Reactions of these $M_2R_2(NMe_2)_4$ compounds with alcohols are dependent on the nature of (i) the alkyl group R, (ii) the alcohol, and (iii) the metal, Mo or W. For example, $M_2(CH_3)_2(NMe_2)_2$ compounds (M = Mo, W) both react with *tert*-butyl alcohol to give $M_2(CH_3)_2(OBu^t)_4$ compounds. However, addition of Pr^iOH to $Mo_2(CH_3)_2(NMe_2)_4$ yields $Mo_2(OPr^i)_6$ (M≡M) and CH_4 (2 equiv). The analogous reaction involving $W_2(CH_3)_2(NMe_2)_4$ has not yet been carried out, but it is known that attempts to prepare $W_2(OPr^i)_6$ have led to $W_4(\mu\text{-}H)_2(OPr^i)_{14}$.[18] The reaction of $Mo_2(C_2H_5)_2(NMe_2)_4$ with Bu^tOH yielded $Mo_2Et(OBu^t)_5$ and ethane.[4b] Using the labeled compound $Mo_2(CH_2CD_3)_2(NMe_2)_4$, we find that addition of Bu^tOH causes the exclusive[16] elimination of CH_2DCD_3. The resulting ethyl ligand in $Mo_2(C_2H_3D_2)(OBu^t)_5$ contains a statistical distribution of deuteriums on the α and β carbons, namely integration indicates that $\alpha:\beta$ = 2:3.

The purpose of this communication is to draw attention to the intriguing chemistry associated with alkyl groups coordinated to the dimolybdenum or ditungsten (M≡M) centers. (1) In $M_2R_2(NMe_2)_4$ compounds, β-hydrogen elimination is either kinetically or thermodynamically not favorable. (2) Addition of CO_2 to $Mo_2(CH_2CH_3)_2(NMe_2)_4$ (M≡M) leads to formation of $Mo_2(O_2CNMe_2)_4$ (M≡M) by an intramolecular mechanism. It seems likely that this involves an initial irreversible β-hydrogen elimination which is then followed by C–H reductive elimination. However, it is not known at what step during CO_2 insertion that this process occurs, nor is it known whether C–H reductive elimination occurs across the M—M triple bond, H—M≡M—Et → M≡M + Et—H, or via an oxidative addition-reductive elimination process at one metal center, $M^{II}{\equiv}M^{IV}(H)(Et) \rightarrow M^{II}{\equiv}M^{II} + Et\text{—}H$. (3) That $W_2(C_2H_5)_2(NMe_2)_4$ should react so differently with CO_2 is also fascinating, and once again points to the elusive nature of $W_2(O_2CX)_4$ (M≡M) compounds.[19] (4) Addition of Bu^tOH to $Mo_2(CH_2CD_3)_2(NMe_2)_4$ which leads to $Mo_2(C_2H_3D_2)(OBu^t)_5$ and CH_2DCD_3 implies that alcoholysis, as with CO_2 insertion (2 above), once again facilitates an irreversible β-hydrogen process which is then followed by C–D reductive elimination. This further implies that formation of the σ-ethyl ligand arises from $CH_2{=}CD_2$ and $Bu^tO\text{—}H$. The statistical distribution of H/D atoms over the α and β carbons in the σ-ethyl ligand thus formed is consistent with a then reversible β-hydrogen elimination process favoring the coordinated ethyl ligand:

$$M\text{—}H + C_2H_4 \rightleftharpoons M\text{—}C_2H_5$$

While all these observations raise intriguing mechanistic questions which cannot be answered at this time, we do note that our observations have at least one parallel with mononuclear transition metal alkyl chemistry: reductive elimination involving C—H bond formation is more facile than reductive elimination involving C—C bond formation.[20]

Acknowledgments. We thank the Office of Naval Research for support of this work. The ^1H NMR spectrum shown in Figure 1a was obtained through the courtesy of Mr. Dean Katahira at Yale University. Mass spectral data were kindly obtained for us by Mr. Peter Cook and Professor D. C. Bradley at Queen Mary College, London.

