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# Short Communications

## An Alternative Method for Preparing 7- and 9-Methylpurines

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*N*-Alkyl derivatives of purine bases are frequently used as model compounds in the studies of the interactions between metal ions and nucleic acid constituents. However, attempts to prepare a desired *N*-alkylated compound have often met with difficulties. This has particularly been the case with the direct methylation of the unsubstituted purine. Albert and Brown,[1] for example, have reported that conventional alkylating procedures, including treatment with methyl iodide, dimethyl sulfate, methyl *p*-toluenesulfonate or formic acid, are unsuccesful in methylation of purine. Later reaction of thallium(I) salt of purine with methyl iodide in DMF has been shown to yield 9-methylpurine and 7,9-dimethylpurinium iodide.[2] Quite recently *N,N*-dimethylformamide dimethyl acetal has been suggested to be an advantageous methylating agent of heterocyclic bases.[3] Treatment of purine with this reagent in refluxing toluene, for example, gives a mixture of 7- and 9-methylpurines in proportion of 3 to 2. We now report that a 1:3 mixture of these compounds can conveniently be prepared in almost 100% yield by allowing purine to react with dimethyl sulfate in acetone in the presence of anhydrous potassium carbonate. The isomers formed can be separated in a preparative scale by passing the methanolic solution of the product mixture through a strong cation exchange resin loaded with magnesium(II) ions. As seen from Fig. 1, the 7-isomer exhibits a considerably larger retention volume (110 $cm^3$) than 9-methylpurine (70 $cm^3$), probably due to more efficient complexing with magnesium(II) ion. By this procedure, amounts of 1 g can satisfactorily be fractionated on a column of 2 × 40 cm.

*Experimental. Preparation of the mixture of 7- and 9-methylpurines.* A suspension of purine (5 mmol, Sigma Chemical Company) and dimethyl sulfate (5 mmol) in dry acetone (150 $cm^3$) was agitated at room temperature on anhydrous potassium carbonate (7 mmol) for two days. Evaporation of the filtrated solution to dryness afforded a 1:3 mixture of 7- and 9-methylpurines, as deduced on the basis of the $^1H$ NMR spectra of the residue. Other products were not detected.

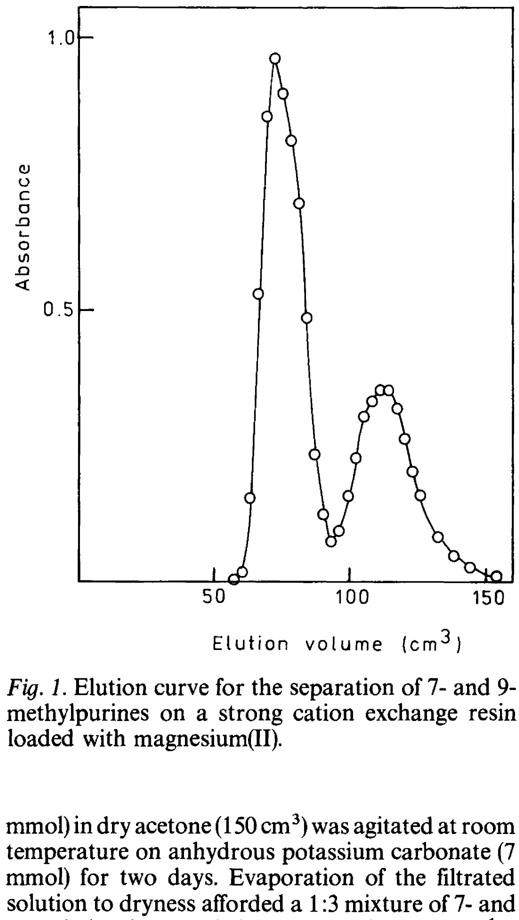


*Fig. 1.* Elution curve for the separation of 7- and 9-methylpurines on a strong cation exchange resin loaded with magnesium(II).

*Separation of 7- and 9-methylpurine.* The isomeric mixture obtained was applicated in 3 $cm^3$ of methanol on strong cation exchange column (Dowex 50 W X2, mesh 100 – 200, 2 × 40 cm) loaded with magnesium(II) ions and eluted with dry methanol (15 $cm^3$ $h^{-1}$). Fractions of 3 $cm^3$ were collected and the appearance of the methylpurines was checked by UV-spectroscopy (dilution 1:350). The elution curve obtained is presented in Fig. 1. The pooled fractions were evaporated to dryness

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and the products were crystallized from ethanol and recrystallized from hot carbon tetrachloride.

7-Methylpurine obtained melted at 178 – 180 °C (lit.[3] 181 – 183 °C) and exhibited the following analytical and spectroscopic data. Found: C 53.81; H 4.49; N 41.74. Calc. for $C_6H_6N_4$: C 53.72; H 4.51; N 41.77. UV (log $\varepsilon$): in 0.1 mol $dm^{-3}$ HCl 257.1 (3.85) nm, in water 265.8 (3.93) nm (lit.[4] in pH 0.23 257.5 (3.83) nm, in pH 9.15 266.5 (3.91) nm). $^1H$ NMR (as ppm from DSS in $D_2O$): $\delta$ 3.91 ($CH_3$,s), 8.76 (H2,s), 8.87 (H6,s), 8.31 (H8,s) (lit.[3] 4.10, 8.95, 9.15, and 8.20 from TMS in $CDCl_3$). $^{13}C$ NMR (as ppm from DSS in $D_2O$): $\delta$ 34.1 ($CH_3$), 154.1 (C-2), 161.1 (C-4), 128.3 (C-5), 143.4 (C-6), 153.2 (C-8) (lit.[5] 32.2, 152.1, 159.3, 126.1, 140.9, and 150.7 in water – dioxan mixture.

9-Methylpurine melted at 160 – 161 °C (lit.[3] 160 – 162 °C) and exhibited the following analytical and spectroscopic data. Found: C 53.71; H 4.52; N 41.69. Calc. for $C_6H_6N_4$: C 53.72; H 4.51; N 41.77. UV (log $\varepsilon$): in 0.1 mol $dm^{-3}$ HCl 262.0 (3.76) nm, in water 263.8 (3.90) nm (lit.[4] in pH 0.62 262.5 (3.77) nm, in pH 8.5 264.0 (3.90) nm. $^1H$ NMR (as ppm from DSS in $D_2O$): $\delta$ 3.83 ($CH_3$,s), 8.74 (H2,s), 8.89 (H6,s), 8.31 (H8,s) (lit.[3] 4.00, 9.00, 9.15, and 8.10 from TMS in $CDCl_3$). $^{13}C$ NMR (as ppm from DSS in $D_2O$): $\delta$ 32.5 ($CH_3$), 153.9 (C-2), 153.3 (C-4), 135.2 (C-5), 149.6 (C-6), 150.9 (C-8) (lit.[5] 30.6, 151.9, 150.9, 132.9, 147.4, and 148.8). When external standard was employed each of the $^{13}C$ shifts diminished by 2 ppm.

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