cipitated in ether, redissolved in chloroform, and reprecipitated in ether; yield 47%. (Evaporation of the first ether fraction yielded 33% of pyran.) Anal. Calcd for $C_{16}H_{14}O_7$: C, 60.38; H, 4.43. Found: C, 59.56; H, 4.45.

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Registry No. 1, 82522-55-2; 2, 82522-57-4; 3, 82522-59-6; 4 82522-58-5; 5, 82522-60-9; 6, 82522-61-0; 7, 82522-62-1; 8a, 82522-63-2; 8b, 82522-64-3; tetramethyl ethylenetetracarboxylate, 1733-15-9; *p*-methoxystyrene, 637-69-4; divinylbenzene, 105-06-6; anethole, 104-46-1; diphenylethylene, 530-48-3; styrene, 100-42-5; isobutyl vinyl ether, 109-53-5; isoprene, 78-79-5; butadiene, 106-99-0; BCMA styrene polymer, 82522-56-3.

Diels–Alder Reaction of Some Trimethylsilyloxy 1,3-Dienes

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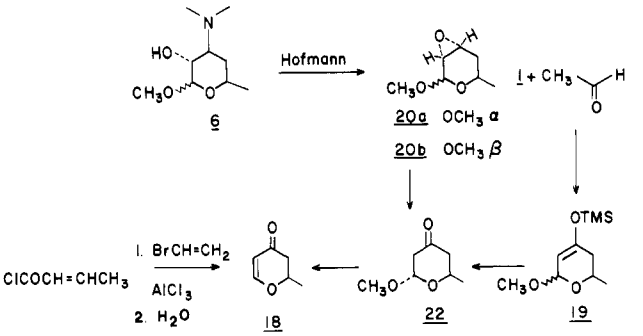
The thermal condensation of five trimethylsilyloxy 1,3-dienes with ethyl mesoxalate led to dihydropyran adducts. The trimethylsilyloxy radical was then removed by hydrolysis. The Danishefsky diene 1 was used to synthesize, with acetaldehyde, the 2,3-dihydro-2-methyl-4-pyrone (18), which was also obtained by two other independent ways.

The trimethylsilyloxy 1,3-dienes are not very popular dienes used in the Diels–Alder condensation. Recently, however, Danishefsky[1,2] reported a synthesis of an interesting diene, 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (1), via the enolization of the corresponding enone and silylation, already available from Aldrich Chemical Co. The progress in the silylation of enolates of vinyl ketones,[3] on the other hand, has aroused an additional interest in this synthesis. For example, Yamamoto,[4] Danishefsky again,[5,6] and Anderson[7] are using the trimethylsilyloxy dienes instead of more conventional alkoxy dienes in their synthesis.

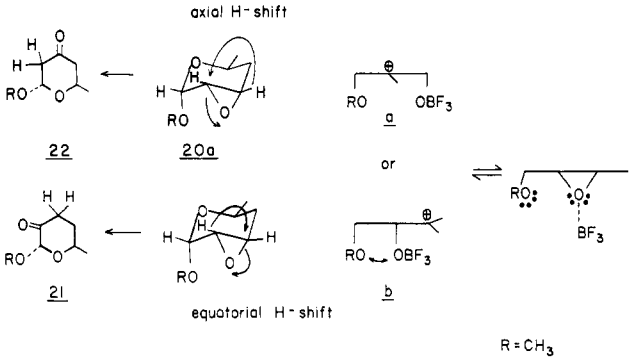
We have been interested in a total sugar synthesis via Diels–Alder condensation of carbonyl dienophiles, particularly ethyl mesoxalate, with dienes. This reaction leads to dihydropyran derivatives. Although acetaldehyde remains the simplest dienophile leading toward the 6-deoxy sugars via Diels–Alder condensation, most similar syntheses have been done with the more reactive carbonyl groups, such as glyoxalate or mesoxalate[6a-c] or, more recently, high-pressure reaction on nonconjugated aldehydes.[6d] We have made a condensation of the following dienes: 1-[(trimethylsilyl)oxy]-1,3-butadiene (2), 2-[(trimethylsilyl)oxy]-1,3-butadiene (3), 3-[(trimethylsilyl)-oxy]-1,3-pentadiene (4), 2-[(trimethylsilyl)oxy]-1,3-cyclohexadiene (5) and Danishefsky's diene 1 with ethyl mesoxalate. The last diene has also been condensed to acetaldehyde in order to confirm the structure of methyl desosaminide (6) degradation product. The thermal condensation of 1 and acetaldehyde leads, in principle, to an interesting 6-deoxy sugar precursor. Finally, the condensation of 1-methoxy-1,3-cyclohexadiene 7 leads to a model cage compound, 8. The trimethylsilyloxy enol ethers have been successfully unblocked to the corresponding ketones via hydrolysis. These ketones could be used for preparation of an interesting variety of sugars via reductive or alkylating routes.

