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Magic Acid Free Generation of Antiaromatic Dications at Room Temperature

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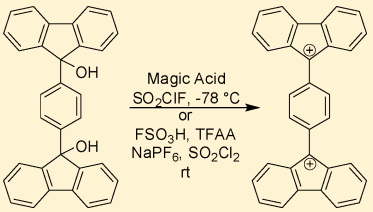
Supporting Information

ABSTRACT: A new method for the generation of dicationic species via ionization of diols is described. The method makes use of milder reagents at room temperatures, an advantage over use of Magic Acid at −78 °C. A series of mono- and dications were synthesized successfully, including previously unattainable species.



Our laboratory has been actively involved in the investigation of antiaromatic dications for some time.[1] Previously, dications have been synthesized by either the oxidation of alkene precursors **1** (Figure 1)[1a,b] or, more

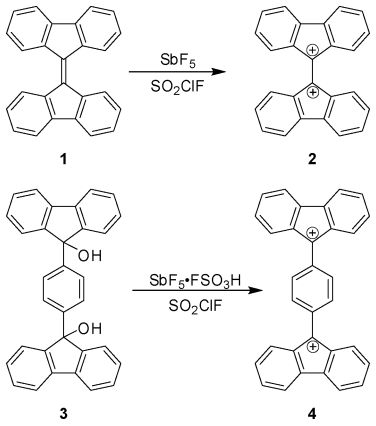


Figure 1. Previously studied bisfluorenyl dications and their generation from neutral species.

recently, the Magic Acid (SbF_5·FSO_3H) promoted ionization of diol precursors **3**.[1c,d] As we continued our investigation into antiaromaticity, in particular the antiaromaticity of indenyl cations, we began to appreciate the need for a new approach to dication synthesis. First, while Magic Acid was effective in the ionization of **3** it was not effective with indenyl diols, presumably due to the oxidation of the indenyl π bond. Second, the synthesis required cold temperatures (−78 to −50 °C) for the synthesis and NMR characterization, respectively, making transfer of viscous reagents at low temperatures more challenging. Lastly, the synthesis required the use of both SbF_5 and SO_2ClF, both of which are dangerously water sensitive, giving off HF upon exposure to trace moisture. Therefore, we set out to determine a way to make antiaromatic dications that can be done at room temperature and which does not require the use of SbF_5. Herein we detail our experimental findings.

In our survey of the literature we noticed that the acid system of choice for the ionization of alcohols to carbocations is almost universally Magic Acid.[2−5] However, Gabbai et al. reported that a mixture of aqueous HBF_4 and trifluoroacetic anhydride (TFAA) could protonate the alcohol groups of a 1,8-disubstituted naphthalenediol to afford a stable dication after loss of water (Figure 2).[6,7] While **6** is presumably more stable

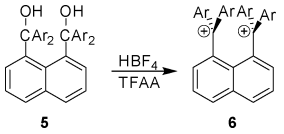


Figure 2. Preparation of dication **6** from diol **5**.[6]

than the dications we are interested in, the synthesis was very intriguing. It made use of safer reagents, could be done at room temperature, and was not water or air sensitive.

Attempting this procedure with **3** yielded **4**; to our knowledge, this is the first antiaromatic dication synthesized at room temperature. Additionally the synthesis was performed open to the air and in the presence of water (although it is believed that the TFAA in essence acts as a drying agent for the HBF_4 and the eliminated water). While we were able to synthesize and characterize the compound by 1D and 2D NMR spectroscopy (Figure 3), we noticed that the deep red solution started to turn darker over a period of ca. 30 min, and black precipitate began to come out of solution. By NMR we noticed that the peaks of **4** slowly disappeared and were replaced by broad indistinguishable peaks (seen in Figure 3). It is worthy of note that the spectra did not match up perfectly with the published spectra of **4**, which is not too surprising given that the dications are prepared in very different solvents (TFAA versus SO_2ClF[1c]) and at different temperatures (24 °C versus −50 °C) and had different counterions (SbF_5·FSO_3^- versus

