Table I. Reaction of Acyl Chlorides with Organocopper Reagents 1[18]

RCu(CN)ZnI	R^4COCl	R^4COR	yield,[a] %
BuCu(CN)ZnI	Ph(CO)Cl	Ph(CO)Bu	85
BuCu(CN)ZnI	$C_5H_{11}(CO)Cl$	$C_5H_{11}(CO)Bu$	85
BuCu(CN)ZnI	c-$C_6H_{11}(CO)Cl$	c-$C_6H_{11}(CO)Bu$	81
i-PrCu(CN)ZnI	Ph(CO)Cl	Ph(CO)-*i*-Pr	88
i-PrCu(CN)ZnI	$ClCH_2CH_2CH_2(CO)Cl$	Cl-$CH_2CH_2CH_2(CO)$-*i*-Pr	90
i-PrCu(CN)ZnI	Ph(OAc)CH(CO)Cl	Ph(OAc)CH(CO)-*i*-Pr	82
sec-BuCu(CN)ZnI	$ClCH_2CH_2CH_2(CO)Cl$	Cl-$CH_2CH_2CH_2(CO)$-*sec*-Bu	94
c-$C_6H_{11}Cu(CN)ZnI$	Ph(CO)Cl	Ph(CO)-c-C_6H_{11}	84
$EtO_2CCH_2CH_2CH_2Cu(CN)ZnI$	Ph(CO)Cl	$Ph(CO)CH_2CH_2CH_2CO_2Et$	87
t-$BuOCOCH(CH_3)CH_2CH_2CH_2Cu(CN)ZnI$	Ph(CO)Cl	$Ph(CO)CH_2CH_2CH_2CH(CH_3)OCO$-*t*-Bu	93
N≡C-$CH_2CH_2CH_2Cu(CN)ZnI$	Ph(CO)Cl	$Ph(CO)CH_2CH_2CH_2CN$	93

[a] Isolated yield.

Table II. Products of Type 5 Obtained by the Reaction of Enones with Organocopper Reagents 1[18]

RCu(CN)ZnI	product of type 5				yield,[a] %
	R^1	R^2	R^3	R	
	Reaction with 2-Cyclohexen-1-one				
BuCu(CN)ZnI	$(CH_2)_3$		H	Bu	97
i-PrCu(CN)ZnI	$(CH_2)_3$		H	*i*-Pr	98
c-$C_6H_{11}Cu(CN)ZnI$	$(CH_2)_3$		H	c-C_6H_{11}	98
$EtO(CO)CH_2CH_2CH_2Cu(CN)ZnI$	$(CH_2)_3$		H	$CH_2CH_2CH_2(CO)OEt$	94
t-$BuO(CO)CH(CH_3)CH_2CH_2CH_2Cu(CN)ZnI$	$(CH_2)_3$		H	$CH_2CH_2CH_2(CH_3)CH(CO)O$-*t*-Bu	94
$N{\equiv}CCH_2CH_2CH_2Cu(CN)ZnI$	$(CH_2)_3$		H	$CH_2CH_2CH_2CN$	97
	Reaction with 2-Cyclopenten-1-one				
$N{\equiv}CCH_2CH_2CH_2Cu(CN)ZnI$	$(CH_2)_2$		H	$CH_2CH_2CH_2CN$	81
	Reaction with *trans*-4-Phenyl-3-buten-2-one				
$N{\equiv}CCH_2CH_2CH_2Cu(CN)ZnI$	CH_3	H	Ph	$CH_2CH_2CH_2CN$	99
	Reaction with 3-Methyl-2-cyclohexen-1-one				
BuCu(CN)ZnI	$(CH_2)_3$		Me	Bu	62

[a] Isolated yield.

