Pergamon

Tetrahedron Letters, Vol. 37, No. 10, pp. 1535-1538, 1996

0040-4039/96 $15.00 + 0.00

S0040-4039(96)00065-2

Attempted Synthesis of *Fjord*-region Containing Polycyclic Fluoranthenes Reveals A Steric-Driven Double Wagner-Meerwein Rearrangement

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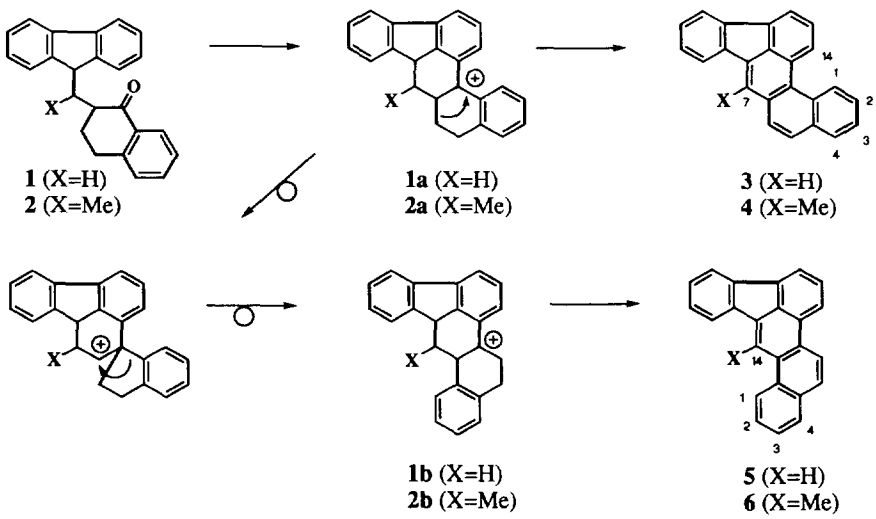
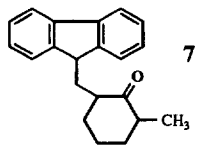
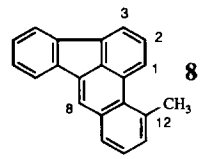
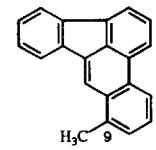
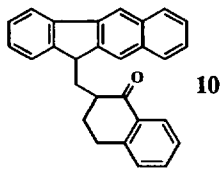
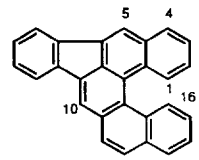
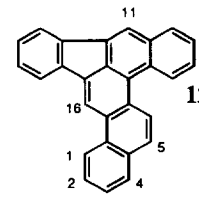
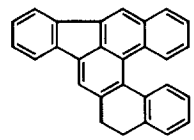
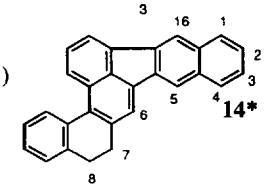
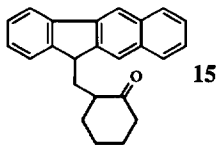
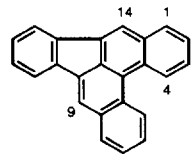
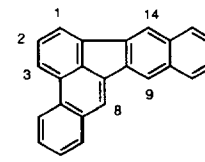
Abstract: *A double Wagner-Meerwein rearrangement takes place commonly in the synthesis of sterically hindered polycyclic fluoranthenes via cyclodehydration reactions and the extent of intramolecular steric crowding within the initially formed tertiary cationic intermediate controls the equilibrium between the expected and the rearranged product.*

An essential feature of Wagner-Meerwein rearrangement is the 1,2-shift of an alkyl or an aryl group to an adjacent carbocationic site, followed by various reactions including a further rearrangement.[1] Although the mechanistic details of the rearrangement have been extensively investigated, relatively little is known concerning the steric factor affecting the rearrangement process. Recently, we reported the acid-catalyzed cyclodehydration of the keto adduct **1**, which furnished a mixture of **3** and **5** (**Scheme 1**) and proposed that the formation of the latter occurs by a double Wagner-Meerwein rearrangement,[2,3] a mechanism similar to that proposed for the conversion of benzo[*c*]phenanthrene to chrysene.[4] In the present study, we conducted similar cyclizations of several appropriately designed keto adducts in order to study further the steric-driven nature of this interesting rearrangement.



