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Synthesis of 1,2,3,4-Tetramethyl- and 1,2,3,4-Tetraethylfluorene through a Dewar Benzene Pathway

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A simple and selective synthesis of 1,2,3,4-tetra(m)ethylfluorenones and -fluorenes was achieved by using Dewar benzenes as important intermediates. The corresponding Dewar benzenes were prepared by reactions of tetraalkylcyclobutadiene–$AlCl_3$ complexes with methyl phenylpropynoate. Their subsequent hydrolysis followed by photochemical rearrangement provided substituted biphenylcarboxylic acids. Treatment of the prepared acids with thionyl chloride gave rise to the fluorenones, which were reduced to the respective fluorenes. A Ru complex with 1,2,3,4-tetraethylfluorenone was prepared.

Introduction

Fluorenes have been shown to coordinate to various transition metal fragments to form either η^5-cyclopentadienyl or η^6-arene complexes. In this respect, the synthesis of such compounds bearing an unsymmetrically substituted fluorene scaffold is of general interest, as it may allow electronic effects in transition-metal complexes and coordination preferences of various metal fragments to be studied. Although several complexes with octamethyl- and nonamethylfluorene ligands have been described,[1,2] to the best of our knowledge, reports concerning the complexation of 1,2,3,4-tetraalkylfluorenes are not available in the literature. Moreover, so far only a handful of methods have been reported for the preparation of such ligands. For instance, two methods for the synthesis of 1,2,3,4-tetramethylfluorene (**1a**) have been described: one is based on the Lewis acid catalyzed alkylation of pristine fluorene, but this reaction is unselective and gives rise to numerous regioisomers (the highest yield of **1a** was 21 %),[3] whereas the other method makes use of a palladium-catalyzed cross-coupling/C–H activation processes (93 % yield of the isolated product from the reaction of pentamethylphenylmagnesium chloride with 1,2-dibromobenzene).[4] In the case of tetraethylfluorene and other alkylated derivatives, only a procedure based on the rearrangement of bis(indenyl)zirconacyclopentadienes has been devised.[5] Interestingly, but perhaps not surprisingly, the presence of 1,2,3,4-tetraalkylated fluorenes has been confirmed in Nature−they were detected in aromatic fractions of Athabasca oil sand bitumens.[6]

Recently, it was shown that highly substituted Dewar benzenes could be used as convenient synthetic intermediates for the preparation of selectively substituted benzenes[7–9] and ter- and quaterphenyls alkylated at the terminal benzene rings.[10] Given that one of the pathways for their preparation utilizes the reaction of a tetralkylcyclobutadiene–aluminum chloride complex with activated alkynes bearing at least one ester group, we envisioned that 1,2,3,4-tetraalkylated fluorenes could be also prepared by a Dewar benzene pathway by taking advantage of the ester functionality present in the molecule. Herein, we would like to report a general and selective synthetic approach toward 1,2,3,4-tetramethyl- and 1,2,3,4-tetraethylfluorenones and the corresponding fluorenes by this strategy.

Results and Discussion

At the outset, the starting Dewar benzenes were synthesized according to a previously reported procedure (Scheme 1).[11] Tetramethylcyclobutadiene- and tetraethylcyclobutadiene–aluminum chloride adducts **2a** and **2b**,[12] respectively, generated in situ from the respective internal alkyne and anhydrous $AlCl_3$, were treated with methyl phenylpropynoate (**3**) in dichloromethane at –15 °C to give corresponding products **4a** and **4b** in 54 and 38 % isolated yield, respectively.

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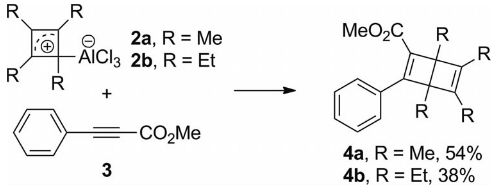
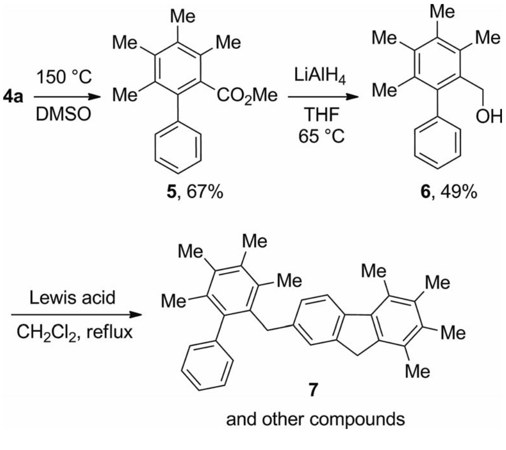