1-butene afford 5-phenyl-6-heptenenitrile (0 °C, 1 h, 88%) and 6-octenenitrile (0 °C, 1 h, 85% cis/trans mixture), respectively. In both cases, less than 4% of the S_N2 substitution products was detected.[19]

Typical Procedure. A suspension of 1.7 g (26 mmol) of zinc (99.99% purity) in 2 mL of THF containing 190 mg (1.0 mmol) of 1,2-dibromoethane was heated to 65 °C for a minute and cooled to 25 °C, and 0.1 mL (0.8 mmol) of chlorotrimethylsilane was added. After 15 min at 25 °C, a solution of the iodide (25 mmol) in 10 mL of THF was slowly added (at 25 °C in the case of a secondary iodide; at 30 °C in the case of a primary iodide). After the end of the addition, the reaction mixture was stirred 12 h at 25–30 °C (or at 35–40 °C in the case of a primary iodide). Usually less than 100 mg of zinc remains, indicating a yield of 90%. The clear, colorless solution was then cooled to −10 °C, and a solution of 1.98 g (22 mmol) of CuCN and 1.9 g (44 mmol) of LiCl (dried at 150 °C for 1 h) in 22 mL of THF was rapidly added. The resulting light green solution was stirred at 0 °C for 10 min and was then ready to use.

(a) Reaction with Acyl Chlorides or Allylic Halides. The acyl chloride or the allylic halide (18.7 mmol) was slowly added to the above prepared solution of the copper reagent 1 at −25 °C. The reaction mixture was then stirred for 3 h at 0 °C. After the usual workup, the residue obtained was purified by distillation or flash chromatography.[18]

(b) Reaction with 2-Cyclohexen-1-one. A solution of 1.73 g (18 mmol) of 2-cyclohexen-1-one and 5.5 mL (43 mmol) of chlorotrimethylsilane in 10 mL of ether was slowly added (0.5 h) to the above prepared solution of the copper reagent cooled at −78 °C. After 3 h of stirring at −78 °C, the reaction mixture was allowed to warm up to 25 °C overnight and then worked up.

The high tolerance of important functional groups like esters, nitriles, and ketones as well as the high stability of new copper reagents RCu(CN)ZnI should find broad applications in organic syntheses. Studies concerning the reactivity of these organometallics toward other electrophiles are currently under way in our laboratory.

Acknowledgment. We thank the Chemistry Department of The University of Michigan for support of this work and La Vieille Montagne Co. (France) for the gift of zinc.

Supplementary Material Available: Spectral data and elemental analyses for new compounds (8 pages). Ordering information is given on any current masthead page.

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(19) R_2Zn in the presence of $CuBr{\cdot}Me_2S$ has been reported to give very high S_N2'/S_N2 product ratios: Nakamura, E.; Aoki, S.; Sekiya, K.; Oshino, H.; Kuwajima, I. *J. Am. Chem. Soc.* **1987**, *109*, 8056. See also: Ochiai, H.; Tamaru, Y.; Tsubaki, K.; Yoshida, Z. *J. Org. Chem.* **1987**, *52*, 4418.

The Low-Temperature, Ionic Diels–Alder Addition of Vinyl Ortho Esters to 1,3-Dienes

Summary: 3,3,3-Triethoxypropene (triethyl orthoacrylate) was added to a series of 1,3-dienes in the presence of trimethylsilyl triflate at −78 to 0 °C to produce 53–83% yields of the adducts of ethyl acrylate and the 1,3-dienes. The products were formed under conditions where ethyl acrylate failed completely to add to the 1,3-dienes and it was demonstrated by both NMR observation of the reactive intermediates and trapping of the initial cationic Diels–Alder product with trimethylsilyl cyanide that the reactive dienophile was the 1,1-diethoxyallyl cation.

Sir: Recent reports from our laboratory have illustrated that allyl cations are powerful Diels–Alder dienophiles which add to 1,3-dienes in high yields at low temperatures.[1] This concept has been extended to the addition of 1-alkoxyallyl cations to 1,3-dienes as a low-temperature, high-yield path to adducts of acrolein and its derivatives.[2] We now report that triethyl orthoacrylate[3] (1) serves as an excellent precursor of the 1,1-diethoxyallyl cation which adds to 1,3-dienes at low temperatures to produce, as the final products, the corresponding adducts of ethyl acrylate.[5,6]

In a typical procedure, 2 equiv of the appropriate 1,3-diene and 1 equiv of triethyl orthoacrylate were dissolved in methylene chloride and the solution was cooled to −78 °C. Trimethylsilyl triflate was then added and the reaction mixture was allowed to warm to ca. 0 °C over the time period specified[7] in Table I, followed by quenching with excess triethylamine. As indicated in Table I, the yield of Diels–Alder adducts ranged from 53% to 83%.

