109214-67-7; (±)-**7Ae**, 109086-81-9; (±)-**7Af**, 109086-82-0; (±)-**7Ag**, 109214-68-8; (±)-**7Bd**, 109087-17-4; (±)-8, 109087-15-2; (±)-8 (*N*-(PhC(O)) deriv), 109087-08-3; (±)-8 (*N*-(*p*-$NO_2C_6HC(O)$) deriv), 109087-09-4; (±)-8 (*N*-(*p*-$MeC_6H_4C(O)$) deriv), 109087-10-7; (±)-**9Aa**, 81969-59-7; (±)-**9Ab**, 109086-83-1; (±)-**9Ac**, 109214-69-9; (±)-**9Ad**, 109214-70-2; (±)-**9Ae**, 109086-84-2; (±)-**9Af**, 109086-85-3; (±)-**9Ag**, 109086-86-4; (±)-**9Bd**, 109087-18-5; (±)-**10**, 29586-59-2; (±)-**10** (*N*-(PhC(O)) deriv), 29673-81-2; (±)-**10** (*N*-(*p*-$NO_2C_6H_4C(O)$) deriv), 109087-11-8; (±)-**10** (*N*-(*p*-$MeC_6H_4C(O)$) deriv), 109087-12-9; (±)-**11Aa**, 109214-71-3; (±)-**11Ab**, 109214-72-4; (±)-**11Ac**, 109214-73-5; (±)-**11Ad**, 109214-74-6; (±)-**11Ae**, 109214-75-7; (±)-**11Af**, 109214-76-8; (±)-**11Ag**, 109214-77-9; (±)-**11Bd**, 109087-19-6; (±)-**12Af**, 109086-87-5; (±)-**12Ag**, 109086-88-6; (±)-**13Aa**, 109086-89-7; (±)-**13Ab**, 109086-90-0; (±)-**13Ac**, 109086-91-1; (±)-**13Ad**, 109086-92-2; (±)-**13Ae**, 109086-93-3; (±)-**13Af**, 109086-94-4; (±)-**13Ag**, 109086-95-5; **14a/15a**, 109086-96-6; **14b/15b**, 109086-97-7; **14c/15c**, 109086-98-8; **16a/17a**, 109086-99-9; **16b/17b**, 109087-00-5; **16c/17c**, 109087-01-6; *p*-$NO_2C_6H_4CHO$, 555-16-8; *m*-$NO_2C_6H_4CHO$, 99-61-6; *p*-ClC_6H_4CHO, 104-88-1; PhCHO, 100-52-7; *p*-MeC_6H_4CHO, 104-87-0; *p*-$MeOC_6H_4CHO$, 123-11-5; *p*-$Me_2NC_6H_4CHO$, 100-10-7; 3-aminopropanol, 156-87-6; *o*-aminobenzyl alcohol, 5344-90-1; *o*-hydroxybenzylamine, 932-30-9.

Supplementary Material Available: Analytical and ^1H NMR data for new 1,3-oxazine derivatives **3a–g**, **5a–g**, **7a–g**, **9a–g**, **11a–g**, **12f,g**, and **13a–g** (9 pages). Ordering information is given on any current masthead page.

Dilithiation of α,β-Disubstituted Activated Olefins: α,β-Dilithiocinnamonitrile

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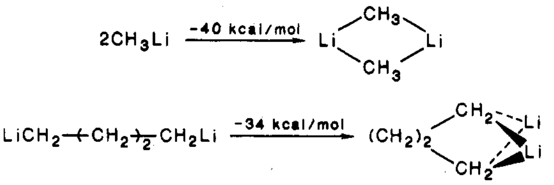
cis- and *trans*-cinnamonitrile were treated with an excess of LDA in an aprotic medium to give a high yield of one preferred isomer of PhC(Li)═C(CN)Li (C.N.-2Li). The chemistry and stereochemistry of its reactions with various electrophiles (MeOD, MeI, IBuI, RCHO, MeSSMe) was studied and discussed. α-Substituted and α,β-disubstituted derivatives of *cis*- and *trans*-cinnamonitrile were obtained. The reaction with MeOD resulted exclusively in a quantitative yield of *trans*-PhCD═CDCN. It is suggested that substitution at C_α takes place first to yield an equilibrium mixture of the corresponding β-lithiated intermediates: *cis*-PhC(Li)═C(E)CN and *trans*-PhC(Li)═C(CN)E. The type and structure of the products obtained in the reaction of this equilibrium mixture with electrophiles depends on factors affecting the nucleophilic reactivity and configurational stability of the C_β–Li bond of each of these two β-lithiated cinnamonitrile derivatives.

Organolithium compounds, usually referred to as "carbanions" because of their chemical behavior, are actually aggregates not only in the solid state but also in solution in coordinating solvents.[1] The tetramerization energy of CH_3Li, for example, is about 125 kcal/mol[2] and even highly coordinating ligands (e.g., TMEDA) are incapable of dissociating this tightly bound cluster. A remarkable number of organic species loosely called "dianions" or "polyanions" are useful synthetic intermediates.[3] The ease of formation of dianions is clearly manifested by the very small $\Delta p\bar{K}_a$ ($pK^2_{CsCHA} - pK^1_{CsCHA}$) values obtained for various carbon acids such as 9,10-dihydroanthracene ($pK_a{}^1 = 30.31$, $pK_a{}^2 = 34.1$),[4] 2,2′-biindenyl[5] ($pK_a{}^1 = 19.8$, $pK_a{}^2 = 20.3$), and 9,9′-bifluorenyl ($pK_a{}^1 = 20.5$; $pK_a{}^2 = 20.7$).[5]

Metallic counterions are intimately involved in stabilizing these polyanionic systems, which might otherwise be unstable because of electrostatic repulsion. Calculations[1,5] and crystallographic studies have clearly shown that double lithium bridging is an extremely common feature of polylithiated compounds. Double lithium bridging might be regarded as the intramolecular equivalent of the dimerization of an organolithium compound. Thus, for example, the cyclization energy for converting extended 1,4-dilithiobutane into the doubly bridged conformation approaches that of the dimerization energy of CH_3Li (eq 1).[6]



(1)

The following are some typical examples of dilithium compounds having a double lithium bridged structure as confirmed by either X-ray crystallography and/or by calculation:

[†] School of Chemistry.

