THE SYNTHESIS OF NEOPHYLLITHIUM AND ITS REACTION WITH ANTHRACENE

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<u>Summary:</u> transmetalation reaction between t-butyllithium and The dineophylmercury produces pure neophyllithium, 1, in a rapid, convenient manner as shown by FT-NMR. Alkylation of anthracene with 1 in HMPA gives 6-10% yields of unrearranged adduct.

A number of alkyllithium reagents (R = Et, n-Pr, i-Pr, n-C₄H₉, sec-C₄H₉, and $t-C_4H_9$ – among others) have been reported to add readily to certain polynuclear aromatic hydrocarbons such as anthracene and pervlene in THF.1-5 As part of an investigation into the mechanism of this reaction we chose to study the addition of neophyllithium(2-methyl-2-phenylpropyllithium, 1) to anthracene. It was our expectation that if the alkylation reaction occurs via a single electron transfer pathway, the possibility for formation of a neophyl radical might lead to rearrangement of the alkyl group. If rearrangement of the neophyl radical were to product would be 9-(1,1-dimethyl-2-phenyl-ethyl-) occur. the expected 9,10-dihydroanthracene(DHA), 2. The benzyldimethyl carbinyl alkyl group in such a rearranged hydrocarbon could be distinguished readily from unrearranged 9-neophyl-9,10-DHA, 3, by the singlet nature of its CH₂ group in the proton NMR.



The preparation of neophyllithium from neophyl chloride's reaction with lithium occurs with 5.3% of rearranged 1,1-dimethyl-2-phenylethyllithium (1,2-phenyl migration).⁶ To avoid having this rearrangement impurity as a contaminant, one can employ the transmetallation reaction of lithium metal with dineophylmercury.7

However, this method was found "to be unpredictable and to fail once in every four attempts" (see footnote 33 in ref.7). In addition neophyllithium is a solid of sparing solubility in pentane (0.1 N solutions are saturated)⁷, and this metal exchange method requires the separation of amalgamated lithium from the desired compound. Thus we sought an alternative synthesis for neophyllithium that would proceed without rearrangement and would avoid the need to separate unreacted lithium metal and lithium amalgam.

Success was achieved through application of the metal exchange method of Schlenk and Holz.⁸ Addition of 8.42 mmole of dineophylmercury in 10 ml of pentane to a two to three fold molar excess of tert-butyllithium (1.7M/pentane) produced a precipitate of neophyllithium after 10 minutes of stirring. See eqn(1).

After chilling to 0° and removal of the supernatant, the precipitate was washed twice with 10 ml portions of pentane. The yield of neophyllithium is 43 \pm 3% as determined by quantitative gas chromatography of t-butylbenzene in a hydrolyzed aliquot of a pentane solution. No isobutylbenzene could be detected. One recrystallization from pentane (100 ml) at -78° produced colorless needles whose solution in C₆D₆ was analyzed by ¹H and ¹³C FT-NMR at 250 MHz. The chemical shifts for neophyllithium are:

	ipso ArH C	meta C	para C	ortho C	quat. C	-CH ₂ Li	(CH3)2 C-
13 _C	153.28	129.81	126.20	124.80	42.03	39.73	35.72
1		7.220	7.029	7.390		-1.077	1.296
'н		2 H (d)	1 H (t)	2 H (d)		2 H (s)	6 H (s)
		J=7.58 Hz	J=7.25 Hz	J≡7.50 Hz			

It is instructive to note that as in the butyllithium isomers⁹, the carbon atom β to the Li atom appears at lower fields than all the other aliphatic carbons. The only detectable impurity in the neophyllithium is a trace of t-butyllithium. Hydrolysis products (t-butylbenzene and isobutane) due to adventitious moisture can also be detected.

Additional evidence for the structure of neophyllithium was provided by

carbonation with gaseous CO₂ to give the known 3-methyl-3-phenylbutyric acid derivative.