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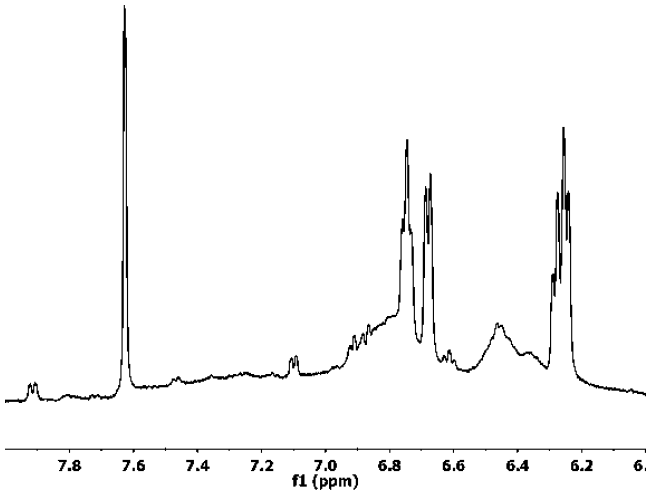


Figure 3. ^{1}H NMR spectra of dication **4** by protonation of **3** with HBF_4 (aq) in TFAA.

BF_4^-). The experimental shifts match up well with the DFT-calculated shifts (see the Supporting Information).

While the initial results were exciting, there were a few shortcomings, primarily that the dications were not particularly stable and showed decomposition in less than 30 min. Believing that the instability was related to the solubility of the dications, we screened a variety of different solvents. We found that diethyl ether accelerated the precipitation of the material (no dications observed by NMR), while chlorinated organic solvents (CH_2Cl_2 and $CHCl_3$) also failed to cleanly provide dication **4**. THF is incompatible with the superacid reaction mixture. The use of SO_2Cl_2 afforded a deep red solution of dications that showed no precipitation.[8]

We found that in the examination of several different superacids (HBF_4, HPF_6, and FSO_3H), addition of TFAA aided in both the stability of the dications and the resolution of the spectra. The aqueous acid/TFAA ratio was kept at 1:10, a ratio that ensured all water would be removed from the aqueous acid solutions. Increasing the amount of TFAA had no further effect. With solutions of FSO_3H, which contained no water, the TFAA to acid ratio was reduced to 1:1. Omitting TFAA from the reaction still led to dication formation but the resultant dications decomposed faster than the dications containing TFAA. We found that FSO_3H proved to be the best acid; it provided **4** cleanly and allowed for the study of counterions such as BF_4^-, PF_6^-, SbF_6^-, and F^- more cleanly than did HBF_4, which would also contain a potentially stabilizing counterion. Through the examination of this series of common counterions, it was discovered that the counterion did not affect the chemical shifts of the dications, but did influence the overall stability. It appears that the size of the counterion is important. With small counterions such as BF_4^- and F^-, dication **4** showed signs of decomposition after 8 h, and was not detectable after 4 days. Larger ions such as SbF_6^- and PF_6^- were able to stabilize the dication, with PF_6^- giving superior stability. Excess counterion provided for the best stabilization of the dication, with equi- and submolar ratios giving rise to dications with shorter lifetimes. This indicates that there is an equilibrium between the counterion salt and the in situ generated counterion FSO_3^- and that greater amounts of salt favor the formation of the more stable complex. Treatment of **3** with FSO_3H, TFAA, and $NaPF_6$ in SO_2Cl_2 at room temperature gave rise to dication **4**, which was much more stable than **4** formed in any other system examined. By NMR, **4** showed no signs of decomposition after 8 h at room temperature and was still the major component after 4 days (Figure 4). To our

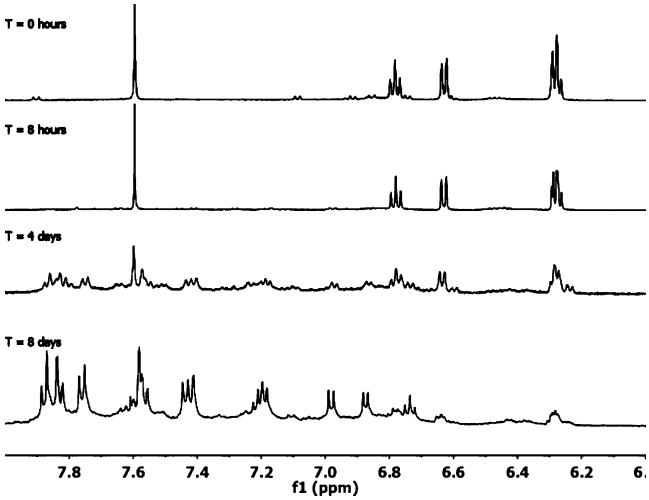


Figure 4. Stacked ^{1}H NMR spectra of dication **4** over time at room temperature.