Scheme 1

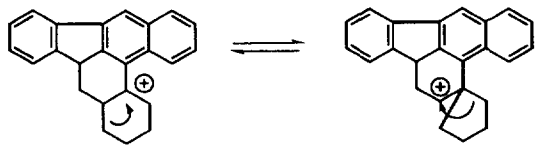
Table 1. Synthesis of polycyclic fluoranthenes *via* a PPA-cyclodehydration reaction.[5]

Entry	Keto-Adduct[7]	Expected Product[11]	Rearranged (or Side*) Product[11]
1	**1**	**3** (40%)	**5** (60%)
2	**2**	**4** (87%)	**6** (13%)
3	 **7**	 **8** (20%)[12]	 **9** (80%)[12]
4	 **10**	 **11** (10%)	 **12** (70%)
		 **13** (10%)	 **14*** (10%)
5	 **15**	 **16** (90%)	 **17*** (10%)[6]

Polyphosphoric acid (PPA)-catalyzed cyclization of **1**, followed by aromatization (DDQ) afforded a 4:6 mixture of **3** and **5** in 80% overall yield (**Scheme 1**). The initially formed cationic intermediate (**1a**) is either aromatized to the expected product **3** or undergoes two Wagner-Meerwein shifts to furnish the rearranged **5**. The corresponding reaction of **2**, the 7-methyl-analog of **1**, however, provided mostly (87%) the expected product (**4**). Such dramatic variation in the product ratio can only be rationalized on steric grounds: *i.e.*, the severe steric crowding in the double pseudo-*fjord* region of the rearranged cationic intermediate (**2b**) shifts equilibrium to the side of that of the expected product (**2a**). Molecular modelling studies indicate that the terminal benzo ring of **6** is significantly distorted than that of **4**.

As expected from the aforementioned steric argument, cyclizations of **7** and **10** (entries 3 and 4, Table 1) favor the rearrangement pathway since the cationic intermediates of the expected products (**8** and

11, respectively) possess highly strained ring systems. The presence of the partially saturated analog **13** in the reaction mixture of entry 4 suggests that the severe molecular deformity of the petahelicene aromatic ring system of **11** suppresses the DDQ oxidation process. Such steric strain also appears to be responsible for the formation of the regioisomeric **14**, since similar ring closure reactions of benzo[*b*]fluorene are known to take place regiospecifically to the naphthalene side.[14,15] Entry 5 in Table 1 is an interesting example of the degenerate, double Wagner-Meerwein rearrangement, in which the structure of the expected and the rearranged product are identical (**16a**, **Scheme 2**). Apparently, as in the case of entry 4, the formation (10%) of the regioisomeric **17**[6] is due to the high steric crowding in the *fjord*-region of **16**.



16a

Scheme 2

In summary, we have shown that a double Wagner-Meerwein rearrangement takes place commonly in the synthesis of sterically hindered polycyclic fluoranthenes *via* cyclodehydration reactions. It was found that the degree of intramolecular steric crowding within the initially formed tertiary cationic intermediate controls the equilibrium between the expected and the rearranged product. The hydrocarbons described in this paper are of interest as standards for environmental analysis and as potential carcinogens and mutagens. Currently, we are exploring possibilities of employing this rearrangement as a way of preparing polycyclic aromatic fluoranthenes that are difficult to obtain otherwise.

Acknowledgments. We thank Sungmi Yoon and Jennifer Kum for their technical help. This work has been partially supported by a grant from the American Cancer Society (#CN-130).

