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A Novel and Practical Synthesis of Polycyclic Fluoranthenes

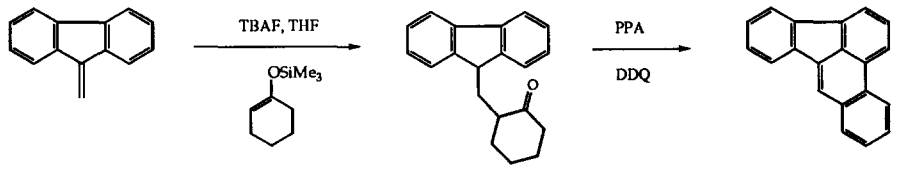
Bongsup P. Cho

Department of Medicinal Chemistry, University of Rhode Island, Kingston, RI 02881

Abstract: *A novel and general preparation of polycyclic fluoranthenes is described. The synthesis involves a Michael addition of silyl enol ethers to dibenzofulvene followed by cyclization and aromatization.*

Polycyclic fluoranthenes are an important class of non-alternant polyarenes containing an indeno ring moiety. Many of these hydrocarbons have been shown to be environmental pollutants and animal carcinogens posing a serious human health risk.[1,2] The availability these compounds and their oxidized metabolites is crucial for their detection in the environment and the determination of their biochemical fate *in vitro* and *in vivo*.[1,3,4] Literature reports for their preparation suffer from a number of drawbacks necessitating the search for better methods for their synthesis. This letter describes an efficient and versatile synthesis of the title compounds.

Retrosynthetic analysis led us to dibenzofulvene (**1**),[5] which is a by-product of fluorenylmethoxycarbonyl (FMOC) deprotection in peptide synthesis. Earlier work by Carpino *et al* demonstrated the ability of **1** to undergo Michael addition with amines.[6,7] Consequently, it was rationalized that an analogous addition by a carbon nucleophile to **1** would give intermediates that can lead to polycyclic fluoranthenes.

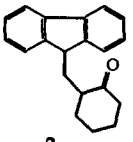
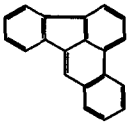
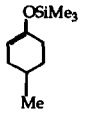
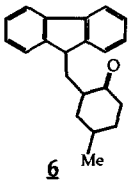
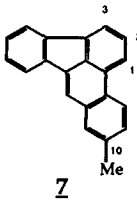
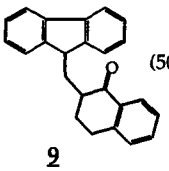
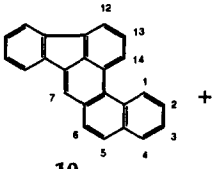
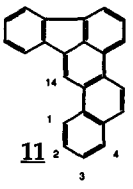
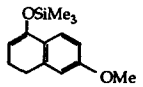
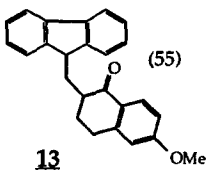
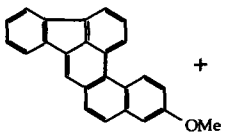
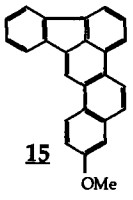


1 **2** **3** **4**

Scheme 1

An illustration of this strategy for the synthesis of benz[e]acepheanthrylene (**4**) is depicted in **Scheme 1**. Tetrabutylammonium fluoride (TBAF)-catalyzed decomposition of the silyl enol ether of cyclohexanone (**2**), followed by Michael addition of the resultant carbanion to **1** furnished the keto adduct **3**. Acid-mediated cyclization of **3** and subsequent aromatization afforded the target hydrocarbon **4** in good overall yield (54% from **1**).

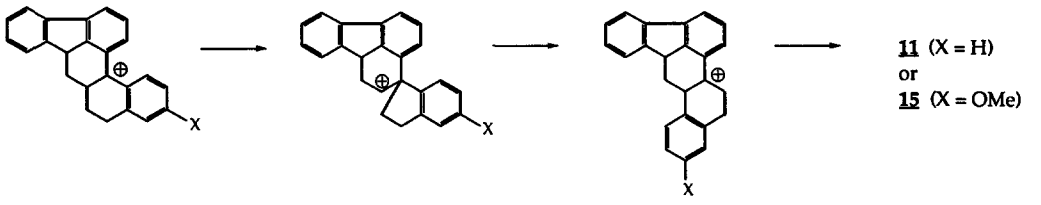
Table 1. Polycyclic Fluoranthenes Synthesized via a Fluoride-catalyzed Addition of Silyl Enol Ethers to Dibenzofulvene (**1**).

Silyl enol ether	Adduct (% yield)[a]	Fluoranthene (% yield)[a]
 **2**	 (68) **3**	 (79) **4**
 **5**	 (42) **6**	 (80) **7**
 **8**	 (50) **9**	 +  (80)[b] **10** **11**
 **12**	 (55) **13**	 +  (84)[b] **14** **15**

[a]Isolated yields [b]Approximately 1:1 ratio.

