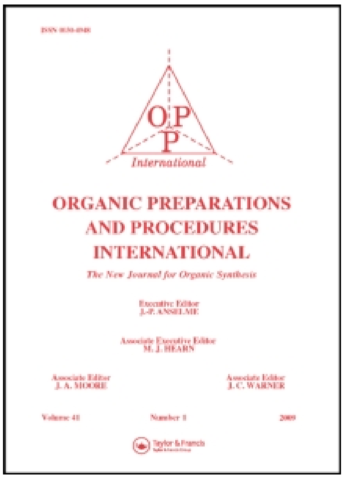
This article was downloaded by:
On: *26 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

2, 6-DIISOPROPYL-4-METHYLPYRYLIUM HEXAFLUOROPHOSPHATE

T. S. Balaban[a]; V. L. Horhoiu[a]; A. T. Balaban[b]
[a] Forschungszentrum Karlsruhe, Institut für Nanotechnologie, Karlsruhe, GERMANY [b] Department of Marine Sciences, Texas A & M University at Galveston, Galveston, TX, USA

To cite this Article Balaban, T. S. , Horhoiu, V. L. and Balaban, A. T.(2007) '2, 6-DIISOPROPYL-4-METHYLPYRYLIUM HEXAFLUOROPHOSPHATE', Organic Preparations and Procedures International, 39: 3, 305 — 309

To link to this Article: DOI: 10.1080/00304940709356017

URL: http://dx.doi.org/10.1080/00304940709356017

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

12. H. E. Baumgarten and R. A. Setterquist, *J. Am. Chem. Soc.*, **81**, 2132 (1959).

13. (a) R. S.Varma, in *"Microwave in Organic Synthesis"*, Loupy, A. (Ed.) Wiley-VCH, Weinheim, Chapter 6, pp 181-218, (**2002**). (b) G. W. Kabalka and R. M. Pagni, *Tetrahedron*, **53**, 7999 (1997). (c) R. S. Varma, *Tetrahedron*, **58**, 1235 (2002).

14. (a) V. K. Yadav and K. G. Babu, *J. Org. Chem.*, **69**, 577 (2004). (b) J. S. Yadav, B. Y. Subba Reddy, M. Srinivas, A. Prabhakar and B. Jagadeesh, *Tetrahedron, Lett.*, **45**, 6033 (2004).

15. A. R. Sardarian and B. Kaboudin, *Synth. Commun.*, **27**, 543 (1997).

16. A. R. Sardarian and B. Kaboudin, *Tetrahedron Lett.*, **38**, 2543 (1997).

17. B. Kaboudin, *Tetrahedron Lett.*, **41**, 3169 (2000).

18. B. Kaboudin and R. Nazari, *Tetrahedron Lett.*, **42**, 8211 (2001).

19. A. K. Gupta, M. Palit, D. K. Dubey and S. K. Raza, *Eur. J. Mass. Spectrom.*, **11**, 119 (2005).

Downloaded At: 18:09 26 January 2011

****

2,6-DIISOPROPYL-4-METHYLPYRYLIUM HEXAFLUOROPHOSPHATE

Submitted by T. S. Balaban,*[†] V. L. Horhoiu,[†] and A. T. Balaban*[‡]
(02/08/07)

[†] *Forschungszentrum Karlsruhe, Institut für Nanotechnologie*
Postfach 3640, D-76021 Karlsruhe, GERMANY
E-mail: silviu.balaban@int.fzk.de

[‡] *Department of Marine Sciences, Texas A&M University at Galveston*
5007 Avenue U, Galveston, TX 77551, USA
E-mail: balabana@tamug.edu

Although the acylation of alkenes has been studied for more than a century, the diacylation to give pyrylium salts was discovered only around 1960 because the diacylation products (the pyrylium salts) being soluble in water, were being unintentionally discarded, despite the fact that sometimes they can be the main reaction product.[1] Although this method (the Balaban-Nenitzescu-Praill synthesis of pyrylium salts) has been known for nearly half a century and many substituted pyrylium salts with identical substituents at positions 2 and 6 have been prepared in

