10. Mårtensson, E. *Acta Chem. Scand.* **17** (1963) 1174.
11. Svennerholm, L. and Thorin, H. *J. Lipid Res.* **3** (1962) 483.
12. Karlsson, K.-A. *To be published.*
13. Wagner, H., Hörhammer, L. and Wolff, P. *Biochem. Z.* **334** (1961) 175.
14. Beiss, U. and Armbruster, O. *Z. Naturforsch.* **136** (1958) 79.
15. Sweeley, C. and Klionsky, B. *J. Biol. Chem.* **238** (1963) 3148.
16. Myrbäck, K. and Willstædt, E. *Arkiv Kemi* **6** (1953) 417.
17. Svennerholm, L. *J. Neurochem.* **1** (1956) 42.
18. Svennerholm, L. *Acta Soc. Med. Upsalien.* **61** (1956) 287.
19. Strid, L. *Acta Chem. Scand.* **15** (1961) 1423.

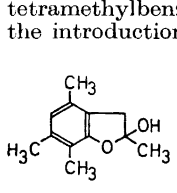
Received October 28, 1963.

## Perchloric Acid Catalysed Acylation of Benzofurans

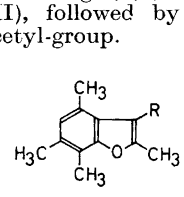
RUNE MAGNUSSON

*Institutionen för organisk kemi, Chalmers Tekniska Högskola, Göteborg, Sweden*

An attempt to convert 2-hydroxy-2,4,6,7-tetramethyl-2,3-dihydrobenzofuran (I)[1] into the corresponding 2-acetoxy compound with acetic anhydride in the presence of perchloric acid gave a yellow crystalline compound, which on treatment with water was converted to colourless 2,4,6,7-tetramethyl-3-benzofuranyl methyl ketone (III). Titration of the acid water phase indicated the simultaneous formation of 0.5 mole of perchloric acid per mole of the ketone III. Thus, instead of the intended acetylation of the 2-hydroxyl-group in I dehydration occurred forming 2,4,6,7-tetramethylbenzofuran (II), followed by the introduction of a 3-acetyl-group.



I



II R=H

III R=COCH$_3$

The yellow product that precipitated from the reaction mixture was obviously a molecular compound of the ketone III with perchloric acid in a mole ratio of 2:1. This interpretation of the reaction was supported by the formation of the same yellow product when 2,4,6,7-tetramethylbenzofuran (II) or the ketone III was treated with acetic anhydride/perchloric acid under the same conditions as compound I. That acylation of 2,4,6,7-tetramethylbenzofuran (II) occurred in the 3-position and not in the 5-position has not been shown experimentally but is very probable since it is known that electrophilic substitution takes place in the 3-position in benzofurans that are substituted in the 2-position with an electron releasing group (*e.g.* $CH_3-$).[2] 2-Benzofuranyl methyl ketone, which was obtained on acylation of benzofuran with acetic anhydride/perchloric acid did not give any isolatable perchloric acid adduct.

Acylation of benzofurans is often difficult because they polymerise in the presence of Friedel-Crafts catalysts.[3] Successful acylations have been carried out with, for instance, boron trifluoride [4] or stannic chloride [2,4] but the yields reported are lower than those now obtained with perchloric acid. Perchloric acid and perchlorates have recently been used as catalysts, inter alia in the acylation of furan.[5]

Molecular compounds of aromatic ketones with perchloric acid are known with mole ratios of both 1:1 and 2:1 (*e.g.* Refs.[6-8]). The tendency to form such compounds varies widely even in related types of compounds; *e.g.* 2-methoxychromones give crystalline addition products with perchloric acid but 4-methoxycoumarins do not.[8]

*Experimental.* Compounds I and II were prepared according to Ref.[1] and the acylation reagent ($Ac_2O/HClO_4$ in ethyl acetate) according to Ref.[9]

*2,4,6,7-Tetramethyl-3-benzofuranyl methyl ketone (III) and its molecular compound with perchloric acid.* A mixture of 2-hydroxy-2,4,6,7-tetramethyl-2,3-dihydrobenzofuran (I, 174 mg) and the acylation reagent (1.5 ml) precipitated a crystalline substance after about 15 min. The mixture was cooled to 0° and the product was filtered off and washed with ethyl acetate, giving pale yellow needles (116 mg), m.p. 110–150° (decomp.). (Equiv. wt. by titration with NaOH: 536. Calc. for a molecular compound 2 $C_{14}H_{16}O_2 \cdot HClO_4$: 533.01).

