C, 72.93; H, 6.80. Found: C, 73.01; H, 6.85.

9,10-Dihydro-9,10-epoxy-9-methoxyanthracene (14). An ice-cooled solution of **13** (300 mg, 1.01 mmol) in 10 mL of THF was treated with 1.1 mmol of TBAF (1.1 mL of 1.0 M in THF). After being stirred for 10 h, the solution was taken up in 100 mL of ether, washed several times with brine, dried, and rotary evaporated to give a quantitative yield of crude but essentially pure **14**, as an oil: ^{1}H NMR δ 3.80 (s, 3 H), 5.97 (s, 1 H), and 6.9–7.4 ppm (m, 8 H); MS calcd for $C_{15}H_{12}O_2$ 224.0837, found 224.0844. No effort was made to purify this product further, because it and related materials (including **13**) were found to be susceptible to air oxidation to anthraquinone.

9,10-Dihydro-9,10-epoxy-9-ethoxy-10-(trimethylsilyl)-anthracene (16). To an ice-bath-cooled solution of 380 mg (1.83 mmol) of **15** and 30 μL (0.21 mmol) of diisopropylamine in 10 mL of THF was added 3.2 mL (4.75 mmol) of *n*-butyllithium in hexane. After 1 h, direct examination of the dark reaction mixture by NMR indicated that all of the **15** had been consumed. A solution of Me_3SiCl (630 μL, 5 mmol) in 3 mL of THF was added dropwise, followed by bromobenzene (0.65 mL, 6.2 mmol) and LTMP (3.1 mmol). The ice bath was removed, and the mixture was stirred for 14 h at room temperature. Workup and chromatographic isolation as described for **13** gave 505 mg (89%) of **16** as an oil: ^{1}H NMR δ 0.39 (s, 9 H), 1.42 (t, 3 H, J = 7 Hz), 4.07 (q, 2 H, J = 7 Hz), and 6.9–7.3 ppm (m, 8 H); MS (chemically induced, methane flow gas) calcd for $C_{19}H_{22}O_2Si$ 310.1388, found 310.1389. In a repetition of this experiment **16** was obtained as a solid, mp 104–106 °C. Anal. Calcd: C, 73.50; H, 7.14. Found: C, 73.84; H, 7.21.

9,10-Dihydro-9,10-epoxy-9-ethoxyanthracene (17). A mixture of 500 mg of **16** (1.6 mmol) and 1.7 mmol of TBAF in 10 mL of THF at 0 °C was stirred for 12 h. Workup as before gave 380 mg (ca. 100%) of essentially pure **17** (oil): ^{1}H NMR δ 1.45 (t, 3 H, J = 7 Hz), 4.10 (q, 2 H, J = 7 Hz), 5.95 (s, 1 H), and 6.9–7.4 ppm (m, 5 H); MS calcd for $C_{16}H_{14}O_2$ 238.0994, found 238.0988.

An attempt to chromatograph this product on silica gel with ether/hexanes (1/5) containing 1% triethylamine caused decomposition, with the slow elution of a yellow solid which proved (mp, NMR, MS) to be anthraquinone. The exact mechanism for this oxidation is not known. Other samples of **16** and **17**, on standing exposed to air, have also been observed to oxidize.

4,9-Epoxy-4-methoxy-2-methyl-3a,4,9,9a-tetrahydro-9-(trimethylsilyl)-1*H*-benz[*f*]isoindole-1,3(2*H*)-dione (18). To an ice-bath-cooled mixture of 1 (380 mg, 2.1 mmol) and Me_3SiCl (1.8 mL, 13.8 mmol) in 13 mL of ether was added 8.3 mmol of LTMP (prepared by addition of *n*-butyllithium in hexane to the amine in 5 mL of ether, with ice bath cooling). The mixture was stirred for 3 h and then 2.0 mL of *tert*-butyl alcohol was added, followed after 0.5 h by *N*-methylmaleimide (300 mg, 2.6 mmol), with stirring continued overnight. The volatiles were removed by rotary evaporation; the residue was taken up in CH_2Cl_2 (150 mL) and washed with 5% aqueous sodium bicarbonate solution (3 × 20 mL). After drying (K_2CO_3) and evaporation, the residue was chromatographed on 40 g of silica gel using ether/hexanes (1/3) with 1% triethylamine. An early fraction (35 mg) contained (by NMR) essentially pure **1c** contaminated by **18**. Subsequent fractions afforded 483 mg (70%) of crystalline **18**: mp 131–132 °C; ^{1}H NMR δ 0.36 (s, 9 H), 2.24 (s, 3 H), 3.53 (d, 1 H, J = 8 Hz, methine proton adjacent to methoxy), 3.68 (s, 3 H), 3.74 (d, 1 H, J = 8 Hz, methine adjacent to trimethylsilyl group), and 7.1–7.3 ppm (m, 4 H); MS calcd for $C_{17}H_{21}NO_4Si$ 331.1239, found 331.1225. Anal. Calcd: C, 61.61; H, 6.39. Found: C, 61.71; H, 6.33.

4,9-Epoxy-4-methoxy-2-methyl-3a,4,9,9a-tetrahydro-1*H*-benz[*f*]isoindole-1,3(2*H*)-dione (19). A sample of **18** (158 mg, 0.47 mmol) in 5 mL of THF at 0 °C was treated with 0.52 mmol of TBAF. The reaction was complete (TLC) within 0.5 h. Excess ether was added and the organic phase was washed several times with brine, then dried over K_2CO_3, and rotary evaporated to give 119 mg (95%) of nearly pure **19**. Recrystallization from hexane/CH_2Cl_2 gave pure **19**: mp 115–116 °C; ^{1}H NMR δ 2.27 (s, 3 H), 3.57 (d, 1 H, J = 8 Hz), 3.70 (s, 3 H), 3.92 (dd, 1 H, J = 8 and 6 Hz), 5.57 (d, 1 H, J = 6 Hz), and 7.2 ppm (br s, 4 H); MS calcd for $C_{14}H_{13}NO_4$ 259.0844, found 259.0848.

The evidence that this is the endo isomer rests on the bridgehead proton signal at 5.57 ppm appearing as a doublet. A small amount of the exo isomer may have been present in the crude product, but the Diels–Alder reaction to form **18** appears to be >95% endo selective.

