

Article

Iminium Salts by Meerwein Alkylation of Ehrlich's Aldehyde

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Abstract: 4-(Dimethylamino)benzaldehyde is alkylated at the N atom by dialkyl sulfates, MeI, or Me₃O BF₄. In contrast, ethylation by Et₃O BF₄ occurs selectively at the O atom yielding a quinoid iminium ion. 4-(Diethylamino)benzaldehyde is alkylated only at O by either Et or Me oxonium reagent. The iminium salts are prone to hydrolysis giving the corresponding hydrotetrafluoroborates. Five crystal structures were determined.

Keywords: alkylation; Ehrlich's aldehyde; iminium salt; quinoid; quinone

1. Introduction

During unrelated work, the need arose for low-melting quaternary ammonium salts (“ionic liquids”) bearing an aldehyde functional group. Our obvious choice was 4-(dimethylamino)benzaldehyde (Ehrlich's aldehyde) as inexpensive starting material which was to be *N*-alkylated. Common alkylating reagents such as dialkyl sulfates or methyl iodide readily gave the desired products [1,2]. However, a surprising selectivity was observed when trialkyloxonium tetrafluoroborates (Meerwein reagents) were employed. Thus, methylation occurred at the N atom as expected, whereas ethylation took place at the

O atom. The crystal structures of the new compounds and byproducts were determined by single crystal X-ray diffraction (Table 1).

2. Results and Discussion

As noted above, for most of the different methods of alkylating 4-(dialkylamino)benzaldehydes (Figure 1a), including the use of trimethyloxonium tetrafluoroborate, the electrophilic attack occurs at the aniline N atom as expected, whereas Meerwein ethylation takes place at the carbonyl O atom, creating the quinoid iminium ion **1** in high yield and purity. Only traces of N-alkyl derivative of 4-(diethylamino)benzaldehyde were observed with either Et or Me oxonium reagent. Iminium ions are very reactive electrophilic intermediates, allowing a large range of nucleophiles to be trapped. For example, cyclizations involving iminium ions belong to the most powerful methods of forming nitrogen-containing heterocycles [3]. They are easily available by various well-established methods, but unprecedented pathways towards new iminium vehicles are emerging by serendipity, thus inviting multifaceted follow-up chemistry [4]. Iminium species are sensitive compounds and are typically prepared immediately prior to use. In the present case, the new iminium salts can be stored under an inert atmosphere for prolonged periods at room temperature. They are however prone to hydrolysis in solution, yielding the corresponding protic salts **2** and **5**, which gave suitable single crystals. Exhibiting the interesting motif of a quinoid spacer between an imine moiety and an enol ether, the new bright green iminium salts **1** and **4** (Figure 1b) belong to the subfamily of quinone imine dyes, featuring specific reactivity patterns on their own [5]. Analogous products of O-alkylation and silylation were obtained from the related 4,4'-bis(dimethylamino)benzophenone [6,7]. Another example was found in 3,6-bis(dimethylamino)-9-ethoxyacridine [8]. The N-alkylated product, 4-(trimethylammonio)benzaldehyde, is known as a useful precursor for 4-fluorobenzaldehyde [9,10]. The product of N-alkylation was converted to the low-melting triflimide **3** by ion metathesis, thus achieving the goal of the initial unrelated project. Protonation of Ehrlich's aldehyde has also been reported to result in low-melting salts [11], and two crystal structures of such salts are known [12,13].

Figure 1. (a) Alkylation of 4-(dialkylamino)benzaldehydes with Meerwein reagents; (b) Colorful reaction of Ehrlich's aldehyde resulting in green crystals of iminium salt **1**.

