J. Chem. Research (S), 1999, 262–263†

Preparation and Characterization of Tetraphenylborate Salts of 2-Aminopyrrole and 1-Alkyl-2-aminopyrroles†

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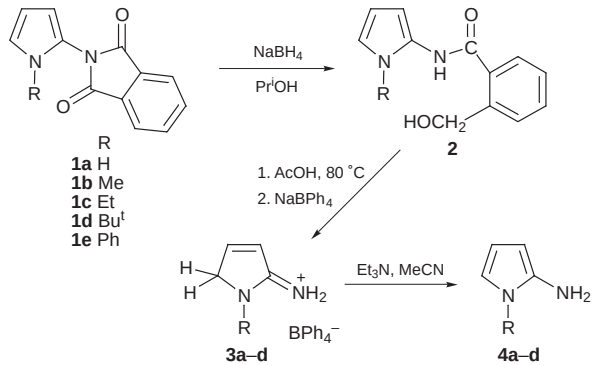
Tetraphenylborate salts of 2-aminopyrrole and 1-alkyl-2-aminopyrroles are prepared and found to be stable.

Recently we reported the first successful synthesis of 2-aminopyrrole and several 1-substituted-2-aminopyrroles in which the pyrrole ring did not contain additional electron-withdrawing groups.[1] In the absence of these electron-withdrawing groups the newly synthesized 2-amino derivatives were stable only in solution and were not isolable.[2] It is of interest, for mechanistic and synthetic studies, to have a readily available source of these 2-aminopyrroles. In this paper we describe the isolation of stable tetraphenylborate salts of the 2-aminopyrroles and the subsequent regeneration of the parent amino derivatives in several solvents.

During the course of previous work it was noted that 2-aminopyrroles appeared to be much more stable in glacial acetic acid than in chloroform.[1] NMR studies indicated that in acetic acid the 2-aminopyrrole was present as the conjugate acid, and this appeared to indicate that the conjugate acid **3** was more stable than the 2-aminopyrrole **4**. Previous workers have isolated trifluoroacetate[3] and perchlorate[4] salts of highly substituted 2-aminopyrroles. With these facts in mind, we sought to isolate the 2-aminopyrroles as their more stable protonated salts. One method of isolating a cation is to precipitate it as a tetraphenylborate salt.[5] This method is particularly appropriate for precipitating monocationic protonated amines and tertiary ammonium ions, as their tetraphenylborate salts are often very insoluble in water. Recently this method was also used to obtain crystalline *N*-acylammonium salts.[6]



Scheme 1

Partial reduction[7] of an *N*-(1-substituent-1*H*-pyrrol-2-yl)-phthalimide[8] **1** with $NaBH_4$ gave the *o*-hydroxymethyl benzamide **2** used to generate the 2-aminopyrrole (Scheme 1). Heating the *o*-hydroxymethylbenzamide in glacial acetic acid for 2 h at 80 °C under nitrogen gave the conjugate acid of the 2-aminopyrrole and phthalide.[1] Addition of an aqueous solution of sodium tetraphenylborate gave an instantaneous precipitate of the tetraphenylborate salt. The solid was filtered off, dried under vacuum and then triturated with small amounts of cold $CHCl_3$ to remove neutral impurities. Tetraphenylborate salts **3a**–**d** were isolated in this manner and characterized by ^1H and ^{13}C NMR spectroscopy (Table 1) and positive-ion FAB mass spectroscopy. ^1H and ^{13}C NMR spectra clearly showed the presence of the CH_2 group expected for the salt **3**. The presence of a CH_2 group was confirmed by DEPT spectra. These results ruled out protonation of the *exo* amino group. The CH_2 group, in some of the ^1H NMR spectra (Table 1), did not have the expected couplings to C^3H and C^4H. Singlets or broad triplets were observed. This is attributed to proton exchange at the CH_2 that causes partial or complete collapse of the expected multiplet.[1] In the case of the 1-phenyl derivative **3e** a black deliquescent material was obtained that could not be further characterized. Salts **3a**–**d** are stable enough to store for reasonably long periods of time. After 10 months at 0 °C, washing the salt with a small amount of $CHCl_3$ yielded material with the same NMR spectral properties and decomposition point as the originally isolated product.[9]

The 2-aminopyrrole can be regenerated by dissolving the salt in DMSO or acetonitrile and adding one or more equivalents of triethylamine. Upon addition of the amine the CH_2 signal of the salt disappeared in the ^1H NMR spectrum and three multiplets[1] diagnostic for a 2-substituted pyrrole appeared. Addition of water to the DMSO solution following the addition of triethylamine, gave a precipitate the ^1H NMR spectrum of which was consistent with triethylammonium tetraphenylborate.

The results of this work demonstrate that simple 2-aminopyrroles can be isolated and stored as their respective tetraphenylborate salts and that they are readily converted back to the amino form. Tetraphenylborate salts can therefore serve as convenient sources of unstable 2-aminopyrrole derivatives, eliminating the need to isolate the 2-aminopyrrole from acetic acid each time that a sample is needed.

