10 °C during the addition. After 15 min more, ca. 2 g of potassium carbonate was added and stirring was continued for another 10 min. The product was distilled at 1 atm to give 71 g (77%) of the desired 1-ethoxyethyl ether, bp mostly 146 °C. NMR and IR spectra were satisfactory.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Registry No. *cis*-**2/3**, 73137-44-7; *trans*-**2/3**, 73137-45-8; *cis*-**5/6**, 73208-56-7; *trans*-**5/6**, 73208-57-8; *cis*-**7/8**, 73137-46-9; *trans*-**7/8**, 73137-47-0; *cis*-**9/10**, 73137-48-1; *trans*-**9/10**, 73137-49-2; *cis*-**13/14**, 73137-50-5; *trans*-**13/14**, 73137-51-6; *cis*-**15/16**, 73137-52-7; *trans*-**15/16**, 73137-53-8; *cis*-**17/18**, 73137-54-9; *trans*-**17/18**, 73137-55-0; *cis*-**19/20**, 73137-56-1; *trans*-**19/20**, 73137-57-2; *cis*-**23/24**, 73137-58-3; *trans*-**23/24**, 73137-59-4; *cis*-**25/26**, 73137-60-7; *trans*-**25/26**, 73137-61-8; *cis*-**27/28**, 73137-62-9; *trans*-**27/28**, 73137-63-0; **29**, 177-23-1; *cis*-**30/31**, 73137-64-1; *trans*-**30/31**, 73137-65-2; **32**, 73046-13-6; **33**, 73137-66-3; **34**, 73208-58-9; PR, 107-19-7; PR THP ether, 6089-04-9; PR 1-ethoxyethyl ether, 18669-04-0; MB, 115-19-5; MB THP ether, 27943-46-0; MB 1-ethoxyethyl ether, 39807-00-6; B, 927-74-2; B THP ether, 40365-61-5; P, 2117-11-5; P THP ether, 58654-09-4; dihydro-5-methyl-2(3*H*)-furanone, 108-29-2; 5-ethyldihydro-2(3*H*)-furanone, 695-06-7; dihydro-5-propyl-2(3*H*)-furanone, 105-21-5; 5-butyldihydro-2(3*H*)-furanone, 104-50-7; dihydro-5-pentyl-2(3*H*)-furanone, 104-61-0; 5-hexyldihydro-2(3*H*)-furanone, 706-14-9; tetrahydro-2*H*-pyran-2-one, 542-28-9; dihydro-2(3*H*)-furanone, 96-48-0; ethyl vinyl ether, 109-92-2.

Supplementary Material Available: ^{13}C NMR data for all compounds and mass spectral data for compounds not previously reported (4 pages). Ordering information is given on any current masthead page.

Alkyllithium Reagents from Alkyl Halides and Lithium Radical Anions[1]

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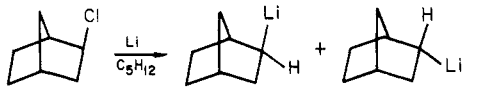
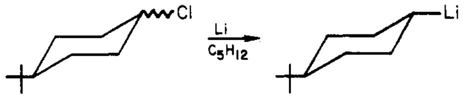
The reaction of alkyl halides with three different lithium radical anions, lithium naphthalene (LiN), lithium di-*tert*-butylnaphthalene (LiDBN), and lithium di-*tert*-butylbiphenyl (LiDBB), was studied. The reaction of alkyl halides with an excess of LiN, LiDBN, or LiDBB in THF at −78 °C leads to a consistently high yield (96–100%) of reduction products (RH, RLi) with a high degree of formation of RLi (anion trapping 93–95%) in the case of LiDBB. LiDBN consistently produces high yields of reduction products (89–99%) with widely variable amounts of anion trapping (21–88%), while LiN provides variable yields of reduction (39–99%) and anion trapping (24–65%). Variation of the concentration of lithium bromide and naphthalene and the ratio of alkyl halide to naphthalene in conjunction with the use of deuterium tracer experiments provided evidence consistent with a competition between metalation of the lithium dihydronaphthalenedicarboxylate by alkyllithium and carbonation of alkyllithium in the carbonation step of the analysis.

Alkyllithium reagents are potentially very valuable synthetic reagents for organic synthesis. Often the yields of products from addition reactions with ketones and nitriles exceed those of the more common Grignard reagents,[2] while synthetic sequences which start with the formation of lithium dialkylcuprates from cuprous halide employ lithium reagents, since the Grignard alternative generally cannot be substituted.[3] However, lithium reagents, other than those commercially available, have not achieved as widespread use as one might expect in view of their superior properties. This can be ascribed to the fact that their preparation from the halide and lithium metal often gives rather low yields or requires considerable "magic" in order to attain high yields.[4,5] For example, Applequist and Chmurny have reported that treatment of *exo*-2-norbornyl chloride with lithium metal in refluxing pentane gives yields of the lithium reagent as high as 33% but averaging about 10%,[6] while Alexandrou was unsuccessful in a variety of attempts to prepare (4-*tert*-butylcyclohexyl)lithium from the bromide.[7] Glaze and Selman later prevailed in the preparation of (4-*tert*-butylcyclohexyl)lithium utilizing the chloride with lithium containing 1% sodium.[8] This illustrates another difficulty of the conventional procedure—bromides give much poorer yields than chlorides. This is undoubtedly due to the greater tendency of bromides to undergo side reactions (coupling) with lithium reagents.