[‡] Faculty of Chemistry.

(1) (a) Schleyer, P. v. R. *Pure Appl. Chem.* **1983**, *55*, 355. (b) Schleyer, P. v. R. *Pure Appl. Chem.* **1984**, *56*, 151 and references therein.

(2) Clark, T.; Schleyer, P. v. R.; Pople, J. A. *J. Chem. Soc., Chem. Commun.* **1978**, 137. Graham, G.; Richtsmeir, S.; Dixon, D. A. *J. Am. Chem. Soc.* **1980**, *102*, 5759.

(3) (a) Kaiser, E. M.; Petty, J. D.; Knustun, P. L. A. *Synthesis* **1977**, 509. (b) Stowell, J. C. *Carbanions in Organic Synthesis*; Wiley Interscience: New York, 1979. (c) Bates, R. B. *Comprehensive Carbanion Chemistry. Part A. Structure and Reactivity*; Studies in Organic Chemistry 5, Buncel, E., Durst, J., Eds.; Elsevier, 1980; Chapter, 1. (d) Bates, R. B.; Hess, B. A., Jr.; Ogle, C. A.; Schaad, L. J. *J. Am. Chem. Soc.* **1981**, *103*, 5022.

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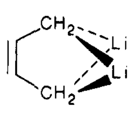
(6) Schleyer, P. v. R.; Kos, A. J.; Kaufmann, E. J. *J. Am. Chem. Soc.* **1983**, *105*, 7617.

(7) Wilhelm, D.; Clark, T.; Schleyer, P. v. R.; Dietrich, H. *J. Chem. Soc., Perkin Trans. 2* **1984**, 915.

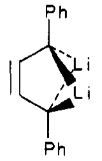
(8) Schleyer, P. v. R.; Kos, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 7928.

(9) Schubert, U.; Neugebauer, W.; Schleyer, P. v. R. *J. Chem. Soc., Chem. Commun.* **1982**, 1185.

0022-3263/87/1952-3825$01.50/0



ref 1a



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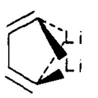

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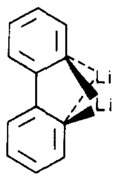
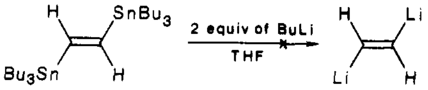


ref 9

1,2-Olefinic dianions have been prepared by various ways of nonelectrochemical deliveries of electrons to acetylenic compounds. Alkali metal mirrors and solutions of alkaline and alkaline earth metal (in amines, ethers, etc.) were useful in producing such dianions.[10-12] *cis*-1,2-Dilithiocyclooctene and *trans*-1,2-dilithio-1,2-dialkylethylenes were recently prepared by reacting the corresponding acetylenes with metallic lithium in diethyl ether.[13] The attempted preparation of *trans*-1,2-dilithioethylene by a tin–lithium exchange reaction (eq 2), failed.[14] The cis and trans isomers of CH(Li)=CHLi were however prepared very recently by Maercker et al. by an Hg–Li exchange reaction, from the corresponding ClHgCH=CHHgCl derivatives.[15]



(2)

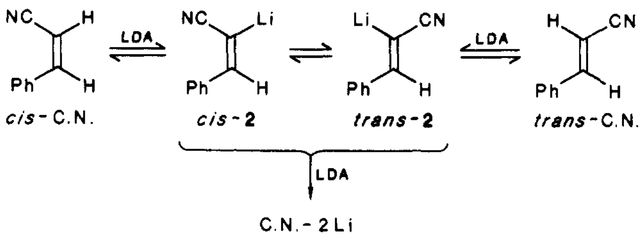
Monolithiation of α-substituted and α,β-disubstituted activated olefins has been carried out by their deprotonation in presence of an excess of *t*-BuLi, LDA, etc. The resulting vinyl lithium compounds were often used as nucleophiles in organic synthesis.[16] In spite of the fact that an excess of the base was used to affect the monolithiation reactions, formation of byproducts derived from the corresponding α,β-dilithium compounds was not reported at all, except for the formation of *tans*-PhC(Me)=C(CN)Me in the cinnamonitrile–LDA–MeI reaction system.[17] The lack of this type of information was somewhat unexpected in view of the generally facile formation of relatively stable dilithium compounds (as described above) and of the possible existence of *cis*- and *trans*-1,2-dilithioalkenes.[13,15]

It was the purpose of the present work to study in some detail this preliminary and first observation of a possible formation of an α,β-dilithiated activated olefin (PhC(Li)=C(CN)Li) by an acid–base-type reaction, with regard to its structural features and with regard to the chemical and stereochemical behavior of this reactive intermediate, in its reactions with various electrophiles.

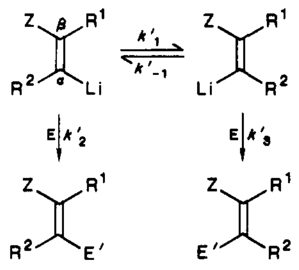
Results and Discussion

The *cis* and *trans* isomers of cinnamonitrile (C.N.) are used in the present work as model olefinic substrates for a preliminary-type study, the wider scope of which is the formation of α,β-dilithiated olefins derived from α,β-disubstituted activated olefins, as well as their properties and applications as nucleophiles.

Scheme I



Scheme II[a]



[a] $R^1 = R^2 = CO_2Me$; Z = NR_2, OR, OPh, SR.

