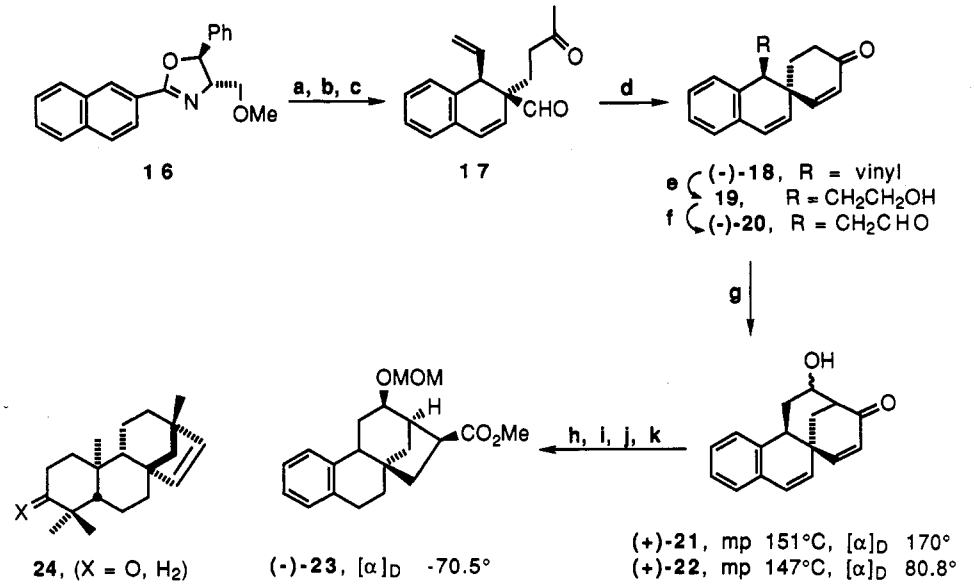
Scheme III[a]



[a] Reagents and conditions: a, MeLi, $Bu_3SnCH{=}CH_2$, THF, −50 °C; b, $ICH_2CH_2(Me)C(OCH_2)_2$; c, (i) MeOTf, $CHCl_2$, (ii) $NaBH_4$, MeOH–THF, (iii) H_3O^+; d, 2.5% KOH–MeOH; e, 9-BBN, H_2O_2, 3 M NaOH, THF; f, Swern oxidation; g, 2.5% KOH–MeOH, rt; h, MOMCl, NaH, THF; i, Pd/C, H_2, MeOH; j, $ArSO_3N_3$, KOH, PTC; k, *hν*, MeOH–Et_2O.

group and ester function on the β-face of **14**. This completed the assembly of the skeletal array related to the scopadulcic acids[17] from the common intermediate (−)-**9** in 44% overall yield. The relationship of **14** to our target **4b** is merely oxidation of the C-ring hydroxyl group.

Finally, we examined the additional scope of this method by utilizing the chiral oxazoline **16** derived from 2-naphthoic acid as an entry into the isomeric tetracyclic system **24**. The latter is present in a number of kaurane diterpene systems such as hibaene[18] and stachenone.[19] Scheme III outlines our route, which is purposely similar to the route previously described (in Scheme II). The acquisition of optically pure tetracyclic ketones **21**, **22** in good overall yield was the principal goal of this aspect of the study and as Scheme III depicts, we have reached this goal. The epimeric ketones could be readily separated (formed in the aldol process as a 1:1 mixture) and characterized. These were carried forward to the model tetracyclic carboxylic esters **23**. Although the last two steps; the α-diazo transfer and subsequent photolysis to the product **23** have not been optimized (27% over both steps), we are comfortable with the overall sequence and versatility shown by the chiral naphthyloxazolines **1** and **16**.

Methodology such as this, although not necessarily in position to reach specific natural products, is considered to be worthy of merit in synthesis. A similar report by Overman[20] nicely demonstrated how general ring closure strategy via palladium-catalyzed polyene cyclizations can provide an entry into the tetracyclic system **4b**, namely the scopadulcic acid skeletal system. The enantioselectivity, efficiency, and simplicity of this approach attest to the potential power of this process. We are continuing our efforts to reach complex systems and are in the process of making appropriate modifications in starting materials.[21]

Acknowledgment. We are grateful to the National Institutes of Health for support of this program.

Supplementary Material Available: Experimental details and physical constants for all compounds (15 pages). Ordering information is given on any current masthead page.

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(18) Ireland, R. E.; Mander, L. N. *Tetrahedron Lett.* **1965**, 2627.
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(21) The installation of the angular methyl at C-10 (aphidicolin numbering) is a major goal of the presently ongoing studies. We would like to *stress* that utilization of the reported approach (from the naphthalene nucleus) to a natural product system containing this C-10 angular methyl group is obviously neither facile nor attractive. Efforts utilizing more appropriately functionalized A and B rings (e.g., 10-methyldecalones) in place of naphthyl systems are currently under study, and preliminary results are encouraging.