(1)

4:1, 10% yield



(2)

35% yield

Clearly, the development of a reaction sequence which would overcome the deficiencies in the traditional preparation of alkyllithium reagents would be a significant step forward for synthetic and mechanistic investigations. With this background in mind, a study aimed at uncovering a

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[1] Reported in part in preliminary form: P. K. Freeman and L. L. Hutchinson, *Tetrahedron Lett.*, 1849 (1976).

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[3] G. H. Posner, *Org. React.*, **22**, 253 (1975); J. F. Normant, *Synthesis*, 1, 63 (1972).

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[5] W. N. Smith, Jr., *J. Organomet. Chem.*, **82**, 7 (1974).

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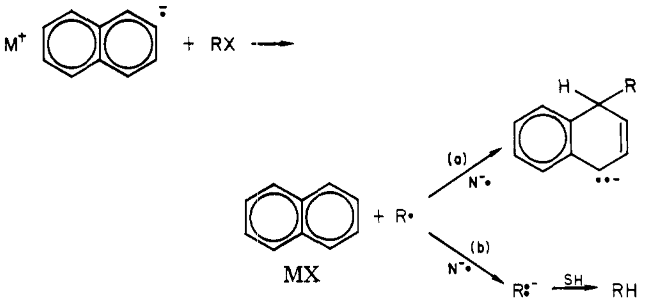
Table I. Survey of Lithium Radical Anion-Alkyl Halide Reactions

	LiN		LiDBN		LiDBB	
halide	% RH^a yield	% anion trapping	% RH yield	% anion trapping	% RH yield	% anion trapping
1-chlorooctane	92 (2)	45 (8)^b	96	49	100 (1)	94 (1)^c
1-bromooctane	79	47			96	91
2-chlorooctane	63 (0)	24 (5)^c	96	21^d	101	87
2-bromooctane	57	25^e			99 (2)	83 (4)^c
3-chloro-3-methylheptane	39 (1)	74 (5)^c	89	81	97	88^d
7-chloronorcarane	99	65^e	99	88	99	95^d

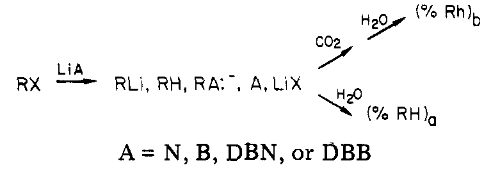
^{a} ±4% estimated error. Numbers in parentheses are standard deviations (SD). ^{b} Average and SD of 8 runs. ^{c} Average and SD of 3 runs. ^{d} Average of 2 runs. ^{e} Warmed to -5 °C to speed up reaction.

Scheme I



M = Na$^+$ or Li$^+$

Scheme II



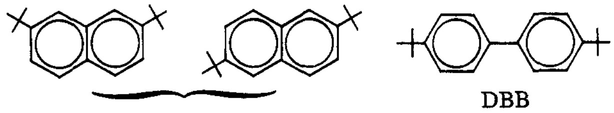
A = N, B, DBN, or DBB

new method for the determination of the configurational equilibrium of carbon-centered radicals led us to the discovery of a versatile new reagent, lithium 4,4′-di-*tert*-butylbiphenyl (LiDBB), which provides for the formation of alkyllithium reagents from alkyl halides in consistently high yields.

While the reactions of aromatic radical anions with alkyl and aryl halides have received a great amount of attention in recent years,[9] the great majority of reports have described the use of sodium naphthalene as the alkali radical anion species and only minimal attention has been given to other systems. The products of the reactions of sodium naphthalene (NaN) and alkyl halides typically partition about equally between hydrocarbons and alkylated dihydronaphthalene, as illustrated in Scheme I. Thus, with NaN the potentially useful anion is formed in a yield most likely in the range 20–70%, and, as an added difficulty, the anion is immediately destroyed by reaction with the solvent[9–13] or with the parent halide.[9,11] Recent reports suggest that the alkyl carbanion may be captured in the presence of $MgCl_2$.[12]

It appeared to us that a dramatic improvement in the synthetic potential for the generation of alkali alkyls might be achieved by (1) substituting Li for Na, which should allow the alkyl carbanion to be trapped in the form of the organolithium reagent,[13] and (2) reducing the ratio of alkylation (route a) to electron transfer (route b) through a simple modification of the structure of the radical anion. Since electron-transfer processes may take place between molecular entities which are separated by as much as 7–9 Å,[14] whereas the transition state for the alkylation of a radical anion should be at a bond-forming distance, increasing the steric requirement of the radical anion might favor (b) over (a). Placing methyl groups on naphthalene would not work well since the protons of the methyl groups would be benzylic and would destroy the lithium reagent. *tert*-Butyl groups, on the other hand, have no acidic protons and appeared to be a very reasonable choice.

A study of the reactions of lithium naphthalene (LiN), lithium biphenyl (LiB), lithium di-*tert*-butylnaphthalene (LiDBN), and lithium di-*tert*-butylbiphenyl (LiDBB) with a spectrum of alkyl halides was thus initiated. The *tert*-butyl-substituted arenes were obtained quite easily by the Friedel–Crafts reaction of *tert*-butyl chloride with naphthalene[15] or biphenyl.[16] The reaction with naphthalene gives an approximately equal mixture of 2,6- and 2,7-di-*tert*-butylnaphthalenes. It is very difficult to separate these isomers by crystallization, and thus the mixture was used in all reactions.



DBN DBB

The technique used in the survey will now be described. To a solution of the radical anion cooled to -78 °C was added an accurately measured quantity of an internal standard (nonane or decane), followed by the halide. In most cases, a large excess of the radical anion was used. After sufficient time had elapsed for completion of the reaction, an aliquot was removed and immediately quenched in water. Vapor-phase chromatographic analysis gave the total yield of hydrocarbon and lithium reagent (RH + RLi) (% RH)$_a$ (Scheme II). After the first aliquot was taken, carbon dioxide was bubbled in until the intense color of the radical anion disappeared, and then a few

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(15) H. M. Crawford and M. C. Glessman, *J. Am. Chem. Soc.*, **76**, 1108 (1954).