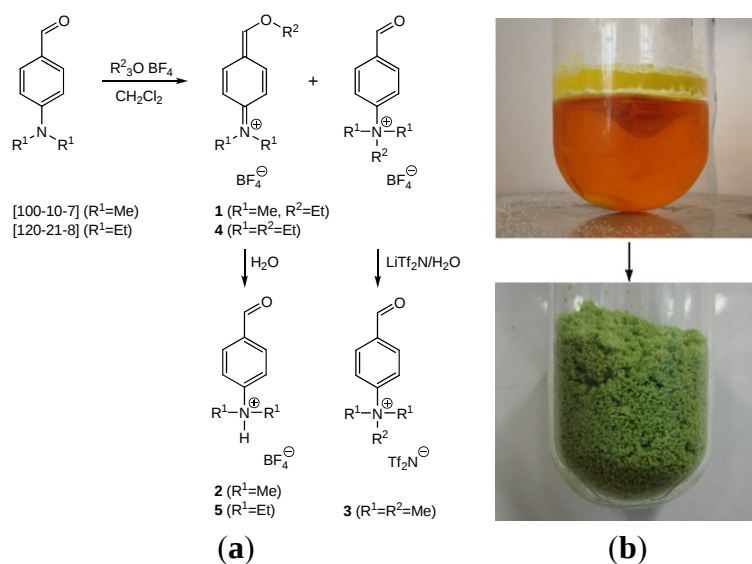


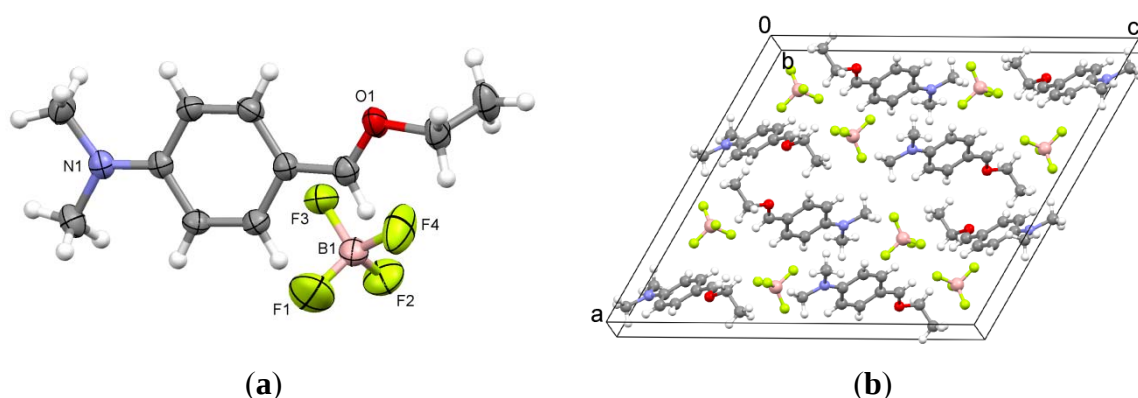
Table 1. Crystal data and structure refinement details.

