eV), *m/e* 164 (5%, M^+).

As the addition of *t*-BuLi to the central bond of highly strained small-ring propellanes[9] has been observed previously,[10] the precursor of **6a** is probably the [1.1.1]propellane **4**, which is formed by ring closure of **5g** and which reacts with the excess of the base leading to **6a**. When the reduction of **5f** was repeated with 1.3 equiv of *t*-BuLi under otherwise identical conditions, a new hydrocarbon was produced in 30% yield, which could be purified by preparative GC (column 4 m, 20% Silicon GE SE-30 on kieselghur, 65 °C). The spectroscopic properties of the hydrocarbon are in accord with structure **4**: ^{1}H NMR (C_6D_6) δ 1.05–1.28 (m, 4 H, 3-H_2, 5-H_2), 1.35–1.63 (m with s at 1.55, 4 H, 4-H_2, 8-H_2), 2.75 (narrow m, 2 H, 2-H, 6-H); ^{13}C NMR (C_6D_6) δ 9.4 (s, C-1, C-7), 18.9 (t, C-4), 20.8 (t, C-3, C-5), 66.6 (t, $J(^{13}C-^1H)$ = 162 Hz, C-8), 86.5 (d, $J(^{13}C-^1H)$ = 159 Hz, C-2, C-6); MS (70 eV), *m/e* 106 (40%, M^+), 91 (100), 78 (55), 65 (20), 51 (30), 39 (35); IR (pentane) 595 cm^{-1}.[3]

The yield of **4** was raised to 55–65% when BuLi, instead of *t*-BuLi, was chosen as a reducing agent for **5f**. **4** proved to be stable against BuLi in ether at −30 °C; in contrast, when **4** was exposed to an excess of *t*-BuLi in pentane/ether (3:2) in the presence of lithium bromide at −30 °C, **6a** after aqueous workup was obtained in high yield. Thiophenol and **4** afforded the thioether **6b**,[11] probably via a radical chain process. The propellane **4** shares with the parent hydrocrbon **1**[3] an unexpected thermal stability: the ^{1}H NMR spectrum of a sample of **4** in C_6D_6 in a sealed NMR tube was unchanged after the sample had been kept at 105 °C for 30 min.

Recently Skattebøl, Baird, et al.[12] have shown that treatment of 1,1-dibromo-2-(chloromethyl)cyclopropanes with methyllithium leads to the formation of 1-bromobicyclo[1.1.0]butanes.[13] This observation combined with the facile ring closure of **5g** giving **4** suggested an efficient synthesis of **1** starting from **7** and proceeding via the bicyclo[1.1.0]butane **3c** as an intermediate: To a solution of **7**[14] in pentane/ether (3:2) at −50 °C, 2.2 equiv of BuLi was added and the mixture was kept for 30 min at this temperature. Aqueous workup followed by distillation of the volatile organic material from a 30 °C bath into a dry-ice trap under vacuum afforded a solution of **1** in pentane/ether.[15] Addition of thiophenol to this fraction produced a 34% yield (based on **7**) of thioether **2d**,[16] indicating that **1** had been formed in a reasonable yield.

Finally we would like to point out that the reaction sequence leading to **4** could be applied to any bicyclo[1.1.0]butane hydrocarbon carrying hydrogen at the bridgehead positions.[17]

Acknowledgment. This investigation was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie. We thank Dr. R. Römer for the mass spectrum of **4**.

(9) For definition, see: Ginsburg, D. "Propellanes", Verlag Chemie: Weinheim, 1975.

(10) Wiberg, K. B.; Walker, F. H.; Pratt, W. E.; Michl, J. *J. Am. Chem. Soc.* **1983**, *105*, 3638–3641 and references therein.

