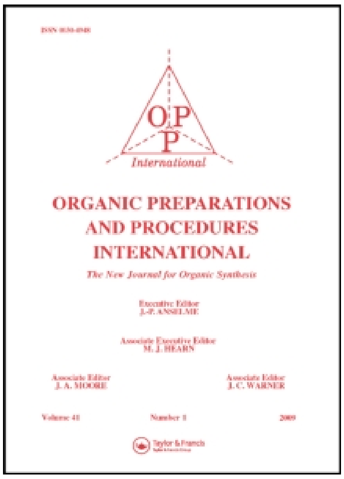

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2,4,6-TRIMETHYLPYRYLIUM SULFOACETATE

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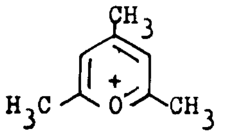
The present procedure reports the preparation of a versatile 2,4,6-trimethylpyrylium salt possessing the sulfoacetate anion.

$$(CH_3CO)_2O + H_2SO_4 \longrightarrow HO_3SCH_2CO_2H + CH_3CO_2H$$

$$3\ (CH_3CO)_2O + H_2C{=}C(CH_3)_2 + HO_3SCH_2CO_2H \longrightarrow$$

$\longrightarrow$



$HO_2CCH_2SO_3^- + 4\ CH_3CO_2H$

Unlike the previously described 2,4,6-trimethylpyrylium salts (perchlorate [1] which is explosive [1,2] and difficultly soluble ; trifluoromethanesulfonate which is expensive ; [3] tetrafluoroborate [4] which is formed in lower yield and requires large amounts of acetic anhydride), the presently described sulfoacetate has the advantages of being prepared in good yield from simple, unexpensive starting materials and of being readily soluble in water (about 900 g./l. at room temperature), methanol, ethanol, acetic acid and other protic solvents (it is insoluble in ethyl ether and little soluble in acetone). In addition, it can be stored indefinitely without decomposition or danger of explosion and the procedure can be scaled up and controlled easily, because the exothermicity is much lower than in the syntheses of other pyrylium salts.[1,4] By anion exchange, the 2,4,6-trimethylpyrylium sulfoacetate can be converted into other 2,4,6-trimethylpyrylium salts such as perchlorate, tetrafluoroborate, iodide, reineckeate, phosphomolybdate, phosphotungstate, etc., which precipitate from concentrated aqueous solutions.

Like other 2,4,6-trimethylpyrylium salts,[1,3,4] the sulfoacetate is a very versatile and useful starting material for the preparation of other heterocyclic or carbocyclic compounds[5] and the present method can be readily extended to other alkyl- and/or aryl-substituted pyrylium salts.

Since the product is new, this is the only method so far reported for its preparation. The procedure is based on the diacetylation of isobutene (or, in lower yield, of t-butanol which is dehydrated in situ)[6] just as in the case of the other 2,4,6-trimethylpyrylium salts mentioned above, namely perchlorate,[1] trifluoromethanesulfonate,[3] and tetrafluoroborate.[4]

The only drawback of the present sulfoacetate is that when employed for the preparation of pyridinium salts by reaction with primary amines, the resulting pyridinium sulfoacetate is often too soluble to crystallize readily ; in this case, it is preferable to convert first the pyrylium sulfoacetate into another salt such as perchlorate (without drying !) thus obviating the need to store the dangerous dry perchlorate, or to add another anion (as the sodium salt) after the reaction between the primary amine and the pyrylium sulfoacetate.

These advantages mentioned above, notably the low cost, the ease of scaling up (we tried successfully with ten times the amounts described below), and the safety in storage and handling of large amounts of this salt, make it the most convenient 2,4,6-trimethylpyrylium salt so far described.[7]

EXPERIMENTAL

In a 3 l. four-necked flask fitted with stirrer, thermometer, reflux condenser, and addition funnel, were placed 2160 g. (2000 ml., 20 moles) of acetic anhydride. Then 210 ml. (384 g., 3.7 moles) of concentrated sulfuric acid (sp. gr. 1.84) was added with stirring at such a rate that the temperature of the liquid reached 80-85° over a period of 5 min. ; in this fashion no external heating was necessary. With larger quantities, cooling was required while with lower amounts, the mixture had to be heated to reach the optimal temperature of 80-85° ; otherwise the reaction followed a different course.[8] The addition funnel was replaced by a fritted gas bubbler. Isobutene (from a metallic container placed on a suitable balance) was bubbled into the reaction mixture with stirring at 80-85° (slight cooling may be necessary) at a flow rate of about 100 g./hr for 2 hrs. After the required amount of isobutene (200 g., 3.5 moles) had been introduced, stirring was continued with mild external heating at 80-85° for 30 min.[9] The resulting acetic acid was completely removed from the dark-brown reaction mixture using a rotatory evaporator under reduced pressure on a boiling water bath.