The trimethylsilyloxy 1,3-dienes react relatively well with ethyl mesoxalate in thermal reaction. However, the catalysis of this condensation via Lewis acids (e.g., aluminum chloride) does not work under various conditions

Scheme I



Scheme II



(1) After submission of this work we were informed by the Referee of our paper that he was completing a synthesis of compound 18 using a Diels–Alder BF_3-catalyzed reaction between the diene 1 and acetaldehyde (yield 17%, compare to 5% of thermal reaction described by us). There is apparently less of a complexation of the methoxy group of the diene 1 by a Lewis acid catalyst than expected.[5d,e]

(2) S. Danishefsky and T. Kitahara, *J. Am. Chem. Soc.*, **96**, 7807 (1974).

(3) (a) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969); (b) M. W. Rathke and D. F. Sullivan, *Synth. Commun.*, **3**, 67 (1973).

(4) K. Yamamoto, S. Suzuki, and J. Tsuji, *Chem. Lett.*, 649 (1978).

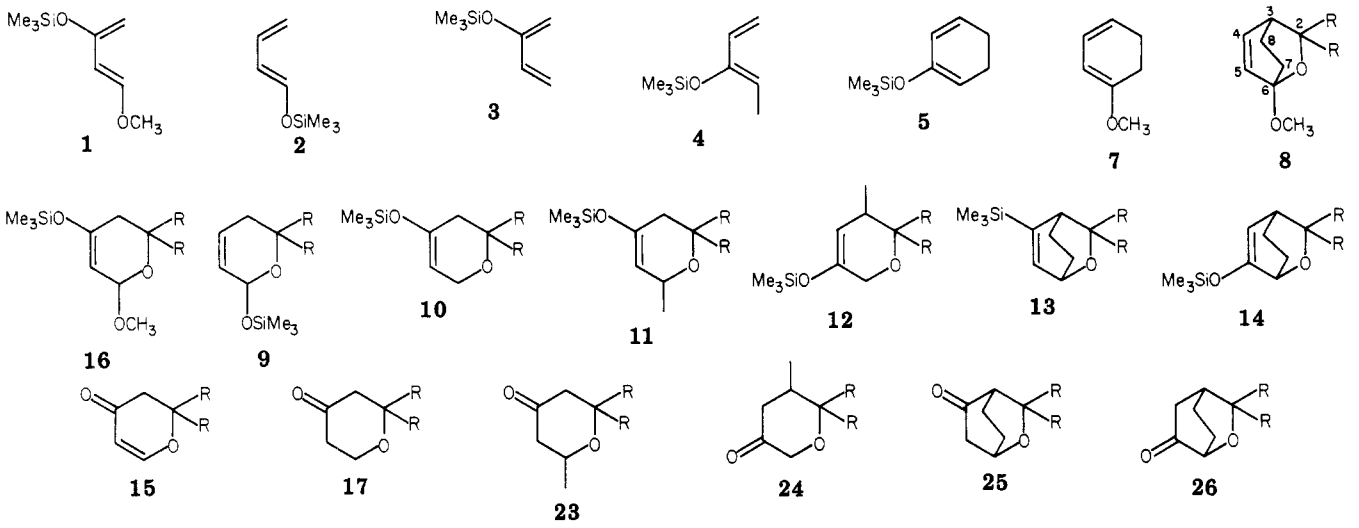
(5) (a) S. Danishefsky, R. K. Singh, and R. B. Gammill, *J. Org. Chem.*, **43**, 379 (1978); see also ref 3 of this paper; (b) S. Danishefsky, M. P. Prisbylla, and S. Hiner, *J. Am. Chem. Soc.*, **100**, 2919 (1978); (c) S. Danishefsky, J. F. Kerwin, Jr., and S. Kobayashi, *J. Am. Chem. Soc.*, **104**, 358 (1982); (d) S. Danishefsky and J. F. Kerwin, Jr., *J. Org. Chem.*, in press; (e) *ibid.*, submitted; (f) S. Danishefsky, N. Kato, D. Askin, and J. F. Kerwin, Jr., *J. Am. Chem. Soc.*, in press.

(6) (a) O. A. Sharygina and S. M. Makin, *Khim. Farm. Zh.*, **3**, 17 (1969); (b) S. David and J. Eustache, *J. Chem. Soc., Perkin Trans. 1*, 2230 (1979); (c) A. Konowal, J. Jurczak, and A. Zamojski, *Rocz. Chem.*, **42**, 2045 (1968); (d) M. Chmielewski and J. Jurczak, *J. Org. Chem.*, **46**, 2230 (1981).