A solution of the olefin was added to an excess of an LDA solution ([LDA]:[C.N.] = 4) at low temperatures. An excess of an electrophile was added following a deprotonation period of t_1 minutes and the reaction was further continued for t_2 minutes. The reaction was stopped by addition of methanol or of an aqueous hydrochloric acid solution. The solvents used were THF and a diethyl ether (DEE)–hexane (3:1) mixture. The electrophiles used were MeOD, MeSSMe, alkyl iodides, aldehydes.

trans-$\text{PhC}^{\beta}\text{D}{=}\text{C}^{\alpha}\text{DCN}$ (**1**) was the only olefinic product obtained on reacting the lithiated cinnamonitrile obtained from either *cis*- or *trans*-C.N. with an excess of MeOD at temperatures ranging from −80 °C to −130 °C. The same results were obtained on using THF or a relatively poor solvating medium—a DEE–hexane (3:1) mixture (Table I, entries 1–4). It should be noted that retention of the cis geometry of the product formed on reacting PhCH=C(CN)Li (obtained from *cis*-C.N.) with an electrophile was observed in DEE–hexane (3:1), whereas complete isomerization took place in THF.[17] Reacting *trans*-PhCH=CHCN and *trans*-PhCD=CDCN with MeOLi–MeOD and MeOLi–MeOH, respectively, under comparable experimental conditions, resulted in each case in recovery of the unexchanged olefinic substrate (entries 5, 6). This indicates that formation of **1** (entries 1–4) is not due to any kind of a lithium methoxide catalyzed H–D exchange taking place in the reaction mixture after addition of the excess of MeOD to the C.N.–LDA reaction mixture. These results suggest that an α,β-dilithio derivative of C.N. is the intermediate formed under the experimental conditions used.

Deuteration of the monolithiated C.N. obtained in the *trans*-C.N.–LDA–THF reaction system resulted in *trans*-PhCH=CDCN.[18] This indicates that the kinetic and thermodynamic acidities of the α-hydrogen atom of this olefin are larger than that of the β-hydrogen atom. One might expect that the acidity of the vinylic β-hydrogen atom of (*trans*-**2**) should be even smaller compared to its acidity in the non-lithiated olefin due to electrostatic repulsion in the resulting dianion. The observed unex-

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[18] Schmidt, R. R.; Speer, H. *Synthesis* **1979**, 797.

Table I. Products of the PhC(Li)=C(CN)Li-Electrophile Reaction System[a]

entry	olefin		[LDA]	electrophile					yield	
		(mmol)	(mmol)		(mmol)	t_1, min	t_2, min	products	g	(%)
1[b]	*cis*-C.N.	(2.5)	10	MeOD	(24)	15	60	*trans*-PhCD=CDCN (**1**)	0.330	(100)
2[c]	*cis*-C.N.	(2.5)	10	MeOD	(24)	25	60	**1**	0.330	(100)
3[d]	*cis*-C.N.	(2.5)	10	MeOD	(24)	10	60	**1**	0.250	(76)
4[e]	*trans*-C.N.	(2.5)	10	MeOD	(24)	10	60	**1**	0.330	(100)
5[f]	*trans*-C.N.	(2)	8	MeOD	(24)	60		*trans*-PhCH=CHCN (**1**)	0.260	(100)
6[g]	**1**	(1.6)	6.4	MeOH	(24)	20		*trans*-PhCD=CDCN (**1**)	0.150	(71)
7	*trans*-C.N.	(2)	8	1. MeOD	(6)	30	2	*trans*-PhCH=CDCN[i]	0.061	(23.7)
				2. MeOH[h]	(6)	t_3 =	15	*trans*-PhCH=CHCN	0.007	(2.7)
								trans-PhCD=CHCN	0.002	(0.77)
8	*trans*-C.N.	(2)	8	MeI	(12)	15	90	*trans*-PhC(Me)=C(CN)Me (*trans*-**4**)	0.150	(48)
								cis-PhCH=C(CN)Me (*cis*-**5**)	0.050	(17.5)
								trans-PhCH=C(CN)Me (*trans*-**5**)	0.030	(10.5)
								CH$_2$=C(Ph)C(Me)$_2$CN (**6**)	0.019	(5.5)
9	*trans*-C.N.	(2)	8	MeI	(12)	15	90	*cis*-**5**	0.036	(12.6)
								6	0.175	(51)
								trans-Ph(Et)=C(CN)Me (*trans*-**7**)	0.016	(4.8)
								CH$_2$=C(Ph)CH(CN)Me (**8**)	0.013	(4.1)
10	*trans*-C.N.	(8)	20	MeI	(16)	20	60	*trans*-**4**	0.462	(33)
								cis-**5**	0.160	(12.3)
								trans-**5**	0.075	(5.8)
								6	0.275	(18)
								trans-**7**	0.033	(2.2)
								8	0.011	(~1)
11	*trans*-C.N.	(2)	8	MeI	(4)	15	90	*cis*-**5**	0.040	(14)
								6	0.146	(46)
								trans-**7**	0.018	(5.3)
								8	0.014	(4.5)
12	*trans*-C.N.	(2)	8	I(CH$_2$)$_4$I	(6)	30	90	*trans*-PhC(BuI)=C(CN)BuI (*trans*-**9**)	0.125	(12)
								cis-PhCH=C(CN)BuI (*cis*-**10**)	0.105	(16.9)
								trans-C.N.	0.040	(15.5)
13	*trans*-C.N.	(2)	8	MeCHO	(30)	30	120	*trans*-PhCH=C(CN)CH(OH)Me (*trans*-**11**)	0.190	(55)
								cis-PhCH=C(CN)CH(OH)Me (*cis*-**11**)	0.090	(26)
14	*trans*-C.N.	(2)	8	EtCHO	(12)	15	90	*trans*-PhCH=C(CN)CH(OH)Et (*trans*-**12**)	0.300	(80)
								cis-PhCH=C(CN)CH(OH)Et (*cis*-**12**)	0.060	(16)
15	*trans*-**12**	(1)	2.5	EtCHO	(3.6)	25	120	*trans*-**12**	0.160	(86)
16	*trans*-**12**	(1)	4.0	EtCHO	(3.6)	25	120	*trans*-**12**	0.150	(80)
17	*trans*-**11**	(0.98)	3.93	MeCHO	(5.9)	30	60	*trans*-**11**	0.155	(88)
				MeOd[j]	(24)	t_3 =	15			
18[b,d]	*cis*-C.N.	(2)	8	MeSSMe	(10)	15	90	*trans*-PhC(SME)=C(CN)SMe (*trans*-**13**)[k]	0.057	(13)
								cis-PhC(SMe)=C(CN)SMe (*cis*-**13**)	0.193	(44)
								trans-PhCH=C(CN)SMe (*trans*-**14**)	*cis*-**14**:*trans*-**14** = 65:35[j]	
								cis-PhCH=C(CN)SMe (*cis*-**14**)		
19[d,l]	*cis*-C.N.	(2)	8	MeSSMe	(12)	10	60	*trans*-**13**	0.150	(34)
								cis-**13**	0.150	(34)
20	*trans*-C.N.	(2)	8	MeSSMe	(12)	15	60	*trans*-**13**[k]	0.085	(19.2)
								cis-**13**	0.025	(5.8)
21[d]	*cis*-C.N.	(2)	5	MeSSMe	(4)[m]	15	60	*trans*-**14**[k]	0.093	(27)
								cis-**14**	0.117	(33)