The mother liquor was washed with bicarbonate solution and evaporated. The residue

(80 mg) was recrystallised from hexane giving colourless plates of ketone III, m.p. 79.5–80.5°. (Found: C 77.82; H 7.73. Calc. for $C_{14}H_{16}O_2$: C 77.75; H 7.46).

The yellow molecular compound with perchloric acid crystallised out from a solution of ketone III in the acylation mixture after a few minutes. The same result was obtained when 2,4,6,7-tetramethylbenzofuran (II) was used as starting material. In the presence of water the molecular compound gave the ketone III in 98 % yield.

*2-Benzofuranyl methyl ketone.* A solution of benzofuran (1.18 g) in the acylation reagent (15 ml) was kept for 2 h at room temperature and then washed with water and sodium bicarbonate solution. The ethyl acetate phase was evaporated and the residue was recrystallised from hexane. The product (1.05 g, 66 %) was sublimed (bath temp. 80°, 1 mm Hg) and the sublimate was identified as 2-benzofuranyl methyl ketone by m.p. 72–73°,[4] dinitrophenylhydrazone, m.p. 265° (decomp.) and reduction to 2-benzofuranylmethylcarbinol, m.p. 40–41°.[10] The reduction was done by stirring the ketone with an aqueous solution of potassium borohydride.

1. Magnusson, R. *Acta Chem. Scand.* **18** (1964). *In press.*
2. Bisagni, M., Buu-Hoi, N. P. and Royer, R. *J. Chem. Soc.* **1955** 3688.
3. Elderfield, R. C. (Ed.) *Heterocyclic Compounds*, John Wiley & Sons, New York 1950, Vol. 2, p. 23.
4. Farrar, M. W. and Levine, R. *J. Am. Chem. Soc.* **72** (1950) 4433.
5. Dorofenko, G. N., Dulenko, V. I. and Antoneko, L. M. *Zh. Obshch. Khim.* **32** (1962) 3047.
6. Pfeiffer, P. *Organische Molekülverbindungen*, Enke, Stuttgart 1922.
7. Hein, F. *Chemische Koordinationslehre*, Hirzel, Leipzig 1957.
8. Cieslak, J., Lewak, S. and Chmielewska, I. *Roczniki Chem.* **33** (1959) 349.
9. Fritz, J. S. and Schenk, G. H. *Anal. Chem.* **31** (1959) 1808.
10. Elliott, E. D. *J. Am. Chem. Soc.* **73** (1951) 754.

Received October 31, 1963.

# The Effects of Protonation, Alkylation and Cooling on the Fluorescence of Purine Nucleosides in Liquid Solution

HANS CHR. BØRRESEN*

*Institute of Clinical Biochemistry, Rikshospitalet, University of Oslo, Oslo, Norway*

In a recent publication [1] we elaborated on the previously known fluorescence of adenosine and guanosine in acid solutions. A reasonable hypothesis derived from this work is that alkylations of these compounds should produce fluorescent derivatives to the extent that the alkyl groups stabilize the same electron pairs as those involved in the protonations. In accordance with this expectation we have found that adenosine and guanosine yield fluorescent derivatives when methylated with dimethyl sulfate. Guanosine also reacts with nitrogen mustard (2,2′-dichloro-N-methyldiethylamine) and diazomethane with a high yield of fluorescent substances.

Dimethyl sulfate and nitrogen mustard are supposed to alkylate the purine nucleosides mainly in the positions which are protonated in acid solutions, *i.e.* N-1 in adenosine and N-7 in guanosine.[2,3] These data are confirmed by our observation that neither the absorption spectra nor the fluorescence activation spectra of the fluorescent derivatives of the purine nucleosides depend on whether the fluorescence has been elicited by protonation or by alkylation, except when diazomethane is used as alkylating agent. The latter reagent is known, however, not to alkylate guanosine at N-7.[4]

When solutions of the fluorescent guanosine derivatives were cooled down to 193°K, the fluorescence intensity increased 10- to 50-fold. A mixture of water (1 volume) and methanol (3 volumes) was used as solvent to avoid freezing (Fig. 1).

The fluorescence of the adenosine derivatives either increased slightly (1-methyl adenosine), or did not change significantly (adenosine at pH 2.5), or even almost disappeared (adenosine triphosphate at pH 3.5) when their solutions were cooled. The absorption spectra of the solutions did not change appreciably on cooling. This

* Fellow of The Norwegian Cancer Society.