The mechanistic steps involved in these Diels–Alder additions were of particular interest to us. Based on our earlier studies, we anticipated that 1 would react with trimethylsilyl triflate to produce the 1,1-diethoxyallyl cation (2) which would add to an appropriate 1,3-diene, such as 1,3-cyclohexadiene, to produce a new cation, 3.

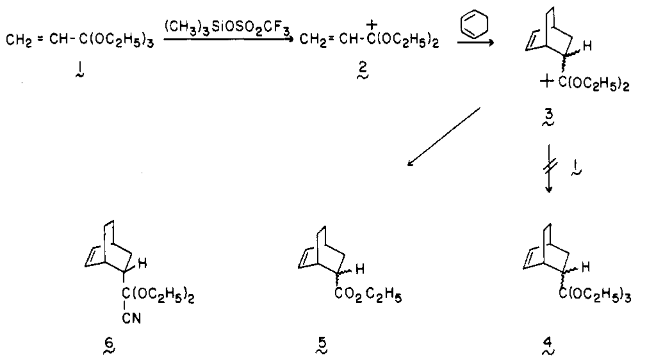
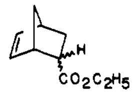
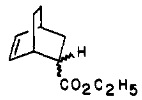
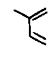
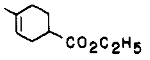
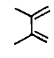
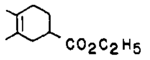
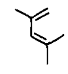
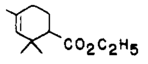
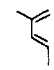
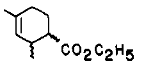


Table I. Yields and Conditions for the Ionic Addition of Triethyl Orthoacrylate to 1,3-Dienes in the Presence of ca. 50 mol % Trimethylsilyl Triflate

diene	product	yield (%)	temp (°C)	time (h)
		83[a]	−78 to −5	3.0
		62[b]	0	0.3
		62	0	1.5
		53	−78 to −10	1.8
		65	−78 to −10	2.0
		81[c]	−78 to 0	2.0

[a] The ratio of endo to exo addition was 16:1. [b] The ratio of endo to exo addition was 6:1. [c] The ratio of cis to trans adducts was 9:1.

Transfer of an ethoxy group to 3 from 1 could then produce 4 and regenerate 2.[8] Interestingly, no trace of 4 could be detected. Instead, only the ethyl ester, 5, was isolated in 62% yield. This raised the question of whether 1 was simply being converted to ethyl acrylate, which, in the presence of trimethylsilyl triflate or acid, was producing 5. However, treatment of a mixture of ethyl acrylate and 1,3-cyclohexadiene with either triflic acid or trimethylsilyl triflate failed to produce 5 under the reaction conditions. Thus, it was established that ethyl acrylate was not the dienophile.

In order to establish that 2 and 3 were intermediates in the formation of 5, the progress of the reaction was followed by ^{1}H NMR. Addition of trimethylsilyl triflate to 1 gave a solution of 2 which showed the following: ^{1}H NMR ($CDCl_3$) δ 7.06 (d, 1 H, $J = 16.4$ Hz), 6.87 (dd, 1 H, $J = 16.4$ Hz, $J = 10.7$ Hz), 6.72 (d, 1 H, $J = 10.7$ Hz), 4.97 (q, 4 H, $J = 7$ Hz), 1.57 (t, 6 H, $J = 7$ Hz). Comparison of these values with those of 1[3] shows a downfield shift of ca. 1.5 ppm for the vinyl hydrogens and the ether methylenes. This material slowly converted to ethyl acrylate. When this reaction was repeated in the presence of 1,3-cyclohexadiene, 2 was not observed. Instead, a new cationic material was observed with the following: ^{1}H NMR ($CDCl_3$) δ 6.37 (t, 1 H, $J = 7$ Hz), 6.17 (t, 1 H, $J = 7$ Hz), 4.89 (br q, 4 H), 3.50 (m, 1 H), 3.04 (br s, 1 H), 2.71 (br s, 1 H), 1.54 (t, 6 H, $J = 7$ Hz). The six methylene hydrogens of the bicyclo[2.2.2]octyl skeleton of 3 overlapped with the related hydrogens of 5 and, as a result, could not be specifically identified. The downfield shift of the ether methylene to δ 4.89 is consistent with the presence of the cationic intermediate 3. This material slowly converted to 5 under the reaction conditions.