[a] If not specified otherwise, the reaction temperature was −90 °C, and the solvent used was THF. [b] Reaction temperature −100 °C. [c] Reaction temperature −130 °C. [d] The solvent used was a DEE–hexane (3:1) mixture. [e] Reaction temperature −80 °C. [f] MeOD was added first to the cooled LDA solution and then was followed by addition of the olefin. After t_2 min the reaction mixture was quenched with aqueous HCl solution. [g] The same as footnote e, but MeOH was used instead of MeOD. [h] MeOD was added after t_1 min, the stirring was continued for t_2 min followed by addition of the MeOD, further stirring for t_3 min, and then quenching by aqueous HCl solution. [i] The yields determined from the ^{1}H NMR spectrum of the mixture dissolved in CDCl$_3$ and in CD$_6$. [j] MeOD was added into the reaction mixture after t_2 and the reaction was further continued for t_3 min. [k] The *trans*-**13** and *cis*-**13** were obtained as a mixture that could not be separated by chromatography. The relative yields were calculated from the ^{1}H NMR spectrum of the mixture. [l] The reaction mixture was actually a DEE–hexane–THF mixture, since *cis*-C.N. dissolved in THF (10 mL) was added dropwise into the cooled solution of LDA, in DEE–hexane. [m] The experimental conditions were aimed at obtaining a monolithiated and a monosubstituted cinnamonitrile.

pected facile formation of the two adjacent C–Li bonds suggests therefore that an additional factor, which stabilizes the (C.N.-2Li), makes the second acidity of cinnamonitrile sufficient, relative to LDA, for the reaction to yield the dilithio compound. It might be reasonably assumed that the stabilizing factor is some form of a multiple lithium bridging. α-Lithiated cinnamonitriles, as well as other α-lithiated olefins, exist as cis–trans equilibrium mixtures (Scheme I).[17,19]

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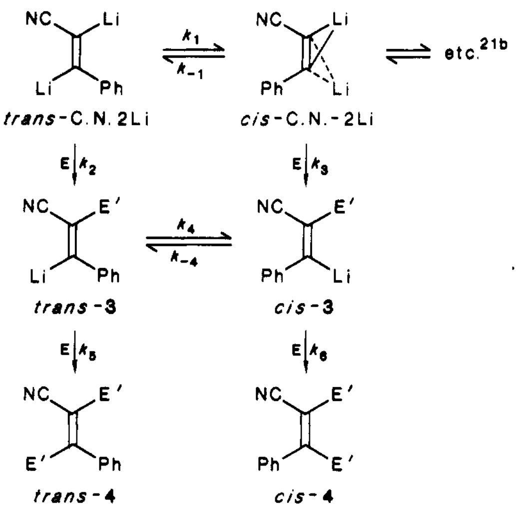
(19) Feit, B. A.; Melamed, U.; Speer, H.; Schmidt, R. R. *J. Chem. Soc., Perkin Trans. 1* 1984, 775 and references cited therein.

Scheme III



It was recently observed that the nucleophilic reactivity of an α-lithiated activated olefin derived from dimethyl fumarate is increased and its configurational stability is decreased by an electron-donating trans β-substituent,[20] namely: $k'_1 > k'_{-1}$ and $k'_2 > k'_3$ (Scheme II). It might be therefore suggested that the β-hydrogen atom of (*cis*-**2**), having a trans electron-withdrawing cyano group, is more acidic as compared to the β-hydrogen of (trans-**2**), which has a lithium atom of the trans position. To summarize, it might be reasonably assumed that the dilithiation of either *cis*-C.N. or *trans*-C.N. is a consecutive two-lithiation process, in which the $C_\alpha(CN)$–H bond is being lithiated first to give a *cis*-**2** $\rightleftharpoons$ *trans*-**2** equilibrium mixture. This equilibrium mixture undergoes a second lithiation via the intermediate *cis*-**2**, yielding C.N.-2Li (Scheme I).

Recent ab initio calculations of geometries and energies of the various possible isomers of 1,2-dilithioethylene resulted in a conclusion that it is the cis-double-bridged structure which is the most stable one.[21a] However, in line with a more recent observation on the preferred cis-to-trans isomerization of LiCH=CHLi,[15] and by applying a more advanced approach of calculation, it has been suggested that the *trans*-1,2-dilithioethylene is somewhat more stable than the cis double-bridged one.[21b] Different types of substituent and medium effects operating in the case of the lithiated derivatives of 1,2-disubstituted activated olefins[19,20] (not accounted for in these calculations) might have of course a profound influence regarding the preferred structure of the derived dilithiated olefinic species in solution. It might be assumed that C.N.-2Li too is actually an equilibrium mixture of isomers differing in their geometry and stability, such as in Scheme III.