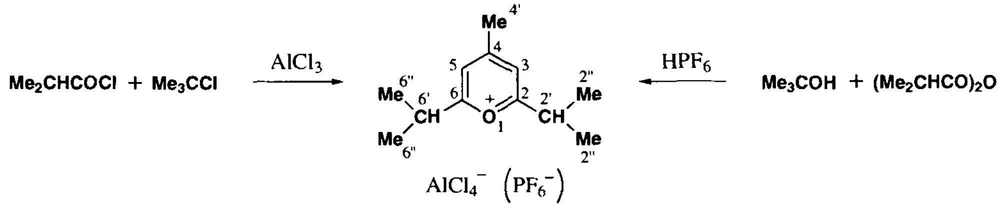
Downloaded At: 18:09 26 January 2011

this way, mostly as perchlorates or tetrafluoroborates, the title compound[2] offers advantages compared to other pyrylium salts because of its hexafluorophosphate anion, as will be detailed later in this paper.

A general overview for the synthesis of pyrylium salts, which includes preparative directions, has been recently published.[3] There are no other practical methods for obtaining the title pyrylium salt. References 3–7 should be consulted for the synthetic utility of pyrylium salts. Pyrylium salts undergo many useful transformations such as conversion to pyridines,[8] 2-acylfurans,[9] indolizines,[10] and *all-cis* tetrahydropyrans,[11] usually in preparatively useful yields. Other uses of pyrylium synthons[6,7] include syntheses of azulenes, pyridinium salts, phosphoranes, benzene and naphthalene derivatives.

The interest of the title compound results from the good yield and purity in which the hexafluorophosphate salt can be isolated. The advantage of this anion resides in its biocompatibility and good solubility in organic solvents. Previously described synthetic procedures for 2,4,6-trimethylpyrylium salts included recourse to the hazardous perchlorate,[12] the tetrafluoroborate,[13] hydrogen sulfate[14] or the more expensive triflate as anions.[15] The advantage of the 2,6-diisopropyl substituents, beside imparting a higher solubility than 2,6-diaryl substituents, is that they are inactive in condensation reactions, which therefore *will promote regiospecific attack at the 4-methyl substituent.* No other 4-methylpyrylium salt is available where this methodology can be employed, except for 2,6-diaryl-4-methylpyrylium or 2,6-di-*tert*-butyl-4-methylpyrylium salts, which lead to compounds with low solubility. The sterically demanding 2,6-di-*tert*-butyl substituents prevent the conversion of pyrylium into pyridinium cations with primary amines, while 2,6-diisopropyl substituted pyrylium salts react readily with primary amines even when buttressing 3,5-dimethyl substituents favor a *tert*-butyl-like conformation of the isopropyl groups.[8] The synthesis of highly fluorescent styrylpyrylium salts, obtained by condensing aromatic aldehydes with the title compound, is described separately; they can be easily converted into fluorescent styrylpyridinium salts.

The preparation of the title pyrylium salt was performed by the Balaban-Nenitzescu-Praill synthesis by the diacylation of isobutene by the isobutyryl cation. Two procedures are presented. In the first, isobutene was generated from *tert*-butyl chloride, and the acylation agent was isobutyryl chloride with anhydrous aluminium chloride as a Lewis acid; at the end of the reaction, addition of hexafluorophosphoric acid precipitated the pyrylium salt; and in the second,[2] isobutene was introduced as *tert*-butanol, with isobutyric anhydride as the acylation agent and with with hexafluorophosphoric acid as the Brønsted acid as shown in the scheme below. The procedure with isobutyryl chloride will be described now for the first time.



EXPERIMENTAL SECTION

Melting points were measured on a Stuart Scientific melting point apparatus SMP3 and are uncorrected. Electospray ionization (ESI) high-resolution mass spectra were recorded using a Bruker Daltonics FT-ICR mass spectrometer equipped with a Bruker ESI/APCI source. ^{1}H and ^{13}C NMR spectra were determined on a Bruker 300 DPI Avance spectrometer at 300 MHz in $CDCl_3$–trifluoroacetic acid. Anhydrous powdered aluminium chloride was purchased from Merck-Schuchardt and all other chemicals were obtained from Aldrich Chemicals.