Acknowledgment. We thank John Gregson for his early work on the preparation and characterization of **1**, Dan Pollart for carrying out a preparation of **16**, Dr. Hugh Webb for obtaining MS data, and Curt Breneman for his indispensible assistance with NOE experiments. Acknowledgment is made to the donors of Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

Regioselectivity of Alkoxyisobenzofuran–Aryne Cycloadditions

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The cycloaddition reactions of some unsymmetrical arynes with 1-ethoxy-3-(trimethylsilyl)isobenzofuran and a naphtho[1,2-*c*]furan analogue were examined for prospective regioselectivity. The arynes, generated by lithium tetramethylpiperidide induced dehydrohalogenation of the appropriate haloaromatics, were 3-bromo-, 3-chloro-, 3-methoxy-, and 3-methylbenzyne, 3,4-pyridyne, and 1,2-naphthalyne. Regioselectivities ranged from nil (50/50 isomer ratio with 3,4-pyridyne) to modest (ca. 80/20). The products are bridgehead trimethylsilylated ketals, which undergo a novel acid-catalyzed rearrangement to 9-alkoxy-10-[(trimethylsilyl)oxy]anthracenes. These position-differentiated anthracenediol analogues are thought to be formed by ring opening, followed by Brook rearrangement. Isomeric ketal pairs were found to react at different rates, and this selective decomposition was used to isolate one of the cycloadduct isomers from the reaction of 3-bromobenzyne. Lithium–bromine exchange followed by methylation was used to determine its structure, and this information in turn was used to clarify the mechanism of the acid-catalyzed reaction.

The question of selectivity in Diels–Alder reactions of substituted benzynes (arynes) has evoked interest since shortly after the recognition of these reactive intermediates. Various schemes have been employed to explore this matter. For example, the identical ratio of A ring/B ring cycloadducts produced when 1,4-dimethoxyanthracene was treated with benzyne generated in six different ways was used to argue that all six methods gave the same inter-

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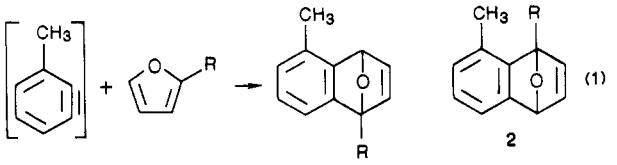
mediate species.[1] In related work, it was shown that the A ring/B ring ratio is sensitive to the substituents present on the anthracene (i.e., benzyne exhibits site selectivity in response to these substituents), and this is also reflected in relative rates as determined by competition kinetics experiments.[2] Similarly, Newman and Kannan queried the role of the precursor in the reaction of 3-methylbenzyne with 2-substituted furans (eq 1). This work also led to

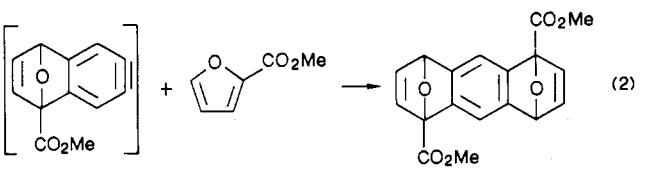


(1)

1 2

the conclusion that the same reactive intermediate was formed regardless of precursor employed.[4] These cycloadditions displayed modest regioselectivity, with product **1** favored over **2**; interestingly, the ratio of **1**/**2** was nearly independent of the substituent R (R = Me, 58/42; *t*-Bu, 63/37; $CH(OCH_2)_2$, 61/39; and CO_2Me, 57/43). While it is difficult to escape the conclusion[4] that these reactions are insensitive to both polar and steric effects, it remains unclear why this insensitivity does not lead to 50/50 product ratios.

Recently Hart and Ok have described reactions involving a 1,4-benzadiyne equivalent, which gave cycloadducts with exclusive or very high regioselectivity.[5] These reactions are thought to occur in a stepwise manner, i.e., formation of first one aryne site, cycloaddition, and the generation of the second aryne site, with the selectivity determined in the final cycloaddition as shown in the example displayed as eq 2. The product **3** was isolated as a single

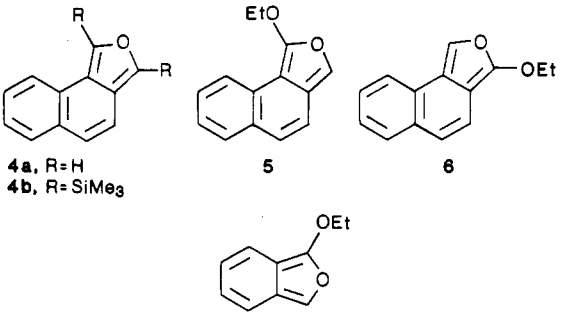


(2)

3

stereo- and regioisomer, with the regiochemistry demonstrated to be that depicted.[5] This result is of special interest since it arises with one of the furans used in Newman's study.[4] Analogous high selectivity was found in Hart and Ok's work for the cycloaddition of 3-bromofuran. In this instance the bromo substituent is even more remote from the centers involved in determining regiochemistry in the product (which is the 2,6-dibromoanthracene derivative).[5] The aryne was generated by $Pb(OAc)_4$ oxidation of the aminobenzotriazole function, one of the general methods which Klanderman and Criswell[1] found to give "normal" benzyne, i.e., there is no a priori reason to expect unusual memory effects in this procedure. From these limited examples, it appears that the regioselectivity of cycloaddition may be strongly dependent on the aryne structure and relatively insensitive to the structure of the diene (furan) partner.

Aside from purely mechanistic interest, there is potential synthetic utility in understanding the factors which control the regioselectivity of aryne cycloadditions. Our interest in this question arose when examining the Diels–Alder reactions of naphtho[1,2-*c*]furan (**4a**) with unsymmetrical dienophiles (e.g., 2-butenolide). These reactions were



4a, R = H
4b, R = $SiMe_3$

5 6

7

devoid of regioselectivity under both kinetically controlled and equilibrium conditions,[6] a rare example of such behavior for a distinctly unsymmetrical system. In contrast, the alkoxy derivatives **5** and **6** gave only one regioisomer each with these unsymmetrical dienophiles,[6] with the products having the structures anticipated from model Diels–Alder reactions of 1-alkoxybutadienes, and earlier work with the simpler analogue **7**.[7]

If the acidic sites of isobenzofurans are masked by trimethylsilylation, the resulting materials are useful for aryne cycloadditions in which the reactive intermediate may be generated by strong base (lithium tetramethylpiperidide, LTMP) induced dehydrohalogenation of the appropriate haloaromatic. This methodology provides a simple and direct entry to various polycyclic aromatic hydrocarbon derivatives.[8] It would clearly be of value to be able to control the regiochemistry of such cycloadditions, in order to synthesize specifically substituted analogues. However, the reactions of bis(trimethylsilyl) derivative **4b** with three unsymmetrical arynes (4-methylbenzyne, 3,4-pyridyne, and 1,2-naphthalyne) are also completely devoid of regioselectivity.[9]

Since the nonselective behavior of **4b** with arynes mirrored that of **4a** with more common dienophiles which are known to give regioselective Diels–Alder reactions with many dienes, we concluded that the benzannulation of isobenzofuran simply does not perturb the system sufficiently to induce regioselectivity. It was clear that diene substrates which exhibited regioselectivity were needed to test for any inherent property of arynes to react with measurable selectivity. Analogues of **5**–**7** appeared to meet this need. Recent improvement in methods for the iso-

(1) Klanderman, B. H.; Criswell, T. R. *J. Am. Chem. Soc.* **1969**, *91*, 510. The methods of benzyne generation included diazotization of anthranilic acid, Mg-induced dehalogenation of *o*-bromofluorobenzene, and $Pb(OAc)_4$ oxidation of 1-aminobenzotriazole. See also: Huisgen, R.; Knorr, R. *Tetrahedron Lett.* **1963**, 1017.

