# Twofold Metallation of 2-Hydroxy-4-methylpyrimidines to form a New Class of Synthetically Useful Dianions

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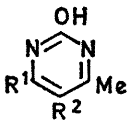
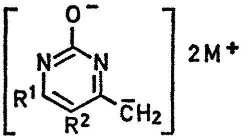
*Summary* Twofold metallation of 2-hydroxy-4-methylpyrimidines (Ia,b) with n-butyl-lithium or sodium amide produces dianions (IIa,b), which can serve as potentially versatile synthetic intermediates by virtue of their selective carbon–carbon condensations with electrophiles.

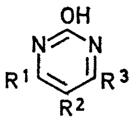
It seemed that twofold metallation of 2-hydroxy-4-methylpyrimidines of type (I) could be effected by means of strong bases to produce the heretofore unreported class of dianions represented by structural formula (II). Further, reactions of dianions (II) with electrophiles might occur preferentially at the exocyclic carbanion site,[1,2] thereby providing a convenient new entry into the synthesis of a variety of substituted pyrimidines. These hypotheses have now been verified, and we report our initial findings.



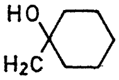
| | $R^1$ | $R^2$ |
|---|---|---|
| (Ia) | Me | Ph |
| (Ib) | Ph | H |



| | $R^1$ | $R^2$ |
|---|---|---|
| (IIa) | Me | Ph |
| (IIb) | Ph | H |



(III)

| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| a; | Me | Ph | $CH_2\overset{OH}{C}(Ph)_2$ |
| b; | Me | Ph | $CH_2CH_2Ph$ |
| c; | Ph | H | $CH_2CH_2Ph$ |
| d; | Ph | H |  |
| e; | P | H | $CH{=}C(Ph)_2$ |

Addition of two molecular equivalents of n-butyl-lithium in hexane to a solution of (Ia) and two molecular equivalents of *NNN'N'*-tetramethylethylenediamine[3] in THF at 0° produced a homogeneous yellow solution of dianion (IIa) (M = Li). Addition of an excess of deuterium oxide to the reaction mixture gave (Ia) containing 80% of one methyl deuterium atom/molecule (n.m.r.). Dianion (IIa) (M = Li) was condensed with benzophenone to form (IIIa), m.p. 144—146°,‡ and alkylated with benzyl chloride to give (IIIb), m.p. 202—204°,‡ in yields of 89 and 76%, respectively. Disodio-derivative (IIa) (M = Na), prepared by treatment of (Ia) with two molecular equivalents of sodium amide in liquid ammonia, was alkylated with benzyl chloride in this medium to produce (IIIb) in 75% yield.

Treatment of (Ib) with two molecular equivalents of n-butyl-lithium in THF–hexane at 0° produced the soluble, red dianion (IIb) (M = Li), which was trapped with benzyl chloride and cyclohexanone to afford (IIIc), m.p. 180—182°,‡ (57%) and (IIId), m.p. 183—184°,‡ (44%). Reaction of dilithio-derivative (IIb) with benzophenone, followed by dehydration of the crude adduct with *p*-toluenesulphonic acid in refluxing benzene, gave (IIIe), m.p. 236—238°,‡ in 67% overall yield. Formation of (IIb) (M = Na) by means of sodium amide in liquid ammonia was demonstrated by its alkylation with benzyl chloride to produce (IIIc) (65%).

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‡ Satisfactory analytical and spectral data were obtained for this compound.

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