Compound	1	2	3	4	5
Chemical formula	C ₁₁ H ₁₆ NO·BF ₄	C ₉ H ₁₂ NO·BF ₄	C ₁₀ H ₁₄ NO·C ₂ F ₆ NO ₄ S ₂	C ₁₃ H ₂₀ NO·BF ₄	C ₁₁ H ₁₆ NO·BF ₄
<i>M</i> _r	265.06	237.01	444.37	293.11	265.06
Crystal system	Monoclinic	Monoclinic	Triclinic	Triclinic	Triclinic
Space group	<i>C</i> 2/ <i>c</i>	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$
<i>a</i> /Å	18.9425 (5)	8.4727 (4)	7.7374 (4)	8.1170 (12)	7.2055 (5)
<i>b</i> /Å	7.4564 (3)	13.5659 (6)	10.3506 (7)	9.2368 (16)	9.0529 (6)
<i>c</i> /Å	21.134 (1)	10.4411 (5)	12.6004 (8)	10.6937 (17)	10.2060 (7)
<i>α</i> /°	90	90	72.577 (6)	67.069 (15)	94.378 (6)
<i>β</i> /°	118.979 (7)	109.730 (6)	73.231 (5)	77.760 (13)	90.403 (6)
<i>γ</i> /°	90	90	72.301 (9)	89.080 (13)	97.839 (5)
<i>V</i> /Å ³	2611.3 (2)	1129.64 (9)	895.34 (10)	719.6 (2)	657.50 (8)
<i>Z</i>	8	4	2	2	2
<i>D</i> _x /g·cm ^{−3}	1.35	1.39	1.65	1.35	1.34
<i>μ</i> /mm ^{−1}	1.08	0.13	0.39	1.03	0.12
Crystal size/mm ³	0.32 × 0.24 × 0.24	0.32 × 0.32 × 0.02	0.28 × 0.16 × 0.12	0.20 × 0.20 × 0.12	0.32 × 0.2 × 0.08
<i>F</i> (000)/e	1104	488	452	308	276
<i>θ</i> range/°	4.8–67.6	2.6–25.2	2.8–25.4	4.6–67.5	3.2–25.3
<i>h</i> , <i>k</i> , <i>l</i> range	−22 ≤ <i>h</i> ≤ 16	−10 ≤ <i>h</i> ≤ 10	−7 ≤ <i>h</i> ≤ 9	−9 ≤ <i>h</i> ≤ 9	−8 ≤ <i>h</i> ≤ 7
	−8 ≤ <i>k</i> ≤ 8	−16 ≤ <i>k</i> ≤ 16	−11 ≤ <i>k</i> ≤ 12	−11 ≤ <i>k</i> ≤ 10	−10 ≤ <i>k</i> ≤ 10
	−19 ≤ <i>l</i> ≤ 25	−11 ≤ <i>l</i> ≤ 12	−14 ≤ <i>l</i> ≤ 15	−10 ≤ <i>l</i> ≤ 12	−12 ≤ <i>l</i> ≤ 9
Measured reflections	7103	10599	5493	4283	4097
Independent reflections (<i>R</i> _{int})	2337 (0.022)	2020 (0.033)	3248 (0.019)	2421 (0.027)	2369 (0.025)
Observed reflections [<i>I</i> ≥ 2σ(<i>I</i>)]	1902	1641	2529	1928	1893
Restraints/parameters	21/185	0/153	0/251	0/188	132/261
<i>R</i> ₁ / <i>wR</i> ₂ [<i>I</i> ≥ 2σ(<i>I</i>)]	0.059/0.172	0.039/0.11	0.029/0.067	0.043/0.108	0.039/0.084
<i>R</i> ₁ / <i>wR</i> ₂ (all data)	0.069/0.181	0.048/0.116	0.039/0.071	0.055/0.119	0.053/0.093
Δρ _{max/min} /e Å ^{−3}	0.50/−0.33	0.32/−0.28	0.35/−0.34	0.18/−0.20	0.17/−0.17

2.1. *N*-(4-(Ethoxymethylene)cyclohexa-2,5-dienylidene)-*N,N*-dimethylammonium Tetrafluoroborate (**1**)

The quinoid nature of the ring can be readily recognized by the presence of two short double bonds, 1.343(4) Å and 1.350(4) Å, and four long single bonds, from 1.418(4) Å to 1.436(5) Å. The two exocyclic bonds, C=N with 1.330(3) Å and C=C with 1.375(4) Å, are clearly double bonds. The molecular structure of the ion pair and the packing in the unit cell ($Z = 8$) are shown in Figure 2.

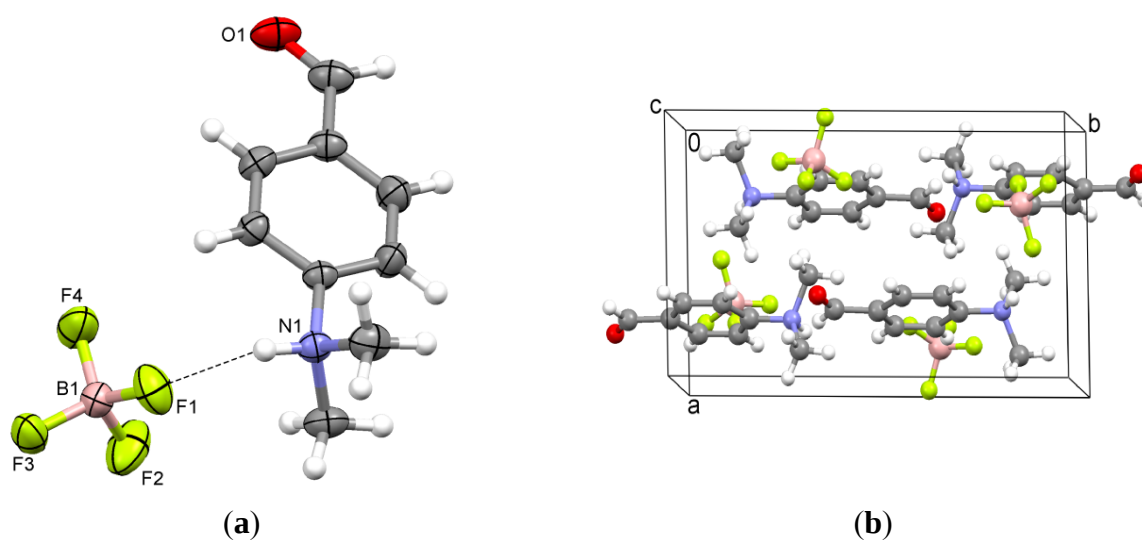
Figure 2. (a) Ion pair (ellipsoids at 50 percent probability level); (b) Packing of compound **1** in the unit cell.