(7) D. R. Anderson and T. H. Koch, *J. Org. Chem.*, **43**, 2726 (1978).

0022-3263/82/1947-3649$01.25/0

Chart I [a]



[a] R = $COOC_2H_5$.

involving solvent, time, temperature, and ratio of substract/catalyst changes. It seems that the complexation of the trimethylsilyloxy group via Lewis acid is either deactivating or just favoring fast polymerization of the diene.

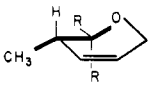
The direct adducts **9–14** (see Chart I) have been obtained with a yield comparable to the corresponding unsilylated dienes having the same carbon number.[14] The Danishefsky diene **1** reacts with both dienophiles (ethyl mesoxalate and acetaldehyde) in a characteristic manner: the condensation is followed by the demethanolysis, as observed by Danishefsky,[1] leading to α,β-unsaturated ketones.

The intermediate silylated enol ethers **16** and **19** are loosing Me_4Si and methanol during simple filtration via a silica gel column. As expected, the thermal reaction with acetaldehyde gives a particularly poor yield of condensation; however, in the total sugar synthesis approach, this is a direct way to synthesize the 6-deoxy sugars.[8]

Compound **18** has been successfully (Scheme I) synthesized in two other ways: from vinyl bromide and crotonyl chloride[9-11] and the retrosynthesis via the Hofmann degradation on methyl desosaminide **6**.[12,13] This reaction leads, according to Newman,[12] to corresponding epoxides **20a** and **20b**. The major epoxide **20a** has been transformed via the corresponding ketone **22** to compound **18**. Looking for a possible explanation of this mechanism, we must point out that there are two H shifts possible on the epoxide (Scheme II): the axial shift leading to the desired ketone **18** and the equatorial shift leading to isomeric ketone **21**.

The dienes **4** and **5** give two isomeric adducts when condensed to ethyl mesoxalate. The major adduct in each series is thus showing meta orientation of $OSiMe_3$ and carboxylate groups. The structural proofs of adducts have been obtained via spectroscopy, especially ^1H and ^{13}C NMR. The CH_3 signal in ^{13}C NMR is shifted, due to the ring oxygen being anti to this carbon by approximately 4.5 ppm upfield if the methyl group is present at the C-3 carbon.[15] This observation confirms the $^0H_2$ (see Chart II) conformation for dihydropyrans established earlier on the basis of ^1H NMR data.[14] A similar shift (upfield) has been observed for the tetrahydropyrone series ($\Delta\delta$ ~3 ppm).

Chart II



The diene **7** gives, with ethyl mesoxalate, an adduct having a methoxy group placed on C-6. The NMR spectra of this adduct are very similar to the adduct obtained from 1,3-cyclohexadiene and the same dienophile.

The hydrolysis of silylated enol ethers **10–12** works well, leading to the corresponding ketones **17**, **23**, and **24**. However, the cage enol ethers **13** and **14** show an amazing resistance (stability) during hydrolysis and refuse to hydrolyze to the corresponding ketones under THF/H^+ conditions. During longer hydrolysis (up to 24 h), these compounds give, via a retro-Diels–Alder reaction, a starting ethyl mesoxalate and a dimer of 2-cyclohexenone instead of the corresponding ketones **25** and **26**.

The potential of trimethylsilyloxy 1,3-dienes for the Diels–Alder reaction, as well as in the total sugar synthesis, is certainly interesting,[5d] in fact, these compounds behave in the thermal reaction as conventional 1,3 dienes.

Experimental Section

Boiling points were not corrected. Nuclear magnetic resonance (^1H and ^{13}C NMR) spectra were recorded in $CDCl_3$ (Me_4Si internal standard) on Varian T 60A and FT 80A spectrometers. The assignment of ^{13}C signals were aided throught the use of the off-resonance technique. The solvents and reagents were distilled before use from an appropriate drying agent. The purity of compounds was checked via the GC analysis performed on a PE 990 gas chromatograph in a programmed temperature manner. This chromatograph was coupled to a Hitachi RM-50 mass spectrometer. The following GC columns were used: for silylated derivatives, 3% SE-30 on WHP 80–120 (3 ft × 0.25 in. o.d.); for