Multiple Rearrangements of 1-Methoxyfluorenylidene to 1-Phenanthrenol

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Summary: Flash vacuum pyrolysis of 1-methoxy-9-diazofluorene (**1**) yielded 1-phenanthrenol (**2**). Experiments with ^2H- and ^{13}C-labeled **1** revealed that the source of C_{10} of **2** is the methoxy carbon of **1**, whereas the likely source of C_9 of **2** is the diazo-substituted carbon of **1**.

The rearrangements of arylcarbenes[1] in the gas phase are of a complexity that rivals that of the rearrangements of carbocations in solution. Even innocent-looking products may have been produced by a long series of rearrangements and automerization. Such rearrangements

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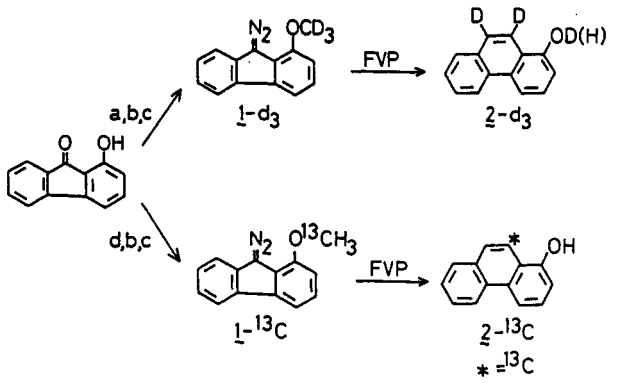
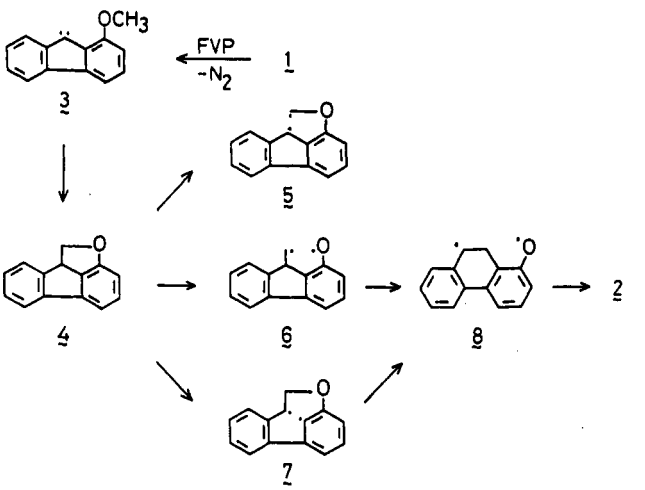
Scheme I[a]



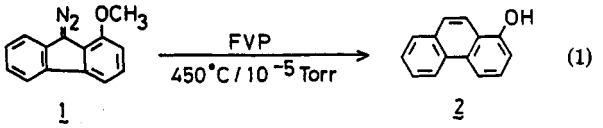
[a] (a) CD_3I/K_2CO_3; (b) $N_2H_4 \cdot H_2O$; (c) MnO_2–SiO_2; (d) $^{13}CH_3I/K_2CO_3$.

Scheme II



therefore have attracted much attention from synthetic chemists because they permit the straightforward synthesis of many useful organic compounds that are not readily obtained from reactions in solution. Such rearrangements have also strongly attracted mechanistic organic chemists because it is not easy to find straightforward paths between reactants and products. We wish to report here an unusual example of the perplexing rearrangements of arylcarbenes in the gas phase.

Flash vacuum pyrolysis (450 °C/10^{-5} Torr) of 1-methoxy-9-diazofluorene (1) afforded 1-phenanthrenol (2, 42%) along with a small amount of 9-methoxyfluorene (eq 1).



(1)

The identity of 2 was easily established by comparing its spectra (^1H and ^{13}C NMR, IR, and MS) with those of an authentic specimen prepared by a literature method.[2]