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Table II. Reduction Potentials of Selected Aromatic Hydrocarbons in DMF

compd	$E_{1/2}$, V[a]	ref
naphthalene	−1.98	19
2,6-di-*tert*-butylnaphthalene	−2.07	19
2,7-di-*tert*-butylnaphthalene	−2.09	19
biphenyl	−2.05	20
4,4′-di-*tert*-butylbiphenyl	−2.14	20
anthracene	−1.46[b]	

[a] Vs. Hg pool. [b] Calculated from titration data for biphenyl vs. anthracene in HMPA.[21]

minutes more. This treatment destroys the lithium reagent by generating carboxylate salts, ketones, and *tert*-alkoxides. An aliquot of this mixture was then taken and treated as before to afford the quantity $(100[(\% \mathrm{RH})_a - (\% \mathrm{RH})_b]/(\% \mathrm{RH})_a)(\% \mathrm{RH})_b$. The percent reduction of the yield of hydrocarbon $[(\% \mathrm{RH})_a - (\% \mathrm{RH})_b]$ is taken to be the percent efficiency in trapping the anion as the lithium reagent.[17] From knowledge of the yield of reduction products, the extent of coupling (alkylation) can be obtained in the case of chlorides by subtraction from 100% since dimerization does not occur. Bromides, however, form around 5% dimers.[18]

Results selected from Tables III–IX are presented in Table I. It is apparent from Table I that lithium di-*tert*-butylbiphenyl (LiDBB) gives excellent yields of lithium reagents. The maximum extent of coupling is a few percent and is probably much less, while anion trapping is typically around 90%. LiDBB closely approaches the ideal of a homogeneous solution of lithium metal in THF, with the DBB moiety functioning only as an inert carrier of an electron, at least in reactions with alkyl halides and radicals.

It is interesting to note that lithium naphthalene or lithium biphenyl, when reacting with CO_2, gives a mixture of the hydrocarbon and the dihydrocarboxylic acids. In contrast, LiDBB gives a 97% isolated recovery of pure DBB. It is not known what the inorganic products are. No experiments with LiDBN have been done specifically on the reaction with water or carbon dioxide. However, it was noticed during the experiments with alkyl halides that while LiDBB produced only a slight cloudiness with carbon dioxide, lithium naphthalene and LiDBN both produced very thick milky suspensions. It is probable that LiDBN reacts normally. Another abnormality of DBB is seen in the fact that while the hydrocarbon reacts quite readily in THF with both lithium and potasssium, no reaction with sodium beyond a very slight coloration of the surface could be induced. Various conditions included temperature variation between 20 and −78 °C while the metal was sliced in situ to expose a fresh surface.

In addition to the steric effect of the *tert*-butyl groups, another factor which may reduce coupling in the case of $DBB^{-\cdot}$ is the 0.16-V higher reduction potential relative to naphthalene (Table II). Biphenyl radical anion undergoes relatively more electron transfer than naphthalene. It has been reported[10c] that sodium biphenyl reacting with 5-hexenyl fluoride gives virtually quantitative yields of reduction products. Unfortunately, lithium biphenyl precipitates out of solution under the conditions used in this study (−78 °C). Nevertheless, one run was made using the tertiary chloride 3-chloro-3-methylheptane (Table VII). The extent of electron transfer is 56%, larger than naphthalene radical anion, which gives only 39% electron transfer. It is likely that for primary and perhaps secondary halides, lithium biphenyl would give almost as high yields of lithium reagents as LiDBB. However, its inhomogeneous nature in THF at −78 °C would seem to complicate the interpretation in mechanistic studies. By combining these results with the literature observation[11b] that sodium anthracene undergoes only 1% electron transfer with even primary substances, the following order of electron transfer vs. coupling can be constructed: DTBB > DTBN > B > N >> A. It is seen from Table II that this is also the order of reduction potentials.

The reaction of lithium naphthalene dianion in diethyl ether with 2-bromooctane gives only 9% electron transfer vs. 57% for lithium naphthalene in THF. Similarly, lithium di-*tert*-butylnaphthalene (as the dianion) gives only 34% electron transfer in diethyl ether vs. 96% in THF (as the radical anion) when allowed to react with 2-bromooctane (Table V). These observations, combined with a consideration of the data of Garst and Barbas[11b] on the reactions of 1,4-diiodobutane with alkali naphthalenes, indicate that loose ion pairs give relatively more electron transfer than contact ion pairs which, in turn, give much more electron transfer than the very tight ion triples of the dianions. Thus, if one is attempting to synthesize alkylated dihydronaphthalenes, the highest yields would be obtained in the least polar solvent.