REFERENCES AND NOTES

1. (a) March, J. *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, Wiley, New York, 4th Ed, **1992**, Chapter 18. (b) Pocker, Y. In *Molecular Rearrangements*; de Mayo, P., Ed. Wiley-Interscience: New York, **1963**, Vol. **1** pp 1-25.
2. Cho, B. P. *Tetrahedron Lett.* **1995**, *36*, 2403-2406.
3. Cho, B. P. and Zhou, L. *15th International Symposium on Polycyclic Aromatic Hydrocarbons: Chemistry, Biology and Environmental Impact*, Belgirate, Italy, **1995**.
4. Cahana, E. R.; Schmidt, G. M.; Shah, K. H. *J. Org. Chem.* **1959**, *24*, 557-559.
5. In a typical experiment, **15** (65 mg, 0.2 mmole) was treated with PPA for 5 hr at 120°C. The resulting hot brown syrup was poured into ice-water, allowed to stand for 1hr, and extracted with ether. The crude residue was treated with DDQ (135 mg, 0.6 mmole) in refluxing benzene for 2 hr and poured onto a short neutral alumina column. The solid which eluted with benzene was recrystalized to give pure dibenz[*a,e*]acephenanthrylene (**16**, 43 mg, 71%, mp 214-215°C, HRMS: $C_{24}H_{14}$, Calcd. for 302.10955; Found 302.10944). Further elution with benzene furnished dibenzo[*b,k*]fluoranthene (**17**, 5 mg, 8%, mp 227-228°C, lit.[6] mp 236°C, HRMS: $C_{24}H_{14}$, Calcd. for 302.10955; Found 302.10944).
6. Buu-Hoï, N. P.; Lavit, D. *J. Chem. Soc.* **1960**, 536-539.

7. Keto adducts were prepared according to the general procedure using an appropriate Michael donor and acceptor (**1**[2,3]; **2**: trimethylsilylenolether of α-tetralone + 6-methyldibenzofulvene[8]; **7**: trimethylsilyl-enolether of 2-methylcyclohexanone[9] + dibenzofluvene;[8] **10** and **15** were prepared by reaction of 11-lithiobenzo[*b*]-fluorene to α-methylenetetralone[10] and α-methyleneyclohexanone,[10] respectively).
8. Nuenschwander, von M.; Vogell, R.; Fahrni, H.-P.; Lehmann, H.; Ruder, J.-P. *Helv. Chim. Acta* **1977**, ***60***, 1073-1087.
9. Fleming, I.; Paterson, I. *Synthesis* **1979**, 736-737.
10. Nakahira, H.; Ryu, I.; Oku, Y.; Ogawa, A.; Kambe, N.; Sonoda, N.; Murai, S. J. *J. Org. Chem.* **1992**, ***57***, 17-28.