(11) Properties of **6b**: ^{1}H NMR ($CDCl_3$) δ 1.45–1.75 (m with s at 1.63, 8 H, 3-H_2, 4-H_2, 5-H_2, 8-H_2), 2.43 (narrow m, 2 H, 2-H, 6-H), 2.58 (s, 1 H, 7-H), 7.05–7.42 (m, 5 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 18.1 (t, C-4), 20.7 (t, C-3, C-5), 30.7 (d, C-7), 48.4 (s, C-1), 49.7 (t, C-8), 58.1 (d, C-2, C-6), 126.8, 128.3, 133.6 (3 d, Ar C), 133.7 (s, Ar C); HRMS calcd for $C_{14}H_{16}{}^{32}S$ 216.09727, found 216.096.

(12) Nilsen, N. O.; Skattebøl, L.; Baird, M. S.; Buxton, S. R.; Slowey, P. *Tetrahedron Lett.* **1984**, 2887–2890.

(13) Düker, A.; Szeimies, G. *Tetrahedron Lett.* **1985**, 3555–3558.

(14) **7** was obtained in 45% yield from commercially available 3-chloro-2-(chloromethyl)-1-propene by addition of dibromocarbene (from bromoform and 50% aqueous sodium hydroxide in dichloromethane at 25 °C under the conditions of phase-transfer catalysis). Properties of **7**: mp 45–46 °C; ^{1}H NMR ($CDCl_3$) δ 1.80 (s, 2 H), 3.91 (s, 4 H); ^{13}C NMR ($CDCl_3$) δ 32.0 (s), 33.9 (t), 35.2 (s), 47.6 (t, 2 C). Anal. C, H.

(15) In addition to **1**, the pentane/ether fraction contained some 1-bromobutane.

(16) Properties of **2d**: ^{1}H NMR ($CDCl_3$) δ 1.90 (s, 6 H), 2.65 (s, 1 H), 7.10–7.30 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 28.6 (d), 45.6 (s), 54.0 (t, 3 C), 127.3, 128.6, 133.4 (3 d), 134.1 (s); HRMS calcd for $C_{11}H_{12}{}^{32}S$ 176.06592, found 176.067.

(17) **Note Added In Proof**: Tetracyclo[4.1.0.$0^{1,5}$.$0^{2,6}$]heptane, the lower homologue of **4**, was obtained in 45% yield from 1-bromo-6-(chloromethyl)-tricyclo[3.1.0.$0^{2,6}$]hexane and methyllithium in ether at −30 °C: ^{1}H NMR (C_6D_6) δ 1.54 (s, 4 H), 2.32 (s, 2 H), 2.73 (s, 2 H); ^{13}C NMR (C_6D_6) δ 11.8 (s), 25.1 (t, 2 C), 70.7 (t), 84.1 (d, 2 C).

Organometallic–Crown Reagents. Anti-Cram Selectivity via R_2CuLi·Crown and Enhanced Cram Selectivity via RLi·Crown and RMgX·Crown

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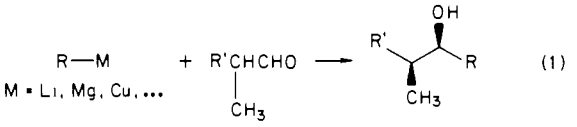
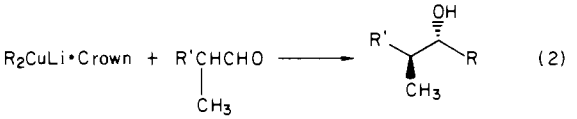
It is widely agreed that the reaction of organometallic reagents with ordinary chiral aldehydes having no ability to be chelated produces the Cram (or Felkin) type isomer predominantly (eq 1). We report herein the surprising stereochemical behavior



(1)

exhibited by R_2CuLi·crown reagents; the anti-Cram isomer is produced preferentially (eq 2). We have also discovered that



(2)

the Cram selectivity is enhanced with RLi(or RMgX)·crown reagents.[1] These findings provide not only a new useful method for 1,2-asymmetric induction but also a conceptual advance in empirical models to rationalize the stereoselectivity in reactions of chiral aldehydes. The results are summarized in Table I.