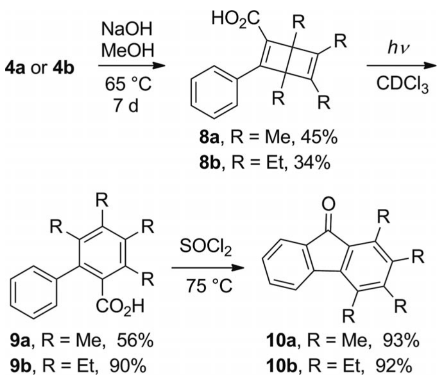
Scheme 1. Preparation of Dewar benzenes **4**.

Compound **4a** was expected to be converted into 1,2,3,4-tetramethylfluorene (**1a**) in a straightforward manner (Scheme 2). The prepared Dewar benzene was quantitatively thermally rearranged in DMSO (150 °C, 20 h) to biphenyl **5**, which was isolated in 67% yield. Subsequent reduction with $LiAlH_4$ provided alcohol **6** in 49% isolated yield. We assumed that alcohol **6** could be converted into expected fluorene **1** upon intramolecular alkylation induced by a Lewis acid. We tried to bring about the intramolecular cyclization by addition of several Lewis acids, including $AlCl_3$, $Bi(OTf)_3$, and $BF_3{\cdot}OEt_2$. However, no reaction took place in the presence of $AlCl_3$ (c = 0.04 mmol L^{-1}) and the starting material was recovered unchanged. The use $Bi(OTf)_3$ (c = 0.04 mmol L^{-1}) resulted in the formation of an inseparable mixture of products. Carrying out the reaction under dilute conditions [c(**6**) = 0.004 mol L^{-1}] did not have any positive effect on the course of the reaction. Finally, the reaction of **6** with $BF_3{\cdot}OEt_2$ also provided an inseparable mixture of various products. In neither case was the presence of desired fluorene **1a** detected in the crude mixture. Instead, compound **7** was isolated, and its structure was tentatively assigned on the basis of ^{1}H NMR and ^{13}C NMR spectroscopy. It is the product of sequential intra- and intermolecular alkylations, and it was present in various amounts along with higher alkylated products.



Scheme 2. Lewis acid mediated reaction of **6**.

An attempt to synthesize tetramethylfluorene by using the previously reported procedure based on the rearrangement of bis(indenyl)tetramethylzirconacyclopentadiene in the presence of $TiCl_4$[5] was also unsuccessful; and this reaction led to a complex mixture in which 1,2,3,4-tetramethylfluorene (**1a**) was not detected. Because the approach outlined above failed to provide the desired products, a different strategy was applied. Dewar benzenes **4a** and **4b** were used again as the starting materials, but they were first hydrolyzed to Dewar benzene carboxylic acids **8a** and **8b** by using NaOH in methanol (65 °C, 1 week). The long reaction times that were typically required[13] probably reflect the steric hindrance of the ester substrates; the use of higher reaction temperatures to increase the reaction rate may lead to undesirable rearrangement of the Dewar benzene scaffold to the benzene one. Acids **8a** and **8b** were isolated in 45 and 34% yield, respectively. Given that conventional thermal rearrangement of carboxylic acid **8a** in DMSO at 120 °C[14] took 1 week to reach full conversion and given that the corresponding benzoic acid was isolated in only 27% yield, the photochemical rearrangement of both acids was attempted next (254 nm, in $CDCl_3$).[15] Gratifyingly, the photochemical conversion of acids **8** into **9** proceeded quantitatively at 20 °C within 24 h. Simple evaporation of the solvent followed by column chromatography on silica gel yielded **9a** and **9b** in 56 and 90% yield, respectively (in the case of the rearrangement of **8a**, the unreacted starting material was recovered). Although it was initially envisioned that these benzoic acids would be converted stepwise into the corresponding acid chlorides and then treated with a Lewis acid to bring about intramolecular acylation, our early experiments showed that the cyclization could be done in one step. Eventually, after trying several reaction conditions, it was found that heating benzoic acids **9a** and **9b** in pure thionyl chloride at 75 °C resulted in smooth, spontaneous intramolecular acylation to give 1,2,3,4-tetralkylfluorenones **10a** and **10b** in high isolated yields (Scheme 3). Thus, 1,2,3,4-tetramethyl-9*H*-fluoren-9-one (**10a**) was obtained in 93% yield, whereas 1,2,3,4-tetraethyl-9*H*-fluoren-9-one (**10b**) was obtained in 92% yield. Recrystallization of the latter compound from hexane furnished crystals suitable for X-ray analysis, which unequivocally corroborated its structure (Figure 1). It showed alternating up–down ethyl groups analogically to hexaethylbenzene.[16]