Deuteration (or protonation) and other reactions of C.N.-2Li with electrophiles are presumably also two-step processes. A partial-deuteration experiment of C.N.-2Li was carried out using a C.N.–LDA–MeOD mixture of a molar ratio of 1:4:3 respectively, followed by addition of 3 equiv of MeOH after a short deuteration period (2 min) (Table I, entry 7). The olefin isolated (27%) consisted of a mixture of *trans*-PhCH=CDCN, *trans*-PhCD=CHCN, and *trans*-PhCH=CHCN (yields ratio of 31:1:3.5, respectively). Similarly, other monosubstituted products obtained in the reaction of C.N.-2Li with various electronphiles, were all α-substituted derivatives (Table I). We therefore suggest that in the full-deuteration experiments the first deuteration step yields preferentially the β-lithiated intermediate, *trans*-PhC(Li)=CDCN, which, thereafter undergoes a second deuteration to give the end product *trans*-PhCD=CDCN (**1**).

Electrophiles are expected to react with each of the isomeric dilithiated olefins at different rate constants, depending on the nucleophilic and electrophilic reactivities of the isomeric lithiated olefins and of the electrophiles, respectively[20] (Scheme II). The relative yields of the products that will be formed will, however, depend on the relative values of all the rate constants involved. Highly reactive electrophiles will be regarded as those for which k_2 and $k_3 \gg k_1$ and k_{-1} and k_5 and $k_6 \gg k_4$ and k_{-4} (Scheme III). MeOD may obviously be classified as an electrophile of this type. It is thus assumed that the rate constants of each of the two deuteration steps (E = MeOD) are much larger than the rate constants of the interconversion of any pair of isomers of C.N.-2Li or of any pair of isomers of the monosubstituted monolithated cinnamonitriles. Consequently, the formation of *trans*-PhCD=CDCN in the deuteration of C.N.-2Li by MeOD may be regarded by itself as an evidence for the trans structure of the monolithiated species formed in the first deuteration step. This further implies that the trans geometry of the dideuterated product might be regarded as an indirect indication that some form of a trans structure is the relatively stable structure of the dilithated species involved—C.N.-2Li.[13,15,21b]

The preferred formation of α-substituted derivatives in the monosubstitution reactions of *trans*-PhCLi=C(CN)Li with MeOD and with the other electrophiles used (Table I) clearly indicates that the basicity and nucleophilicity of its α-carbon atom are larger compared to that of the β-carbon atom. Each of the two electropositive lithium atoms of *trans*-C.N.-2Li is expected to increase the basicity and nucleophilicity of the other trans carbon atom.[20] The above-mentioned experimental results suggest that the α-lithium atom is less influencial in this respect than the β-lithium atom, probably due to the larger I^- effect of the α-cyano group as compared to that of the β-phenyl group.

Reaction of a solution of C.N.-2Li with excess of MeI resulted mainly in one disubstitution product—*trans*-PhC(CH_3)=C(CN)CH_3 (*trans*-**4**) (and/or some of its derivatives) together with the α-methyl derivative of *cis*-C.N. (*cis*-**5**) which was the major monosubstitution product (Table I, entries 8–11). Monosubstitution products at C_β were not detected at all. A similar result was obtained on using 1,4-diiodobutane as the electrophile (entry 12). It might therefore be suggested that an equilibrium mixture of the two isomeric α-methyl-β-lithio-C.N. (*trans*-**3** and *cis*-**3**) (E′ = Me) is formed first in the reaction of C.N.-2Li with MeI (Scheme III). It should be mentioned in this regard that reaction of 3,4-dilithiooctene with MeOD and with $(CH_3)_2SO_4$ resulted in *trans*-3,4-dideuteriooctene and *trans*-3,4-dimethyloctene, respectively.[13] As shown above (Scheme II), the configurational stability of a lithiated activated olefin is decreased, and its nucleophilic reactivity is increased by an electron-donating trans β-substituent.[20] The sole formation of the monosubstitution product *cis*-**5**, or its formation in a large excess of *trans*-**5** suggests, in accordance, that the lithiated olefin of type *cis*-**3** (E′ = Me, BuI) is the main constituent of the corresponding *cis*-**3** $\rightleftharpoons$ *trans*-**3** equilibrium mixture, this being due to the relative configurational instability of the C_β–Li bond affected by the trans C_α-alkyl group of *trans*-**3**. However, MeI, being

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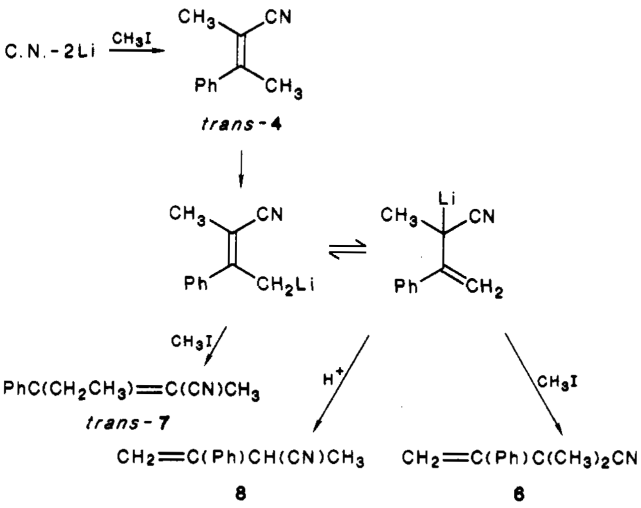
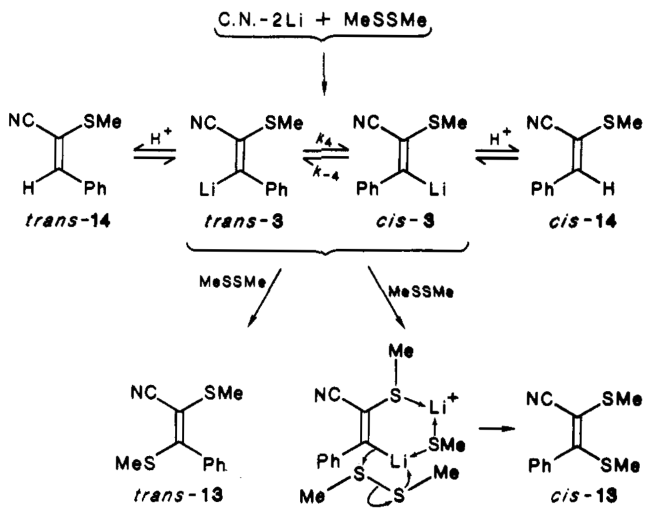
(20) (a) Feit, B. A.; Haag, B.; Schmidt, R. R. *J. Chem. Soc., Perkin Trans. 1*, in press, and references cited therein. (b) Lafont, D.; Hoch, M.; Schmidt, R. R. *J. Carbohydr. Chem.* **1986**, *5*, 601.