References and Notes

(1) (a) G. Wilkinson, *Science*, **185**, 109 (1974); (b) M. F. Lappert, P. J. Davidson, and R. Pearce, *Acc. Chem. Res.*, **7**, 209 (1974); (c) R. R. Schrock and G. W. Parshall, *Chem. Rev.*, **76**, 243 (1976).
(2) J. K. Kochi in "Organometallic Mechanisms and Catalysis", Academic Press, New York, 1978.
(3) M. Akiyama, M. H. Chisholm, F. A. Cotton, M. W. Extine, and C. A. Murillo, *Inorg. Chem.*, **16**, 2407 (1977).
(4) (a) The preparation and structure of $Mo_2(CH_3)_2(NMe_2)_4$ has been reported: M. H. Chisholm, F. A. Cotton, M. W. Extine, and C. A. Murillo, *Inorg. Chem.*, **17**, 2338 (1978). (b) The preparation and reactivity of $Mo_2(C_2H_5)_2(NMe_2)_4$ was previously reported: M. H. Chisholm, D. A. Haitko, and C. A. Murillo, *J. Am. Chem. Soc.*, **100**, 6262 (1978).
(5) Satisfactory analytical data have been obtained. All compounds showed molecular ions in the mass spectrometer, $M_2R_2(NMe_2)_4^+$, and we thank Professor D. C. Bradley and Mr. Peter Cook at Queen Mary College for kindly obtaining these valuable spectra for us. This collaboration was promoted by a NATO grant to D.C.B. and M.H.C.
(6) We have no rationale for this observation; our intuition would have suggested the opposite trend.
(7) For an assignment of proximal and distal *N*-Me resonances, see M. H. Chisholm, F. A. Cotton, B. A. Frenz, W. W. Reichert, L. W. Shive, and B. R. Stults, *J. Am. Chem. Soc.*, **98**, 4469 (1976).
(8) For a detailed discussion, see the variable-temperature ^{13}C NMR studies carried out on $W_2(CH_3)_2(NEt_2)_4$: M. H. Chisholm, F. A. Cotton, M. W. Extine, M. Millar, and B. R. Stults, *Inorg. Chem.*, **15**, 2244 (1976).
(9) *tert*-Butyl transition metal complexes (and to a lesser extent isopropyl complexes) are relatively rare. See ref 2. The reversible β-H elimination from an alkyl metal complex *without* attendant reductive elimination of alkane was elegantly studied in alkyl gold(III) chemistry. The isomerization of *trans-tert*-butyldimethyl(triphenylphosphine)gold(III) proceeds spontaneously at 25 °C in ethereal solution to produce the *trans*-isobutyldimethyl(triphenylphosphine)gold(III) complex in *quantitative* yield. See A. Tamaki and J. K. Kochi, *J. Chem. Soc. Chem. Commun.*, 423 (1973).
(10) Prepared from the reaction between CD_3CH_2Br and Li shot in hexane and purified by sublimation at 65 °C, 10^{-6} cmHg. CD_3CH_2Br was obtained from Merck Sharp & Dohme.
(11) The mechanism of this insertion has been shown to proceed via an amine catalyzed sequence: M. H. Chisholm and M. W. Extine, *J. Am. Chem. Soc.*, **99**, 792 (1977).