That 2 was formed by the FVP of 1 was initially surprising. The formation of 2 must have involved the rearrangement of 1-methoxyfluorenylidene (3). To elucidate the mechanism of this rather puzzling rearrangement, experiments with ^2H- and ^{13}C-labeled 1 were performed. The results shed light at least on the source of the atoms at C_9 and C_{10} of the newly constructed aromatic ring of 2. Thus, 1-(methoxy-d_3)-9-diazofluorene (1-d_3) was prepared as summarized in Scheme I and was then subjected to FVP. ^1H NMR analysis of the product, 2-d_3[4], showed that the two doublets at 7.75 and 8.17 ppm in the spectrum of undeuterated 2, which were assignable to H_9 and H_{10} protons, respectively, were not present in the spectrum of 2-d_3 and that the intensity of the signal due to the hydroxy proton was greatly reduced. The patterns of the other signals were essentially unchanged. A comparison of the intensities of the pertinent signals in the spectra of 2 and 2-d_3 showed that the deuterium atoms had been preferentially (>97%) incorporated at C_9 and C_{10} and in the phenolic hydroxyl group without loss of deuterium. FVP of [*methoxy*-^{13}C]-1-methoxy-9-diazofluorene (1-^{13}C)[5] produced 2-^{13}C.[6] Therein, the ^{13}C label was located exclusively at C_{10}, judging from the large ^{13}C–H coupling constant of the H_{10} signals observed in the ^1H NMR spectrum. The ^{13}C NMR spectrum showed exclusive enhancement (>97%) of the peak at 119.9 ppm due to C_9. A comparison of the intensities of the pertinent signals in the spectra of 2 and 2-^{13}C showed that >97% of the ^{13}C label was located at C_{10}. These labeling experiments clearly showed that the source of C_{10} of 2 is the methoxy carbon of 1, whereas the likely source of C_9 of 2 is the diazo-substituted carbon of 1 and that the two hydrogen atoms at C_9 and C_{10} of 2 are contributed by the methoxy group of 1.

A mechanism that explains the available facts is summarized in Scheme II. Thus, pyrolysis of 1 must generate fluorenylidene 3. Most arylcarbenes generated in the gas phase that cannot readily rearrange by, e.g., a hydrogen or alkyl group shift usually undergo carbene to carbene rearrangement. Such rearrangements have not been observed for fluorenylidenes. This is partly because ring strain would be developed by the movement required in relocating the carbene center located in benzocyclopentano bridge. Thus, fluorenylidene 3 is forced to insert into a C–H bond of the 1-methoxy group, to give oxacyclopenta[*jk*]fluorene (4), which is also presumed to be a

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(2) Mosetting, E.; Duvall, M. *J. Am. Chem. Soc.* **1937**, *59*, 367. ^1H NMR (100 MHz, $CDCl_3$) δ 5.34 (s, 1 H, OH), 6.95 (d, J = 8.0 Hz, 1 H), 7.43 (d, J = 8.0 Hz, 1 H), 7.55–7.68 (m, 2 H), 7.75 (d, J = 8.0 Hz, 1 H, H_9), 7.85–7.94 (m, 2 H), 8.17 (d, J = 8.0 Hz, 1 H, H_{10}), 8.29 (d, J = 8.0 Hz, 1 H), 8.56–8.07 (m, 2 H); ^{13}C NMR (22.6 MHz, $CDCl_3$) δ (rel intensity) 110.5 (0.68), 114.7 (0.47), 120.4 (0.68), 123.1 (0.68), 125.8 (0.86), 126.4 (1.00), 126.5 (0.74), 126.6 (0.74), 128.5 (0.59), 130.2 (0.21), 131.9 (0.12), 132.3 (0.27), 152.8 (0.21); MS *m/e* 194 (100, M^+), 165 (91.8), 77 (30.3).

(3) ^1H NMR (100 MHz, $CDCl_3$) δ 6.87 (d, J = 8.0 Hz, 1 H), 7.26–7.58 (m, 4 H), 7.64 (d, J = 8.0 Hz, 1 H) 7.90–8.08 (m, 1 H); IR (KBr) 2065 cm^{-1}.

(4) ^1H NMR (100 MHz, $CDCl_3$) δ 5.26 (s, <0.5 H), 6.88 (d, J = 8.0 Hz, 1 H), 7.35 (d, J = 8.0 Hz, 1 H), 7.42–7.60 (m, 2 H), 7.75–7.85 (m, 1 H), 8.18 (d, J = 8.0 Hz, 1 H), 8.50–8.59 (m, 1 H); MS *m/e* 196 (100, M^+), 167 (90.1), 78 (31.3).

(5) ^1H NMR (100 MHz, $CDCl_3$) δ 3.87 (d, $J_{^{13}C-H}$ = 142 Hz, 3 H), 6.64 (d, J = 8.0 Hz, 1 H), 6.97–7.30 (m, 4 H), 7.39 (d, J = 8.0 Hz, 1 H), 7.68–7.81 (m, 1 H); IR (KBr) 2050 cm^{-1}.