In order to establish the intermediacy of 3 on even firmer grounds, an attempt was made to trap 3 intermolecularly. A mixture of 1,3-cyclohexadiene (2 equiv), 1 (1 equiv), and trimethylsilyl cyanide (1.2 equiv) in methylene chloride

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[1] Gassman, P. G.; Singleton, D. A. *J. Am. Chem. Soc.* **1984**, *106*, 6086. Gassman, P. G.; Singleton, D. A. *Ibid.* **1984**, *106*, 7993. Gassman, P. G.; Singleton, D. A. *J. Org. Chem.* **1986**, *51*, 3075. Gassman, P. G.; Singleton, D. A. *Tetrahedron Lett.* **1987**, *28*, 5969. See also: Poutsma, M. L. *J. Org. Chem.* **1968**, *33*, 4080. Escher, A.; Übersax, B.; Neuenschwander, M. *Chimia* **1981**, *35*, 251. Hoffmann, H. M. R.; Vathke-Ernst, H. *Chem. Ber.* **1981**, *114*, 1182, 1464, 1548, 2208. Giguere, R. J.; von Ilsemann, G.; Hoffmann, H. M. R. *J. Org. Chem.* **1982**, *47*, 4948. Lazlo, P.; Lucchetti, J. *Tetrahedron Lett.* **1984**, *25*, 2147 and references therein.

[2] Gassman, P. G.; Singleton, D. A.; Wilwerding, J. J.; Chavan, S. P. *J. Am. Chem. Soc.* **1987**, *109*, 2182.

[3] Triethyl orthoacrylate was prepared in 82% yield through the dehydrobromination of triethyl α-bromoorthopropionate[4] with potassium *tert*-butoxide in dimethyl sulfoxide at room temperature: bp 162–164 °C; ^{1}H NMR ($CDCl_3$) δ 5.59 (dd, 1 H, $J = 17.4$ Hz, $J = 9.2$ Hz), 5.51 (dd, 1 H, $J = 17.4$ Hz, $J = 3.4$ Hz), 5.34 (dd, 1 H, $J = 9.2$ Hz, $J = 3.4$ Hz), 3.40 (q, 6 H, $J = 7.1$ Hz), 1.12 (t, 9 H, $J = 7.1$ Hz); ^{13}C NMR ($CDCl_3$) δ 134.59 (d), 119.87 (t), 112.16 (s), 57.29 (t), 14.93 (q).

[4] Walters, P.; McElvain, S. *J. Am. Chem. Soc.* **1940**, *62*, 1482. Beyerstedt, F.; McElvain, S. *Ibid.* **1937**, *59*, 2266. Stetter, H.; Uerdingen, W. *Synthesis* **1973**, 207.

[5] Satisfactory elemental analyses and/or exact mass molecular weights were obtained on all new compounds. In all cases ^{13}C NMR, ^{1}H NMR, and IR spectra were consistent with the assigned structure.

[6] For mechanistic precedence for this reaction and for an alternate path to the same type of reaction intermediate, see: Roush, W. R.; Gillis, H. R.; Essenfeld, A. P. *J. Org. Chem.* **1984**, *49*, 4674.

[7] For 1,3-cyclohexadiene and isoprene, the reactions were run at 0 °C because slightly improved yields were obtained at that temperature.

[8] Perst, H. *Oxonium Ions in Organic Chemistry*; Verlag Chemie: Weinheim, 1971. Kabu, S. *Angew Chem., Int. Ed. Engl.* **1966**, 675. Pindur, U.; Muller, J.; Flo, C.; Witzel, H. *Chem. Soc. Rev.* **1987**, *16*, 75.

was prepared at −78 °C, allowed to warm to 25 °C, and stirred for 12 h. No reaction occurred. At this point, trimethylsilyl triflate (0.2 equiv) was added and the reaction mixture was stirred for 12 h. Workup gave 25% of **5** and 24% of **6**.[9,10] The isolation of **6** adds substantial support to the hypothesis that **3** is the reactive intermediate in the path from **1** to **5**.