(2) Klanderman, B. H.; Criswell, T. R. *J. Org. Chem.* **1969**, *34*, 3426. The k_{rel} values spanned a range of slightly over 10^2, with 9,10-dicyanoanthracene the slowest, and 9,10-dimethylanthracene the most reactive system examined. The relative rates of substituted anthracenes with maleic anhydride as the dienophile[3] cover a much broader range (>10^4). While there is an approximate correlation between substituent and reactivity for the two cycloadditions, there are some interesting exceptions. For example, 9,10-dimethoxyanthracene is ca. 3 times more reactive than anthracene with benzyne, whereas the ratio is inverted for the reaction with maleic anhydride.[3]

(3) Mielert, A.; Braig, C.; Sauer, J.; Martelli, J.; Sustmann, R. *Liebigs Ann. Chem.* **1980**, 954.

(4) Newman, M. S.; Kannan, R. *J. Org. Chem.* **1976**, *41*, 3356. The 3-methylbenzyne was formed by diazotization of the two methyl-substituted anthranilic acids and by dehalogenation of the two isomeric bromofluorotoluenes.

(5) Hart, H.; Ok, D. *J. Org. Chem.* **1986**, *51*, 979.

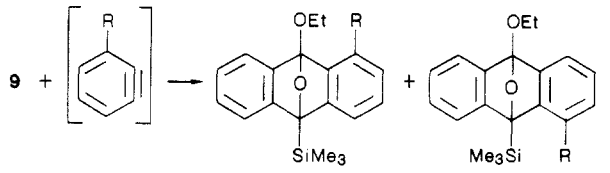
(6) Cornejo, J.; Ghodsi, S.; Johnson, R. D.; Woodling, R.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 3869.

(7) Makhlouf, M. A.; Rickborn, B. *J. Org. Chem.* **1981**, *46*, 2734.

(8) (a) Crump, S. L.; Netka, J.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 2746. (b) Netka, J.; Crump, S. L.; Rickborn, B. *Ibid.* **1986**, *51*, 1189. (c) Camenzind, R.; Rickborn, B. *Ibid.* **1986**, *51*, 1914.

(9) Pollart, D. J.; Rickborn, B. *J. Org. Chem.* **1986**, *51*, 3155.

Table I. Regioselectivity of 3-Substituted Benzyne Reactions with 9



13 14

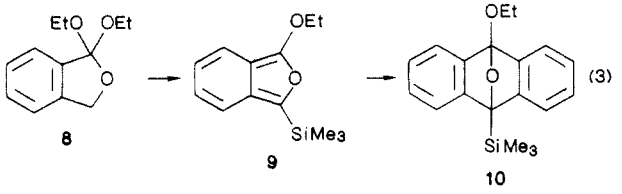
R =	ratio[a] 13:14	yield (%)[b]
CH_3 (a)	60:40	74
Cl (b)	53:47	74
Br (c)	63:37	62
OCH_3 (d)	80:20	52[c]

[a] The ratio was determined by NMR at the crude product stage, to avoid possible selective losses on chromatography. [b] The yields are of nearly pure (by NMR) material obtained by rapid chromatography and vacuum evaporation of volatiles. [c] This yield is after chromatography and crystallization of the individual isomers, which were obtained in 43% and 9%, respectively.

lation of 1-alkoxyisobenzofurans (in solution)[10] and conversion to 3-trimethylsilylated derivatives[11] were used to prepare substrates suitable for LTMP-induced aryne-forming conditions. The initial attempt to utilize this approach did indeed give a modestly regioselective reaction[9] and encouraged the further study reported here.

Results and Discussion

(a) Reactions of the Trimethylsilylated Ketal. The ortho ester **8** was treated with *n*-butyllithium and a catalytic amount of $LiNR_2$ to generate 1-ethoxy-3-lithioisobenzofuran, which was in turn treated with Me_3SiCl to form 1-ethoxy-3-(trimethylsilyl)isobenzofuran (**9**). No attempt was made to isolate these hydrolytically very unstable ketene acetals. The solution containing **9** was treated with chlorobenzene and LTMP and stirred for several hours at room temperature. This procedure gave the benzyne derivative **10** in excellent yield.[11] Similar procedures were used for analogues of **9** and the other arynes examined in this study.

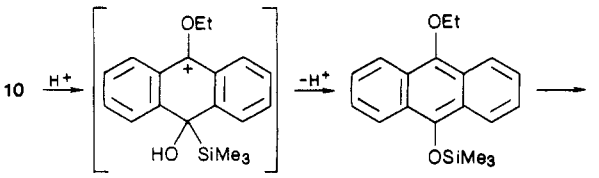


8 9 10

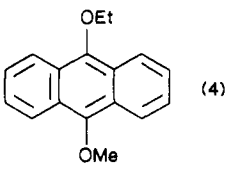
Although it was possible to isolate pure **10** by careful chromatography on deactivated alumina, in general such silylated ketals proved very susceptible to decomposition and/or oxidation. They are very acid-sensitive, and even NMR solvents caused slow reaction. It was possible to effect protiodesilylation with degassed tetrabutylammonium fluoride (TBAF) solutions as described previously,[11] but quinone formation was a commonly observed complication, and the resulting ketals were also generally too sensitive to purify by chromatography. These materials have in most instances been characterized only by spectroscopic means and further reactions described below.

Reduction of **10** with Zn dust in refluxing AcOH[8c,9] gave anthracene contaminated by ca. 15% of 9,10-dihydroanthracene (identified by NMR) in overall quantitative yield.

An interesting reaction of **10** was discovered while attempting to identify the product(s) of the decomposition observed in NMR samples on standing. Treatment of purified **10** with a *catalytic* (ca. 1%) amount of trifluoroacetic acid (TFA) caused a rapid reaction. The NMR spectrum (which was the same for samples formed directly in NMR tubes or after vacuum removal of volatiles) showed that the product retained both the trimethylsilyl and ethoxy groups, with all other proton absorptions found as part of two equal area multiplets in the aromatic region. The MS of a freshly prepared sample indicated that it is an isomer of **10**. We believe this rather unstable (readily oxidized to anthraquinone on standing)[12] material has the structure **11**, formed by initial acid-catalyzed cleavage at the ketal center, followed by a facile Brook rearrangement as suggested in eq 4.