Scheme 3. Synthesis of fluorenones **10a** and **10b**.

In the last step, the carbonyl moiety in fluorenones **10a** and **10b** was reduced to a methylene group to give 1,2,3,4-tetramethylfluorene (**1a**) and 1,2,3,4-tetraethylfluorene (**1b**; Scheme 4). Attempts to use the classical Wolff–Kishner reduction or its later modification[18] for the reduction of **10a** were unsuccessful. The reaction did not take place and the

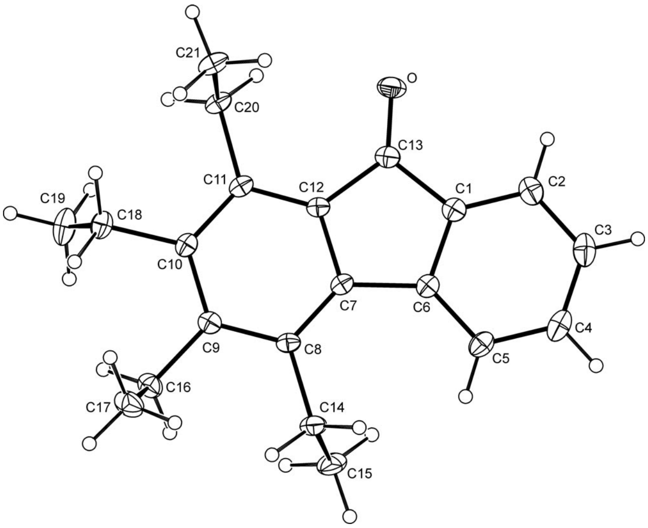
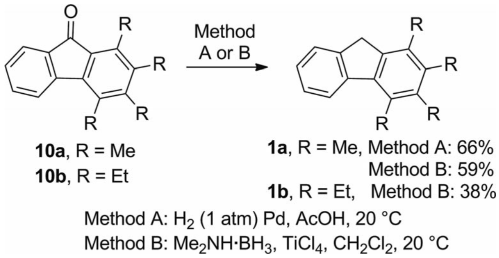


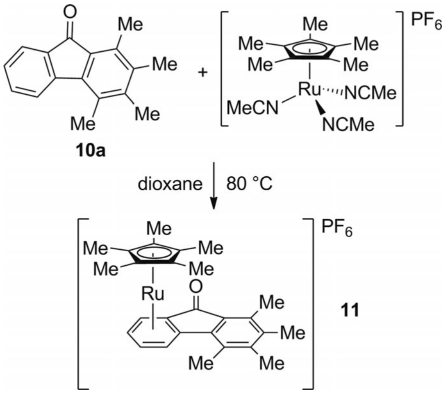
Figure 1. PLATON[17] drawing of 1,2,3,4-tetraethylfluorenone (**10b**) showing atom labeling and displacement ellipsoids at the 30% probability level. Note the alternating up–down arrangement of the ethyl substituents.

starting material was recovered. In contrast, catalytic hydrogenation with Pd/C in acetic acid[19] proved to be the method of choice for this transformation, as it provided desired fluorene **1a** in 66% isolated yield. Interestingly, this methodology was not successful for the reduction of **10b**. In this instance, reduction of the carbonyl group was achieved by using the $Me_2NH\cdot BH_3$ complex in the presence of titanium(IV) chloride,[20] and after workup, **1b** was isolated in 38% yield. The same reaction conditions were also used for the reduction of **10a** to afford fluorene **1a** in 59% yield.