astonishment, **4** was still detectable, albeit in small amounts, after 8 days at room temperature. To date these are the most stable, longest lasting antiaromatic dications that we or others have made. The primary advantage to this new procedure for making dications is the ease of use of the reagents; there is no need for inert atmosphere techniques and the reactions can be done at room temperature. This allows for much quicker turnover between reactions and rapid monitoring by NMR. Additionally, the conditions do not require the oxidization by SbF_5 and therefore should allow the ionization of diol precursors that are sensitive to oxidation.

To prove the overall utility of our new method and to prove it comparable to Magic Acid, we set out to explore another cationic system which has been studied previously using low temperatures and Magic Acid (Scheme 1). Olah et al. made the

Scheme 1. Synthesis of Monocation 8

7 8

9-phenylfluorenyl cation (**8**) in 1980 by treating alcohol **5** with Magic Acid at −78 °C and characterized the systems using both ^{1}H and ^{13}C NMR spectroscopy.[9,10] Using the aforementioned conditions, **8** was synthesized at room temperature and proved to be stable for an extended period of time, with no decomposition evident after 24 h; see the Supporting Information.

The extended stability and the ambient temperature offer a sizable advantage over previous methods used to study these types of molecules. Previously, our group has been unsuccessful at obtaining ^{13}C NMR data for many dications as the samples would decompose before a suitable carbon spectrum could be obtained. Using this new approach, we were successfully able to

obtain ^{13}C data for both **4** and **8**. Analysis of the two spectra reveled similarities between the two compounds, particularly the carbocation centers that appear at δ 205.2 (**4**) and 204.4 (**8**) ppm. Because of the ambient temperature, ^{13}C data can be safely collected overnight without constantly supplying the spectrometer with liquid nitrogen.

The ultimate goal of this study, however, was to allow access to dications that were incompatible with Magic Acid. In our ongoing study of antiaromaticity, we were interested in the synthesis of indenyl cations as they are, computationally, more antiaromatic than the fluorenyl systems that we have been studying.[9] As mentioned previously, attempts to study indenyl cations such as dication **10** by Magic Acid (1:1 FSO_3H/SBF_5) protonation were unsuccessful (Figure 5a, Scheme 2). The ^1H NMR spectrum exhibits broad, indistinguishable peaks. Attempting the reaction with the newly developed procedure, however, led only to decomposition. While this was very disappointing, we considered that the increased antiaromaticity (and therefore decreased stability) could cause **10** to be unstable at room temperature. Performing the reaction at −78 °C using SO_2ClF as solvent rather than SO_2Cl_2 successfully afforded **10** which could be analyzed by ^1H NMR spectroscopy. Of special interest is the fact that the ^1H spectrum obtained by this method is very clean, with well-resolved peaks and a clean baseline, another advantage over Magic Acid. This is the first example of an indenyl cation prepared by ionization of an alcohol precursor.

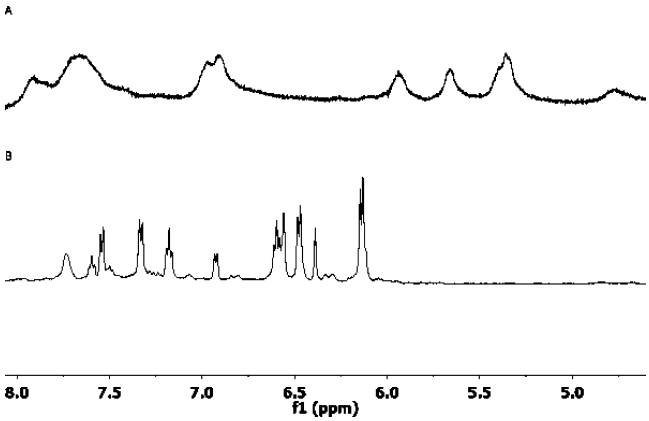
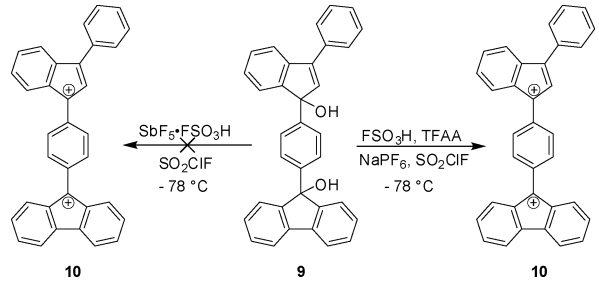


Figure 5. ^1H NMR spectra of dication **10** taken at −50 °C: (A) reaction performed using Magic Acid; (B) reaction performed using $FSO_3H/TFAA/NaPF_6/SO_2ClF$ at −78 °C.