Preparation of 2,6-Diisopropyl-4-methylpyrylium Hexafluorophosphate:

From t-Butyl Chloride and Isobutyryl Chloride.- A 1L 3-necked flask equipped with a mechanical stirrer, immersion thermometer, reflux condenser (with calcium chloride protection against atmospheric moisture, and pressure equalizing addition funnel) containing isobutyryl chloride (98%, 101.0 g, 0.95 mol, 99.3 mL) was cooled to –10° to 0°C with an external ice-salt bath. Then, through a wide-bore rubber tube was added powdered anhydrous aluminium chloride (62.3 g, 0.47 mol) under stirring in several small portions. After complete dissolution of the $AlCl_3$, *tert*-butyl chloride (43.9 g, 51.6 mL, 0.47 mol) was added dropwise at 0-5°C. The evolved hydrogen chloride was absorbed in an Erlenmeyer flask with water at the bottom (taking care that the level of the liquid was at least 5 cm below the end of the tube through which HCl arrived). After completion of the addition, the reaction mixture was stirred at room temperature for 70 hrs, after which it was poured under stirring onto crushed ice containing 10 mL of conc. hydrochloric acid. Any water-insoluble by-products were then extracted twice with diethyl ether. The aqueous solution containing the pyrylium tetrachloroaluminate was treated with 60% hexafluorophosphoric acid (114.0 g, 0.47 mol, 69.0 mL). The resulting off-white precipitate was collected with suction and washed on the filter paper repeatedly (4-5 times) with ethyl ether. The resulting white precipitate was recrystallized from ethanol-water (1:1 vol.) to afford 70.8 g (0.22 mol, 46%) of white crystals, mp 197-198°C. The previously reported mp was 186°C.[2]

High-resolution MS: Calcd for $C_{12}H_{19}O^+$: m/z = 179.14300. Found: 179.14291. MALDI-MS [in anthracenetriol (dithranol) matrix, positive mode]: 179.85 (M+1, 38%), 178.85 (M, 100%). $C_{12}H_{19}O^+ PF_6^-$ requires 179.14 for the cation.

^{1}H-NMR (300 MHz, $CDCl_3$-TFA): δ 1.47 (d, J = 6.9 Hz, 12H, H-2'' and H-6''), 2.79 (s, 3H, H-4'), 3.42 (septet, J = 6.9 Hz, 2H, H-2' and H-6'), 7.72 (s, 2H, H-3 and H-5). ^{13}C-NMR (75 MHz, $CDCl_3$-TFA): δ 19.58 (C-2'' and C-6''), 23.63 (C-4'), 34.66 (C-2' and C-6'), 121.02 (C-3 and C-5), 176.41 (C-4), 185.57 (C-2 and C-6).

From t-Butanol and Isobutyric Anhydride.- To a 1L 3-necked flask equipped with mechanical or powerful magnetic stirrer, immersion thermometer, reflux condenser, Nalgene dropping funnel, and containing isobutyric anhydride (332 mL, 316 g, 2.0 mol) and *tert*-butanol (95.6 mL, 74.1 g, 1.0 mol) was added dropwise 60% hexafluorophosphoric acid (147 mL, 243 g, 1.0 mol). The rate of addition should be about 1 mL/min at first so as to lead to a fairly rapid rise in temperature till 60-70°C. The remaining hexafluorophosphoric acid must be added at a rate such