(21) (a) Apeloig, Y.; Clark, T.; Kos, A. J.; Jemmis, E. D.; Schleyer, P. v. R. *Isr. J. Chem.* **1980**, *20*, 43. (b) Schleyer, P. v. R.; Kaufmann, E.; Kos, A. J.; Clark, T.; Pople, J. A. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 169.

Scheme IV



Scheme V



a very much weaker electrophile as compared to MeOH, is expected to react preferentially in the second alkylation step with the more reactive nucleophile *trans*-**3** ($k_5 > k_6$), thus affecting a shift of the *cis*-**3** ⇌ *trans*-**3** equilibrium toward formation of the reaction product derived from *trans*-**3**, in spite of k_4 being larger than k_{-4} (Scheme III). Similar complete selectivities were observed for the reactions of $Ph_2C{=}O$ and PhCHO with equilibrium mixtures of dimethyl α-lithio-β-substituted fumarates and maleates, the β-substituent being an electron-donating group.[20] In analogy, the exclusive formation of the trans dialkylation products *trans*-**4**, (E′ = Me) and *trans*-**9** (E′ = BuI) suggest that $k_5 > k_4$ and k_6 (Scheme III) for this reaction system. It should be noted that alkylation of either PhCH=C(CN)Li or C.N.-2Li in THF using MeI results in different isomers of α-methylcinnamonitrile in each case. *trans*-$PhCH{=}C(CN)CH_3$ is obtained from the monolithiated olefin,[17,18] while *cis*-$PhCH{=}C(CN)CH_3$ is the prefered product obtained from the dilithiated olefin. This might be due to the above-mentioned predominance of *cis*-**3** in the *cis*-**3** ⇌ *trans*-**3** equilibrium mixture.

Products derived from the in situ allylic deprotonation of *trans*-$PhC(CH_3){=}C(CN)CH_3$ (*trans*-**4**) were also formed in the C.N.-2Li–MeI reaction system (entries 8–11) (Scheme IV). The main product of these was $CH_2{=}C(Ph)C(CH_3)_2CN$ (**6**), which in some case (entries 9, 11) was even the main reaction product. The other minor (<5%) products were *trans*-$PhC(CH_2CH_3){=}C(CN)CH_3$ (trans-**7**) and $CH_2{=}C(Ph)CH(CH_3)CN$ (**8**).

The results of the reaction of C.N.-2Li with aldehydes (Table I, entries 13, 14) were clearly different from those obtained with the alkyl iodides as electrophiles. Disubstitution products were *not* obtained at all, and the mixture of monosubstitution products consisted mainly of the ones derived from *trans*-cinnamonitrile, in spite of the expected isomerization of *trans*-**3** (E′ = $CH(R)O^-Li^+$; R = Me, Et) to the corresponding cis isomers (due to $k_4 > k_{-4}$) (Scheme III). The fact that a second substitution at C_β did not take place could not be due to the nonformation of the corresponding β-lithiated species of the types *trans*-**3** and *cis*-**3**) (Scheme III). These intermediates must have been formed since it is the C.N.-2Li which reacts with RCHO in the first step. The fact that a second substitution at C_β did not take place was varified experimentally by reacting the α-carbinol derivatives *trans*-**11** and *trans*-**12** with the corresponding aldehydes in the presence of an excess of LDA (entries 15–17). The starting materials were recovered in high yields. No substitution at C_β was observed and no deuteriation of the C_β–Li bond was detected after quenching the reaction mixture with MeOD (entry 17). These results might be due to either insolubility of the lithium alkoxides of the type *trans*-**3** and *cis*-**3** (E′ = $CH(R)O^-Li^+$), or to a protonation of these intermediates by the i-Pr_2NH or the aldehyde present, being faster than both their interconversion and their reaction with the electrophile RCHO.

The reaction of C.N.-2Li with MeSSMe gave a mixture of two isomeric disubstitution products PhC(SMe)=C(CN)SMe (*cis,trans*-**13**) as main products (~60%), together with (in some cases) an isomeric mixture of PhCH=C(CN)SMe (*cis,trans*-**14**) (Table I, entries 18–20). Assignment of a cis geometry to one of the two isomeric disubstitution products based on their NMR spectra was not possible. None of the two showed the downfield shift of the two orto hydrogens of the phenyl group, which was typical of all other *cis*-C.N. derivatives (Table II). However, a cis structure could be assigned to one of the two PhCH=C(CN)SMe isomers, which showed this typical downfield shift (Table II). Formation of a cis–trans mixture of PhC(SMe)=C(CN)SMe was in contrast to the sole formation of *trans*-PhC(Me)=C(CN)Me in the C.N.-2Li–MeI reaction system. Formation of *cis*-**13** in addition to the expected *trans*-**13** might be due to the following reasons: (a) MeSSMe, being a more reactive electrophile than MeI, reacts less selectively[20a] and will therefore give also the product derived from the less reactive nucleophile (*cis*-**3**, E′ = SMe). (b) A possible participation of the C_α-SMe group and the MeS^-Li^+ formed, in a multicenter-type stabilization of the C_β–Li bond of *cis*-**3**, and not of *trans*-**3**, might also be a contributing factor favoring the formation of *cis*-PhC(SMe)=C(CN)SMe (Scheme V). It might be reasonably assumed that the internally coordinated monolithio intermediates derived from *cis*-C.N., *cis*-PhC(Li)=C(CN)SMe, should be relatively more stable and favored in the poorly solvating medium DEE–hexane (3:1) (entries 18, 19), as compared to THF (entry 18). In favor of this assumption was the fact that the yields of *cis*-**14** were higher than those of *trans*-**14** in DEE–hexane (entries 18, 21) as compared to THF (entry 20) or to a mixture of THF and DEE–hexane (entry 19). The major component of the *cis,trans*-**13** obtained in DEE–hexane is therefore arbitararily assigned as a derivative of *cis*-C.N. (Table I and II).