11



(4)

12

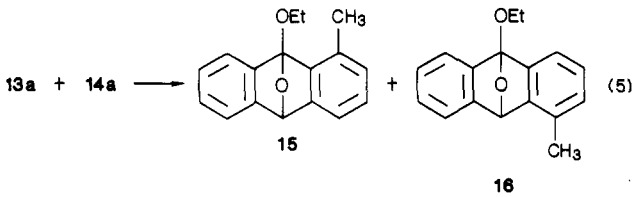
The differentiated reactivity of the two functional groups in this dihydroxyanthracene derivative may have synthetic value. While we have not attempted to exploit this feature, it was found that treatment of **11** with K_2CO_3 in acetone containing dimethyl sulfate effected the formation of 9-ethoxy-10-methoxyanthracene (**12**). In order to prepare a known derivative as further structural evidence, this procedure was repeated with the *O*-methyl analogue of **10**.[11] The expected 9,10-dimethoxyanthracene was isolated from this sequence.

Several attempts were made to form the triptycene derivative of **11** by cycloaddition with benzyne (generated by the LTMP method or by *n*-butyllithium treatment of *o*-dibromobenzene); these were uniformly unsuccessful, for reasons not understood at this time (9,10-dimethoxyanthracene is reported to be more reactive than anthracene itself in Diels–Alder reactions with benzyne).[2]

(b) Regioselectivity of Aryne Cycloadditions. The reactions of **9** with four 3-substituted benzynes (3-Me, OMe, Cl, and Br) exhibited regioselectivity ranging from barely perceptible (Cl) to modest (OMe). The results are displayed in Table I. For all of these arynes the major cycloadduct formed has structure **13**, with the aryne substituent proximal to the OEt group, determined as outlined below.

Protiodesilylation of the 3-methylbenzyne adducts (**13a** + **14a**) by treatment with TBAF in N_2-purged THF gave (**15** + **16**), in quantitative crude yield and unchanged ratio as judged by integration of the methyl peaks at 2.41 (major) and 2.32 ppm, and the bridgehead proton signals at 6.01 and 5.90 ppm (major). Presaturation of the 2.41

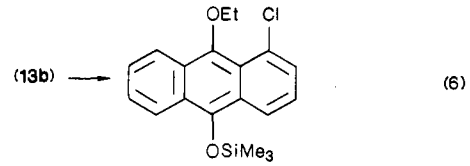
(10) Mir-Mohamad-Sadeghy, B.; Rickborn, B. *J. Org. Chem.* **1984**, *49*, 1477.
(11) Mirsadeghi, S.; Rickborn, B. *J. Org. Chem.*, previous paper in this issue.
(12) Although not necessarily related to the oxidation of **11**, bis(trimethylsilyl) ethers of hydroquinones have been shown to be easily oxidized electrochemically in anhydrous solvents.[13]
(13) Stewart, R. F.; Miller, L. L. *J. Am. Chem. Soc.* **1980**, *102*, 4999.



15 16

ppm methyl signal caused no enhancement of either bridgehead proton absorption. Presaturation of the (minor) 2.32 ppm methyl group, however, caused an 11% NOE of the (minor) bridgehead signal at 6.01 ppm, establishing the structure **16** for the minor isomer.

The reaction of 3-chlorobenzyne (LTMP and *o*-dichlorobenzene) with **9** exhibited negligible regioselectivity. As judged by integration of the Me_3Si peaks in the crude product, the isomers were formed in a ratio of 53/47 (signals at 0.39 and 0.43 ppm, respectively). A feature of potential synthetic value was found when this product mixture was treated with TFA. The reaction was much slower than that of similar materials lacking halogen (e.g., **10**) and exhibited substantial isomer selectivity. An NMR tube experiment with ca. 0.05 equiv of TFA indicated that after 4 days the 0.39 ppm peak had disappeared and had been replaced by another singlet of nearly equal area at 0.32 ppm. We believe the latter is due to **17**, formed by selective rearrangement of **13b** (eq 6). The effect of the



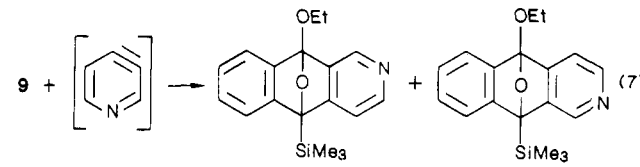
17

halo substituent is reminiscent of that observed in the TFA-induced reactions of the bis(trimethylsilyl)-9,10-epoxyanthracenes studied previously,[8b,c] i.e., overall rate diminution with very selective cleavage at the position proximal to the (peri) halogen. This behavior is assumed to be caused by the same factors which lead to rate depression coupled with ortho, para directing effects in electrophilic substitution reactions of haloaromatics.

The reaction of 3-bromobenzyne (from *o*-dibromobenzene) with **9** gave two cycloadducts in a ratio of 63/37 (integration of Me_3Si in ^1H NMR). Several attempts were made to ascertain the major/minor isomer structures (i.e., **13c** or **14c**) by lithium-bromine exchange (MeLi) followed by methylation (MeI), to give **13a** + **14a**. The results were inconclusive because a nearly 50/50 mixture of the methylated species was formed in each instance, in modest overall yield. The mixture of **13c**/**14c** was therefore subjected to TFA, in the expectation that **13c** would be the more reactive isomer. The major component was consumed faster, allowing the isolation of the minor isomer by chromatography. This material was subjected to the Li–Br exchange, methylation procedure. Only **14a** (of the two methylated isomers) was formed. Since **14a** can arise only from **14c**, this establishes that **14c** is the minor, and **13c** the major isomer of the reaction with 3-bromobenzyne. It also proves that **13c** is the more reactive isomer with TFA, and by analogy reinforces the structural conclusions drawn in the 3-chlorobenzyne reaction.

The reaction of **9** with 3-methoxybenzyne was the most selective of the series, leading to an 80/20 ratio of the products **13d**/**14d**. Alone of all the product mixtures examined in this work, these isomers were easily separated by column chromatography and a pure sample of each was obtained. An attempt to identify isomer structure by protiodesilylation followed by difference NOE spectroscopy was unsuccessful; neither isomer showed a measurable NOE between the methoxy and bridgehead proton (although a large NOE of the aromatic proton ortho to the methoxy group was seen for both **13d** and **14d**). The structural assignments in this instance rest on the kinetic argument that, for the same reasons as in the halo substituted materials, **13d** should be more reactive to acid than **14d**. Treatment of a ca. 1/1 mixture of the two with a catalytic amount of TFA caused the more rapid loss of the "major" isomer, which was thus assigned structure **13d**. As additional evidence of gross structure, it was shown that both isomers on exposure to acid and air were converted to known 1-methoxy-9,10-anthraquinone.