(12) All these compounds show molecular ions in the mass spectrometer and are believed to be directly analogous to the structurally characterized diethylcarbamato analogue $W_2(CH_3)_2(O_2CNEt_2)_4$: M. H. Chisholm, F. A. Cotton, M. W. Extine, and B. R. Stults, *Inorg. Chem.*, **16**, 603 (1977).
(13) $Mo_2(O_2CNMe_2)_4$ is formed as a fine yellow precipitate in this reaction. It shows a strong molecular ion $Mo_2(O_2CNMe_2)_4^+$ and a doubly charged molecular ion $Mo_2(O_2CNMe_2)_4^{2+}$. In all respects it appears like $Mo_2(O_2CR)_4$ compounds for which scores have been structurally characterized and all of which contain a Mo–Mo quadruple bond.
(14) From R. M. Lynden-Bell and N. Sheppard, *Proc. R. Soc. A.*, **269**, 1385 (1965): for ethylene $J_{cis}(^1H\text{–}^1H) = +11.7$, $J_{trans}(^1H\text{–}^1H) = 19.1$, and $J_{gem}(^1H\text{–}^1H) = +2.5$ Hz; $\gamma(^1H) = 2.675 \times 10^4$ radians/(s·G), $\gamma_{^2H} = 4.107 \times 10^3$ radians/s·G. Using this data it was possible to calculate the splittings of $CD_2{=}CH_2$, *trans*-CHD=CHD and *cis*-CHD=CHD. The calculated splittings were obtained by using the program entitled NMRCAL, a part of the Nicolet-80 system. For each of the isomeric dideuterioethylenes a centered three-line pattern was observed with the only apparent distinguishing characteristic being the separation between the outer lines. The calculated vs. observed splittings in hertz for each dideuterioethylene are as follows: 1,1-dideuterioethylene, 4.8 (4.8); 1,2-*cis*-dideuterioethylene, 3.3 (3.3); and *trans*-1,2-dideuterioethylene, 2.2 (2.2).
(15) From Merck Sharp & Dohme.
(16) By exclusively, we mean within the limits of NMR detection which is at least 95%.
(17) Alkyllithium and alkylaluminum compounds are well known to undergo β-H elimination under thermolysis[2] but we are not aware of anyone reporting the formation of ethylene upon the addition of water. It quite possibly is formed under our conditions because $LiCH_2CD_3$ is present in excess as D_2O is added and therefore thermolysis is a competitive reaction owing to local heating effects which accompany hydrolysis. See also B. J. Wakefield in "The Chemistry of Organolithium Compounds", Pergamon Press, Elmsford, N.Y., and Oxford, 1974, Chapter 15.
(18) M. Akiyama, D. Little, M. H. Chisholm, D. A. Haitko, F. A. Cotton, and M. W. Extine, *J. Am. Chem. Soc.*, **101**, 2504 (1979).
(19) A. Bino, F. A. Cotton, Z. Dosi, S. Koch, H. Kuepers, M. Millar, and J. C. Sekutowski, *Inorg. Chem.*, **17**, 3245 (1978).
(20) J. R. Norton, *Acc. Chem. Res.*, **12**, 139 (1979), and references therein.