Scheme 4. Reduction of fluorenones **10** to fluorenes **1**.

Finally, complexation of fluorenone **10a** with $[Ru(\eta^5\text{-}C_5Me_5)(MeCN)_3][PF_6]$ was attempted. Heating a mixture of these two compounds in warm dioxane resulted in the formation of η^6-fluorenone complex **11** in 25% isolated yield (Scheme 5). Its structure was unequivocally confirmed by single-crystal X-ray analysis for the solvate **11**·MeCN (Figure 2). Analysis of the crude reaction mixture (after evaporation) by NMR spectroscopy revealed only the presence of complex **11** and unreacted **10a**. Other products (including possible isomers of **11**) were not detected. The preferential coordination of the bulky (η^5-pentamethylcyclopentadienyl)ruthenium cation to the unsubstituted benzene ring of the fluorenone moiety could be attributed to the lower steric hindrance of the π ligands surrounding the Ru^{II} ion, which may outweigh the anticipated preference for the coordination to the more electron-rich alkylated benzene ring.



Scheme 5. Synthesis of Cp*Ru–fluorenone complex **11**.

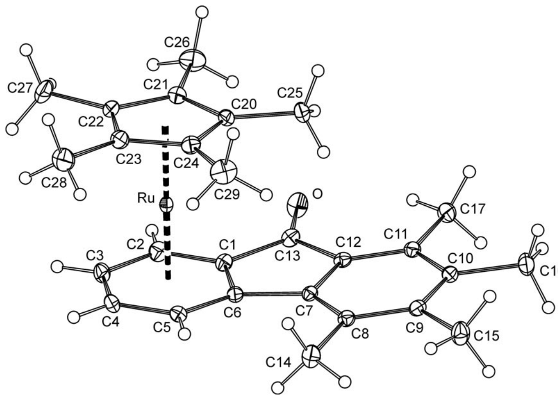


Figure 2. PLATON plot of the cation in the structure of **11**·MeCN. Displacement ellipsoids are scaled to the 30% probability level.

According to a search in the Cambridge Structural Database,[21] structurally characterized transition-metal complexes with π-coordinated fluorenone are restricted to only several representatives, namely, to two cobalt complexes in which unsubstituted fluorenone forms a η^5:η^6-bridge between two $(\eta^5\text{-}C_5R_5)Co^I$ fragments[22] and the CpRu complex $[Ru(\eta^5\text{-}C_5H_5)(\eta^6\text{-fluorenone})][PF_6]$.[23] The π-coordinated aromatic rings in **11** are practically parallel [dihedral angle 1.2(1)°], which in turn corresponds to marginal variation in the individual Ru–C distances [2.190(2)–2.233(2) and 2.177(2)–2.192(2) Å for the coordinated cyclopentadienyl and benzene ring, respectively]. The 14 atoms constituting the fluorenone skeleton [i.e., C(1–13) and O] are coplanar within ca. 0.09 Å, and the C–C distances within the coordinated benzene ring [1.411(3)–1.423(3) Å] are slightly longer than those found in the uncoordinated benzene ring in **11** [1.388(3)–1.415(3) Å] and even for the unsubstituted ring in the molecule of **1b** [1.382(2)–1.405(2) Å]. The C=O bond remains unaffected by coordination [cf., C=O 1.218(2) Å for **1b** and 1.215(3) Å for **11**].

Conclusions

In conclusion, we have presented a new and concise method for the synthesis of 1,2,3,4-tetra(m)ethylfluorenones and -fluorenes by making use of Dewar benzenes as the key synthetic intermediates. Moreover, we demonstrated that borane-based reductants are suitable for the reduction of fluorenones to fluorenes. Last, but not least, the preferential coordination of the ruthenium atom in complex **11** to the less sterically hindered and the less electron-rich benzene ring suggests that the unsymmetrically substituted fluorenones and fluorenes accessible by this newly discovered route might exert interesting coordination chemistry with transition metals.

CCDC-873451 (for **10b**) and -873452 (for **11**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Experimental procedures, copies of the ^{1}H NMR and ^{13}C NMR spectra for all new compounds, and crystallographic data for **10b** and **11**.

Acknowledgments

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