2.2. 4-(Dimethylamino)benzaldehyde hydrotetrafluoroborate (**2**)

This protic salt was obtained by hydrolysis of the quinone **1**. An interionic hydrogen bond is observed between N1-H and F1. The H...F distance is 1.99(3) Å and the N...F distance, 2.818(2) Å. The N...H...F angle was found to be 152(2)°. The bond lengths in the ring, ranging from 1.378(2) Å to 1.391(3) Å, reveal its aromatic character. The two exocyclic bonds, C-N with 1.478(2) Å and C-C with 1.473(3) Å, are typical single bonds. The molecular structure of the ion pair and the packing in the unit cell ($Z = 4$) are shown in Figure 3.

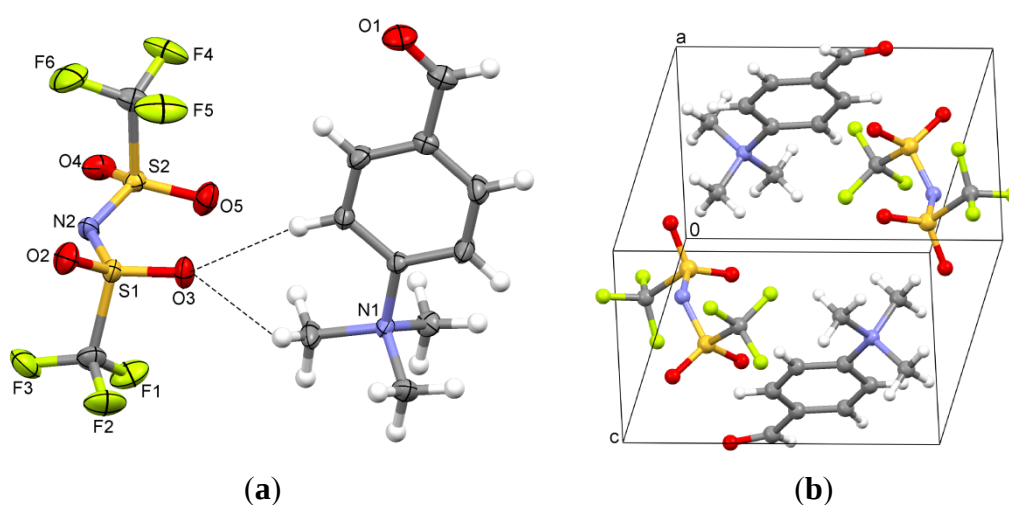
Figure 3. (a) Ion pair (ellipsoids at 50 percent probability level); (b) Packing of compound **2** in the unit cell.



2.3. 4-(Trimethylammonio)benzaldehyde bis(trifluoromethylsulfonyl)imide (3)

The 4-(trimethylammonio)benzaldehyde cation obtained by methylation of Ehrlich's aldehyde using $\text{Me}_3\text{O BF}_4$ was converted by ion metathesis and isolated as triflimide, a low-melting salt. Again, the bond lengths in the ring, ranging from 1.379(3) Å to 1.386(2) Å, indicate an aromatic system. The exocyclic single bonds, C-N with 1.500(2) Å and C-C with 1.482(3) Å, are longer than in the protic salt **2**. The triflimide anion adopts a typical *anti* conformation [14] with a C-S1...S2-C torsion angle of 167.1(1)° and exhibits only weak C-H...O interactions with the cation. The molecular structure of the ion pair and the packing in the unit cell ($Z = 2$) are shown in Figure 4.