A consideration of the factors which control the extent of anion trapping, as indicated by the carbon dioxide quench method (Table I), is prompted by the fact that LiDBB gives results vastly different from either lithium naphthalene or LiDBN. LiDBB gives anion trapping values consistently near 90%, while the values for lithium naphthalene and LiDBN vary from 21 to 88%. One is also struck by the close tracking between lithium naphthalene and LiDBN. How is it possible for LiDBB to give 87% anion trapping, while under identical conditions lithium naphthalene and LiDBN give less than 25%? If for some reason LiDBB gives the lithium reagent directly, while lithium naphthalene and LiDBN give the free anion, which would presumably react very rapidly with solvent, then addition of a large excess of lithium bromide should increase the extent of anion trapping. The addition of sufficient lithium bromide to make the solution 0.4 M failed to affect the anion trapping (runs 8 and 9, Table VI). Increasing either the naphthalene or lithium quantities also did not affect the percent of anion trapping. This shows that disproportionation to the dianion was not the cause of the low yields (runs 7 and 8, Table III). Running the reaction of lithium naphthalene at −63 °C rather than −78 °C did not much affect the anion trapping, although increasing the reaction temperature to 0 °C did cut it in about half (runs 9 and 10, Table III). Entry 17, Table III, was run to test the hypothesis that adventitious water was destroying the lithium reagent. The addition of bromobutane in large excess before adding 1-chlorooctane would create enough butyllithium to protect the octyllithium from destruction by small quantities of a proton source.

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[17] The term "anion trapping" is derived from literature usage. It is very rare to see the metal ion represented in the electron transfers, which implies that the anion generated is free, even though this may not have been intended in all cases. Considering the high cation affinity of an alkyl anion, the low dielectric constant for the solvents used, and the fact that the radical anions exist as ion pairs, it is not likely that free anions play a significant role in the mechanistic scheme. In this section "anion trapping" implies only the phenomenological outcome of an experiment designed to determine the fraction of reduction products which contain a carbon–lithium bond.

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[21] M. Szwarc, Ed., "Ions and Ion Pairs in Organic Reactions", Vol. 2, Wiley, New York, 1974, p 38.

Table III. Reaction of 1-Chlorooctane with Lithium Radical Anions

run	conditions[a]	radical anion	hydrocarbon yield, %	indicated RLi yield, % of HC
1	A	$N^{-\cdot}$	93	53
2	B	$N^{-\cdot}$	92	39
3	B	$N^{-\cdot}$	88	40
4	B	$N^{-\cdot}$	92	37
5	B	$N^{-\cdot}$	91	35
6	B	$N^{-\cdot}$	94	60
7	B (excess N)	$N^{-\cdot}$	91	48
8	B (excess Li)	$N^{-\cdot}$	90	45
9	B (−63 °C)	$N^{-\cdot}$	91	35
10	B (0 °C)	$N^{-\cdot}$	79	25
11	B (in DME)[b]	$N^{-\cdot}$	78	53
12	A (sodium, room temperature)	$N^{-\cdot}$	44	
13	A	$DBB^{-\cdot}$	101	94
14	B	$DBB^{-\cdot}$	100	95
15	B	$DBB^{-\cdot}$	99	94
16	B	$DBN^{-\cdot}$	96	49
17	A, scavenged[c]	$N^{-\cdot}$	96	56

[a] Conditions for the preparation of the radical anion solutions: (A) THF, 30 mL; aromatic hydrocarbon, 6 mmol; alkali metal, 5 mmol, which results in a solution 0.17 M in radical anion; (B) as in A, but with the addition of 1.56 mequiv of Br_2, which produces a solution 0.11 M in radical anion and 0.05 M in LiBr. Halide (13% of required stoichiometry) added to radical anion solution at −78 °C unless otherwise noted. [b] Not homogeneous. [c] Bromobutane added before 1-chlorooctane (1-bromobutane–1-chlorooctane 2.5:1).

Table IV. Reaction of 1-Bromooctane with Lithium Radical Anions

run	conditions[a]	radical anion	hydrocarbon yield, %	indicated RLi yield, % of HC
1	A	$N^{-\cdot}$	79	47
2	100% stoich	$N^{-\cdot}$	76	93
3	A	$DBB^{-\cdot}$	96	94
4	B	$DBB^{-\cdot}$	96	91
5	A (potassium)	$N^{-\cdot}$	25[b]	
6	A	$N^{-\cdot}$	80	41
7	A	$N^{-\cdot}$	80	44
8	A, 87% stoich	$N^{-\cdot}$	78	83
9	A, 45%	$N^{-\cdot}$	79	56

[a] Standard conditions A and B described in footnote *a*, Table III, and in Experimental Section. [b] An approximately 70% yield of dimer was detected by VPC.

Table V. Reaction of 2-Bromooctane with Lithium Radical Anions

run	conditions[a]	radical anion	hydrocarbon yield, %	indicated RLi yield, % of HC
1	A	$N^{-\cdot}$	57	29
2	B	$N^{-\cdot}$	57	21
3	100% stoich	$N^{-\cdot}$	51	52
4	dianion	N^{2-}	9	49
5	dianion	DBN^{2-}	34	42
6	A	$DBB^{-\cdot}$	100	87
7	B	$DBB^{-\cdot}$	101	79
8	B	$DBB^{-\cdot}$	97	82
9	A, −60 °C	$DBB^{-\cdot}$	94	70
10	A, −50 °C	$DBB^{-\cdot}$	94	72
11	inverse	$DBB^{-\cdot}$	82[b]	46
12	A, potassium	$DBB^{-\cdot}$	64[b]	

[a] Standard conditions A and B described in footnote *a*, Table III, and in Experimental Section. [b] Including ca. 20% olefin.

Table VI. Reaction of 2-Chlorooctane with Lithium Radical Anions

run	conditions[a]	radical anion	hydrocarbon yield, %	indicated RLi yield, % of HC
1	A	$N^{-\cdot}$	63	30
2	B	$N^{-\cdot}$	63	21
3	B	$N^{-\cdot}$	63	22
4	A	$DBB^{-\cdot}$	104	87
5	B	$DBB^{-\cdot}$	101	87
6	B	$DBB^{-\cdot}$	101	81
7	100% stoich	$DBB^{-\cdot}$	95	86
8	A (+1 g of LiBr)	$DBN^{-\cdot}$	97	21
9	B	$DBN^{-\cdot}$	95	21

[a] Standard conditions A and B described in footnote *a*, Table III, and in Experimental Section.