11. Although these regioisomers were isolated either by recrystallization/column chromatography (**3**, **4**, **9**, **12**, **16**, **17**) or by HPLC (**5**, **6**, **8**, **11**, **13**, **14**), the relative % ratio given here is based on ^{1}H NMR integration of crude product taken after DDQ aromatization. Characterization of these compounds were made with the aid of elemental analyses, high resolution mass spectra (within the limits of ±1 mmu, Mass Spectrometer Lab., Univ. of Illinois), and ^{1}NMR (COSY and NOE experiments).[13] HPLC analyses were carried out on a Waters LC system with a Hitachi L-3000 photodiode-array detector (Ultrasphere analytical column with 1 mL/min of isocratic 100 % methanol). All NMR spectra (Bruker AM300) were recorded in $CDCl_3$ with internal TMS standard: **4**; HPLC, 12.52 min. ^{1}H NMR δ 9.18 (d, H1), 8.95 (d, H14), 8.33 (d, H6), 8.23 (m, H8), 8.1-8.0 (m, 4H), 7.80 (m), 7.75 (m), 7.67 (m), 7.46 (m, H9,10), 3.26 (s, CH_3). **6**; HPLC, 12.17 min: ^{1}H NMR δ 8.72 (m, H1), 8.68 (d, H6), 8.53 (d, H7), 8.19 (m, H13), 8.02 (m, 2H), 7.77 (m, H8), 7.70 (m), 7.63 (m), 7.52 (m), 7.47 (m), 3.52 (s, CH_3). **8**; HPLC, 8.24 min: δ 8.81 (d, H1), 8.30 (s, H8), 8.07-7.94 (5H), 7.89-7.78 (2H), 7.56 (2H), 7.44 (2H), 3.20 (CH_3). **9**; HPLC, 7.33 min: ^{1}H NMR δ 8.57 (d), 8.50 (s, H8), 8.49 (d), 8.07, 8.01, 7.95, 7.78, 7.59, 7.50, 7.43 (2H), 2.90 (CH_3). **11**; HPLC, 12.88 min: ^{1}H NMR δ 8.83 (d, H1), 8.80 (d, H16), 8.38 (s, H5), 8.30 (s, H10), 8.10 (d, H4), 8.03 (H6,7), 8.01 (H11), 7.98 (m, H12,13), 7.60 (m, H14), 7.57 (m, H3), 7.47 (m, H7,8), 7.41 (m, H2,15). **12**; HPLC, 16.35 min: ^{1}H NMR δ 9.33 (s, H16), 9.29 (d, H7), 9.25 (d, H6), 8.99 (d, H1), 8.36 (s, H11), 8.19 (m, H10), 8.15 (m, H15), 8.05 (m, H4,5,12), 7.69 (m, H2,8), 7.71 (d, H3), 7.68 (d, H9), 7.50 (m, H13,14). **13**; HPLC, 11.85 min: ^{1}H NMR δ 8.65 (d, H1), 8.21 (s, H5), 8.01 (m, H4,9), 7.84 (m, H6), 7.85 (s, H10), 7.72 (d, H14), 7.51 (m, H3), 7.40 (m, H7,8,16), 7.29 (m, H2), 7.25 (H15), 7.13 (H13), 3.10 (m, H12), 2.90 (m, H11). **14**; HPLC, 17.64 min: ^{1}H NMR δ 8.44 (d, H13), 8.33 (s, H5), 8.32 (s, H16), 8.02 (m, H12,15), 7.98 (s, H6), 7.95 (m, H1,4), 7.72 (dd, H14), 7.50 (m, H2,3), 7.41 (m, H10,11), 7.33 (m, H9), 3.10 (m, H7), 2.90 (m, H8). **16**; ^{1}H NMR δ 9.25 (d, H4,5), 8.28 (s, H9,14), 8.09 (dd), 7.96 (dd), 7.68 (m), 7.60 (m), 7.39 (m, H11,12). **17**; ^{1}H NMR δ 8.62 (d, H4), 8.43 (d, H3), 8.37 (s, H8), 8.28 (s, H9), 8.26 (s, H14), 8.03 (m), 7.91 (m), 7.77 (m), 7.62 (m), 7.45 (m, H11,12).

12. Amin, S.; Huie, K.; Hussain, N.; Balanikas, G.; Hecht, S. S. *J. Org. Chem.* **1985**, ***50***, 1948-1954.
13. Cho, B. P.; Harvey, R. G. *J. Org. Chem.* **1987**, ***52***, 5679-6884.
14. Amin, S.; Hussain, N.; Brielmann, H.; Hecht, S. S. *J. Org. Chem.* **1984**, ***49***, 1091-1095.
15. Rice, J. E.; Hussain, N.; LaVoie, E. J. *Polynucl. Aromat. Hydrocarbons: Meas., Means, Metab., Int. Sympo., 11th*, 741-751, **1991**.

(*Received in USA* 6 *December* 1995; *revised* 19 *December* 1995; *accepted* 21 *December* 1995)