Malcolm H. Chisholm,* Deborah A. Haitko
Department of Chemistry, Indiana University
Bloomington, Indiana 47405
Received April 20, 1979

Stereospecific Total Synthesis of *dl*-Austamide

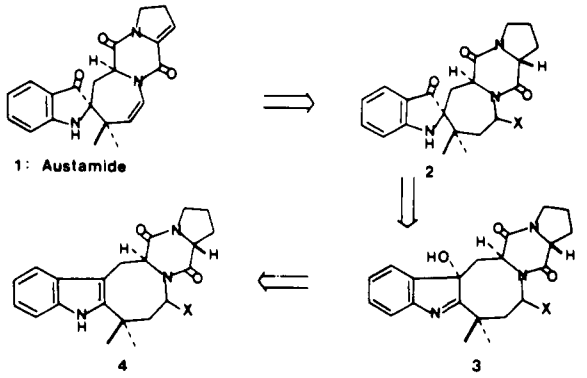
Sir:

Austamide (**1**) is a toxic metabolite of *Aspergillus ustus* whose isolation and structure elucidation was described by Steyn in 1971.[1] Herein we report the first stereospecific total synthesis of *dl*-austamide.

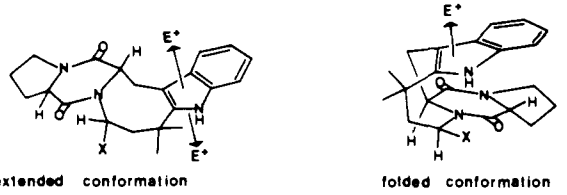
Austamide contains elements of great synthetic difficulty, possessing two labile enamide functionalities as well as the delicate ψ-indoxyl chromophore. In addition, it is necessary to control the relative stereochemistry of two asymmetric centers, one of which is located at a spiro ring junction. Our synthetic strategy is outlined in Scheme I. The cornerstone of

0002-7863/79/1501-6786$01.00/0

Scheme I



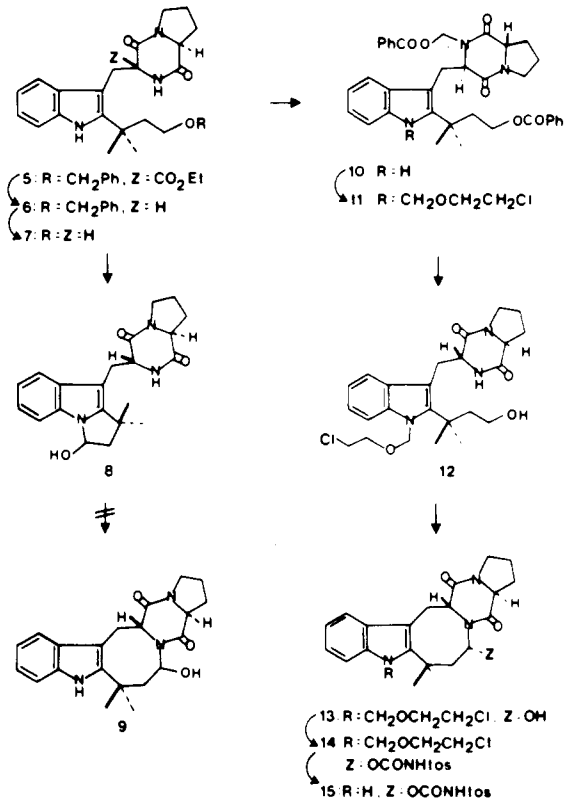
Scheme II



this strategy is the stereospecific oxidation and rearrangement of an appropriate indole derivative via the corresponding 3-hydroxyindoline. As previously described,[2] the acid- or base-catalyzed pinacol-type rearrangement of a 3-hydroxyindoline to a ψ-indoxyl must proceed stereospecifically, and hence the overall stereochemical outcome of the oxidative rearrangement sequence is determined by the stereochemistry of the oxidation (i.e., **4** to **3**). Examination of the Dreiding models reveals that the direction of attack of some hypothetical electrophile, E^+, depends on the conformation of the indole **4**. As shown in Scheme II, oxidation via the extended conformation would not be expected to be stereospecific. If, however, the oxidation occurs predominantly via the folded conformation, attack of an electrophile should occur preferentially from the α face of the indole to give a 3-hydroxyindoline with the desired stereochemistry. On the basis of our previously reported model studies[2] as well as NMR studies on similar systems,[1] we would expect the oxidative rearrangement of such a system to give a ψ-indoxyl with identical relative stereochemistry with that of austamide itself. It has been suggested that the biogenesis of austamide may involve a similar oxidative rearrangement.[3]

The preparation of an appropriate indole precursor to austamide is outlined in Scheme III. The diketopiperazine ester **5**, whose synthesis was previously described,[2] was hydrolyzed (1 N NaOH, dioxane) and decarboxylated in refluxing dioxane to give the *trans*-diketopiperazine **6**[4] (mp 207–208 °C) in 93% yield along with a small amount of the cis isomer (stereospecificity, 13:1). Hydrogenolysis in 1:1 methanol–acetic acid afforded the alcohol **7**[4,5] (mp 131–132 °C) in 92% yield. Oxidation of this alcohol was best accomplished by stirring with excess MnO_2 in acetonitrile.[6] Under these conditions the *N,O*-hemiacetal **8**[4,7] (amorphous solid) was formed. In no case was the free aldehyde detected and attempts to isomerize the *N,O*-hemiacetal **8** to the desired *N*-acyl-*N,O*-hemiacetal **9** proved fruitless. Thus it became necessary to block indole nitrogen. However, since the diketopiperazine nitrogen of **7** is more reactive than the indole nitrogen toward intermolecular alkylation, this position had to be protected prior to the protection of indole nitrogen. Accordingly, the alcohol **7** was hydroxymethylated (K_2CO_3, aqueous HCHO, dioxane, 100 °C) and benzoylated to give the benzoate **10**[4,8] (amorphous solid) in 75% overall yield. Owing to the failure of several conventional protecting groups (CH_3OCH_2–, CH_3O-