Again, very little effect was observed.

Another possible reason for the low yields of anion trapping which came to mind is that the very reactive first-formed alkyllithium monomer might be metalating the naphthalene. Such metalations are known to occur much more rapidly with TMEDA complexes of alkyllithiums[2] and much more rapidly with alkyl dimers than with normal tetramers and hexamers.[22] The conditions were changed to test this hypothesis such that, rather than using a large excess of radical anion, the reaction was run on a completely stoichiometric scale. If metalation of naphthalene were taking place, then one should be able to observe a reduction in the percent recovery of naphthalene upon carbonation. When this experiment was run, two things were apparent. First, there was less than 1% reduction in the recovery yield of naphthalene, where an 18% reduction was expected on the basis of the untrapped anion product observed. Second, the extent of anion trapping, as revealed by the carbon dioxide quench method, jumped from 47 to 93% for 1-bromooctane (runs 1 and 2, Table IV). The effect on anion trapping of going from the usual stoichiometry (ca. 13%) to 100% for 2-bromooctane was also quite sizeable (25 to 52%; runs 1, 2, and 3, Table V), but no effect was observed for 3-chloro-3-methylheptane (74 to 70%; runs 1, 2, and 3, Table VII). When the reaction of lithium naphthalene with 1-bromooctane was run at medium degrees of stoichiometry, the percent of anion trapping was also intermediate (runs 8 and 9, Table IV). From these results it can be deduced that the anion is probably completely trapped as the lithium reagent, but that upon carbonation the lithium reagent is somehow converted into the hydrocarbon when excess radical anion is present.

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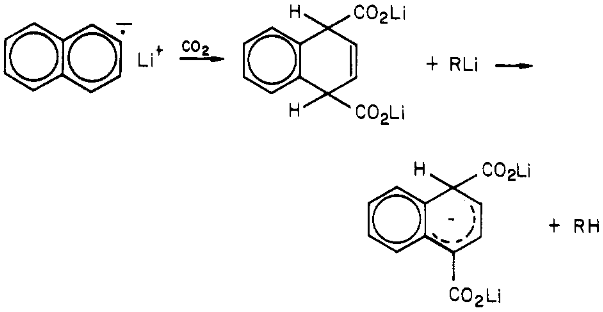
[22] W. H. Glaze and C. H. Freeman, *J. Am. Chem. Soc.*, 91, 7198 (1969).

Table VII. Reaction of 3-Chloro-3-methylheptane with Lithium Radical Anions

run	conditions[a]	radical anion	hydrocarbon yield, %	indicated RLi yield, % of HC
1	A	$N^{-}\cdot$	39	78
2	B	$N^{-}\cdot$	38	69
3	100% stoich	$N^{-}\cdot$	35	70
4	B	$N^{-}\cdot$	40	76
5	B[b]	$B^{-}\cdot$	56	79
6	A	$DBB^{-}\cdot$	95	87
7	B	$DBN^{-}\cdot$	89	81
8	B	$DBB^{-}\cdot$	98	90

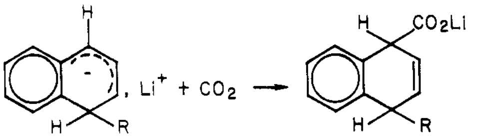
[a] Standard conditions A and B described in footnote a, Table III, and in Experimental Section. [b] LiB seemed to precipitate.

All of the above data can be accommodated by the suggestion that in all cases the percent anion trapping is high, but that the reaction sequence in eq 3 is operative

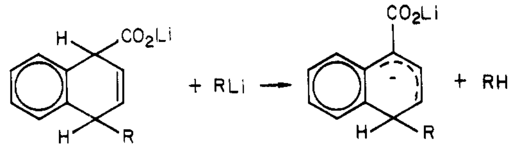


(3)

with the second step competitive with the reaction of alkyllithium with carbon dioxide.[23] This easily explains why LiDBB gives high anion trapping by the carbon dioxide quench method, while lithium naphthalene and LiDBN do not. Unlike lithium naphthalene and presumably LiDBN, which give dicarboxylic acid salts upon reaction with carbon dioxide, LiDBB gives back DBB unchanged. This also explains why going from those conditions where a large excess of radical anion is present to where no excess is present induces a large jump in the degree of anion trapping for 1-bromooctane, but not for 3-chloro-3-methylheptane. In the former case, little or no coupling is observed, while in the latter case, a large amount of coupling does take place. Thus, even when excess radical anion is not present, the tertiary lithium reagent can abstract a proton (eq 4 and 5).



(4)



(5)

Quite obviously, this explanation is open to experimental test. Treatment of a lithium naphthalene solution with 0.24 equiv of 1-chlorooctane, followed by the usual procedure, gave the result of 53% anion trapping. Repeating this experiment with a lithium naphthalene solution made from naphthalene-d_8 gave 69% anion trapping. The octane produced after carbonation was isolated and subjected to low-voltage mass spectral analysis. The octane produced was found to be 90.8 ± 0.5 monodeuterated. This experiment proves that the hydrocarbon found after the carbon dioxide quench was formed by abstraction of a proton from naphthalene. It has previously been shown that metalation does not take place. Additional evidence that the anion is nearly completely trapped as the lithium reagent was obtained by addition of deuterium oxide to a reaction run exactly as just described but without the carbon dioxide quench. The octane was found to be 96.0 ± 0.9% monodeuterated. This is slightly greater than the percent anion trapping, as indicated by the carbon dioxide quench in the case of 1-chlorooctane and LiDBB. It is probable that the lithium incorporations produced in all the other substrates by lithium naphthalene and LiDBN are just as high as, or slightly higher than, those indicated by the carbon dioxide quench in the case of LiDBB. Even with LiDBB, the percent anion trapping figures are probably just lower limits.