(1) For organolithium reactions in the presence of crown ethers and cryptates, see: (a) Pierre, J. L.; Handel, H.; Perraud, R. *Tetrahedron Lett.* **1977**, 2013. (b) Biellmann, J. F.; Vicens, J. J. *Ibid.* **1974**, 2915. (c) Atlani, P. M.; Biellmann, J. F.; Dube, S.; Vicens, J. J. *Ibid* **1974**, 2665. (d) Chassaing, G.; Marquet, A. *Tetrahedron* **1978**, *34*, 1399. (e) Maruoka, K.; Yamamoto, H. J. *Synth. Org. Chem. Jpn.* **1985**, *43*, 437. For reduction with metal hydrides, see: (f) Handel, H.; Pierre, J. L. *Tetrahedron Lett.* **1976**, 741; *Tetrahedron* **1975**, *31*, 997; **1975**, *31*, 2799. (g) Pierre, J. L.; Handle, H.; Perraud, R. *Ibid.* **1975**, *31*, 2795. (h) Loupy, A.; S-Penne, J. *Tetrahedron Lett.* **1978**, 2571. (i) Loupy, A.; S-Penne, J.; Tchoubar, B. *Ibid.* **1976**, 1677. (j) Lee, H. S.; Isagawa, K.; Toyoda, H.; Otsuji, Y. *Chem. Lett.* **1984**, 363 and 673. For Grignard reactions, see: (k) Richey, H. G., Jr.; King, B. A. *J. Am. Chem. Soc.* **1982**, *104*, 4672 and references cited therein.

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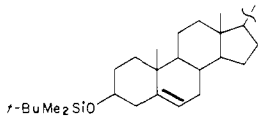
Table I. Reactions of RLi·Crown, RMgX·Crown and Cuprate–Crown Reagents[a]

entry	aldehyde	RM	crown (coronand)	Cram/anti-Cram[b]	Yield, %[c]
1	$PhC(CH_3)HCHO$	BuLi	15-C-5	>30/1	91
2		BuLi	12-C-4	8/1	93
3		BuLi	18-C-6	10/1	93
4		BuLi		5/1	91
5		$CH_2{=}CHCH_2Li$	18-C-6	>30/1	87
6		$CH_2{=}CHCH_2Li$	15-C-5	12/1	87
7		MeLi	18-C-6	7/1	90
8		MeLi	5-221	9/1	86
9		MeLi		4/1	91
10		MeMgBr	K-222	7/1	95
11		EtMgBr	K-221	9/1	90
12		EtMgBr	K-222	7/1	90
13		EtMgBr	K-21	9/1	90
14		EtMgBr		4/1	92
15		Et_2Mg		8/1	92
16		Et_2Mg	15-C-5	14/1	75
17		Et_2Mg	K-211	11/1	90
18		Bu_2CuLi	18-C-6	1/4.2	95
19		Bu_2CuLi	15-C-5	1/2	95
20		Bu_2CuLi	K-21	1/5	80
21		Bu_2CuLi	K-22	1/4	88
22		$Bu_5Cu_3Li_2$	18-C-6	1/4.4	96
23		$Bu_2CuCNLi_2$	15-C-5	1/2	95
24		Bu_2CuLi		3/1	95
25		Me_2CuLi	K-21	1/1	30[d]
26		$Me_2Cu{\cdot}MgBr$	K-21	1/2	90
27		$Me_2Cu{\cdot}MgBr$	K-22	1/2	95
28	$CH_3CH_2C(CH_3)HCHO$	BuLi	15-C-5	2/1	93
29		$Bu_5Cu_3Li_2$	15-C-5	1/2	95
30	$PhCH_2C(CH_3)HCHO$	BuLi	15-C-5	2/1	94
31		BuLi		1.2/1	94
32		Bu_2CuLi	18-C-6	1/2	95
33	$C_6H_{11}C(CH_3)HCHO$	BuLi	15-C-5	10/1	89
34		BuLi	18-C-6	5/1	89
35		Bu_2CuLi	18-C-6	1/2	90
36		$Bu_5Cu_3Li_2$	18-C-6	1/2	90
37		Bu_2CuLi	K-21	1/4	88
38		Et_2Mg	K-211	11/1	90
39	St-$C(CH_3)HCHO$[e]	BuLi	15-C-5	9/1	85
40		Et_2Mg		7/1	87
41		Bu_2CuLi	18-C-6	1/2	90