Experimental Section

Materials. THF was refluxed over sodium and then distilled. A solution of sodium diphenylketyl in the distilled THF was prepared, and the required amount of the THF was directly

Table II. ^{1}H NMR[a] and Mass Spectral Data of the Reaction Products

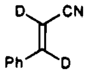
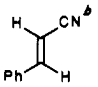
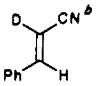
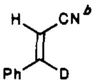
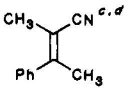
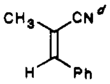
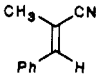
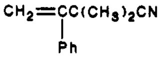
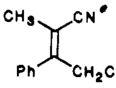
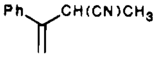
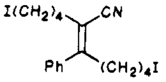
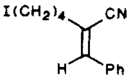
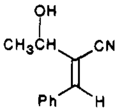
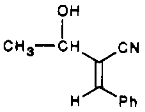
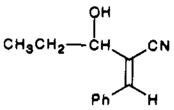
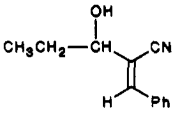
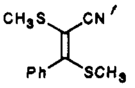
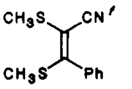
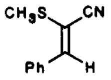
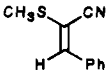
product	formula	ppm							m/e	anal. found (required)		
										C	H	N
 **1**	$C_9H_5D_2N$				7.35–7.76				131			
	C_9H_7N	5.08 (d)	6.64 (d)	6.70–6.84 (m, 2 H)	6.89–7.07 (m, 3 H)							
	C_9H_6DN		6.64 (m)	6.70–6.84 (m, 2 H)	6.89–7.07 (m, 3 H)							
	C_9H_6DN	4.95 (s)		6.70–6.84 (m, 2 H)	6.89–7.07 (m, 3 H)							
 *trans*-**4**	$C_{11}H_{11}N$	1.84 (m, 3 H)	2.36 (m, 3 H)	7.10–7.53 (m, 5 H)					157			
 *cis*-**5**	$C_{10}H_9N$	2.15 (d, 3 H)	6.94 (d, 1 H)	7.30–7.45 (m, 3 H)	7.67–7.72 (m, 2 H)				143			
 *trans*-**5**	$C_{10}H_9N$	2.15 (d, 3 H)	7.21 (d, 1 H)	7.30–7.45 (m, 5 H)					143			
 $CH_2{=}\underset{Ph}{\underset{\vert}{C}}C(CH_3)_2CN$ **6**	$C_{12}H_{13}N$	1.53 (s, 6 H)	5.15 (s, 1 H)	5.59 (s, 1 H)	7.25–7.55 (m, 5 H)					84.11 (84.17)	7.71 (7.65)	8.07 (8.18)
 *trans*-**7**		0.96 (t, 3 H)	2.07 (s, 3 H)	2.55 (q, 2 H)	7.29–7.40 (m, 5 H)							
 **8**		1.46 (d, 3 H)	3.86 (q, 1 H)	5.46 (s, 1 H)	5.56 (s, 1 H)	7.36–7.45 (m, 5 H)						
 *trans*-**9**		1.88–1.90 (m, 8 H)	2.12 (t, 2 H)	2.76 (t, 2 H)	3.05 (t, 2 H)	3.14 (t, 2 H)		7.20–7.50 (m, 5 H)				
 *cis*-**10**	$C_{13}H_{14}IN$	1.7–1.95 (m, 4 H)	2.44 (t, 2 H)	3.22 (t, 2 H)	6.95 (s, 1 H)	7.07–7.10 (m, 2 H)	7.33–7.46 (m, 3 H)		311	50.74 (50.18)	4.82 (4.54)	3.94 (4.50)
 *trans*-**11**	$C_{11}H_{11}NO$	1.53 (d, 3 H)	2.13 (br s, 1 H)	4.86 (q, 1 H)	7.16–7.55 (m, 6 H)					76.31 (76.28)	6.58 (6.40)	7.95 (8.09)
 *cis*-**11**	$C_{11}H_{11}NO$	1.53 (d, 3 H)	2.06 (br s, 1 H)	4.56 (q, 1 H)	7.31–7.53 (m, 3 H)	7.63–7.88 (m, 3 H)				75.99 (76.28)	6.41 (6.40)	8.09 (8.09)
 *trans*-**12**	$C_{12}H_{13}NO$	0.98 (t, 3 H)	1.70–1.95 (q, 2 H)	2.61 (br s, 1 H)	4.55 (t, 1 H)	7.34–7.46 (m, 6 H)			187			