Scheme 2. Synthesis of Indenyl−Fluorenyl Dication 10



In summary, we have developed a Magic Acid free method for synthesizing antiaromatic dications at room temperature. The milder reaction conditions will allow us to study more sensitive systems, which we are currently pursuing. We have shown that this method can be extended to other cationic systems and allows for the study of systems under more desirable conditions. Using these procedures has allowed for the synthesis of indenyl cations which are not compatible with Magic Acid.

EXPERIMENTAL SECTION

General Procedure A for the Formation of Dications. In an NMR tube, 10 mg of diol was added along with $NaPF_6$ (30 mg) and a sealed capillary containing acetone-d_6. In a separate centrifuge tube SO_2Cl_2 (0.5 mL), TFAA (0.25 mL), and FSO_3H (0.25 mL) were combined open to the air and mixed via vortex. Approximately 0.7 mL of the acid solution was transferred to the NMR tube. The NMR tube was capped and the sample was analyzed by NMR spectroscopy (500 MHz spectrometer) at 24 °C.

Bisfluorenyl Dication 4. Diol **3** was reacted according to general procedure A: ^1H NMR (acetone-d_6) δ 7.60 (s, 4H), 6.78 (t, J = 7.5 Hz, 4H), 6.63 (d, J = 7.6 Hz, 4H), 6.28 (m, 8H); ^{13}C NMR (acetone-d_6) δ 205.2, 152.5, 152.0, 144.5, 142.8, 138.3, 134.4, 133.3, 128.0.

9-Phenylflorenyl Cation 8. Alcohol **7** was reacted according to general procedure A: ^1H NMR (acetone-d_6) δ 7.61 (t, J = 7.5 Hz, 1H), 7.43 (d, J = 7.4 Hz, 2H), 7.28 (t, J = 7.9 Hz, 2H), 6.82 (t, J = 7.5 Hz, 2H), 6.78 (d, J = 7.6 Hz, 2H), 6.42 (m, 4H); ^{13}C NMR (acetone-d_6) δ 204.4, 149.6, 146.9, 142.8, 141.4, 139.8, 134.1, 131.9, 131.8, 130.4, 124.9.

3-Phenylindenyl−Fluorenyl Dication 10. Diol **9**[10] was reacted according to general procedure A using SO_2ClF as a solvent. The reaction was carried out at −78 °C, and the reaction was monitored by ^1H NMR at −50 °C: ^1H NMR (acetone-d_6) δ 7.73 (br s, 2H), 7.59 (t, J = 6.9 Hz, 1H), 7.54 (d, J = 7.9 Hz, 2H), 7.33 (d, J = 7.5 Hz, 2H), 7.18 (t, J = 6.9 Hz, 2H), 6.92 (d, J = 7.0 Hz, 1H), 6.59 (m, 5H), 6.48 (d, J = 7.6 Hz, 2H), 6.39 (s, 1H), 6.14 (m, 4H).

Synthesis of 9-(4-(1-Hydroxy-3-phenyl-1*H*-inden-1-yl)-phenyl)-9*H*-fluoren-9-ol (9). See the Supporting Information for the synthetic scheme and NMR spectra. In a dry 100 mL round-bottom flask was dissolved 1,4-dibromobenzene (1.9 g, 8.3 mmol) in dry THF (41 mL) and the solution cooled to −78 °C under Ar. *n*-Butyllithium (3.2 mL, 2.5 M in hexanes) was added dropwise, and the solution was stirred for 1 h after complete addition. In a separate 250 mL round-bottom flask, 3-phenyl-1-indanone (1.3 g, 6.3 mmol) was dissolved in dry THF (31 mL) and cooled to −78 °C under Ar. After the monolithiated dibromobenzene stirred for 1 h at −78 °C, the lithiate was transferred by cannula to the solution of 3-phenyl-1-indanone, which was allowed to warm to rt overnight. H_2SO_4 (30 mL, 5 M) was then added to the reaction and allowed to stir for 20 min. The reaction was then extracted 3× with diethyl ether and washed with aq $NaHCO_3$ (1×) and brine (2×). The organic layer was dried over $MgSO_4$ and filtered through a plug of silica. Column chromatography of the crude material eluting with hexanes afforded 1-(4-bromophenyl)-3-phenyl-1-indene (1.65 g, 76%) as a yellow solid.