(8) Similar to the condensation on ethyl pyruvate, K. Jankowski and R. Luce, *Tetrahedron Lett.*, 2069 (1974).
(9) T. Matsumoto, Japanese Patent 6929255 (1966).
(10) K. Nakanishi, M. Nagao, and K. Okada, *Yakugaku Zaschi*, 88, 1044 (1968).
(11) N. K. Kochetkov, A. Ya. Khorin, B. P. Gottish, and A. N. Nesmeyanov, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk*, 1053 (1956).
(12) H. Newman, *J. Org. Chem.*, **29**, 1461 (1964); *Chem. Ind. (London)*, 372 (1963).
(13) K. Jankowski, E. Luce, and G. Bérubé, *Carbohydr. Res.*, submitted.
(14) K. Jankowski and J. Couturier, *J. Org. Chem.*, **37**, 3997 (1972); see also ref 5 of this paper.
(15) K. Jankowski, A. Zamojski, and J. Couturier, *Pol. J. Chem.*, **53**, 1683 (1979).
(16) A. Bozouin, J. Dunogues, and M. LeFort, French Patent, 1436568 (1966).
(17) P. Cazeau and E. Frainnet, *Bull. Soc. Chim. Fr.*, 1658 (1972).

others, 3% OV-101 on WHP 80-120 (6 ft × 0.25 in. o.d.). The mass spectra were recorded in the electronic impact mode at 70 eV (200 °C, source 250 °C). All new compounds gave a satisfactory elementary (C and H) analysis. The ethyl mesoxalate, as well as dienes 1 and 7, were purchased from Aldrich Chemical Co.

Synthesis of Trimethylsilyloxy Dienes. The House procedure,[3,16,17] from the corresponding α,β-unsaturated ketones, was followed with three additional consecutive washings of pentane solution of the diene by HCl (1%), saturated $NaHCO_3$, saturated NaCl, and once with water. The distillation of dienes was done under low vacuum.

1-[(Trimethylsilyl)oxy]-1,3-butadiene (2): bp 80–83 °C (40 mmHg); yield 69%; MS, m/z 142 (M^+, 32), 73 (100), 127 (42), 75 (21), 99 (17), 101 (15); ^1H NMR δ 6.8 (H-1), 5.3 (H-2), 6.0 (H-3), 5.1 (H-4), 0.25 (CH_3Si), ($J_{1,2}$ = 13.0 Hz, $J_{4,4'}$ = 12.0 Hz); ^{13}C NMR δ 140.0 (C-1), 113.4 (C-2), 130.3 (C-3), 112.3 (C-4), 2.3 (CH_3Si).

2-[(Trimethylsilyl)oxy]-1,3-butadiene (3): bp 25–28 °C (12 mmHg); yield 40%; MS, m/z 142 (41, M^+), 75 (100), 127 (93), 77 (67), 73 (64), 85 (55); ^1H NMR δ 4.17 (H-1), 6.40 (H-3), 5.1 and 5.6 (H-4) ($J_{3,4}$ = 17.0 Hz, $J_{3,4'}$ = 10.0 Hz, $J_{4,4'}$ = 3.0 Hz).

3-[(Trimethylsilyl)oxy]-1,3-pentadiene (4): bp 50–57 °C (25 mmHg); yield 15%; MS, m/z 156 (41, M^+), 75 (100), 73 (51), 127 (37), 155 (30), 141 (26); ^1H NMR δ 4.6–6.3 (H-1, H-2, and H-4) 1.6 (CH_3–C), 0.2 (CH_3Si) (J_{H,CH_3} = 6.0 Hz).

2-[(Trimethylsilyl)oxy]-1,3-cyclohexadiene (5): bp 33–37 °C (0.01 mmHg); yield 80%; MS, m/z 168 (M^+, 90), 73 (100), 75 (30), 153 (20), 151 (40); ^1H NMR δ 2.05 (CH_2), 0.27 ($SiCH_3$), 5.0–6.05 (H-1, H-3, and H-4).

Condensation of Trimethylsilyloxy 1,3-Dienes with Ethyl Mesoxalate. A thick-wall tube was charged with a mixture of 1.1 g (7 mmol) of ethyl mesoxalate and the equivalent quantity of the diene. After degassing, the tube was sealed while the contents remained frozen. The sealed tube was heated in the sand bath for 24 h at 150–160 °C and then cooled in a liquid nitrogen bath and opened. The adducts were purified by microdistillation.