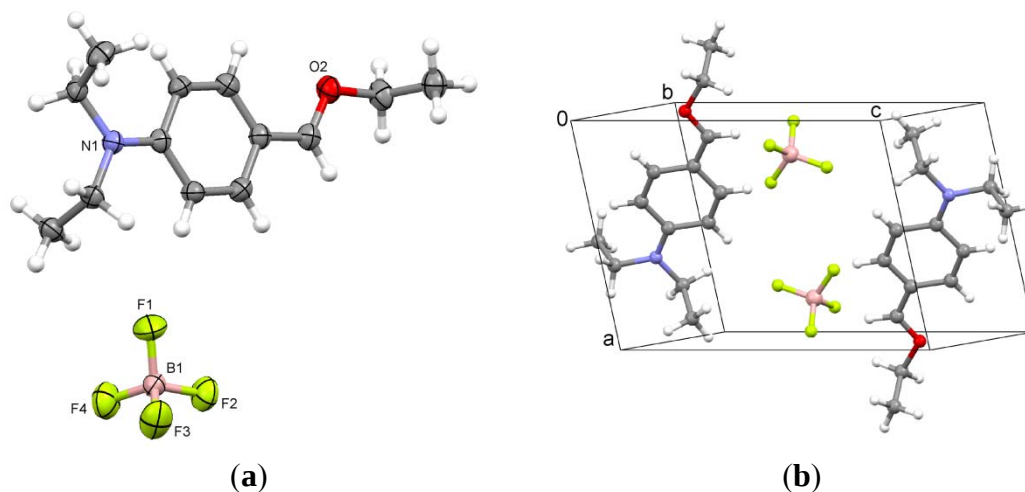
Figure 4. (a) Ion pair (ellipsoids at 50 percent level); (b) Packing of compound **3**.



2.4. *N*-(4-(Ethoxymethylene)cyclohexa-2,5-dienylidene)-*N,N*-diethylammonium Tetrafluoroborate (4)

Again, the quinoid character of the ring can be seen by the presence of two short double bonds, 1.356(2) Å and 1.359(2) Å, and four long single bonds, from 1.420(3) Å to 1.439(2) Å. The two exocyclic bonds, C=N with 1.336(2) Å and C=C with 1.379(2) Å, are clearly double bonds. The molecular structure of the ion pair and the packing in the unit cell ($Z = 2$) are shown in Figure 5.

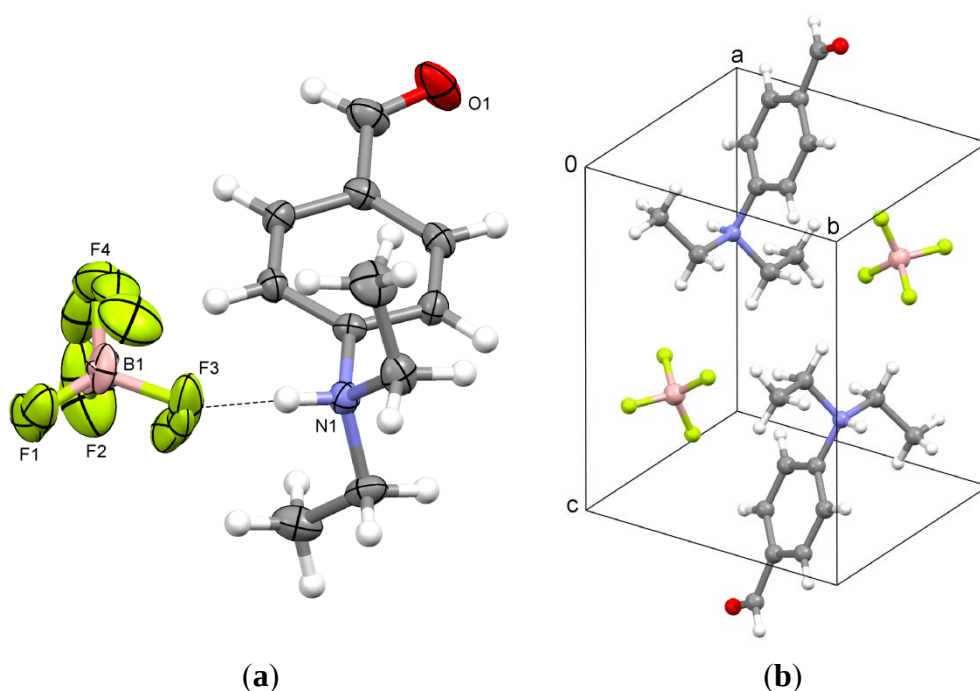
Figure 5. (a) Ion pair (ellipsoids at 50 percent level); (b) Packing of compound **4**.