[a] A general procedure is described in ref 2 and 3. K-211 = Kryptofix 211. [b] The isomer ratio was determined by 400-MHz ^1H NMR and ^{13}C NMR analyses of the reaction mixture. [c] Determined by ^1H NMR spectra of the product through a short column of silica gel. [d] A major product was 2-phenylpropanol. [e] St =



In the reaction of 2-phenylpropionaldehyde, BuLi·15-C-5 provided the Cram isomer almost exclusively (entry 1).[2] Other crown ethers, such as 12-C-4 and 18-C-6, were less effective than 15-C-5 (entries 2 and 3) but still produced the Cram isomer more predominantly than BuLi itself (entry 4). Allyllithium–18-C-6 was more effective than the corresponding 15-C-5 reagent (entries 5 and 6), and thus the most effective size of crown ethers depended on the R group of RLi. MeLi·K-211 was more effective than MeLi·18-C-6 (entries 7–9). Although enhancement of Cram selectivity was not observed with RMgX·18-C-6 and RMgX·15-C-5, use of kryptofixes exhibited the selectivity elevation (entries 10–14). Quite interestingly, Et_2Mg itself and Et_2Mg·crown gave the Cram isomer with greater selectivity than EtMgX and EtMgX·crown, respectively (entries 15–17).

Although Bu_2CuLi produced the Cram isomer preferentially as a matter of course (entry 24), Bu_2CuLi·crown gave the anti-Cram isomer predominantly (entries 18–21).[3] Other cuprates such as $Bu_5Cu_3Li_2$ and $Bu_2CuCNLi_2$[4] also produced the anti-Cram isomer preferentially, when they were treated with the coronands (entries 22 and 23). Although Me_2CuLi·K-21 gave the product in a ratio of 1:1 (entry 25), $Me_2CuMgBr$–kryptofix reagents produced the anti-Cram isomer predominantly (entries 26 and 27).

With other aldehydes, a similar trend was observed (entries 28–41). When the R′ substituent of aldehydes (eq 1 and 2) was a primary alkyl group, both Cram and anti-Cram selectivities were low (entries 28–32), but the selectivity inversion was again observed. In conclusion, (i) the enhanced Cram selectivity was realized when RLi and Grignard reagents were treated with coronands before addition of aldehydes. (ii) For RLi, 18-C-6 or

(2) RLi·crown and RMgX·crown reagents were prepared as follows. To an THF (or ether) solution of crown ether (2 mmol) cooled at −78 °C under N_2 was added RLi or RMgX (2 mmol) in an appropriate solvent. The aldehyde (1 mmol) was added and the mixture was allowed to warm to room temperature. Quenching with H_2O, drying, and filtration through a short column of silica gel using ether as eluant provided the alcohol.

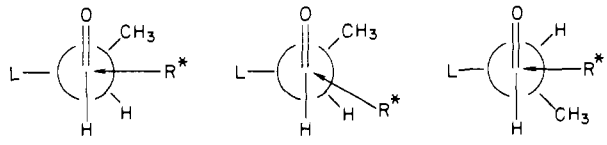
(3) To an THF (or ether) solution of cuprate (2 mmol) cooled at −78 °C under N_2 was added crown ether (2 mmol) in THF, and then the aldehyde (1 mmol) was added. For $Bu_5Cu_3Li_2$ and $Bu_2CuCNLi_2$, 2 equiv of crown ether were used.

(4) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *24*, 5005. Lipshutz kindly informed us in his referee report that they also investigated the effect of 12-C-4 on the cuprate reaction. The normal reactivity of cuprates was essentially lost in the presence of 12-C-4. For the fate of the alkoxide products in terms of their effect on BuLi and cuprates, see: Lipshutz, B. H.; Kozlowski, J. A.; Breneman, C. M. *J. Am. Chem. Soc.* **1985**, *107*, 3197.