Diethyl 2-[(Trimethylsilyl)oxy]-5,6-dihydro-α-pyran-6,6-dicarboxylate (9). This adduct was obtained from the diene **2** and ethyl mesoxalate as a yellow liquid: bp 155–158 °C (0.2 mmHg); yield 55%; MS, m/z 316 (M^+, 10), 73 (100), 242 (58), 169 (45), 75 (35), 153 (32), 315 (20), 301 (13); ^1H NMR δ 5.60 (H-2), 5.36 (H-3), 5.85 (H-4), 2.50 (H-5 ax), 2.80 (H-5 eq), 4.31 (CH_2CH_3), 1.27 (CH_2CH_3), 0.31 (CH_3Si) ($J_{2,3}$ = 1.30 Hz, $J_{3,5}$ = −1.5 Hz, $J_{3,4}$ = 10.0 Hz, $J_{5,5}$ = −15.0 Hz, $J_{CH_2CH_3}$ = 7.5 Hz); ^{13}C NMR δ 89.9 (C-2), 127.5 (C-3), 124.6 (C-4), 28.3 (C-5), 78.2 (C-6), 168.7 (CO), 61.8 (CH_2CH_3), 13.9 (CH_2CH_3), 0.17 (CH_3Si).

Diethyl 4-[(Trimethylsilyl)oxy]-5,6-dihydro-α-pyran-6,6-dicarboxylate (10). The adduct was obtained from the diene **3** and ethyl mesoxalate as a yellow pale oil: bp 145–147 °C (0.25 mmHg); yield 30%; MS, m/z 316 (M^+, 8), 243 (100), 244 (63), 73 (53), 75 (38), 171 (20), 215 (18), 270 (15); ^1H NMR δ 4.68 (H-2 ax), 4.45 (H-2 eq), 4.50 (H-3), 2.60 (H-5 ax), 2.80 (H-5 eq), 4.27 (CH_2CH_3), 1.30 (CH_2CH_3), 0.22 (CH_3Si) ($J_{2,2}$ = −13.0 Hz, $J_{2,3}$ = 2.0 Hz, $J_{3,5}$ = −1.5 Hz, $J_{5,5}$ = −14.5 Hz, $J_{CH_2CH_3}$ = 7.0 Hz); ^{13}C NMR δ 62.3 (C-2), 145.1 (C-3), 100.4 (C-4), 33.7 (C-5), 80.3 (C-6), 167.6 (C=O), 61.9 (CH_2CH_3), 13.9 (CH_2CH_3), 1.6 (CH_3Si).

Diethyl 2-Methyl-4-[(trimethylsilyl)oxy]-5,6-dihydro-α-pyran-6,6-dicarboxylate (11) and 5-Methyl-3-[(trimethylsilyl)oxy]-5,6-dihydro-α-pyran-6,6-dicarboxylate (12). These two adducts were obtained from the diene **4** and mesoxalate as a yellow oil and separated on the GC effluent splitter: bp range 160–165 °C (0.25 mmHg); total yield 24%, **11**/**12** ratio 3:2.

11: MS, m/z 330 (M^+, 1), 73 (100), 75 (48), 55 (40), 257 (30), 170 (25), 141 (22), 238 (15); ^1H NMR 4.19 (H-2), 4.68 (H-3), 2.85 (H-5), 4.25 (CH_2CH_3), 1.30 (CH_2CH_3), 1.25 (2-CH_3) ($J_{CH_2CH_3}$ = 7.5 Hz, $J_{2\text{-}CH_3}$ = 6.8 Hz) ^{13}C NMR δ 70.4 (C-2), 151.0 (C-3), 98.9 (C-4), 33.8 (C-5), 78.6 (C-6), 167.9 (C=O), 61.8 (CH_2CH_3), 13.9 (CH_2CH_3), 18.9 (2-CH_3), 1.9 (CH_3Si).

12: ^1H NMR δ 3.62 (H-2), 4.28 (H-4), 2.99 (H-5), 4.25 (CH_2CH_3), 1.30 (CH_2CH_3), 1.10 (5-CH_3) ($J_{CH_2CH_3}$ = 7.5 Hz, $J_{5\text{-}CH_3}$ = 7.0; ^{13}C NMR δ 48.1 (C-2), 151.0 (C-3), 98.1 (C-4), 37.6 (C-5), 78.6 (C-6), 167.6 (C=O), 61.8 (CH_2CH_3), 13.9 (CH_2CH_3), 14.5 (5-CH_3), 1.8 (CH_3Si).

Diethyl 4-[(Trimethylsilyl)oxy]-1-oxabicyclo[2.2.2^{3,6}]oct-4-ene-2,2-dicarboxylate (13) and Diethyl 5-[(Trimethylsilyl)oxy]-1-oxabicyclo[2.2.2^{3,6}]oct-4-ene-2,2-dicarboxylate (14). [The numbering of the bicyclic compounds conform neither to IUPAC nor Chemical Abstracts Service recomendations; please refer to Chart I for the numbering used in this paper.] These two adducts were obtained from diene **5** and ethyl mesoxalate as a semisolid material and were separated on the GC effluent splitter: bp 165 °C (0.2 mmHg); total yield 41%; **13**/**14** ratio 55:45.