This methodology has been readily extended to the preparation of other substituted fluoranthenes. As shown in **Table 1**, 10-methylbenz[e]acephenanthrylene (**7**) was obtained in 34% overall yield *via* an analogous sequence using **5** as a Michael donor. The cyclization of **9**, which was obtained in a similar manner from the silyl enol ether of a-tetralone (**8**), afforded the desired compound **10** and the rearranged isomeric product **11** in equal amounts. The pure isomers were obtained by silica gel column chromatography followed by recrystallization. The ^{1}H NMR spectrum of **10** showed two doublets for highly deshielded protons at 9.26 and 9.05 ppm.[8] These were respectively assigned to H1 and H14 in the sterically compressed fjord-region. Structural assignment of the rearranged product **11** was based upon comparison of its spectroscopic data (UV, ^{1}H and ^{13}C NMR) and chromatographic behavior (TLC and

HPLC) with those of an authentic sample.[9,10] It should be pointed out that recent syntheses of **7**[11] and **10**[12] were achieved by a less convenient high-temperature vacuum pyrolysis in poor overall yields. The methoxy substituted keto-adduct **13**, obtained analogously from **12**, underwent a similar cyclization/aromatization sequence to furnish a 1:1 mixture of **14** and **15**. These hitherto unknown compounds are not readily accessible by other methods and could be used as precursors for the synthesis of their diol epoxide metabolites.[1]



Scheme 2

The formation of **11** and **15** may take place by a double Wagner-Meerwein rearrangement (**Scheme 2**), a mechanism similar to that proposed for the acid-catalyzed conversion of benzo[c]phenanthrene to chrysene.[13] The high steric crowding in the fjord-region appears to be the driving force for their formation, since such transformation was not observed in the less hindered bay-region compounds **4** and **7**. Efforts are currently directed at preparing derivatives with substituents that could help us better understand the mechanism of the rearrangement.

In a typical experiment, a 5-mL THF solution containing a mixture of dibenzofulvene (**1**, 303 mg, 1.7 mmole)[5] and 1-cyclohexenyltrimethylsilane (**2**, 341 mg, 2.0 mmole, Aldrich) was added rapidly to TBAF (523 mg, 2.0 mmole) in THF at 5°C. After stirring for 2 hr at room temperature, the reaction was quenched with water and extracted with ether and the residue was chromatographed on silica gel (ethyl acetate:hexanes) to yield **3** (68%); m.p. 76-77°C (ethanol). The keto adduct **3** (276 mg, 1 mmole) was reacted with polyphosphoric acid (PPA) for 2 hr at 120°C. The resulting hot orange syrup was poured into ice-water, allowed to stand for 1 hr, and extracted with ether. The crude product was treated with DDQ (1.14 g, 5 mmole) in refluxing benzene for 1.5 hr and poured onto a short neutral alumina column. The solid which eluted with benzene was crystallized from ethanol to give **4** (199 mg, 79%), which exhibited spectroscopic characteristics identical to those of an authentic sample.[9,10]

In summary, a novel and general synthesis of polycyclic fluoranthenes was described. It is applicable for the preparation of substituted derivatives that are otherwise difficult to obtain by classical methods. Extension of this chemistry to prepare compounds as precursors to oxidized metabolites and as standards for environmental pollutants is now in progress.

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8. All new compounds in **Table 1** gave satisfactory ^{1}H NMR ($CDCl_3$)and C,H-elemental analyses within ± 0.3% (**3**, **9**, **10**, **13**, **14**). Compounds **10**, **14**, **15** have the following physical and spectroscopic characteristics. The ^{1}H NMR resonance assignments were aided by COSY and long-range COSY experiments.

   Dibenz[e,l]acephenanthrylene (**10**): m.p. 131-134°C (CH_2Cl_2:hexanes); ^{1}H NMR, δ 9.26 (H1, d, $J_{1,2}$=8.5 Hz), 9.05 (H14, d, $J_{13,14}$=8.5Hz), 8.35 (H7, s), 8.10-7.80 (H12,4,6,11, 5,8, m), 7.85 (H13, dd, $J_{13,14}$=8.5 Hz, $J_{12,13}$=7.7 Hz), 7.76 (H2, dd), 7.66 (H3, dd), 7.44 (H9,10, m).

   3-Methoxydibenz[e,l]acephenanthrylene (**14**): m.p. 206-208°C (CH_2Cl_2:hexanes); ^{1}H NMR, δ 9.16 (H1, d, $J_{1,2}$=9.2 Hz), 8.98 (H14, d, $J_{13,14}$=8.5 Hz), 8.32 (H7, s), 8.05 (H12, d, $J_{12,13}$=7.4 Hz), 8.03-7.95 (H8,6,11, m), 7.87 (H5, d, $J_{5,6}$=7.7 Hz), 7.84 (H13, dd), 7.45-7.42 (H9,10, m), 7.42 (H2), 7.39 (H4, bs).

   3-Methoxyindeno[1,2,3-hi]chrysene (**15**): m.p. 180-182°C (CH_2Cl_2:hexanes); ^{1}H NMR δ 9.16 (H14, s), 8.85 (H1, d, $J_{1,2}$=9.2 Hz), 8.69 (H6, d, $J_{5,6}$=8.8 Hz), 8.54 (H7, d, $J_{7,8}$=8.5 Hz), 8.12 (H13, m), 8.02 (H9, d, $J_{8,9}$=7.0 Hz), 7.96 (H5, d, $J_{5,6}$=8.8 Hz), 7.96 (H10, m), 7.81 (H8, dd, $J_{7,8}$=8.5 Hz, $J_{8,9}$=7.0 Hz), 7.45 (H11, m), 7.44 (H12, m), 7.39 (H2, dd, $J_{1,2}$=9.2 Hz, $J_{2,4}$=2.9 Hz).
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