Table VIII. Reactions of 7-Chloronorcarane with Lithium Radical Anions

run	conditions[a]	radical anion	hydrocarbon yield, %	indicated RLi yield, % of HC
1	A	$DBB^{-}\cdot$	99	95
2	B	$DBB^{-}\cdot$	99	94
3	A (+1 g of LiBr)	$DBN^{-}\cdot$	99	88
4	B (warm to −5 °C)	$N^{-}\cdot$	99	65

[a] Standard conditions A and B described in footnote a, Table III.

General Considerations on the Use of LiDBB for Lithium Reagent Synthesis. For at least some substrates, it is important that the reaction be run at −78 °C or colder. From entries 9 and 10 of Table V, we see that the yield of anion trapping drops from 83 to 70% when the reaction with 2-bromooctane is run at −60 °C, even though secondary lithium reagents are stable in THF below about −50 °C. Inverse addition of LiDBB to 2-bromooctane, although synthetically desirable, also gives poor results (run 11, Table V). This is undoubtedly due to the fact that the lithium reagent and unreacted bromide are in contact for perhaps 0.5 h by this method, but less than a fraction of a second by the normal addition. Lithium DBB has advantages over lithium naphthalene in reactions with secondary cyclopropyl chlorides because this reaction is excessively slow with lithium naphthalene, but is over within 5 min with LiDBB. Since LiDBB gives essentially 100% electron transfer, it would seem that it ought to be possible to use DBB in a catalytic fashion. This would require the use of a lithium dispersion to allow fast enough formation of the radical anion at −78 °C. It might be possible to use less than 10% of the theoretical amount of DBB, thus making separation of products from the DBB easier.

Experimental Section

General Laboratory Procedures and Conditions. All temperatures are uncorrected. NMR spectra were obtained on a Varian HA-100 spectrometer (100 MHz). IR spectra were recorded on a Perkin-Elmer 621 infrared spectrophotometer. Mass spectra were run by using an Atlas CH7 mass spectrometer. VPC analyses were carried out on a Varian Aerograph A90-P2. Unless otherwise noted, the detector and injector temperatures were set at 230 °C. The flow rate for 0.25-in. columns was generally set to 60 mL/min, with ca. 20 mL/min for $^{1}/_{8}$-in. columns. The columns used were the following: A, 4 ft × 0.25 in. 5% CW20M

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[23] For examples of metalation with alkyl- or aryllithium reagents of C–H which is benzylic and allylic, see ref 2, p 29. For examples of metalation of C_α of carboxylate salts, see P. E. Pfeffer, L. S. Silbert, and J. M. Chirinko, Jr., *J. Org. Chem.*, **37**, 451 (1972); P. E. Pfeffer and L. S. Silbert, *ibid.*, **35**, 262 (1970); P. L. Creger, *J. Am. Chem. Soc.*, **89**, 2500 (1967); F. F. Blicke and H. Raffelson, *ibid.*, **74**, 1731 (1952).

Table IX. Reaction of Some Selected Halides with Lithium Di-*tert*-butylbiphenyl

run	halide	conditions[a]	radical anion	hydrocarbon yield, %	indicated RLi yield, % of HC
1	4-*tert*-butylchlorocyclohexane	B	DBB$^{-\cdot}$	99	88
2	4-*tert*-butyl-1-chlorocyclohexene	B[b]	DBB$^{-\cdot}$	104	76
3	*anti*-3-chlorotricyclo[3.2.1.0^{2,4}]octane	B	DBB$^{-\cdot}$	99	89

[a] Standard conditions A and B described in footnote *a*, Table III. [b] Too slow at −78 °C, warmed to −20 °C.

on 30–60 Chromosorb W; B, 10 ft × 0.25 in. 10% SE-30 on Anakrom 110–120 AS; C, 10 ft × 0.25 in. 10% Ucon water soluble with 1% KOH on 60–40 Chromosorb W; D, 8 ft × 0.25 in. 10% CW20M on 30–60 Chromosorb W; E, 20 ft × $^{1}/_{8}$ in. 8% Apiezon-N on 80–100 Chromosorb WAS; and F, 15 ft × 0.25 in. 5% OV-17 on 60–80 Chromosorb G.

Ether solvents were distilled from sodium benzophenone dianion and stored over 4-Å molecular sieves under nitrogen. Errors are standard deviations on multiple integrations (VPC or NMR) unless otherwise noted. The term high vacuum as used in this paper means 10^{-5} torr or less.

General Conditions for the Preparation of Radical Anion Solutions. A 100-mL three-neck 14/20 morton flask containing a 2.5-cm glass covered magnetic stirring bar was simultaneously dried and filled with argon by passing a steady stream of the gas in through the right-hand neck of the flask with alternately one and then the other of the two stoppers floating in the exiting argon stream while the flask with a high-temperature heat gun was being heated. After the flask had cooled to about 35 °C, the weighed amount of aromatic hydrocarbon was added through a briskly exiting stream of argon via a 14/20 funnel. The required amount of solvent was then added by carefully pouring from the storage container while passing a rapid stream of argon through the flask. The space above the liquid in the storage container was blown out with nitrogen as soon as possible (within 10 s) after the addition. The required amount of alkali metal was weighed out on an analytical balance to within 1–2 mg of the target weight. An oversize piece was first weighed and then trimmed to the proper weight with a knife to clean off any oxide crust. Lithium was handled with tweezers in the open air, as only a very slight amount of oxidation occurred during the short time the metal was exposed to the atmosphere. Potassium and sodium, however, had to be coated at all times with mineral oil to prevent excessive oxidation and reaction with atmospheric moisture. The piece of metal was then placed in the center of the flask, and, with a rapid flow of argon, portions of the metal were flattened with curved surgical scissors so as to maximize the clean surface area and cut into the solution. A 35-mg piece of lithium typically was cut into at most three pieces. This procedure was found to result in a more rapid formation of the radical anion than by cutting many small pieces of lithium into the solution.