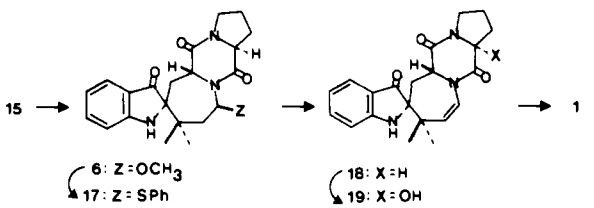
Scheme III



$CH_2CH_2OCH_2$–, CH_3SCH_2–), we had the opportunity to develop a new protecting group for indole nitrogen,[9] the 2-chloroethoxymethylene group. We imagined that such a group could be removed by a combination of cyanide ion and base, reagents expected to be compatible with the remaining functionality. Alkylation of the benzoate **10** with 2-chloroethyl chloromethyl ether[10] in DMF–THF (1:4) with KH as a base afforded the protected benzoate **11**[4] in 50% yield. Hydrolysis of **11** with 1 N NaOH in dioxane gave the protected alcohol **12**[4,11] (amorphous solid) in 61% yield. Oxidation was effected as before to give the desired protected *N*-acyl-*N,O*-hemiacetal **13**[4,12] (amorphous solid) in 65% yield. The protected tosyl carbamate **14**[4] (amorphous solid) was prepared in 89% yield from **13** in the usual manner (Tos-NCO, CH_2Cl_2). The 2-chloroethoxymethylene group was removed by refluxing with KCN in acetonitrile in the presence of 18-crown-6 to afford the tosyl carbamate **15**[4,13] (mp 171–173 °C) in 84% yield.

The oxidation and rearrangement of this compound as well as the conversion of the resulting indoxyl into austamide is outlined in Scheme IV. The protected tosyl carbamate **15** was oxidized with *m*-chloroperbenzoic acid (MCPBA) in methylene chloride at room temperature and the resulting 3-hydroxyindoline was rearranged with sodium methoxide in refluxing methanol to afford the methoxy indoxyl **16**[4,14] (amorphous solid) in an overall yield of 53% as the only stereoisomer detected. This compound was treated with excess thiophenol in the presence of boron trifluoride etherate to give the thiophenyl indoxyl **17**[4] (amorphous solid) in 95% yield. The sulfide was oxidized to the corresponding sulfoxide (MCPBA,

Scheme IV



K_2CO_3, $CaCO_3$, CH_2Cl_2) which was pyrolyzed in situ (*o*-dichlorobenzene, 150 °C) to give *trans*-dihydroaustamide **18**[4,15] (mp 110–115 °C) in 50% overall yield. This material was identical in all respects (NMR, UV, MS, TLC) with an authentic sample of (12*R*)-dihydroaustamide prepared by hydrogenation of austamide.[1]

The dianion of **18** was formed with lithium diisopropylamide (2 equiv) in tetrahydrofuran at −78 °C, which in turn was quenched with 2 equiv of diphenyl disulfide at −78 °C to room temperature. In this manner the tertiary alcohol **19**[4,16] as a mixture of stereoisomers (amorphous solid) was formed as the major product after aqueous workup. This alcohol was treated with excess triethylamine and mesyl chloride in methylene chloride at room temperature to give *dl*-austamide (**1**) in 40% overall yield. The synthetic material was identical in all respects (NMR, UV, MS, TLC) with an authentic sample.