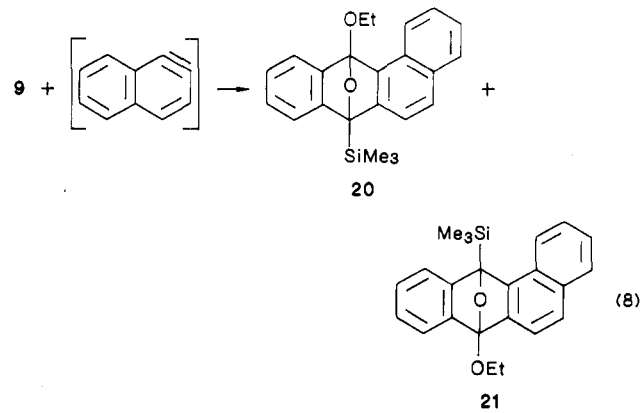
Treatment of 3-bromopyridine with LTMP forms 3,4-pyridyne, which with **9** gave the two cycloadducts **18** + **19** in equal amounts (50 ± 2%), as judged by integration of



18 19

the Me_3Si absorptions and the singlets (small meta coupling) of the peri protons adjacent to nitrogen. Although the isolated yields in this instance were modest (typically 35% after chromatography), the ratio of products was the same in several runs, encouraging the view that this outcome accurately reflects the intrinsic lack of regioselective capability of this aryne. The nitrogen thus serves simply as a marker group in this reaction.

LTMP treatment of 1-bromonaphthalene was used to generate 1,2-naphthalyne; in the presence of **9** the cycloadducts **20** and **21** (eq 8) were formed, in a ratio of 63/37.

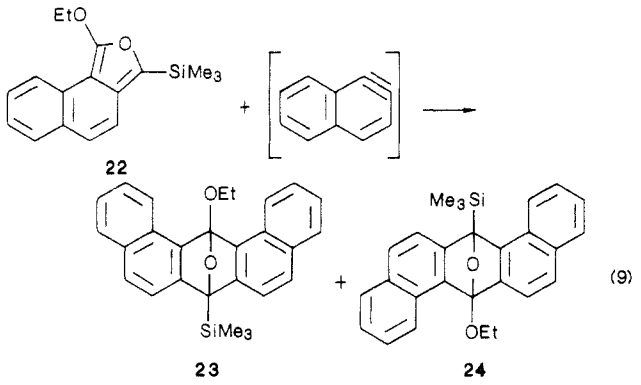


20 21

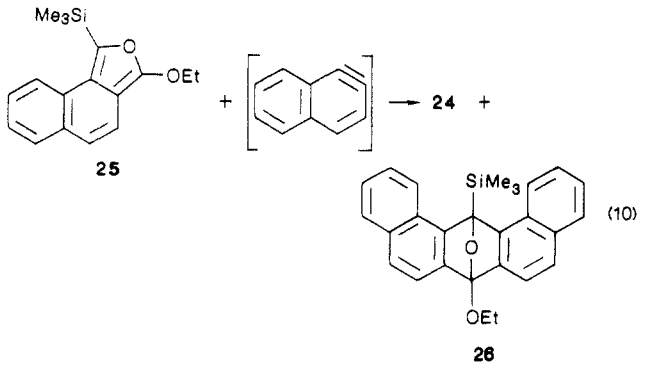
The assignment of structures was tentatively made on the basis of the chemical shifts of the Me_3Si groups, which appeared at 0.45 (major) and 0.50 ppm (minor). This assignment was reinforced by the spectrum of TBAF protiodesilylated material, which exhibited bridgehead proton signals at 6.09 (major) and 6.45 ppm (minor), in the same ratio (65/35) as the mixture of **20**/**21**.

The reaction which originally encouraged this study is shown in eq 9. The dibenz[*a*,*j*]anthracene derivative **23** was the major product of this cycloaddition, with the ratio of **23**/**24** = 66/34.[9] Note that this is essentially the same ratio as found for the reaction of 1,2-naphthalyne with **9** (eq 8), suggesting that the benzannulation of isobenzofuran has a negligible effect on the outcome (i.e., like the nitrogen in pyridyne, it serves only as a marker group or label).

The isomer of **22** in which the ethoxy and Me_3Si groups are transposed (**25**) was of special interest in this context. If it is assumed that (a) the (electronic, steric?) effect of



the ethoxy and Me_3Si groups exert the same influence in the reactions of **9**, **22**, and **25** and (b) the benzannulation has no effect on the outcome, then the ratio of **24**/**26** in eq 10 should be 66/34 (note the dibenz[*a*,*h*] isomer is



predicted to be the major product here, unlike the results of eq 9). The actual ratio of **24**/**26** that is formed is 74/26, which supports the view that these assumptions are approximately correct.

What are the factors which control the (modest) regioselectivities found in these reactions? Certain generalizations emerge. Regardless of the nature of the substituent on the aryne, all of the reactions examined gave as the major product the isomer in which the substituent is proximal to the ethoxy group of the IBF (and hence distal from the Me_3Si group). This holds for methyl, benzo-ring, halo, and methoxy substituents on the aryne, with no discernible order in terms of polar or steric effects.

The Me_3Si group imparts little regioselectivity (70/30 = ortho/meta) in the cycloaddition of α-acetoxyacrylonitrile with 1-(trimethylsilyl)isobenzofuran.[14] Similar and even lower levels of selectivity have been reported for 1-(trimethylsilyl)-1,3-butadiene and other unsymmetrical dienophiles.[15,16] The overall effect of this substituent appears to be rate depressing for the butadiene, and recently it has been shown[17] that 1,3-bis(trimethylsilyl)isobenzofuran is significantly slower than isobenzofuran itself in cycloaddition with *N*-methylmaleimide. While it is not clear that any of these observations need pertain to cycloadditions with arynes, to the extent that this extension holds, it appears that the net effect of the Me_3Si group counters that of OEt. It is still not possible to distribute credit between electronic and steric effects for either the overall regiochemistry or even the variations associated with the different aryne substituents. Rogers and Averill[18] have described triptycene-forming reactions between 1,8-disubstituted anthracenes and 3-substituted benzynes, in which the aryne substituent has a significant effect on the regiochemical outcome. For example, it was reported that 1,8-dichloroanthracene gave mainly syn product (s/a = ca. 3/1) with 3-methylbenzyne, while the anti product dominated (s/a = ca. 1/3) the reaction with 3-chlorobenzyne. The results were rationalized on the basis of an induced dipole perturbation of the dienophile (aryne) FMO. One might expect a parallel relative outcome in other cycloadditions of these same arynes, but our results stand in contrast to this expectation; both the 3-methyl- and 3-halobenzynes lead to the same dominant regiochemistry in the present study.

The cycloadditions described in this study involve very reactive partners, i.e., arynes are probably the most reactive dienophiles known, and isobenzofurans the most reactive *isolable* dienes. These factors imply a very low activation energy and an "early" transition state. It is significant that, in spite of these features, the reactions in most instances exhibit some selectivity.