Downloaded At: 18:09 26 January 2011

that the temperature remains in the 80-90°C range. A lower temperature favors crystallization of the title pyrylium salt making stirring difficult, whereas a higher temperature leads to the evolution of isobutene, lowering the yield. Stirring was continued till the temperature dropped below 50°C; the mixture was then cooled to room temperature. The off-white precipitate was collected with suction and washed thoroughly 4-5 times with ethyl ether. Hexafluorophosphoric acid (unlike perchloric or tetrafluoroboric acids) forms a colorless crystalline salt with the monoacylation product. This salt is also present in the precipitate; on exposure to humid air, this salt decomposes into hexafluorophosphoric acid (which corrodes glass containers) and isopropyl isobutenyl ketone with a characteristic terpenoid-like smell. Recrystallization from ethanol-water (1:1 vol.) *must* be performed for removal of traces of secondary products, and affords 168 g, (52%) of white solid, mp. 197-198°C. This compound was identical to the product prepared in *Procedure 1*.

REFERENCES

1. A. Hassner and C. Stummer, *Organic Syntheses Based on Name Reactions*, 2nd Edition, Elsevier, Amsterdam, 2002.

2. I. Ghiviriga, E. W. Czerwinski and A. T. Balaban, *Croatica Chim. Acta*, **77**, 391 (2004).

3. T. S. Balaban and A. T. Balaban. "*Pyrylium Salts, Science of Synthesis. Houben-Weyl Methods of Molecular Transformations*" (ed. E. J. Thomas), Vol. 14, pp. 11-200, Georg Thieme Verlag, Stuttgart: 2003; W. Schroth and A. T. Balaban, "Pyrylium salts" (in German). In "*Methoden der Organischen Chemie (Houben-Weyl)*", Vol. **E7b**, Hetarene II (Teil 2), (Ed. R. P. Kreher), Georg Thieme Verlag: Stuttgart, 1992, pp. 755.

4. A. T. Balaban, A. Dinculescu, G. N. Dorofeenko, G. W. Fischer, A. V. Koblik, V. V. Mezheritskii and W. Schroth, "*Pyrylium Salts: Syntheses, Reactions and Physical Properties*", *Adv. Het. Chem., Suppl. Vol. 2*, (ed. A. R. Katritzky), Academic Press, New York, 1982.

5. A. T. Balaban, "Trimethylpyrylium" in Vol. 7, pp. 5224-5227; "Triphenylpyrylium", in Vol. 8, pp. 5407-5411. In *Encyclopedia of Reagents for Organic Synthesis* (ed. L. A. Paquette), Wiley, New York, 1996.

6. A. T. Balaban, "Pyrylium Salts as Useful Synthons", in *Organic Synthesis: Modern Trends* (Proc. 6th IUPAC Internat. Symp. on Organic Synthesis, Moscow), (ed. O. Chizov), Blackwell, Oxford, 1987, p. 263.

7. A. T. Balaban, "The Pyrylium Cation as a Synthon in Organic Chemistry", in *New Trends in Heterocyclic Chemistry*, (eds. R. B. Mitra, N. R. Ayyangar, V. N Gogte, R. M. Acheson and N. Cromwell), Elsevier, Amsterdam, 1979, pp. 79.

8. A. T. Balaban, I. Ghiviriga, E. W. Czerwinski, P. De and R. Faust, *J. Org. Chem.*, **69**, 536 (2004).

Downloaded At: 18:09 26 January 2011

9. A. T. Balaban, *Org. Prep. Proced. Int.*, **1**, 63 (1969).

10. A. Dinculescu, T. S. Balaban and A. T. Balaban, *Tetrahedron Lett.*, **28**, 3145 (1987).

11. G. Mihai and T. S Balaban, *Z. Naturforsch.*, **41b**, 502 (1986).

12. A. T. Balaban and C. D. Nenitzescu, *Org. Synth. Coll. Vol.* **5**, 1106 (1973).

13. A. T. Balaban and A. J. Boulton, *Org. Synth. Coll. Vol.* **5**, 1112 (1973).

14. A. Dinculescu and A. T.Balaban, *Org. Prep. Proced. Int.*, **14**, 39 (1982).

15. A. T. Balaban and A. J. Boulton, *Org. Synth. Coll. Vol.* **5**, 1114 (1973).

Downloaded At: 18:09 26 January 2011