1-(4-Bromophenyl)-3-phenyl-1-indene (1.65 g, 4.75 mmol) and $NaHCO_3$ (2.0 g, 23.75 mmol) were dissolved in H_2O (50 mL) and EtOAc (50 mL), and the mixture was stirred vigorously with a magnetic stirrer. Acetone (3.5 mL, 47.5 mmol) was added, and the biphasic solution was allowed to stir for 10 min. A solution of Oxone (2.92 g, 4.75 mmol) in H_2O (50 mL) was then added by addition funnel over 1 h. The reaction was monitored by TLC and then extracted with EtOAc (2×), washed with H_2O and brine, and then dried over $MgSO_4$. The solvent was removed in vacuo. The crude oil was then dissolved in dry THF (100 mL) and cooled to −78 °C under Ar. Freshly prepared LDA (2 equiv) was transferred by cannula to the epoxide, and the reaction was allowed to stir for 3 h as it warmed to rt. The reaction was quenched with 10% HCl and extracted with diethyl ether (3×). The crude alcohol was purified by column chromatography (10% EtOAc in hexanes) to give 1-(4-bromophenyl)-3-phenyl-1*H*-inden-1-ol (0.92 g, 54%) as an orange oil.

1-(4-Bromophenyl)-3-phenyl-1*H*-inden-1-ol (0.92 g, 2.5 mmol) was dissolved in dry THF (40 mL) and cooled to −78 °C under Ar. *n*-Butyllithium (2.1 mL, 2.5 M in hexanes) was added dropwise and then

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allowed to stir for 1 h. In a separate flask, fluorenone (0.52 g, 2.9 mmol) was dissolved in dry THF (20 mL), cooled to −78 °C under Ar, and then transferred by cannula to the lithiate. The reaction was allowed to warm to rt overnight, quenched with aq NH_4Cl, extracted with diethyl ether (3×), washed with H_2O (1×) and brine (1×), and dried over Na_2SO_4. The crude alcohol was purified by column chromatography (20% DCM in hexanes), followed by recrystallization with toluene/hexanes and preparative TLC on silica with 2:1 hexanes/toluene, to give **9** (0.53 g, 46%) as a tan solid: ^{13}C NMR (126 MHz, $CDCl_3$) δ 83.52, 84.47, 120.05, 121.17, 123.71, 124.80, 125.24, 125.48, 126.96, 127.50, 128.36, 128.63, 129.07, 134.49, 138.91, 138.98, 139.50, 140.04, 141.46, 142.40, 143.97, 150.22, 150.24, 150.67; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 7.5 Hz, 2H), 7.58 (d, J = 8.3 Hz, 2H), 7.49−7.18 (m, 17H), 6.40 (s, 1H). Anal. Calcd for $C_{34}H_{22}O_2$: C, 87.90; H, 5.21; O, 6.89. Found: C, 85.12; H, 5.82. Note: after three successive methods of purification, we were unable to obtain analytically pure material. See the Supporting Information for ^1H and ^{13}C NMR spectra that show traces of an impurity.

■ ASSOCIATED CONTENT

Supporting Information

Comparison of computational versus experimental ^1H chemical shifts for **4** and **10**; spectroscopic data for **4**, **8**, and **10**; synthetic scheme and spectral information for **9**; Cartesian coordinates and total energy for **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) Solvents SO_2 and SO_2ClF have been used in the formation of carbocations since the first use of superacid systems, presumably because the carbocations were anticipated to be sufficiently unstable that characterization would require low temperatures, and solvents which were not viscous at those temperatures. SO_2Cl_2 seemed to be a reasonable extension from SO_2ClF when we were looking for a solvent that was more tractable at room temperature. We have seen no evidence of chlorination with SO_2Cl_2 under these superacid conditions.

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