The Dianion Derived from *N*-Methylphthalimide

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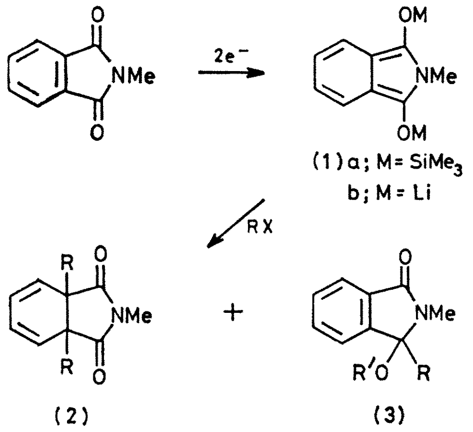
Summary Reduction of *N*-methylphthalimide with lithium in liquid ammonia provides a stable dianion which has been alkylated with various reagents

REDUCTION of *N*-methylphthalimide by lithium metal[1] in liquid NH_3 was investigated as a route to the 1,3-oxygenated isoindole (**1a**) which might serve as an intermediate in



(1) a; M = SiMe$_3$
b; M = Li

(2)

(3)

SCHEME

RX	Product (% yield)	
	(2)	(3)[a]
MeI	R=Me (36)	R=Me, R'=H (37)[b]
Br[CH$_2$]Br	RR= –[CH$_2$]$_3$– (12)	RR'= –[CH$_2$]$_3$– (44)
EtI	Trace[c]	R=Et, R'=H (85)
PhCH$_2$Br	Trace[c]	R=CH$_2$Ph, R'=H (96)
CH$_2$=CHCH$_2$Br	None	R=CH$_2$CH=CH$_2$, R'=H (83)[b]
Me$_3$SiCl	—	R=H, R'=SiMe$_3$ (85)

[a] Small amounts of the dialkylated product (**3**; R,R' = alkyl) may be formed depending on reaction time and conditions.
[b] W. S. Ang and B. Halton, *Aust. J. Chem.*, 1971, **24**, 851.
[c] Apparent mixture of isomers, yield <2%.

anthracyclinone synthesis.[2] Addition of *N*-methylphthalimide in tetrahydrofuran (THF) to 2·1 equiv. of lithium metal in liquid NH$_3$ at –78 °C gave a deep purple solution of the dianion (**1b**) which was characterized by reaction with various alkylating agents (Scheme).

The products isolated after quenching and work-up support the proposed dianion intermediate. The ratio of bridgehead to benzylic alkylation products (**2**) : (**3**) appears to vary with the reactivity and steric bulk of the electrophile. While the products (**2**) resulted from regiospecific alkylation adjacent to the carbanion-stabilizing carbonyl groups of (**1b**), *umpolung* of the carbonyl centre, giving rise to the products (**3**), was the preferred pathway observed with the larger alkylating agents. Interestingly, no trace of the bridgehead alkylated product (**2**) was observed with allyl bromide. This result may in part be due to a facile enolate–Cope rearrangement[3] following initial alkylation at the ring-fusion position. Silylation of the dianion (**1b**) with a variety of reagents gave only the monosilylated product (**3**; R = H, R' = SiMe$_3$).

In conclusion, reduction of *N*-methylphthalimide occurs readily and cleanly to give the highly reactive and heretofore unknown dianion (**1b**). Application of this reaction as a method for preparing functionalized isoindoles and other heterocycles,[4] as well as 1,3-dienes not easily accessible by alternative means, is being investigated.

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[1] For a recent application of dissolving metal reduction of benzoic acid derivatives see: J. A. Marshall and P. G. M. Wuts, *J. Org. Chem.*, 1977, **42**, 1794.

[2] For application of isobenzofuran to anthracyclinone synthesis see: A. S. Kende, D. P. Curran, Y. Tsay, and J. E. Mills, *Tetrahedron Lett.*, 1977, **40**, 3537.

[3] Regeneration of the aromatic system could provide the driving force necessary to shift the equilibrium away from the commonly observed direction; D. A. Evans, D. J. Baillargeon, and J. W. Nelson, *J. Am. Chem. Soc.*, 1978, **100**, 2242.

[4] Intermediates of type (**3**) have been utilized recently; V. Scartoni, R. Fiaschi, S. Catalano, I. Morelli, and A. Marsili, *J. Chem. Soc., Perkin Trans.* 1, 1979, 1547.