2.5. 4-(Diethylamino)benzaldehyde Hydrotetrafluoroborate (5)

The hydrolysis of quinone **4** gave this protic salt, in analogy to the conversion of **1** to **2**. The anion exhibits positional disorder (ratio of components 0.33:0.26:0.41). A short hydrogen bond, as in compound **2**, is observed between N1-H and F3. The bond lengths in the ring, from 1.376(2) Å to 1.388(2) Å, indicate aromatic character. The two exocyclic bonds, C-N with 1.476(2) Å and C-C with 1.474(2) Å, are of almost equal length as in salt **2**. The molecular structure of the ion pair and the packing in the unit cell ($Z = 2$) are shown in Figure 6.

Figure 6. (a) Ion pair (ellipsoids at 50 percent probability level); (b) Packing of compound **5** in the unit cell.



3. Experimental Section

Intensity data were collected on an Oxford Diffraction Gemini-R Ultra diffractometer with graphite-monochromatized Cu $K\alpha$ (**1** and **4**) or Mo $K\alpha$ (**2**, **3**, and **5**) radiation. Data were measured via ω scans, and an empirical absorption correction (multi-scan) was applied. CCDC reference numbers: 921104–921108. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

3.1. *N*-(4-(Ethoxymethylene)cyclohexa-2,5-dienylidene)-*N,N*-dimethylammonium Tetrafluoroborate (**1**) and 4-(Dimethylamino)benzaldehyde Hydrotetrafluoroborate (**2**)

4-(Dimethylamino)benzaldehyde (5.94 g, 39.8 mmol) was added to a solution of Et₃O BF₄ (7.57 g, 39.8 mmol) in anhydrous CH₂Cl₂ (10 mL) in an argon atmosphere. The colour of the solution changed from yellow to red to brown and finally to green after 3 hours of stirring at room temperature. After 3.5 h anhydrous Et₂O (50 mL) was added, and a green solid precipitated. The solid was washed with

anhydrous Et₂O and dried. Single crystals of **1** and **2** were grown concomitantly by diffusion of hexane into a CH₂Cl₂ solution under inert gas.

1: ¹H NMR (300 MHz, DMSO-d₆): 1.46 (t, 3H), 3.38 (s, 6H), 4.73 (q, 2H), 7.11 (d, *J* = 9.5 Hz, 2H), 7.87 (d, *J* = 9.5 Hz, 2H), 8.68 (s, 1H) ppm; ¹³C NMR (75 MHz, DMSO-d₆): 14.9, 41.3 (2C), 76.5, 115.2 (2C), 128.0, 138.0, 159.7, 180.5 ppm.

2: ¹H NMR (300 MHz, DMSO-d₆): 3.04 (s, 6H), 6.79 (d, *J* = 8.9 Hz, 2H), 7.68 (d, *J* = 8.9 Hz, 2H), 9.66 (s, 1H) ppm; ¹³C NMR (75 MHz, DMSO-d₆): 39.7 (2C), 111.1 (2C), 124.6, 131.6 (2C), 154.2, 189.9 ppm.