Experimental Section

The ortho esters used in this work have been described previously.[6,10] Combustion analyses were performed by MicAnal, Tucson, AZ. ^1H NMR spectra were recorded at 300 MHz in $CDCl_3$ unless otherwise stated. Compound **10** and its analogue with OMe in place of OEt were prepared as described.[11] All reactions were carried out under an atmosphere of dry nitrogen. Within measurement accuracy, repeated reactions gave identical isomer ratios even when yields varied, indicating that the regiochemical outcome was not an artifact of selective decomposition.

9-Ethoxy-10-[(trimethylsilyl)oxy]anthracene (11). Treatment of 6.3 mg (0.0203 mmol) of **10** in 0.5 mL of $CDCl_3$ with 0.001 mmol of TFA gave, after 10 min at room temperature, complete reaction (NMR). Removal of the volatiles under vacuum andd reexamination showed the same material contaminated with ca. 5% of anthraquinone and other impurities. Samples of **11** and related materials which were allowed to stand exposed to the atmosphere were converted to quinones, as judged by NMR. A freshly prepared sample of **11** had MS calcd for $C_{19}H_{22}O_2Si$, 310.1389; found, 310.1399. ^1H NMR: 0.34 (s, 9 H), 1.62 (t, 3 H, J = 7 Hz), 4.25 (q, 2 H, J = 7 Hz), 7.39–7.49 (sym m, 4 H), and 8.18–8.28 ppm (sym m, 4 H).

9-Methoxy-10-[(trimethylsilyl)oxy]anthracene. Treatment of the analogue of **10** which contained OMe in place of OEt under similar conditions gave material with the following: ^1H NMR 0.34 (s, 9 H), 4.11 (s, 3 H), 7.39–7.52 (sym m, 4 H), and 8.18–8.30 ppm (sym m, 4 H); MS calcd for $C_{18}H_{20}O_2Si$ 296.1232, found 296.1210.

9-Ethoxy-10-methoxyanthracene (12). To a stirred solution of 70 mg (0.225 mmol) of **10** in 2 mL of benzene was added 1.5 μL (0.019 mmol) of TFA. After 20 min evaporation gave an orange oil with suspended yellow solid, which was taken up in 5 mL of reagent grade acetone, purged with a stream of N_2, and treated with 200 mg of K_2CO_3 followed by 43 μL (0.45 mmol) of dimethyl sulfate. After stirring for 24 h, the mixture was poured into a mixture of water and ether. The aqueous phase was extracted twice with CH_2Cl_2, and the combined organic layers were dried and evaporated to give 57 mg (100%) of nearly pure product. Chromatography on activity III alumina with 50:50 CH_2Cl_2/hexanes gave **12** with mp 124–125 °C. After recrystallization from isopropyl alcohol it had the following: mp 127.5–128.5 °C; ^1H NMR 1.63 (t, 3 H, J = 7 Hz), 4.12 (s, 3 H), 4.25 (q, 2 H, J = 7 Hz), 7.45–7.53 (m, 4 H), and 8.25–8.34 ppm (m, 4 H). Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.73; H, 6.42.

9,10-Dimethoxyanthracene. The procedure was repeated with 60 mg of 9,10-dihydro-9,10-epoxy-9-methoxy-10-(trimethylsilyl)anthracene (in place of **10**), and the dimethyl sulfate step reaction time was reduced to 1 h. Crude product was obtained in 85% yield (41 mg). Chromatography (as above, with 0.5% Et_3N

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(15) Fleming, I; Percival, A. *J. Chem. Soc., Chem. Commun.* **1976**, 681. It was estimated that 1-(trimethylsilyl)-1,3-butadiene was 5 to 100 times less reactive than butadiene, depending upon the dienophile.
(16) Jung, M. E.; Gaede, B. *Tetrahedron* **1979**, *35*, 621.
(17) Unpublished work of D. Tobia, UCSB. A competition kinetics experiment gave a lower limit on the ratio k(unsubst)/k(bis-silylated) ≥ 14.
(18) Rogers, M. E.; Averill, B. A. *J. Org. Chem.* **1986**, *51*, 3308.

added to the solvent) followed by recrystallization from ethanol gave pure 9,10-dimethoxyanthracene, mp 205–205.5 °C (lit.[19] mp 203 °C).

Reactions of Arynes with 1-Ethoxy-3-(trimethylsilyl)-isobenzofuran. The general procedure given next for the generation/reaction of 3-methylbenzyne was followed for other arynes; only modifications are noted. Unless otherwise indicated, attempts to obtain products of sufficient purity for combustion analysis led to decomposition.

1-Methyl- and 4-Methyl-9,10-dihydro-9,10-epoxy-9-ethoxy-10-(trimethylsilyl)anthracene (13a + 14a). To a stirred solution of **9** (prepared[11] from 1.027 mmol of the ortho ester **8**) in 6 mL of THF (ice bath) was added 0.407 mL (3.48 mmol) of *o*-chlorotoluene, followed by 1.74 mmol of LTMP (prepared in the usual way by addition of *n*-butyllithium to the amine in 3.5 mL of THF). The ice bath was removed and the mixture was stirred for 26 h. It was then poured into a mixture of 5% $NaHCO_3$ and ether; the layers were separated and the aqueous phase was extracted once with ether. The combined ether phase was washed with brine containing $NaHCO_3$, dried over K_2CO_3, and vacuum evaporated to give a dark oil. An NMR spectrum was taken at this stage for determination of product isomer ratio. The residue was chromatographed with 20 g of activity III neutral alumina, with 5% ether/hexanes (0.5% Et_3N), to afford 243 mg (74%) of product as a discolored oil: ^1H NMR 0.385 and 0.392 (s, trimethylsilyl groups, ratio in crude 58:42; ratio after chromatography 60:40), 2.35 and 2.40 (s, methyl groups, ratio 35:65), 1.42 (t, 3 H, J = 7 Hz), 3.89–4.13 (m, 2 H), and 6.70–7.34 ppm (m, 7 H); MS calcd for $C_{20}H_{24}O_2Si$ 324.1545, found 324.1547.

Protodesilylation. The general procedure given in detail for the reaction of **13a + 14a** with TBAF was followed for other protiodesilylations.

1-Methyl- and 4-Methyl-9,10-dihydro-9,10-epoxy-9-ethoxyanthracene (15 + 16). To a stirred solution of 103 mg (0.317 mmol) of **13a/14a** (ca. 60/40) in 5 mL of N_2-degassed THF (ice bath) was added 0.35 mL (0.35 mmol) of 1 M TBAF in THF. After 1 h the bath was removed and stirring was continued for 2 h at ambient temperature. Workup with aqueous bicarbonate and ether in the usual way gave 80 mg (100%) of products as an orange oil: ^1H NMR 1.435 and 1.437 (t, total 3 H), 2.32 and 2.41 (s, CH_3 groups, ratio ca. 30/70), 3.92–4.15 (m), 5.90 and 6.01 (s, bridgehead protons, ratio 68/32), and 6.76–7.36 ppm (m). The variations in ratios are indicative of error limits in measurement of NMR integrals; MS calcd for $C_{17}H_{16}O_2$ 252.1150, found 252.1140.