The reactions described constitute a low-temperature path to formal Diels–Alder adducts between ethyl acrylate and 1,3-dienes. It is clear that the 1,1-diethoxyallyl cation is an extremely powerful dienophile in comparison to ethyl acrylate, even when the ethyl acrylate is used in the presence of triflic acid. This low-temperature process offers a unique method for production of the described adducts under very mild conditions.

Acknowledgment. We are indebted to the Institute of General Medical Sciences of the National Institutes of Health for Grant GM35962 which supported this investigation and to the Smith Kline & French Laboratories for financial support.

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[9] ^{1}H NMR ($CDCl_3$): δ 6.33 (t, 1 H, $J = 7$ Hz), 6.26 (t, 1 H, $J = 7$ Hz), 3.62 (m, 4 H), 2.69 (br s, 1 H), 2.58 (m, 1 H), 2.22 (t, 1 H, $J = 7$ Hz), 1.73 (ddd, 1 H, $J = 13$ Hz, $J = 9.9$ Hz, $J = 3.1$ Hz), 1.52–1.16 (m, 5 H), 1.24 (t, 3 H, $J = 7$ Hz), 1.19 (t, 3 H, $J = 7$ Hz). ^{13}C NMR ($CDCl_3$): δ 134.71 (d), 131.65 (d), 116.03 (s), 102.16 (s), 59.56 (t), 59.43 (t), 43.43 (d), 30.26 (t), 29.93 (d), 29.62 (d), 27.49 (t), 23.39 (t), 14.93 (q), 14.87 (q). IR (neat): 2230 cm^{-1}.

[10] While this experiment was carried out at 25 °C, slightly lower yields of the same products were obtained at −78 °C followed by warming to 0 °C.

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Received January 25, 1988

Double Diastereoselectivity in Addition of Metalated Propionitrile to Enones

Summary: Metalated propionitrile undergoes diminished selectivity for axial attack with cyclohexanones compared to metalated acetonitrile. Nevertheless, this more hindered nucleophile shows as high, or even higher, axial selectivity with cyclohexenones. Also, the newly created stereogenic center α to the nitrile is created with good diastereoselectivity as well.

Sir: The previous tenant that the stereochemistry of addition to six-membered ring ketones intrinsically favors an equatorial attack has come under increasing challenge experimentally.[1–3] An explanation for an intrinsic preference for axial attack pits torsional strain, which favors axial attack, against steric strain, which favors equatorial attack.[4,5] Recent calculations have suggested that the axial preference increases from 1.2 kcal in the case of cyclohexanones to 2.0 kcal for cyclohexenones.[5] In order to probe the magnitude of this preference, we examined the diastereoselectivity of addition of a more sterically demanding nucleophile, propionitrile anion. We report that, quite surprisingly, not only does this nucleophile maintain a high preference for axial selectivity with cyclohexenones but that there is also a high diastereoselectivity at the newly created stereogenic center α to the nitrile. The studies provide further experimental support for the proposal that the competition between torsional and steric strain accounts for the stereoselectivity of addition and suggest that metalated nitriles have a highly ordered transition state in carbonyl additions.

We initially studied the addition of metalated propionitrile to 4-*tert*-butylcyclohexanone (eq 1, Scheme I). While the preference for axial attack deteriorated (**1**[6]:**2**[7] 1.3:1 for $M^+ = Li^+$, 2.5:1 for $M^+ = K^+$) it still dominated. Use of the aluminum modifier MAD,[8] which gives rise to enhanced axial attack with nonstabilized nucleophiles, led to a predominance of equatorial attack (1:2, 1:1.8). Assignment of configuration derived from our previously established ^{13}C NMR chemical shift correlations.[3a] The signal for the methine carbon atom of the propionitrile side chain appears at higher field for the axial isomer (**1**, δ 30.8) than for the equatorial isomer (**2**, δ 38.2) as a result of steric compression. In addition, the carbinol carbon appears at lower field for an equatorial hydroxyl group (**1**, δ 71.4) than for an axial hydroxyl group (**2**, δ 70.9).[9]