The hot viscous residue was transferred into a 5 l. Erlenmeyer flask provided with a stopper, and was mixed after cooling to 40° with 4 l. of acetone. The stoppered flask was then cooled to -10°, and after 3-4 hrs. brownish crystals of 2,4,6-trimethylpyrylium sulfoacetate deposited ; crystallization can be appreciably facilitated by seeding with previously prepared crystals of the same product. The crystals were collected and washed on a Buchner funnel with three 350 ml. portions of acetone by interrupting the suction each time and mixing the crystals with the washing liquid by means of a spatula. There was obtained, after drying, 400-430 g. (43-47 %) of crude tan-colored product, mp. 114-116°; this product can be used for most purposes without further purification.

The filtrate and the acetone washings afforded after concentration and treatment with 70 % perchloric acid an extra amount of the less soluble 2,4,6-trimethylpyrylium perchlorate,[1] mp. 244°; if 35 % fluoroboric is used, 2,4,6-trimethylpyrylium tetrafluoroborate,[4] mp. 220° is obtained. The total yield of pyrylium salts was thus raised to 50-55 %. If the sulfoacetate-containing reaction mixture (before removal of the acetic acid) was treated with 70% perchloric acid and (after cooling) with ethyl ether to complete the precipitation, the yield of 2,4,6-trimethylpyrylium perchlorate was 58-62% , higher than that of the previous method which employed *t*-butanol instead of isobutene.[1]

An analytical sample of 2,4,6-trimethylpyrylium sulfoacetate was prepared as follows : 100 g. of the crude sulfoacetate was dissolved in 300 ml. methanol at room temperature, stirred with Norite for 30 min., filtered, and precipitated with 1 l. of acetone. The white crystals (75% recovery) had a mp. 115-116°.

<u>Anal</u>. Calcd. for $C_{10}H_{11}O_6S$: C, 45.79 ; H, 5.38 ; S, 12.22
Found : C, 46.20 ; H, 5.74 ; S, 11.86

^{1}H-NMR (F_3CCO_2H) : δ 2.83 (s, 3H, 4-Me), 2.98 (s, 6H, 2,6-Me_2), 4.43 (s, 2H, CH_2), 7.85 (s, 2H, 3,5-H_2).

^{13}C-NMR (4:1 mixture of F_3CCO_2H and CD_2Cl_2) : δ 21.83 (q, 2C, 2,6-Me_2), 24.30 (q, 1C, 4-Me), 57.29 (t, 1C, CH_2), 124.94 (d, 2C, 3,5-C_2), 172.46 (s, 1C, CO_2H), 177.61 (s, 1C, 4-C), 180.48 (s, 2C, 2,6-C_2).

The ^{1}H- [10] and ^{13}C-NMR spectra [11] of 2,4,6-trimethylpyrylium perchlorate were consistent with the above data.

In addition to peaks due to the cation,[12] the IR spectrum of the 2,4,6-trimethylpyrylium sulfoacetate (KBr pellet) showed C=O bands at 1720 and 1735 cm^{-1}.

MS : In addition to the prominent peaks at m/e = 122, 107, 79 and 77 reported for 2,4,6-trimethylpyrylium iodide,[13] a peak at m/e = 226 appears, corresponding to the elimination of two water molecules from the sulfoacetate.

A simplified but lower-yield procedure replacing the gaseous isobutene by <u>t</u>-butanol (which is dehydrated during the reaction) proceeded as described above using 330 ml. (260 g., 3.5 moles) of <u>t</u>-butanol which was added dropwise at 80-85° into the sulfoacetic acid-containing reaction mixture over 2 hrs. The work-up was as described above, but the yield of crude sulfoacetate was only 35-38%.

Since the product is neither hygroscopic nor corrosive, it may be stored in plastic bags or containers.

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8. If the introduction of isobutene into the sulfoacetic acid-containing reaction mixture is carried out at room temperature instead of 80-85°, another 2,4,6-trimethylpyrylium salt is obtained in low yield instead of the above sulfoacetate, as white crystals, mp. 175° (ethanol-acetone) ; *Anal*. Found : C, 41.6 ; H, 5.1 ; S, 18.7. On treatment with perchloric acid, this compound precipitates quantitatively 2,4,6-trimethylpyrylium perchlorate. The structure of the sulfur-containing anion of this product has not yet been elucidated. The ^{1}H-NMR spectrum displayed two singlets at δ 4.38 (4H) and 5.90 (2H), and the ^{13}C-NMR spectrum showed three peaks at δ 58.56 t, 127.79 s, and 131.89 t; there was no C=O band in the IR or ^{13}C-NMR spectra.
9. Despite the high temperature, the weight of the reaction flask indicated that practically the whole amount of C_4H_8 was retained in the reaction mixture under these conditions.
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