A difference NOE experiment gave the results described in the text, showing that **16** is the minor isomer formed in this reaction, and hence **14a** is the minor isomer formed in the aryne cycloaddition.

1-Chloro- and 4-Chloro-9,10-dihydro-9,10-epoxy-9-ethoxy-10-(trimethylsilyl)anthracene (13b + 14b). A solution of **9** (from 1.027 mmol of **8**) in 6 mL of THF (ice bath) was treated with 0.392 mL (3.48 mmol) of *o*-chlorotoluene, followed by 1.74 mmol of LTMP in 3 mL of THF. The mixture was stirred at room temperature for 22 h. The usual workup and chromatography on 40 g of alumina (3% ether/hexanes) gave 261 mg (74%) of essentially pure **13b + 14b** as a yellow oil: ^1H NMR 0.388 and 0.424 (s, 9 H total, the former constituting 53%), 1.42 and 1.45 (t, 3 H total, J = 7 Hz), 3.95–4.15 (m, 2 H), and 6.90–7.45 ppm (m, 7 H). The ratio of the two trimethylsilyl singlets was 55/45 in the crude, and 53/47 after chromatography.

1-Bromo- and 4-Bromo-9,10-dihydro-9,10-epoxy-9-ethoxy-10-(trimethylsilyl)anthracene (13c + 14c). On the same scale as the preceeding experiment, **9** was treated with *o*-dibromobenzene and LTMP for 22 h. Chromatography (20 g of silica gel, 2% ether/hexanes with 1% Et_3N) afforded 304 mg (76%) of a yellow oil, estimated by NMR to be ca. 90% pure: ^1H NMR 0.39 and 0.46 (s, Me_3Si groups, ratio 64/36), 1.43 (major) and 1.46 (t, 3 H total, J = 7 Hz), 4.00–4.12 (m, 2 H), 6.80–7.46 (m, 7 H).

Isolation, Lithium/Bromine Exchange, and Methylation of 14c To Form 14a. A solution of 125 mg of **13c + 14c** (from the preceding experiment) in 1.5 mL of $CDCl_3$ was treated with 5 μL (0.064 mmol) of TFA. After 3.5 h, examination of the sample by NMR showed nearly complete consumption of the major isomer (**13c**). The mixture was then taken up in ether, washed with 5% $NaHCO_3$, dried, and evaporated to give an orange oil, which by NMR was mostly **14c** and free of **13c**. This crude material was taken up in 5 mL of THF and treated with 1.5 mmol of MeLi (in ether). After 0.5 h at room temperature, 2.4 mmol of MeI was added. Workup in the usual manner after 0.5 h gave a dark oil, which was chromatographed on 20 g of activity III alumina (hexanes) to afford 33 mg of **14a** as an oil: ^1H NMR 0.392 (s, 9 H), 1.43 (t, 3 H, J = 7 Hz), 2.35 (s, 3 H), 4.07 (q, 2 H, J = 7 Hz), 6.76 (br d, 1 H, J = 8 Hz), 6.90 (approx t, 1 H, J = 8 Hz), 6.94–7.02 (m, 2 H), 7.14 (br d, 1 H, J = 7 Hz), 7.19–7.29 (m, 2 H).

1-Methoxy- and 4-Methoxy-9,10-dihydro-9,10-epoxy-9-ethoxy-10-(trimethylsilyl)anthracene (13d + 14d). The usual scale was used in a reaction of **9** and *o*-bromoanisole/LTMP, with a reaction time of 21 h. Normal workup gave a dark oil which was chromatographed on 20 g of silica gel (1% Et_3N, 5% ether, hexanes) to give 85 mg (24%) of minor isomer contaminated by starting *o*-bromoanisole, followed by 150 mg (43%) of essentially pure major isomer. Analytical samples were obtained by recrystallization from hexanes.

13d (major isomer): mp 108–110 °C; ^1H NMR 0.38 (s, 9 H), 1.43 (t, 3 H, J = 7 Hz), 3.83 (s, 3 H), 4.08 (br q, 2 H, J = 7 Hz), 6.59 (d, 1 H, J = 7.5 Hz), 6.87 (dd, 1 H, J = 7, 0.5 Hz), 6.92–7.03 (m, 3 H), 7.18 (br d, 1 H, J = 7 Hz), and 7.40 ppm (br d, 1 H, J = 7 Hz). Anal. Calcd for $C_{20}H_{24}O_3Si$: C, 70.55; H, 7.10. Found: C, 70.89; H, 7.19.

14d (minor isomer): mp 142.5–143 °C; ^1H NMR 0.34 (s, 9 H), 1.42 (t, 3 H, J = 7 Hz), 3.78 (s, 3 H), 4.07 (q, 2 H, J = 7 Hz), 6.57 (dd, 1 H, J = 7.5, 1.5 Hz), 6.91–7.02 (m, 4 H), and 7.21–7.32 ppm (sym m, 2 H). Anal. Found: C, 70.66; H, 7.14.

1-Methoxy-9,10-anthraquinone. A mixture of **13d** and **14d** (4 mg of each, 0.023 mmol total) in 0.5 mL of acetone-d_6 was treated with 1.3×10^{-4} mmol of TFA in 0.5 mL of CCl_4, in an NMR tube. After 0.5 h the singlets at 0.38 and 3.83 ppm due to **13d** had disappeared, while the analogous peaks for **14d** remained. After 13 h, **14d** had also been consumed. Exposure to air resulted in the formation of 1-methoxy-9,10-anthraquinone; it was isolated by chromatography, as a pale yellow solid, mp 171–172 °C (lit.[20] mp 175–176 °C). The ^1H NMR spectrum corresponded to the description in the literature.[20]

Reaction of 9 with 3,4-Pyridyne: Benz[*g*]isoquinoline Derivatives (18 + 19). On the usual scale (1.027 mmol of **8**), treatment with 0.355 mL (3.48 mmol) of 3-bromopyridine and 1.74 mmol of LTMP and a reaction time of 4 h afforded a black oil. Elution through 25 g of activity III basic alumina with 30% ether/hexanes gave 111 mg (35%) of a discolored but by NMR essentially pure mixture of isomers: ^1H NMR 0.390 and 0.412 (s, 9 H total, ratio 49/51 before chromatography, 50/50 after), 1.43 and 1.45 (two identical t, 3 H total, J = 7 Hz), 4.0–4.14 (m, 2 H), 6.98–7.38 (m, 5 H total from both isomers), 8.27 (d, 0.5 H, J = 5 Hz), 8.32 (d, 0.5 H, J = 4.5 Hz), 8.43 (d, 0.5 H, J = 1 Hz), and 8.50 (d, 0.5 H, J = 1 Hz); the last two absorptions are due to the peri protons adjacent to nitrogen, and reinforced the conclusion that **18** and **19** were formed in equal amounts; MS calcd for $C_{18}H_{21}NO_2Si$ 311.1341, found 311.1330.

