ACRIDINE FORMATION BY THE REACTION OF 2-NONAFLUOROBUTYLANILINE WITH 2-MESITYLMAGNESIUM BROMIDE

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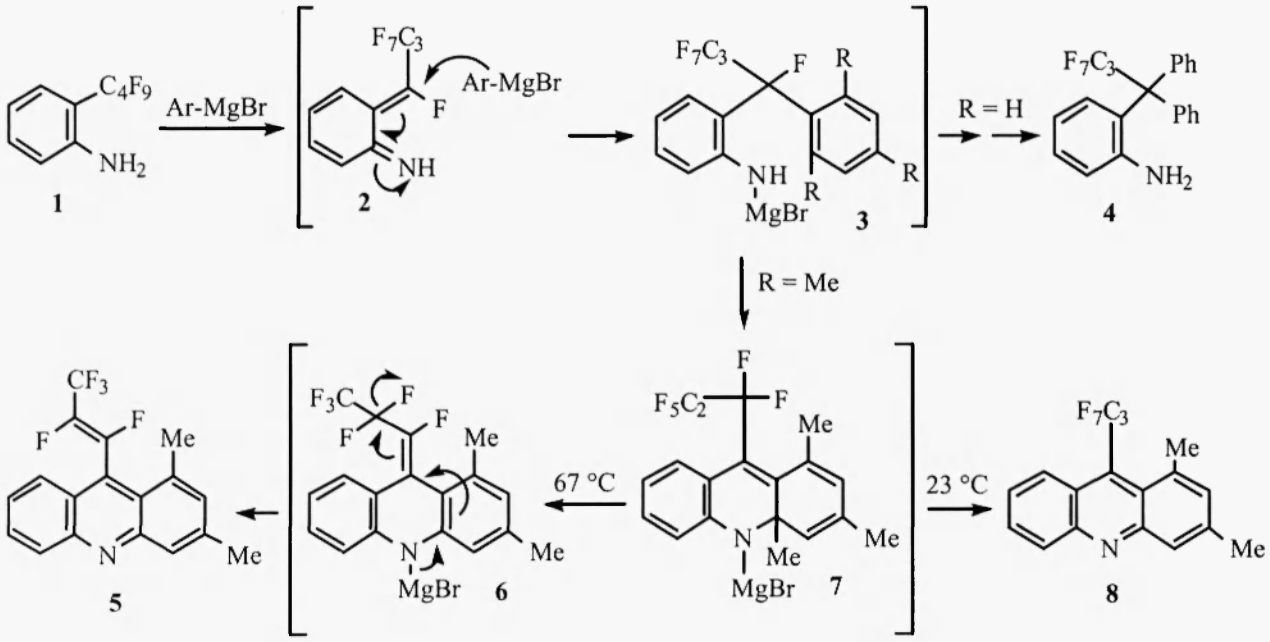
Abstract: The title reaction conducted in THF at 23 °C and under reflux furnishes 1,3-dimethyl-9-perfluoropropylacridine (**8**) and 1,3-dimethyl-9-[(*E*)-1-perfluoropropenyl]acridine (**5**), respectively.

Recently, we have reported synthesis of perfluoroalkyltriarylmethanes (molecular propellers) such as **4** by the reaction of 2-perfluoroalkylanilines with phenylmagnesium bromide.[1] The mechanistic pathway, shown for **4**, involves elimination of fluoride from anion derived from **1** followed by addition of PhMgBr to the resultant intermediate product **2** to generate an adduct **3**. Compound **4** is produced in a similar elimination-addition reaction with **3**.

In an attempt to synthesize a triarylmethane that would be more sterically congested than **4**, the substrate **1** (3 mmol) was allowed to react with 2-mesitylmagnesium bromide (10 mmol) in anhydrous THF (50 mL). The reactions were conducted at 23 °C and under reflux conditions. For the 23 °C reaction the GC-MS analysis showed the absence of **1** after 24 h, and under the reflux conditions the reaction was completed after 6 h. A single, albeit different, major product was observed in each case. To our surprise, however, none of the mass spectra, including those for a number of minor products, could be correlated with the expected analog of **4**.



Following standard workup[1] and chromatography on silica gel (hexanes/ether, 4:1) the product of the reaction at 23 °C was identified as 1,3-dimethyl-9-perfluoropropylacridine [**8**, yield 30%, mp 90-93 °C (from hexanes)]. A similar chromatographic separation of the mixture obtained under reflux conditions gave 1,3-dimethyl-9[(*E*)-1-perfluoropropenyl]acridine [**5**, yield 65%, mp 85-87 °C]. Compounds **5** and **8** gave satisfactory results of elemental analysis and were characterized[2] by MS, ^{1}H NMR and ^{19}F NMR. In particular, their ^{1}H NMR spectra are similar as expected for a similarly substituted acridine system. In the ^{19}F NMR spectrum of **5** the large coupling constant of 140 Hz between fluorine atoms F1 and F2 of the perfluoropropenyl substituent is indicative of *E*-stereochemistry.[3]

It is suggested that the formation of either acridine **5** or **8** involves the intermediary of the same dihydroacridine derivative **7** that is generated by intramolecular S_N2' cyclization of **3** (R = Me) or electrocyclization of a mesityl-substituted analog of **2** (not shown) derived from **3**. This unusual intramolecular reaction can be explained in terms of greatly increased steric congestion in **3** (R = Me) in comparison to that of **3** (R = H). Aromatization of **7** to give **8** requires a formal elimination of MeMgBr. This process may take place within aggregated higher-order structures of **7** that are expected to be present at low temperatures. On the other hand, an increase in temperature causes a decrease in aggregation of organometallic compounds. This phenomenon may be responsible for the elimination of fluoride ion and a C4a-methyl group from **7** by a nucleophilic attack of an external nucleophile at the C4a-methyl group to generate **6**. The intermediate product **6** is the suggested direct precursor to **5**. Additional studies of these novel transformations by using a variety of aryl Grignard reagents are in progress.

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References and Notes

1. L. Strekowski, H. Lee, S.-Y. Lin, A. Czarny and D. Van Derveer, J. Org. Chem. **65**, 7703 (2000)

2. **5**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.57 (s, 3-Me), 2.85 (s, 1-Me), 7.33 (s, 2-H), 7.65 (t, J=8 Hz, 6-H or 7-H), 7.82 (t, J=8 Hz, 6-H or 7-H), 7.96 (s, 4-H), 8.03 (d, J=8 Hz, 8-H), 8.26 (d, J=8 Hz, 5-H); MS m/z 253 (40, M^+-CF_3-Me), 268 (80, M^+ -CF_3), 322 (35, M^+ -Me), 337 (100, M^+). **8**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (s, 3-Me), 2.71 (narrow m, due to H-F couplings, 1-Me), 7.35 (s, 2-H), 7.57 (t, J=8 Hz, 6-H or 7-H), 7.75 (t, J=8 Hz, 6-H or 7-H), 7.85 (s, 4-H), 8.21 (d, J=8 Hz, 8-H), 8.34 (d, J=8 Hz, 5-H); MS m/z 256 (100, M^+-C_2F_5), 356 (10, M^+-F), 375 (75, M^+)

3. R.S. Macomber, A Complete Introduction to Modern NMR, Wiley-Interscience, New York, 1998, p 141

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