The color of the radical anion spread throughout the solution within 10–20 s after the first piece was dropped in. The solution was cooled to 0 °C in the case of lithium radical anions to prevent excessive decomposition during the formation. The solution was stirred rapidly until no unreacted metal could be discerned in the dark solution. This required typically 3–4 h for LiDBB formation in THF.

Standard conditions A: THF (30 mL), aromatic hydrocarbon (6 mmol), and alkali metal (5 mmol) were treated as in the general conditions above. This results in a solution 0.17 M in radical anion.

Standard conditions B: as in A above but with the addition of 20 μL (1.56 mequiv) of Br_2. This results in a solution 0.11 M in radical anion and 0.05 M in LiBr.

General Conditions for Quantitative Radical Anion–Alkyl Halide Reactions. To the radical anion solution as prepared above and cooled to −78 °C by a dry ice–isopropyl alcohol bath was added 60 μL of the internal standard, followed by 60 μL of the halide. For most halides this amount represents 13% of the stoichiometrically required halide. Whenever a sample was added to or withdrawn from the reaction flask, a brisk flow of argon was used to prevent introduction of atmospheric gases. The stoppers were removed only to the extent required for the insertion of the syringe or pipet. In all cases, the halide was ejected from the syringe as rapidly as possible (less than 0.5 s) with the very fine spray sweeping across the radical anion solution. The stirring rate (glass-covered magnetic stir bar) was set as high as possible. The reactions of secondary and tertiary chlorides and bromides, as well as primary and cyclopropyl bromides, with lithium naphthalene (LiN) or lithium di-*tert*-butylbiphenyl (LiDBB), are complete in less than a few seconds. Primary chlorides require 30 s with LiDBB, while secondary cyclopropyl chlorides require as much as 5 min. LiN requires about 30 times as long as LiDBB.

Aliquots were taken with a dried disposable pipet with a shortened tip. The pipet was filled with nitrogen and the liquid was expelled by introduction of nitrogen from a rubber balloon attached to the inlet of the pipet bulb. When the first aliquot was taken, the liquid was sucked up and then ejected directly into 2 mL of water in a 2-dram vial as rapidly as possible—total time for the solution to be in contact with the pipet was typically less than 3 s. To the THF layer was then added 0.5 mL of pentane, and then water was added until the vial was full. The cap was then replaced and the vial inverted and agitated to extract as much THF into the water as possible. The water was then removed, fresh water added, and the vial again agitated and then stored with the cap down. The pentane layer is effectively sealed by the glass on the top and sides and by the water on the bottom. Vials allowed to stand upright lost the pentane in short order and the relative composition of product to internal standard was not stable. Vials stored in the upside-down manner were stable indefinitely.

After the second aliquot was taken, CO_2 was bubbled in until the solution went colorless and for 1 min longer. The CO_2 was generated from dry ice in a 50-mL flask and dried by passing through Drierite. Commercial "Bone Dry" CO_2 (Matheson) gave identical results. The CO_2 quench was worked up in a manner identical with the previous aliquot.

The water and CO_2 quench aliquots were analyzed on column E at 100 °C with the aid of a Hewlett-Packard 3373B integrator. Integration ratios were consistent to within 1%. The reduction of percent yield of hydrocarbon after the CO_2 quench is taken to be the indicated RLi yield (see Tables III–IX).

Response Factors. Response factors were obtained by running through the full procedures (except the CO_2 quench) given above, but using the product in place of starting material. The response factors so obtained were as much as 10% different from those obtained by simply analyzing a known solution of internal standard and product. The weight–weight response factors determined by this procedure are the following: for octane vs. nonane, 1.056 ± 0.02; for tricyclo[3.2.1.0^{2,4}]octane vs. decane, 1.24 ± 0.02; for 4-*tert*-butylcyclohexene vs. nonane, 1.29 ± 0.03; for norcarane vs. nonane, 1.164 ± 0.007. 3-Methylheptane is assumed to have the same response factor as octane, and *tert*-butylcyclohexane is assumed to be the same as 4-*tert*-butylcyclohexene.

Special Conditions

Evaporative Additions. A solution of LiDBB was made in the usual way under conditions A, and, after the lithium had dissolved, the flask was attached to the high-vacuum line and degassed. A previously degassed sample of the halide was then allowed to evaporate into the −78 °C solution over a period of 30 min. The top half of the reaction flask was heated periodically with a heat gun to prevent the halide from condensing and running in as a liquid. Aliquots were taken as usual. Due to the necessity of heating the top of the flask while cooling the bottom, the actual temperature of the solution may be somewhat higher than −78 °C.

Stoichiometric Reactions. Full stoichiometry (100%) experiments were run as usual except that 6 mmol of both aromatic hydrocarbon and lithium were used to make the radical anion solution, and the halide was added dropwise until the color of the radical anion just disappeared, leaving an intense red color. Lower ratios of halide to radical anion were run under conditions A with the calcuated amount of halide added as usual.