15-C-5 gave the best result. (iii) For RMgX, kryptofixes such as K-21, K-22, K-211, K-221, and K-222 were effective. (iv) The selectivity inversion was observed with cuprate–crown reagents, and both kryptofixes and simple crown ethers were effective for achieving the anti-Cram selectivity.

To make sure that the isomer ratio is based on kinetic control, the reactions were quenched (i) immediately after addition of 2-phenylpropionaldehyde at −78 °C, (ii) at −20 °C, and (iii) after 2 days at room temperature. With BuLi·15-C-5, the conversion was low at −78 °C, but the ratio was essentially identical under three different conditions (ii, iii, and entry 1). Although 2 equiv of BuLi·crown reagents were used in Table I, use of an equivalent amount of the reagent produced the alcohol in high yield under a prolonged reaction period, normally 18 h, at room temperature. The reaction of Bu_2CuLi·18-C-6 was also quenched under the three different conditions. The reaction was more rapid than that of BuLi·15-C-5. Here again, the same isomer ratio was obtained at the four different conditions (i–iii and entry 18).

The enhanced Cram selectivity with RLi·crown and Grignard–crown reagents is in good agreement with a prediction made by Anh.[5] The complexation of M^+ by crown-type compounds must diminish the electrophilic assistance of M^+ toward carbonyl group, leading to an increased Cram selectivity irrespective of perpendicular (**1**)[6] or nonperpendicular (**2**) attack. In fact, the



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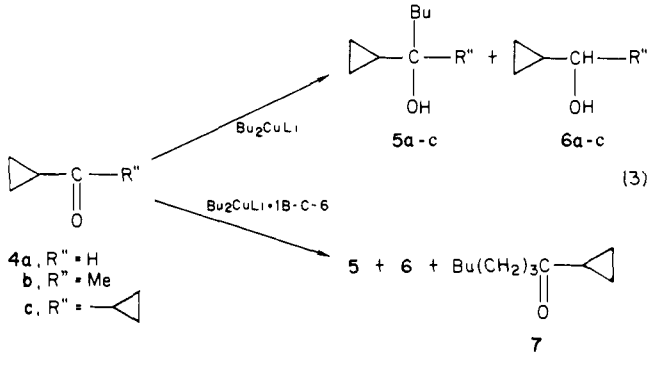
enhanced Cram selectivity (8:1) of Et_2Mg in comparison with the selectivity (4:1) of EtMgBr clearly indicates an important role of the complexation; it can be easily presumed from the Lewis acidity that the electrophilic assistance of RMgX is greater than that of R_2Mg. Besides, the crown presumably assists in increasing the state of aggregation.[7] This hypothesis is supported by an observation that the reactivity of the organometallic–crown reagents decreased markedly in comparison with the uncomplexed reagents. Consequently, both loss of the complexation and increase of the state of aggregation operate to enhance the Cram selectivity.

The anti-Cram selectivity with cuprate–crown reagents suggests the intervention of a radical mechanism.[8] Accordingly, we examined the reaction of Bu_2CuLi·18-C-6 with cyclopropylcarbonyl compounds (**4**) (eq 3). With **4a**, both Bu_2CuLi and Bu_2CuLi·18-C-6 gave the butylated alcohol **5a** in an essentially quantitative yield. With **4b**, both reagents afforded **5b** in 75–82% yield along with **6b** (1%) and the self-condensed aldol product (8–15%). A marked difference between both the reagents was not observed. However, the ring-opening product **7** was obtained in the reaction of **4c** with Bu_2CuLi·18-C-6: **7** (39%), **6c** (39%), **5c** (10%), and the recovered **4c** (12%). With Bu_2CuLi, **7** was not produced: **5c** (89%), **6c** (1%), and the recovered **4c** (10%).