3.2. 4-(Trimethylammonio)benzaldehyde Bis(trifluoromethylsulfonyl)imide (**3**)

4-(Dimethylamino)benzaldehyde (1.53 g, 10.3 mmol) was added to a solution of Me₃O BF₄ (1.52 g, 10.3 mmol) in anhydrous CH₂Cl₂ (50 mL) under inert gas. The colour of the solution changed from yellow to orange to yellow-light green. After stirring at room temperature for 20 h anhydrous Et₂O (50 mL) was added, and a light orange solid formed, which was vacuum-dried. Then K₂CO₃ (1.42 g, 10.3 mmol), lithium bis(trifluoromethylsulfonyl)imide (1.71 g, 5.96 mmol), and H₂O (50 mL) were added and stirred at room temperature for 1 h. The formation of a heavy organic phase was observed. The aqueous phase was discarded, and the lower phase was washed twice with Et₂O. After addition of CH₂Cl₂ (50 mL) the organic phase was washed twice with water. The solvent was removed, and the resulting light-green product was vacuum-dried. Single crystals were obtained by diffusion of hexane into a solution in anhydrous CH₂Cl₂. m.p. 67–69 °C.

¹H NMR (300 MHz, DMSO-d₆): 3.65 (s, 9H), 8.14–8.23 (m, 4H), 10.11 (s, 1H) ppm; ¹³C NMR (75 MHz, DMSO-d₆): 56.4 (3C), 119.5 (q, *J* = 322 Hz), 121.8 (2C), 130.9 (2C), 136.8, 151.1, 192.2 ppm.

3.3. N-(4-(Ethoxymethylene)cyclohexa-2,5-dienylidene)-N,N-diethylammonium Tetrafluoroborate (**4**)

4-(Diethylamino)benzaldehyde (5.25 g, 29.6 mmol) was added to a solution of Et₃O BF₄ (5.62 g, 29.6 mmol) in anhydrous CH₂Cl₂ (15 mL) under argon. The color of the solution changed from yellow to orange to yellow-green after 24 h of stirring at room temperature. Anhydrous Et₂O (10 mL) was added to precipitate a light green solid, which was filtered and dried. Single crystals were grown by diffusion of hexane into a solution in anhydrous CH₂Cl₂.

¹H NMR (300 MHz, DMSO-d₆): 1.23 (t, 6H), 1.46 (t, 3H), 3.74 (q, 4H), 4.73 (q, 2H), 7.13 (d, *J* = 9.2 Hz, 2H), 7.87 (d, *J* = 9.2 Hz, 2H), 8.69 (s, 1H) ppm; ¹³C NMR (75 MHz, DMSO-d₆): 12.6 (2C), 15.0, 46.2 (2C), 76.5, 115.0 (2C), 128.4, 138.4, 158.3, 180.3 ppm.

3.4. 4-(Diethylamino)benzaldehyde Hydrotetrafluoroborate (**5**)

4-(Diethylamino)benzaldehyde (1.80 g, 10.2 mmol) was added to a solution of Me₃O BF₄ (1.50 g, 10.2 mmol) in anhydrous CH₂Cl₂ (30 mL) under inert gas. The orange suspension turned into a green solution after stirring at room temperature for 24 h. Addition of anhydrous Et₂O (10 mL) precipitated a light green solid. Unfortunately, only the hydrolyzed product crystallized by diffusion of hexane into a solution in CH₂Cl₂.

^1H NMR (300 MHz, DMSO- d_6): 1.11 (t, $J = 7.0$ Hz, 6H), 3.43 (q, $J = 7.0$ Hz, 4H), 6.79 (d, $J = 8.9$ Hz, 2H), 7.67 (d, $J = 8.9$ Hz, 2H), 9.64 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO- d_6): 12.3 (2C), 44.5 (2C), 111.3 (2C), 124.7, 132.0 (2C), 151.6, 189.7 ppm.

4. Conclusions

Of course, it would be far beyond the scope of this study, and even a chemist's lifespan could be consumed, to supplement this preliminary report by a representative selection of subsequent conversions. Consequently, this communication is focused mainly on crystallography. However, due to the affordability and ease with which these carbon-substituted representatives are accessible, it is also intended to stimulate further exploration of such iminium derivatives.

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