Table II (Continued)

product	formula	ppm							m/e	anal. found (required)		
										C	H	N
 *cis*-**12**	$C_{12}H_{13}NO$	1.02 (t, 3 H)	1.83 (q, 2 H)	2.40 (br s, 1 H)	4.33 (t, 1 H)	7.33 (s, 1 H)	7.35–7.45 (m, 3 H)	7.45–7.70 (m, 2 H)	187	76.84 (76.98)	7.22 (7.00)	7.41 (7.48)
 *trans*-**13**	$C_{11}H_{11}N$-S_2	1.99 (s, 3 H)	2.57 (s, 3 H)	7.17–7.60 (m, 5 H)					221			
 *cis*-**13**	$C_{11}H_{11}N$-S_2	2.02 (s, 3 H)	2.37 (s, 3 H)	7.17–7.60 (m, 5 H)						59.95 (59.69)	5.12 (5.01)	6.08 (6.33)
 *trans*-**14**	$C_{10}H_9NS$	2.57 (s, 3 H)	7.36–7.66 (m, 6 H)						175	68.08 (68.54)	5.34 (5.18)	7.88 (7.99)
 *cis*-**14**	$C_{10}H_9NS$	2.51 (s, 3 H)	7.34–7.45 (m, 4 H)	7.69–7.78 (m, 2 H)					175			

[a] ^1H NMR spectra were recorded in $CDCl_3$ as solvent and Me_4Si as an internal standard. [b] ^1H NMR spectrum was that of a mixture of *trans*-PhCH=CHCN, *trans*-PhCH=CDCN, and *trans*-PhCD=CHCN (in C_6D_6) recovered from the reaction mixture of entry. [c] The CH_3 absorption bands for the *E* (1.83, 2.36 ppm) and for the *Z* isomers (2.04, 2.14 ppm) are given in the literature.[23] [d] A downfield shift of two out of the five H atoms of the phenyl group is identical with the ^1H NMR spectra of *cis*-1-cyano-2-phenylolefins (and not to the corresponding trans isomers). Assignment of cis or trans geometry to the reaction products obtained was based on this observation. Examples of this deshielding effect of the cyano group are shown in the NMR data of some α,β-unsaturated nitriles (δ, $CDCl_3$) *cis*-cinnamonitrile (5.40, d, 1 H; 7.10–7.55, m, 3 H; 7.53–8.00, m, 2 H), *trans*-cinnamonitrile n(5.85, d, 1 H; 7.35, d, 1 H; 7.05–7.73, m, 5 H), fluoren-9-ylideneacetonitrile (5.91, s, 1 H; 7.10–7.90, m, 7 H; 8.20–8.60, m, 1 H),[24] fluoren-9-ylidenemalonitrile (7.18–7.43, m, 6 H; 8.31, m, 2 H);[25] α-methyl-*cis*-cinnamonitrile (2.06, s, 3 H; 6.80, bs, 1 H; 7.30, m, 3 H; 7.60, m, 2 H).[26] [f] the ^1H NMR spectrum was that of *trans*-**13** and *cis*-**13** which could not be separated by chromatography.

distilled from this solution into the reaction flask. DEE and hexane were refluxed over sodium and then distilled twice over sodium and were kept over sodium. The required amounts of each of the two was directly distilled into the reaction flask. LDA was prepared for each experiment in the reaction flask by adding an equimolar amount of *t*-BuLi (dissolved in hexane) into the cooled *i*-Pr_2NH–solvent solution. All manipulations and all the reactions of cinnamonitrile with the various electrophiles in the presence of LDA were carried out under thoroughly dried oxygen-free nitrogen and under anhydrous conditions. *cis*-Cinnamonitrile was prepared by isomerization of *trans*-cinnamonitrile.[22] The electrophiles used (acetaldehyde, propionaldehyde, methyl iodide, 1,4-diiodobutane, dimethyl disulfide) were distilled before use. Absolute CH_3OD was used for the deuteriation experiments.

A General Procedure for Preparation of C.N.-2Li and Its Reaction with Electrophiles. The solvent (THF, or DEE and hexane) was distilled into the reaction flask and to an attached dropping funnel. The flask was cooled to the reaction temperature (which was kept to the end of the experiment), and diisopropylamine followed by *t*-BuLi was added into the cooled stirred solvent. A solution of the electrophile in the solvent used was prepared in the dropping funnel. The *i*-Pr_2NH–*t*-BuLi mixture was stirred for 30 min, and the cinnamonitrile was then added in one portion by the use of a syringe. The color of the reaction mixture became immediately dark red-brown. Stirring was continued for t_1 minutes to affect deprotonation of the olefin. The solution of the electrophile was then added dropwise from the dropping funnel, during 10 min. In the deuteriation experiments, the alcohol itself was added into the reaction flask in one portion by using a syringe. The reaction mixture was further stirred for t_2 minutes and then quenched by MeOH or aqueous hydrochloric acid solution to stop the reaction. This was followed by extraction with ether. The crude mixture of products recovered from the etheral extracts was first purified by chromatography on a short silica gel column and then was separated into its components by a medium pressure chromatography system on a silica gel column, using a light petroleum ether(40–60 °C)–ethyl acetate mixture as eluent.

Data concerning the reactants used and their concentrations, t_1 and t_2 values, the products obtained, and their yields are given for each experiment in Table I. Structural formulas of the products obtained, ^1H NMR data, and mass spectral data are given in Table II.

Registry No. 1, 107681-77-6; *trans*-**4**, 35684-72-1; *cis*-**5**, 26157-51-7; *trans*-**5**, 53587-72-7; **6**, 72012-47-6; *trans*-**7**, 35684-76-5; **8**, 107681-78-7; *trans*-**9**, 107711-10-4; *cis*-**10**, 107711-11-5; *trans*-**11**, 107681-76-5; *cis*-**11**, 86536-72-3; *trans*-**12**, 107681-75-4; *cis*-**12**, 72676-47-2; *trans*-**13**, 107681-79-8; *cis*-**13**, 107681-80-1; *trans*-**14**, 95757-64-5; *cis*-**14**, 95757-63-4; *cis*-C.N., 24840-05-9; *trans*-C.N., 1885-38-7; MeOD, 1455-13-6; MeI, 74-88-4; $I(CH_2)_4I$, 628-21-7; MeCHO, 75-07-0; EtCHO, 123-38-6; MeSSMe, 624-92-0.

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