Repeating the reaction of the lithiated propionitrile with 4-*tert*-butylcyclohexenone led to four products according to capillary gas chromatography in a ratio of 2.5:1:44:7.4 (order of increasing retention time) in 75% yield.[10] Flash chromatography separated the last two compounds from the first two. Hydrogenation (H_2, PtO_2, HOAc, room temperature, 3 atm) of mixtures of these latter two compounds ranging from 1:1.3 to 10.1:1 gave only **1**—a fact that allowed us to assign the latter two compounds as **3**[6] and **4**.[7] Therefore, the ratio of axial to equatorial attack in this case was 14.7:1. Furthermore, a surprisingly 6:1 ratio of the two isomers epimeric at the carbon bearing the methyl group was produced. The assignment of the major diastereomer as **3** derived from analogy (vide infra).

To examine the generality of this double diastereoselectivity, we added lithiated propionitrile to the enones **7**, **8**, and **9** as summarized in eq 3–5, Scheme II. X-ray crystallography established the stereochemistry of **10**[6] as depicted. ^{13}C NMR shifts showed the normal trends. The

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[1] For acetylide additions, see: Hennion, G. F.; O'Shea, F. X. *J. Am. Chem. Soc.* **1958**, *80*, 614. Akhrem, A. A.; Kamernitskii, A. V.; Prohoda, A. M. *Zh. Org. Khim.* **1967**, *3*, 50. Rocquet, F.; Battioni, J. P.; Capmau, M.-L.; Chodkiewicz, W. *C.R. Hebd. Seances Acad. Sci., Ser. C* **1969**, *26B*, 1449. Stork, G.; Stryker, J. M. *Tetrahedron Lett.* **1983**, *24*, 4887. Kuwajima, I.; Nakamura, E.; Hashimoto, K. *Tetrahedron* **1983**, *39*, 975. Fleming, I.; Terrett, N. K. *J. Organomet. Chem.* **1984**, *264*, 99.

[2] For sulfur ylide additions, see: Corey, E. J.; Chaykovsky, M. J. *J. Am. Chem. Soc.* **1965**, *87*, 1353. Ballantine, J. D.; Sykes, P. J. *J. Chem. Soc. C* **1970**, 731.

[3] (a) Trost, B. M.; Florez, J.; Jebaratnam, D. J. *J. Am. Chem. Soc.* **1987**, *109*, 613. (b) Also see: Bellassoued, M.; Dardoize, F.; Gaudemar-Bardone, F.; Gaudemar, M.; Goasdoue, N. *Tetrahedron* **1979**, *32*, 2713. Irdiss, N.; Perry, M.; Maroni-Bernaud, Y.; Roux-Schmitt, M.-C.; Seyden-Penn, J. *J. Chem. Res. Synop.* **1978**, 128.

[4] Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1968**, 2205. Cherest, M. *Tetrahedron* **1980**, *36*, 1593. Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 908. Also see: Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540.

[5] Wu, Y.-D.; Houk, K. N.; Trost, B. M. *J. Am. Chem. Soc.* **1987**, *109*, 5560. Also see: Toromanoff, E. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Eds.; Interscience: New York, 1967; Vol. 2, p 157. Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 738.

[6] This compound has been fully characterized spectroscopically and elemental composition established by high resolution mass spectroscopy or combustion analysis.

[7] This compound has been characterized spectroscopically.

[8] MAD = methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide). See: Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 4573.

[9] Stothers, J. B. *Carbon-13 NMR Spectroscopy*; Academic Press: New York, 1972. Senda, Y.; Ishiyama, J.; Imaizumi, S. *Tetrahedron* **1975**, *31*, 1601.

[10] The use of the potassium salt gave a 1:1:6.8:4.4 ratio. While axial selectivity remained, albeit diminished in magnitude, facial selectivity with respect to the nitrile disappeared. The source of the difference between Li and K as a counterion may relate to differences in aggregation or structure. Such a large effect was not noted in the case of metalated acetonitrile.

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