(6) ^1H NMR (100 MHz, $CDCl_3$) δ 5.42 (s, 1 H), 6.88 (d, J = 8.0 Hz, 1 H), 7.26 (d, J = 8.0 Hz, 1 H), 7.45–7.61 (m, 2 H), 7.67 (d, J = 8.0 Hz, 1 H), 7.75–7.86 (m, 1 H), 8.11 (d, $J_{^{13}C-H}$ = 144 Hz, 1 H), 8.19 (d, J = 8.0 Hz, 1 H), 8.50–8.67 (m, 1 H); ^{13}C NMR (22.6 MHz, $CDCl_3$) δ (rel intensity) 110.7 (0.38), 115.3 (0.38), 119.9 (58.2), 123.1 (0.44), 126.5 (0.81), 126.7 (1.00), 127.8 (0.25), 128.4 (0.38), 28.7 (0.38), 131.0 (0.06), 132.2 (0.13), 151.9 (0.13); MS *m/e* 195 (100, M^+), 165 (93.0), 78 (32.0).

strained ring compound. 1,2-Dihydrocyclopenta[*jk*]-fluorene, a carbon analogue of **4**, has, for example, been shown[7] to possess a "bent" benzene ring. On the other hand, that no trace of **4** was detected when **3** was generated either photolytically or thermally in solution at much lower temperatures suggests that high energy is required for **4** to be formed. Thus, **4** would be expected to undergo bond cleavage at the pyrolysis temperature. If the respective bond strengths, ring strains, and stabilities of the biradicals that would be formed by bond cleavage are taken into account, then there are three possible bonds, i.e., a, b, and c, which may be cleaved upon thermolysis. Breaking bond a would be favored because the doubly stabilized biradical **5** would be formed. Unfortunately, however, one cannot easily draw a reasonable pathway leading from **5** to the observed product. Hence, breaking bond a seems unproductive. Cleavage of bond b, on the other hand, would produce diradical **6**, which could isomerize to **8** by way of a somewhat unusual 1,2-phenyl shift. 1,2-Shifts of aryl groups in free radicals are not unprecedented.[8] Moreover, the isomerization of **6** to **8** would be favored because a more stable biradical would be formed. Biradical **8** could then rearrange to the stable aromatic compound **2** by way of a 1,4-hydrogen shift. Cleavage of bond c would also release ring strain in **4** and form biradical **7**. This species could undergo a 1,3 O → C shift of the bridging methylene chain to yield biradical **8**. Although the pathway triggered by the cleavage of bond b seems most reasonable, more detailed studies, which would include theoretical calculations, are required.

One would expect **4** not to be unduly unstable because its carbon analogue has been isolated.[7] All attempts to isolate, or even to detect, **4** were, however, unsuccessful. The apparent instability of **4** can be explained, at least in part, in terms of chemical activation.[9] Because a high energy of activation is required to form **3** and also because the subsequent insertion of the carbene into the C–H bond of the methoxy group is highly exothermic, a highly reactive **4** is produced, one that is much more energetic than the pyrolysis temperature would indicate. Therefore, **4** fragments as soon as it forms.

Reports of the gas-phase rearrangements of carbenes have been heavily weighted with those that deal with substituted phenylcarbenes and diphenylcarbenes, probably because such species undergo repeated carbene to carbene rearrangement until they are trapped by a proximate reactive center to yield stable products that are often synthetically useful. In marked contrast, almost no reports of the gas-phase reactions of fluorenylidene systems have appeared because such species obviously infrequently undergo similar rearrangements and, therefore, are not expected to give any useful products. The reaction described here is the first example of a gas-phase reaction of fluorenylidene that produces a significant product in fairly good yield in "one-pot" fashion. The reaction is driven by the relief of ring strain in the initially formed product **4**, which is the result of an interaction of the carbene center and the substituent at the 1-position. The reaction, therefore, should be applicable to other 1-substituted fluorenylidenes. Investigations of such a possibility are in progress in this laboratory.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan.

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tert-Butyloxycarbonyl and Benzyloxycarbonyl Amino Acid Fluorides. New, Stable Rapid-Acting Acylating Agents for Peptide Synthesis

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Summary: A new class of rapid-acting acylating agents, α-BOC and Z amino acid fluorides are obtained as stable, often crystalline, compounds by treatment of the protected amino acid with cyanuric fluoride.

Recently the synthesis of stable FMOC amino acid fluorides substituted in the side chain with *tert*-butyloxycarbonyl (BOC) and other acid-sensitive *tert*-butyl-bearing protecting groups was described.[1] Generally the corresponding acid *chlorides* bearing such side chains were either too sensitive to be obtained or were subject to facile degradation on storage. Similarly, α-BOC-protected amino acid chlorides are not accessible except in situ at very low temperatures.[2] Long-term storage is not practical. The corresponding benzyloxycarbonyl (Z) derivatives are more stable and were in fact synthesized and used by Bergmann and Zervas[3] during the early days of rational peptide synthesis following the classic discovery of the Z function. Unfortunately even these chlorides proved not to be generally storable, undergoing both hydrolysis and conversion to the corresponding Leuch's anhydrides[4] and mainly for that reason rapidly went out of fashion. Very recently new in situ methods for the preparation of Z amino acid chlorides have been described.[5] At least partly in response to the problems encountered by early investigators in the

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