(3)

Formation of **7** evidently indicates the intervention of an electron-transfer process. Increase of the reduction product **6c** also supports the participation of a radical mechanism. With **4a** and **4b**, the transfer of the Bu group to an intermediate (anion radical) must be rapid, preventing the ring cleavage. Taken together, R_2CuLi·crown (presumably R_2Cu^-·Li^+⊂crown) possesses greater ability to transer electrons than R_2CuLi itself.[9]

The anti-Cram selectivity can be explained as follows, though it is highly speculative. If an electron-transfer mechanism is involved, **1–3** put more negative charge on oxygen than the normal transition state for a nucleophilic addition. It is therefore felt that the oxygen is, in effect, made larger, destabilizing the conformation **1** (and **2**) by increasing the CH_3–O^- interaction. Further, the directionality of R* attack must change in the radical mechanism. In fact, a perpendicular attack is proposed for a radical reaction of propene.[10] If the perpendicular attack is involved in the present reaction, **3** is more stable than **1** owing to the CH_3–O^- interaction, leading to the predominant formation of the anti-Cram isomer. We are now studying the related reactions of various organometallic–crown and enolate–crown reagents and will report these works shortly.

Acknowledgment. Thanks are given to Ryuichi Imamura for ^1H and ^{13}C NMR measurements.

(5) (a) Anh, N. T. *Top. Curr. Chem.* **1980**, *88*, 145. (b) Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61.

(6) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199, 2205.

(7) In fact, such a phenomenon is known in Grignard reagents.[1k]

(8) A radical mechanism has been suggested for the anti-Cram selectivity in certain ketone reactions. Argona, O.; P-Ossorio, R.; P-Rubalcaba, A.; Quiroga, M. L. *J. Chem. Soc., Chem. Commun.* **1982**, 452. A-Ibarra, C.; Arjona, O.; P-Ossorio, R.; P-Rubalcaba, A.; Quiroga, M. L.; Santesmases, M. J. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1645. **Note Added in Proof**: In a communication that appeared subsequent to submission of this manuscript, Professor H. Yamamoto and co-workers report the anti-Cram selectivity via certain aluminum reagents: Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 4573.

(9) Our preliminary investigation on ate complexes–crown reagents, such as R_4BM·crown and R_4AlM·crown, revealed the radical reactivity of these complexed organometallics.

(10) Padden-Row, M. N.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 7162.

^{113}Cd Chemical Shifts of Cadmium–Iodide Complexes in Supercooled Aqueous Solution

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It has been suggested that metal nuclide chemical shifts will vary in a linear progression in cation–solvent systems where a single species first solvation sphere is replaced in a stepwise manner by a different solvent, i.e., $MX_4 \rightarrow MX_3Y \rightarrow MX_2Y_2 \rightarrow MXY_3 \rightarrow MY_4$.[1,2] Assumption of the generality of such trends has led to the development of powerful metal nuclide NMR chemical shift methods for evaluation of solvation sphere composition (e.g., preferential solvation) in mixed-solvent systems.[3-5] Here, under conditions of rapid chemical exchange, the single observed chemical shift is taken to be the average of the chemical shifts in the pure solvents weighted according to the mole fraction of each solvent in the contact solvation shell.[1]

The competitive or preferential solvation problem is equivalent to the ligand displacement problem[4] and some precedent for such

(1) Frankel, L. S.; Stengle, T. R.; Langford, C. H. *Chem. Commun.* **1965**, 393.

(2) Frankel, L. S.; Langford, C. H.; Stengle, T. R. *J. Phys. Chem.* **1970**, 1376.

(3) Langford, C. H.; Tong, J. P. K. *Acc. Chem. Res.* **1977**, *10*, 258.

(4) Bryant, R. G. In "NMR of Newly Accessible Nuclei"; Laszlo, P., Ed.; Academic Press: New York, 1983; Vol. 1, p 135.

(5) Lindman, B.; Forsen, S. In "NMR and the Periodic Table"; Harris, R. K., Mann, B. E., Eds.; Academic Press: New York, 1978; p 129.

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