13: MS, m/z 330 (M^+, 5), 73 (100), 75 (82), 55 (37), 42 (30), 257 (25), 170 (21); ^1H NMR δ 4.17 (H-6), 5.95 (H-5), 3.32 (H-3), 2.36 (H-7), 1.92 (H-8), 4.30 (CH_2CH_3), 1.31 (CH_2CH_3), 0.25 (CH_3Si) ($J_{5,6}$ = 6.7 Hz, $J_{7,8}$ = 4.5 Hz (average), $J_{CH_2CH_3}$ = 7.1 Hz, $J_{3,5}$ = −1.8 Hz; ^{13}C NMR δ 62.3 (C-6), 130.3 (C-5), 148.9 (C-4), 41.2 (C-3), 80.7 (C-2), 36.8 (C-7), 23.7 (C-8), 62.0 (CH_2CH_3), 14.1 (CH_2CH_3), 2.05 (CH_3Si).

14: MS, m/z 330 (M^+, 2), 73 (100), 75 (61), 55 (30), 42 (30), 257 (10); ^1H NMR δ 6.70 (H-6), 5.80 (H-4), 3.15 (H-3), 2.36 (H-7), 1.92 (H-8), 4.30 (CH_2CH_3), 1.31 (CH_2CH_3), 0.25 (CH_3Si) ($J_{4,6}$ = −2.9 Hz, $J_{3,4}$ = 5.2 Hz, $J_{7,8}$ = 4.5 Hz (average), $J_{CH_2CH_3}$ = 7.0 Hz; ^{13}C NMR δ 62.1 (C-6), 130.9 (C-5), 149.7 (C-4), 36.8 (C-2), 80.7 (C-3), 36.8 (C-7), 23.7 (C-8), 169.4 (C=O), 62.0 (CH_2CH_3), 14.1 (CH_2CH_3), 2.0 (CH_3Si).

Diethyl 2,3-Dihydro-4-pyrone-2,2-dicarboxylate (15). The adduct has been obtained from diene **1** and ethyl mesoxalate purified by chromatography on the silica gel column and distilled: bp 100 °C (0.25 mmHg); yield 30%; MS, m/z 242 (M^+, 31), 170 (100), 98 (93), 142 (81), 72 (70), 128 (60), 100 (58); ^1H NMR δ 7.42 (H-6), 5.49 (H-5), 3.14 (H-3), 4.32 (CH_2CH_3), 1.31 (CH_2CH_3) ($J_{5,6}$ = 6.1 Hz, $J_{CH_2CH_3}$ = 7.0 Hz); ^{13}C NMR δ 84.6 (C-2), 40.7 (C-3), 187.7 (C-4), 108.2 (C-5), 160.4 (C-6), 165.4 (COO), 63.3 (CH_2CH_3), 13.9 (CH_2CH_3) ($J_{C_3H_3}$ = 134.7 Hz, $J_{C_5H_5}$ = 170.4 Hz, $J_{C_6H_6}$ = 192.8 Hz, for ethyl group = 147.0 for methylene group, 127.4 for methyl group).

Diethyl 6-Methoxy-1-oxabicyclo[2.2.2^{3,6}]oct-4-ene-2,2-dicarboxylate (8). The adduct has been obtained from diene **7** and ethyl mesoxalate: bp 150–155 °C (0.15 mmHg); yield 64%; MS, m/z 284 (M^+, 20), 138 (100), 212 (88), 110 (20), 78 (18), 139 (15), 194 (12), 136 (10); ^1H NMR δ 4.97 (H-5), 6.16 (H-4), 2.32 (H-3), 2.40 (H-7 and H-8), 4.27 (CH_2CH_3), 1.30 (CH_2CH_3), 3.54 (CH_3O) ($J_{4,5}$ = 8.0 Hz, $J_{CH_2CH_3}$ = 7.0 Hz); ^{13}C NMR δ 160.1 (C-6), 122.9 (C-5), 124.9 (C-4), 92.1 (C-3), 81.2 (C-2), 27.6 (C-7), 24.6 (C-8), 169.9 (C=O), 62.6 (CH_2CH_3), 14.0 (CH_2CH_3), 54.7 (CH_3O).

2,3-Dihydro-2-methyl-4-pyrone (18). This adduct was obtained by three different ways: (A) from crotonyl chloride and vinyl bromide,[9] instead of chloride,[11] and Nakanishi[10] methods [bp 50 °C (5–6 mmHg); yield 70%]; (B) via condensation of acetaldehyde and the Danishefsky diene **1** purified by chromatography [bp 40–45 °C (2–3 mmHg); yield 5%; ^1H NMR 4.55 (H-2), 2.35 (H-3), 5.25 (H-5), 7.30 (H-6), 1.45 (CH_3) ($J_{2\text{-}CH_3}$ = 6.5 Hz, $J_{5,6}$ = 6.0 Hz, $J_{2,3}$ = 8.0 Hz); ^{13}C NMR δ 162.5 (C-2), 106.0 (C-3), 191.8 (C-4), 43.2 (C-5), 75.5 (C-6), 20.5 (CH_3); and (C) synthesis of **18** via Hofmann's degradation on **6**, followed by epoxide **20a** rearrangement.