Acknowledgment. We thank Dr. Steyn for a sample of austamide. Financial assistance from the National Science Foundation is gratefully acknowledged.

References and Notes

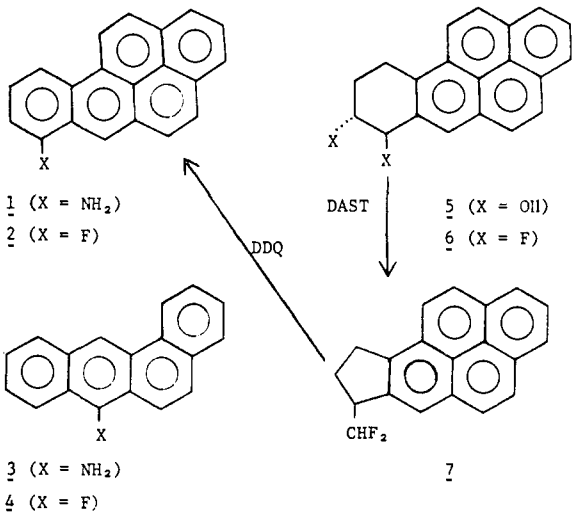
(1) Steyn, P. S. *Tetrahedron Lett.* **1971**, 331–3334; *Tetrahedron* **1973**, *29*, 107–120.
(2) Hutchison, A. J.; Kishi, Y. *Tetrahedron Lett.* **1978**, 539–542.
(3) See for example, Sames, P. G. *Fortschr. Chem Org. Naturst.* **1975**, *32*, 51–117.
(4) Satisfactory spectroscopic data were obtained for this susbtance.
(5) NMR ($CDCl_3$): δ 1.50 (6 H, s), 2.01 (2 H, t, *J* = 7 Hz); MS *m/e* 369 (M^+, 9%), 216 (100), 172 (51).
(6) Harrison, I. T. *Proc. Chem. Soc.* **1964**, 110.
(7) NMR ($CDCl_3$): δ 1.28 (6 H, s); MS *m/e* 349 (M^+ − 18, 15%), 196 (100).
(8) NMR ($CDCl_3$): δ 1.61 (6 H, s), 2.25 (2 H, t, *J* = 7 Hz), MS *m/e* 607 (M^+, 4%), 320 (100), 198 (75).
(9) A paper describing the use of this protecting group is presently in preparation.
(10) Salmi, E. J; Leimu, R.; Kallio, H. *Suom. Kemistil. B* **1944**, *17*, 17–19.
(11) NMR ($CDCl_3$): δ 1.55 (3 H, s), 1.62 (3 H, s); MS *m/e* 381 (M^+ − 80, 12%), 228 (100), 198 (63).
(12) NMR ($CDCl_3$): δ 1.43 (3 H, s), 1.80 (3 H, s); MS *m/e* 461 (M^+, 9%), 459 (M^+, 21), 73 (100).
(13) NMR ($CDCl_3$): δ 1.31 (3 H, s), 1.61 (3 H, s), 2.44 (3 H, s); MS *m/e* 564 (M^+ − 197, 19%), 196 (100).
(14) NMR ($CDCl_3$): δ .85 (3 H, s), 1.03 (3 H, s), 3.25 (3 H, s); UV (MeOH) λ 392 nm (log ε 3.46), 256 (3.86), 232 (4.40); MS *m/e* 397 (M^+, 10%), 365 (74), 309 (100).
(15) NOTE ADDED IN PROOF. Subsequent investigations have uncovered a new method to effect the conversion of **18** into austamide which is superior to that described in the text both in terms of overall yield and reproducibility. A solution of **18** in tetrahydrofuran was stirred under oxygen atmosphere in the presence of benzoyl peroxide at 50 °C for 24 h, after which the reaction mixture was treated with excess methyl sulfide at room temperature. In this manner a 72% yield of 12,13-dihydro-12-hydroxyaustamide, the stereoisomer with respect to X of **19**, was obtained which was found to be identical with the authentic sample by comparison of their NMR spectra. Treatment of this substance with methanesulfonyl chloride and triethylamine in methylene chloride as described in the text gave a 63% yield of *dl*-austamide (**1**). We are indebted to Dr. Steyn for the NMR spectrum of natural 12,13-dihydro-12-hydroxyaustamide.
(16) The gross structure **19** corresponds to that of one of the minor metabolites isolated from *A. ustus:* Steyn, P. S.; Vleggaar, R. *Phytochemistry* **1956**, *15*, 355–356.