Experimental

General Procedure for Preparation of Tetraphenlborate Salts.—The *o*-hydroxymethyl benzamide **2** was dissolved in glacial acetic acid (1 mmol ml^{-1}) and heated at 80 °C for 2 h under a nitrogen atmosphere.[1] A concentrated aqueous solution of sodium tetraphenylborate (4 equiv.) was added to the reaction mixture and the resulting precipitate was filtered and then dried in a vacuum desiccator overnight. The salt was washed with cold chloroform and characterized. Prior to any subsequent use the salt was washed again with a small volume of cold chloroform. Material purified in this way was essentially pure (NMR). Salts can also be by purified by recrystallization from methanol, though with a large loss of material. Melting points are of recrystallized materials and yields, of salts that

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† This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 ^{1}H and ^{13}C chemical shifts (δ) of tetraphenylborate salts **3**

	^{1}H						^{13}C				
R	CH_2^a	C^4H	CS^3H	NH_2 (*exo*)	Other	J^b/Hz	CH_2	C^4	C^3	C^2	Other
H[c]	4.42(brt)	6.57(dt)	7.46(dt)	8.5(br), 8.8 (br)	9.5(br)(NH)[d]	5.8, 1.7	56.2	122.6	152.8	168.4	
Me[e]	4.49(brt)	6.46(dt)	7.44(dt)	8.8(br), 9.2 (br)	3.18(s)	6.0, 1.7	61.3	122.3	149.0	164.4	31.7
Et[e]	4.52(s)	6.46(dt)	7.48(d)	8.8(br), 9.2 (br)	3.60(q), 1.18(t)	6.0, 1.6	58.9	122.3	149.1	164.7	39.4, 12.5
Bu^t[e]	4.70(s)	6.42(d)	7.42(d)	8.3(br), 9.2 (br)	1.46(s)	5.9, 1.5	58.9[f]	123.6	147.6	162.6	56.2, 26.5
Bu^t[c]	4.61(t)	6.50(dt)	7.24(dt)	7.9(br), 8.6 (br)	1.58(s)	5.9, 1.5					

[a] dt = doublet of triplets; br = broad; q = quartet; t = triplet; s = singlet; d = doublet. [b] Large coupling constant (J_{34}); small coupling constant $J_{35} = J_{45}$. [c] In $(CD_3)_2CO$. [d] Pyrrole NH maybe interchangeable with one of the values of exocyclic amino protons. [e] In $(CD_3)_2SO$. [f] Determined to be CH_2 by DEPT.

have been washed with chloroform but not recrystallized. Table 1 summarizes the ^{1}H and ^{13}C NMR data. Tetraphenylborate salt **3a** (R = H): 87% yield; mp 161–162 °C (decomp); FABMS (glycerol) *m/z* (relative intensity) 83 (100, M^+). Tetraphenylborate salt **3b** (R = Me): 95% yield; mp 171–173 °C (decomp); FABMS (4-nitrobenzyl alcohol) *m/z* (relative intensity) 97 (100, M^+). Tetraphenylborate salt **3c** (R = Et): 92% yield; mp 164–165 °C (decomp); FABMS (4-nitrobenzyl alcohol) *m/z* (relative intensity) 111 (100, M^+). Tetraphenylborate salt **3d** (R = Bu^t): 98% yield; mp 163–165 °C; FABMS (4-nitrobenzyl alcohol) *m/z* (relative intensity) 139 (100, M^+).

This work was funded by the National Science Foundation and the American Cyanamid Company. We thank Dr. Robert Minard of Penn State for the FAB mass spectra.

Received, 23rd November 1998; Accepted, 13th January 1999
Paper E/8/09138B

References

1 M. De Rosa, R. P. Issac and G. Houghton, *Tetrahedron Lett.*, 1995, **36**, 9261; M. De Rosa, R. P. Issac, M. Marquez, M. Orozco, F. J. Luque and M. D. Timken, *J. Chem. Soc., Perkin Trans. 2* submitted for publication.
2 G. Cirrincione, A. M. Almerico, E. Aiello and G. Dattolo, in *Pyrroles, Part Two, The Synthesis, Reactivity and Physical Properties of Substituted Pyrroles*, ed. R. A. Jones, Wiley, New York, 1992, ch. 3.
3 H. Wamhoff and B. Wehling, *Synthesis*, 1976, 51.
4 J. A. S. Laks, J. R. Ross, S. M. Bayomi and J. W. Sowell, Sr., *Synthesis*, 1986, 291.
5 K. Vytras, *Am. Lab.*, 1979, 93 and references therein.
6 J. A. King, Jr. and G. L. Bryant, Jr., *J. Org. Chem.*, 1992, **57**, 5136.
7 J. O. Osby, M. G. Martin and B. Ganem, *Tetrahedron Lett.*, 1984, **25**, 2093.
8 M. De Rosa, G. Cabrera Nieto and F. Ferrer Gago, *J. Org. Chem.*, 1989, **54**, 5347.
9 An attempt was made to precipitate the hexafluorophosphate or tetrafluoroborate salts, but no solid precipitated when aqueous solutions containing these anions were added to **3** in acetic acid.