Neophyllithium did not react with anthracene in THF at any temperature between -78° and +25° C. It appears to deprotonate THF (see ref.6). Furthermore, it did not react with anthracene in diethyl ether at 25° C during 2.0 hr. and the addition of tetramethylethylene diamine with an additional hour of reaction time produced no effect. Conversely, in hexamethylphosphoramide(HMPA), 6.0-10% yields of unrearranged 9-neophyl-9,10-DHA were secured in runs at 25° and 55° . These samples possessed ¹H and ¹³C NMR spectra identical with those of an authentic sample synthesized from anthrone and neophylmagnesium chloride¹⁰. This result is in harmony with the work of Panek who showed that anthracene alkylation by n-C₄H₉Li is enhanced by addition of HMPA to the ether solvent.¹¹ No trace of rearrangement in the neophyl group could be found. Only t-butylbenzene could be detected after hydrolysis. It would appear from the failure of neophyllithium to undergo rearrangement during alkylation of anthracene in HMPA that a polar rather than a single electron process is involved in alkylation of aromatic hydrocarbons.

Perylene is known to be alkylated readily by butyllithium^{1 a} in THF and by ethyllithium in boiling benzene.^{1b} But reaction of neophyllithium with perylene in boiling benzene for 15.0 hr. did not give alkylation.

5-hexenyllithium is known to undergo a unimolecular cyclization to cyclopentylmethyllithium at significant rates over the temperature range from -10° to $+20^{\circ}$. ¹² Alkylation of anthracene by 5-hexenyllithium at room temperature gave only 9-cyclopentylmethyl-9,10-DHA¹³. No alkylation product of anthracene by 5-hexenyllithium could be found. Lowering of the reaction temperature to -28° or -78° resulted in no alkylation of anthracene at all. Thus intramolecular cyclization of 5-hexenyllithium is more facile than intermolecular addition to anthracene.

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(10) Sieglitz, A. and Marx, R., <u>Ber.</u> (1923), 1621. Reduction of 9-neophylanthracene to the DHA was accomplished with Na and isoamyl alcohol. The ¹H NMR spectrum for 9-neophyl-9,10-DHA gave δ_{ArH} (7.296 d, 7.284 d, 7.177-7.024 sextet, 6.809 d); $\delta_{benzylic}(3 \text{ H}, \delta_{g}=4.112, \delta_{g}=3.754, J_{gg}=17.6 \text{ Hz}, \delta_{10}=3.788)$; $\delta_{CH2}(2 \text{ H}, 2.036 \text{ d}, J=6.378 \text{ Hz})$; $\delta_{(CH3)2C}$ (6 H, 1.236). The ¹³C NMR spectrum showed ten aromatic carbon signals(δ = 148.17, 142.67, 136.86, 128.09, 127.51, 127,46, 126.29, 126.041, 125.81, 125.58) and five aliphatic carbon signals($\delta_{C10}=50.43, \delta_{Cg}=44.92, \delta_{guat}=38.57, \delta_{CH2}=36.05, \delta_{(CH3)2C}=30.0$).

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(13) The proton NMR spectrum integrated correctly. $\delta_{ArH}(8 \text{ H}, 7.16-7.29 \text{ m});$ $\delta_{benzylic}(3 \text{ H}, \delta_9=4.119, \delta_{9}=3.842, J_{99}=18.2 \text{ Hz}, \delta_{10}=3.918); \delta_{aliph.}(11 \text{ H}, .850-1.8 \text{ four multiplets}).$ The ¹³C NMR spectrum showed five aromatic signals($\delta=141.20$, 136.20, 127.79, 126.07, 125.92) and six aliphatic signals ($\delta_{C10}=46.71$, $\delta_{C9}=43.96$, $\delta_{-CH2}=37.39$, $\delta_{ring CH2's}=32.88$ and 25.38). Yields were not optimized; melting point 54°-56°.

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