Alan J. Hutchison, Yoshito Kishi*
Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138
Received May 29, 1979

A Novel Synthesis of 7-Fluorobenzo[*a*]pyrene Involving Two New Molecular Rearrangements[1]

Sir:

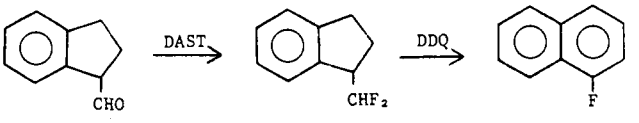
Because of our interest in the possible metabolic pathways by which benzo[*a*]pyrene produces cancer we sought to convert 7-aminobenzo[*a*]pyrene (**1**) into 7-fluorobenzo[*a*]pyrene (**2**) desired for testing. However, only very small amounts of **2** could be produced from **1** by conventional diazotization via the diazonium fluoroborate[2,3] and none at all using the modified procedure recently described for converting 7-aminobenz[*a*]-anthracene (**3**) into 7-fluorobenz[*a*]anthracene[4] (**4**).



We then turned to *trans*-7,8-dihydroxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene[5] (**5**) in the hope that treatment with diethylaminosulfur trifluoride (DAST)[6,7] would yield the corresponding difluoride (**6**), which might be converted into 7- or 8-fluorobenzo[*a*]pyrene or a mixture of the two.[8] Treatment of **5** with DAST produced a compound which on heating in benzene with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) afforded **2** in 60% overall yield from **5**. Examination of the NMR spectra[9] of the intermediate difluoro compound showed that rearrangement into 7-difluoromethyl-8,9-dihydro-7(*H*)-cyclopenta[*a*]pyrene (**7**) had taken place. This rearrangement is surprising, especially since it has been mentioned that the OH group in isobutyl alcohol can be replaced by F without causing extensive rearrangement or dehydration.[7]

Perhaps even more surprising is the rearrangement of **7** into **2** in high yield on heating in benzene with DDQ, a reagent noted mainly for its ability to oxidize by extracting two hydrogens. The formation of **2** from **7** provides an example of what may become a new method for synthesis of fluorinated aromatic compounds as shown in Scheme I.

Scheme I



We are studying the synthesis of nuclear substituted compounds of type **8**, the conversion of these two compounds of type **9** by treatment with DAST,[10] and the effect of DDQ and other reagents on the rearrangement of **9** to **10**. It is also of interest to see if dichlorides, dibromides, and dimethoxy compounds analogous to **9** can be caused to rearrange to compounds of type **10**. Typical experimental procedures follow.

To a stirred suspension of 0.90 g of **5** in 250 mL of CH_2Cl_2 at −78 °C was added 1.5 g of DAST.[6,7] After 30 min the temperature was allowed to rise to 0 °C and the mixture became clear. After water was added, the organic product was isolated and treated at reflux in benzene containing 0.90 g of DDQ for 16 h. Chromatography over basic alumina afforded 0.50 g (60%) of **2**, mp 174–175 °C. Anal.[11] ($C_{20}H_{11}F$) C, H, F.

In another experiment similar to the above, the crude product from the DAST treatment was chromatographed over neutral alumina to yield (40%) pure **7**, mp 112–113 °C. Anal.[11] ($C_{20}H_{14}F_2$) C, H, F. A sample of pure **7** gave **2** in 82% yield on treatment with DDQ as above.

0002-7863/79/1501-6788$01.00/0