The degradation was carried out on 100 mg of compound according to Newman's procedure:[12] yield 40%; ratio of α/β anomers of **20a** to **20b**, 2:1. We isolated the α anomer (**20a**) using the effluent splitter.

A solution of the epoxide **20a** (50 mg) in benzene (5 mL) was treated with 0.5 mL of boron trifluoride etherate. The mixture became turbid and dark after a few minutes. After 20 min, 5% sodium acetate solution was added, and the products were isolated via ether extraction. The extracts were chromatographed on the alumina, giving 56% of the pyrone **18**: bp 50–55 °C (4–5 mmHg), lit.[10] bp 50 °C (5 mmHg).

Removal of the Trimethylsilyl Group: Hydrolysis of Adducts 10–12. Adducts (1 g) were poured into a mixture of 15 mL of THF and 15 mL of HCl (N 0.1) and stired vigorously for 20 min. The mixture was extracted with ether (3 × 30 mL) and then washed with 3 × 30 mL of saturated $NaHCO_3$, 2 × 25 mL of saturated NaCl, and 2 × 25 mL of water. The extract was dried over $MgSO_4$ for 30 min and then evaporated in vacuo and distilled.

Ethyl 2,3,5,6-tetrahydro-4-pyrone-2,2-dicarboxylate (17): bp 160 °C (0.2 mmHg); yield 62%; MS, m/z 244 (M^+, 1), 155 (100), 171 (70), 173 (36), 43 (25), 42 (20), 143 (18); ^1H NMR δ 4.13 (H-6), 2.55 (H-5), 2.90 (H-3), 4.30 (CH_2CH_3), 1.21 (CH_3) ($J_{5,6}$ = 6.15 Hz, $J_{CH_2CH_3}$ = 7.35 Hz); ^{13}C NMR δ 62.6 (C-6), 44.7 (C-5), 201.8 (C-4), 40.4 (C-3), 80.6 (C-6), 62.0 (CH_2CH_3), 13.9 (CH_3), 167.3 (COO).

Ethyl 6-methyl-2,3,5,6-tetrahydro-4-pyrone-2,2-dicarboxylate (23): bp 160–165 °C (0.25 mmHg); yield 42%; MS,

m/z 258 (M^+, 5), 111 (100), 185 (90), 55 (85), 15 (82), 83 (77), 173 (64), 216 (41); ^1H NMR δ 4.1 (H-6), 2.55 (H-5), 2.7 (H-3), 4.30 (CH_2CH_3), 1.30 (CH_2CH_3), 145 (CH_3) ($J_{5,6}$ = 5.8 Hz, J_{CH_2,CH_3} = 7.1 Hz, $J_{6\text{-}CH_3}$ = 7.0); ^{13}C NMR δ 62.5 (C-6), 33.9 (C-5), 196.9 (C-4), 27.5 (C-3), 80.0 (C-6), 62.2 (CH_2CH_3), 14.1 (CH_2CH_3), 15.3 (CH_3), 166.4 (COO).

Ethyl 3-methyl-2,4,5,6-tetrahydro-5-pyrone-2,2-dicarboxylate (24): bp 165 °C (0.2 mmHg); yield 40%; ^1H NMR δ 3.9 (H-6), 2.65 (H-4), 3.00 (H-3), 4.30 (CH_2CH_3), 1.30 (CH_2CH_3), 1.20 (CH_3) ($J_{3,4}$ = 4.5 Hz, $J_{3\text{-}CH_3}$ = 6.8 Hz, J_{CH_2,CH_3} = 7.10 Hz); ^{13}C NMR δ 48.1 (C-6), 200.8 (C-5), 37.6 (C-4), 27.5 (C-3), 85.8 (C-6), 62.4 (CH_2CH_3), 14.1 (CH_2CH_3), 12.3 (CH_3).

