

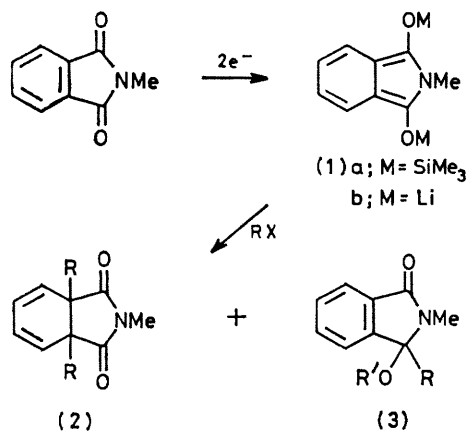
The Dianion Derived from *N*-Methylphthalimide

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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 metal¹ in liquid NH₃ was investigated as a route to the 1,3-oxygenated isoindole (**1a**) which might serve as an intermediate in



SCHEME

RX	Product (% yield)	
	(2)	(3) ^a
MeI	R=Me (36)	R=Me, R'=H (37) ^b
Br[CH ₂] ₂ Br	RR = -[CH ₂] ₂ - (12)	RR' = -[CH ₂] ₂ - (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 NH₃ 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 regioselective 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 rearrangement³ 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' = SiMe₃).

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.