7,12-Dihydro-7,12-epoxy-12-ethoxy-7-(trimethylsilyl)-benz[*a*]anthracene and 7,12-Dihydro-7,12-epoxy-7-ethoxy-12-(trimethylsilyl)benz[*a*]anthracene (20 + 21). To the solution of **9** (from 1.027 mmol of **8**) prepared in the usual way was added 0.286 mL (2.05 mmol) of 1-bromonaphthalene, followed by 1.74 mmol of LTMP. After 20 h, the usual workup gave a dark oil, which afforded 218 mg (59%) of **20 + 21** after chromatography (30 g alumina, 2% ether/hexanes): ^1H NMR 0.45 and 0.50 (s, 9 H total, ratio:crude = 63/37, after chromatography 64/36), 1.48 and 1.51 (t, 3 H total, latter major, J = 7 Hz), 4.03–4.25 (m, 2 H), and 6.85–8.4 ppm (m, containing two unequal pairs of d at 7.80 and 7.98 (minor isomer), and 7.76 and 8.37 ppm (major isomer), respectively); MS calcd for $C_{23}H_{24}O_2Si$ 360.1546, found 360.1514.

7,14-Dihydro-7,14-epoxy-7-ethoxy-14-(trimethylsilyl)dibenz[*a,j*]anthracene (26) and Its Dibenz[*a,h*]anthracene Isomer (24). To a magnetically stirred solution of 80 mg (0.309 mmol) of 3,3-diethoxy-1,3-dihydrobenzo[*e*]isobenzofuran[6] and 5

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μL (0.03 mmol) of tetramethylpiperidine in 2 mL of ether (ice bath) was added 0.97 mL (1.55 mmol) of *n*-butyllithium in hexane. After 1 h 0.22 mL (1.7 mmol) of Me_3SiCl was added, with stirring continued for 0.5 h with the ice bath removed. Then 86 μL (0.62 mmol) of 1-bromonaphthalene was added, followed by 1.55 mmol of LTMP in 2 mL of ether. The mixture was stirred for 5 h and then worked up in the usual manner to obtain a dark oil. A portion was set aside for protiodesilylation as described below, while the major amount was chromatographed on 20 g of activity III alumina (7% ether/hexanes) to give 95 mg (75%) of product as an oil: ^1H NMR 0.56 (br s, 9 H, overlapping trimethylsilyl groups), 1.50–1.59 (3 H, overlapping triplets), 4.10–4.32 (m, 2 H), 7.25–7.80 (m), 8.0 (d, J = 8.5 Hz), 8.16 (d, J = 8.5 Hz), 8.38 (d, J = 8.5 Hz); the ratio of the three doublets in the aromatic region was 41/26/33 before chromatography and 41/26/32 after, indicating that no fractionation had taken place; MS calcd for $C_{27}H_{26}O_2Si$ 410.1702, found, 410.1747.

The portion of crude product mentioned above was taken up in 5 mL of THF and treated with 0.11 mmol of TBAF at ambient temperature (under N_2) for 10 min. After the normal isolation procedure, the crude product was examined by NMR; the spectrum contained no absorptions at 0.56 ppm (indicating complete reaction) and exhibited two singlets at 6.6 and 7.0 ppm, in a ratio of 74/26; MS calcd for $C_{24}H_{18}O_2$ 338.1307, found 338.1311. Attempted isolation/purification of these products caused decomposition, probably to quinones. The major cycloadduct **24** had NMR features identical with those of the minor product of eq 9, and its protiodesilylation product[9] was also correlated in this manner.

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Fluorination of Alkanes by Chlorine Trifluoride. Hydride Abstraction Mechanism

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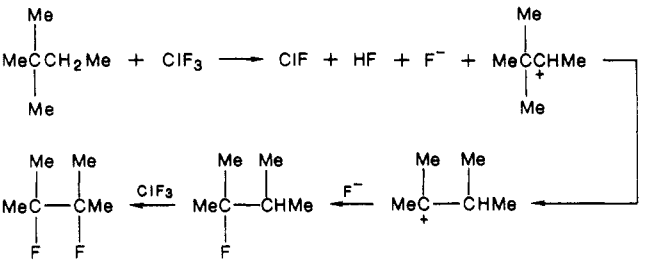
Addition of chlorine trifluoride to a solution of alkane in Freon or liquid carbon dioxide at −75 °C gives good yields of monofluoroalkane along with difluoro- and trifluoroalkanes in amounts dependent on reactant proportions. The inorganic products are HF and ClF. The reaction is highly selective for 3° over 2° positions. Methane and hexamethylethane are unreactive. Neohexane fluorinates with rearrangement, but 2-fluoro-3,3-dimethylbutane exposed to the postreaction medium does not rearrange. A hydride abstraction mechanism is inferred.

A recent paper from this laboratory describes the chemistry and thermochemistry of explosions produced by rapid mixing of liquid chlorine trifluoride with liquid hydrocarbons and halocarbons.[1] A thought-provoking aspect of these reactions is that gaseous mixtures of ClF_3 with methane or propane at room temperature with partial pressures near 1 atm each do not react over a period of hours[1,2] whereas liquid mixtures explode violently with an induction period of less than 1 ms at all temperatures down to the melting point of ClF_3, −76 °C. This behavior suggests an ionic rather than a free-radical mechanism. In an effort to learn more about the initial stages of the reaction, we added ClF_3 at −75 °C to dilute solutions of hydrocarbons in inert solvents such as 1,2-dichloro-1,1,2,2-tetrafluoroethane (Freon 114) and dichlorodifluoromethane (Freon 112) in open vessels, and liquid carbon dioxide in a pressure vessel. To our surprise, we found that under certain conditions alkanes and cycloalkanes are smoothly fluorinated with excellent yield according to eq 1. The fluoroalkane products have been

$$RH + ClF_3 \rightarrow RF + HF + ClF \quad (1)$$

identified and quantified by GC/MS, and the formation of ClF was shown by trapping with cyclohexene and ethylene to give *trans*-1-chloro-2-fluorocyclohexane and 1-chloro-2-fluoroethane.

Scheme I



The products shown in eq 1 will react further if allowed to warm to room temperature, but reaction can be arrested at this stage by scavenging the ClF with ethylene or any higher olefin or a suitable reducing agent such as hydrogen sulfide. If ClF is allowed to react further, it gives products containing both chlorine and fluorine. Incorporation of chlorine also results from too-rapid addition of ClF_3. This may occur by a cage process of the type proposed by Skell and Baxter[3] for multiple substitution in free-radical chlorination. Another possibility is that it results from HF-catalyzed elimination of HF in localized regions of high temperature followed by addition of ClF.

Mechanism

With the original intention of evaluating the selectivity ratio for replacement of hydrogen on methyl and methy-

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