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Synthetic Approaches to 9-Chloro-7-(*o*-fluorophenyl)-5*H*-dibenz[*c*,*e*]azepine

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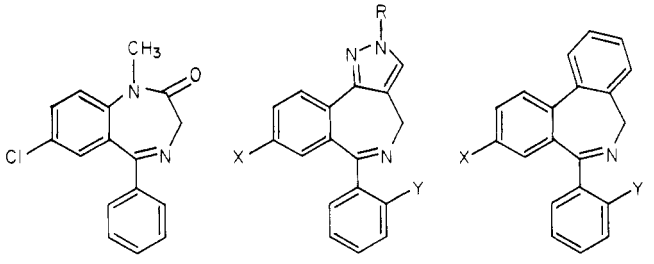
A retrosynthetic analysis of the title compound 1, a potential new anxiolytic agent, is presented. The regiospecific formation of an aryl–aryl bond is considered as the key step. Two synthetic approaches are described which are based on the nucleophilic aromatic substitution of 2-(methoxyaryl)oxazolines. The nature of the organometallic nucleophile, particularly with respect to its need for coordinating ligands, is of crucial importance for the success of these reactions. In the second synthesis, the vinyl lactam **22** is used as the immediate precursor to 1. The vinyl lactam functionality and the quaternary oxazoline **7** are found to be the only derivatives of the carboxyl group with sufficient reactivity toward the labile (*o*-fluorophenyl)lithium. The two syntheses of 1 proceed in ten and eight steps, respectively, with an overall yield of 22–23%.

Extensive structure–activity studies[1,2] on the anxiolytic properties of benzodiazepines reveal that the amide group represents one of the more promising functionalities for molecular modifications. Specifically, it was the transgression from an N-substituted amide to a five-membered heterocycle, such as a triazole, which produced agents with high potency and selectivity, thus leading to a whole new array of additional structural variations.

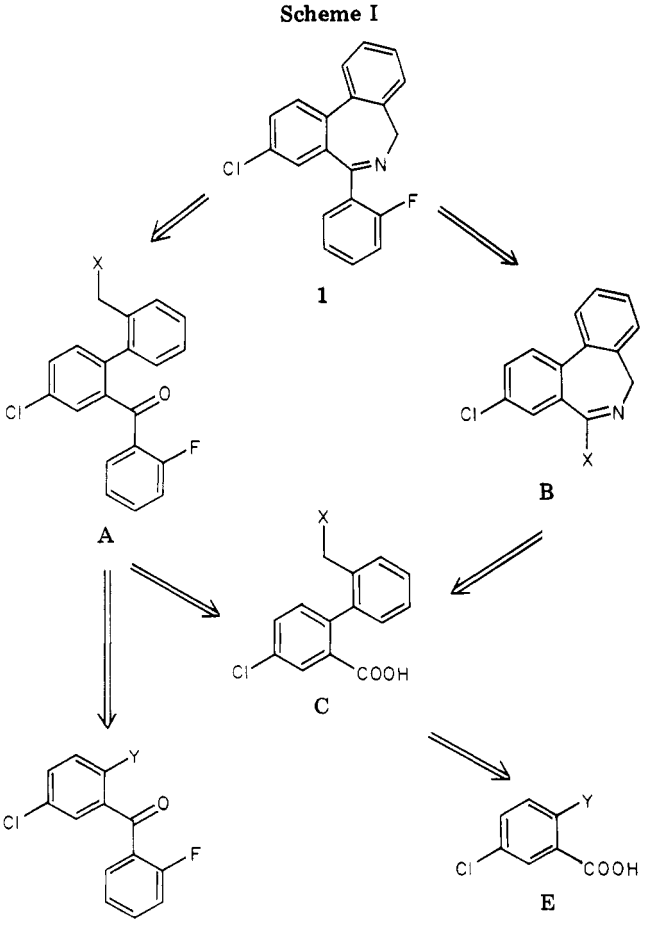
Our own interest in this field was based on the hypothesis that the desired pharmacological profile should be maintained in a benzazepine system, that is by replacing the amide functionality in diazepam by two sp^2-hybridized



diazepam I II

carbon atoms. This hypothesis proved to be correct, as we have shown with several pyrazolobenzazepine (I) systems.[3] More recent studies were designed to explore the pharmacological potential of dibenzazepines of type II, that is of molecules in which the five-membered heterocycle of triazolobenzodiazepines, for example, or of the pyrazolobenzazepines of type I has been replaced by a carbocyclic aromatic ring. This and the following paper report on

Scheme I



three different syntheses of these compounds.

Retrosynthetic Analysis. The chlorofluoro derivative 1 was chosen as a synthetic target on the basis of the

(1) Gschwend, H. W. "Anxiolytics"; Fielding, S., Lal, H. Ed.; Futura Publishing Co.: Mt. Kisco, NY, 1979; p 1.
(2) Sternbach, L. H. *J. Med. Chem.* **1979**, *22*, 1.
(3) U.S. Patent 3 947 585, 1976. U.S. Patent 4 022 801, 1976. U.S. Patent 4 028 381, 1977.

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