Inverse Addition. A 100-mL flask, equipped with a glass-covered stirring bar, was dried under a high vacuum for 1–2 h, and 30 mL of THF was transferred in from THF which had been dried over sodium benzophenone dianion. The flask was pressurized with nitrogen, and one of the stoppers was replaced with a septum stopper. The THF was cooled to the appropriate temperature and the internal standard was added, followed by the halide. A solution of LiDBB made under conditions A was then added dropwise at such a rate that 30–45 min was required for completion. The solution slowly took on a red color until the last drop, which caused the solution to turn green to blue-green. The quench with H_2O did not result in the usual formation of an organic phase, presumably due to the lessened amount of organic solute present. Thus the ratio of product to internal standard may be in considerable error (see internal standard section above).

Reaction of Lithium Naphthalene Dianion and Di-*tert*-butylnaphthalene Dianion with Alkyl Halides in Ether. The title dianions were prepared by treatment of 4.8 mmol of the corresponding hydrocarbon with 4.5 mmol of Li in 30 mL of diethyl ether as described for the radical anions. The temperature of the ether solution was maintained below −20 °C to prevent decomposition. Li seems to react more readily with DBN than with naphthalene. After all the lithium had dissolved, the deep purple solution was cooled to the appropriate temperature, and the internal standard and halide were added. Aliquots were then taken as previously described except that no pentane was added.

Reaction of Lithium Naphthalene-d_8 with 1-Chlorooctane. A lithium naphthalene solution was made from 0.340 g of naphthalene-d_8, 17 mg of Li, and 15 mL of THF (approximately half normal scale). To this solution, cooled to −78 °C, was added 50.0 μL of nonane, followed by 50.0 μL (43.3 mg) of 1-chlorooctane. The reaction was then treated as described above under general conditions. After the CO_2 quench aliquot had been taken, H_2O was added and the reaction worked up in the usual way. VPC collection of the octane using column F at 75 °C was followed by low-voltage mass spectral analysis, 90.8 ± 0.5% d_1, 0.2 ± 0.3% d_2. VPC analysis of the aliquots revealed that the yield of octane was 91% with an indicated RLi yield of 69%.

Repetition of the above sequence with undeuterated naphthalene, but not including the collection and analysis of the octane, indicated an 89% yield of octane with an indicated RLi yield of 53%. The deuterium isotope effect can be calculated as being 2.0 by assuming a competition between reaction of RLi with CO_2 or with the dihydronaphthalenedicarboxylate (see Discussion).

Reaction of Lithium Naphthalene with 1-Chlorooctane Followed by Deuterolysis. A solution of LiN was made under the same conditions as immediately above. Reaction with 50 μL (43.3 mg) of 1-chlorooctane was followed 15 min later by the addition of 0.75 mL of D_2O. Workup as usual was followed by VPC collection from column F at 75 °C. Low-voltage mass spectral analysis revealed the octane to be 96.0 ± 0.9% d_1 and 0.3 ± 0.3% d_2.

Registry No. 1-Chlorooctane, 111-85-3; 1-bromooctane, 111-83-1; 2-chlorooctane, 628-61-5; 2-bromooctane, 557-35-7; 3-chloro-3-methylheptane, 5272-02-6; 7-chloronorcarane, 1588-50-7; 1-lithiooctane, 3314-49-6; 2-lithiooctane, 61182-93-2; 3-lithio-3-methylheptane, 61182-94-3; 7-lithionorcarane, 61182-95-4; LiN, 7308-67-0; Li(2,6-DBN), 73049-04-4; Li(2,7-DBN), 73049-06-6; LiDBB, 61217-61-6; 4-*tert*-butyl-1-chlorocyclohexane, 62056-46-6; 3-chlorotricyclo[3.2.1.$0^{2,4}$]octane, 73088-62-7; 4-*tert*-butyl-1-lithiocyclohexane, 17530-01-7; 3-lithiotricyclo[3.2.1.$0^{2,4}$]octane, 73049-05-5; 4-*tert*-butyl-1-chlorocyclohexene, 6832-09-3.

Nickel Catalysis in Halogen Exchange with Aryl and Vinylic Halides

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Halogen exchange between haloarenes and inorganic halide salts is readily induced by catalytic amounts of certain nickel complexes. Exchange of *cis*- and *trans*-β-bromostyrenes with chloride is stereospecific. Although various nickel complexes with different formal oxidation states such as $Ni^0(PEt_3)_4$, $Ni^IIl(PEt_3)_3$, and $ArNi^{II}Br(PEt_3)_2$ may be employed as catalysts (or catalyst precursors), others such as $Ni^{II}Br_2$ or $Ni^{II}Br_2(PEt_3)_2$ are completely ineffective. The distinction between the two classes of nickel complexes lies in whether they are converted under reaction conditions to nickel(I) species, assigned as the active catalyst. The latter is supported by the study of direct halide exchange between haloarenes and arylnickel(II) halides, in which a radical-chain process showing an induction period and inhibition by quinones and nitro aromatics is attributed to a labile nickel(I) species. A mechanism for nickel(I) catalysis of halide exchange is proposed.

Introduction

Nucleophilic substitutions on aromatic systems are generally quite slow in the absence of catalysts.[1-4] Metal complexes, particularly those of copper(I), have been used extensively to effect halide exchange.[5-10]

Nickel complexes have recently been found to catalyze the substitution of aryl halides with nucleophiles such as amines, phosphines, and cyanide.[11-13] Such substitution processes are of synthetic value, particularly when viewed from the broader perspective of carbon-centered nucleophiles leading to the formation of aryl–carbon bonds.[14] Indeed in the course of our recent studies of the nickel-induced coupling of aryl halides to biaryls,[15] we discovered

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