liquid was then fractionally distilled: yield 88%; bp 57–59 °C (1.0 mm). mp 68.0°C (20.0 mm); 3H NMR (CDCl3) δ 0.26 (s, 6 H, N-Si(CH3)2), 0.54 (s, 9 H, N-Si(CH3)2), 2.05 (s, 3 H, CH3C), 2.79 (s, 3 H, NCH3), 0.84 (s, 9 H, N-Si(CH3)2), 2.05 (s, 3 H, CH3C), 2.79 (s, 3 H, NCH3), mass spectrum, m/e (relative intensity) 187 (M+*, 11), 127 (17), 130 (100), 147 (74), 73 (66), 59 (93). Anal. Calc'd for C6H15NO: C, 61.43; H, 9.82; N, 6.49. Found: C, 61.42; H, 9.83; N, 6.47.

N-Methyl-N-(tert-butyldimethylsilyl)formamide (MTBSF).

Synthesis of MTBSF is the same as that for MTBTA except that 29.5 g (0.5 mol) of acetamide was used in place of N-methylacetamide: yield 88%; bp 57–59 °C (1.0 mm); mp 32 °C (moist solid); 1H NMR (CDCl3) δ 0.26 (s, 6 H, N-Si(CH3)2), 0.93 (s, 9 H, Si(CH3)2), 2.76 (s, 3 H, NCH3), 2.87 (s, 1 H, HC), mass spectrum, m/e (relative intensity) 173 (M+*), 185 (22), 147 (74), 116 (100), 59 (86). Anal. Calc'd for C6H15NO: C, 55.44; H, 11.05; N, 8.08; Si, 16.20. Found: C, 55.63; H, 10.88; N, 8.19; Si, 15.99.

N, O-Bis(tert-butyldimethylsilyl)acetamide (BMTBSA).

Synthesis of BMTBSA is the same as for MTBTA except that 29.5 g (0.5 mol) of acetamide was used in place of N-methylacetamide: yield 88.7%; bp 91–92 °C (2.0 mm); dm 4 0.859; 'H NMR (CDCl3) δ 2.03 (s, 3 H, CH,COCH3), 2.25 (s, 3 H, COCH3), 2.79 (s, 3 H, NCH3), 3.47 (s, 3 H, OCH3), 3.98 (s, 3 H, OCH3), 4.81 (dd, J 12, 4 Hz), 5.91 (s, 1 H, HCOCH3), 7.19 (dd, J 4.7, 1.3 Hz), 7.30 (d, J 8.0 Hz), 7.33 (d, J 8.0 Hz), 7.35 (d, J 8.0 Hz), 7.40 (d, J 8.0 Hz). Anal. Calc'd for C18H36NO5S: C, 55.14; H, 8.42; N, 3.47; S, 7.47; Found: C, 55.28; H, 8.39; N, 3.51; S, 7.53.

Reactions of Enamines with Trifluoroacetic Anhydride: Trifluoroacetylation and the Formation of 1,3-Oxazines

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In relation to our work on the synthesis of analogues of the antitumor antibiotic mitomycin C, we are currently interested in the reactions of pyrrolizines, prepared by reaction of 1-(1-pyrrolidinyl)cycloalkanes and dimethyl acetylenedicarboxylate (DMAD), with trifluoroacetic anhydride (TFA). Kametani et al. used this reagent for the conversion of pyrroloindoles into azocines.1 Recently, we have reported that one of the pyrroloindoles that we have synthesized, viz., methyl 7a,8,9,10-tetrahydro-7-(methoxy carbonyl)-7H-benzo[g]pyrrolo[1,2-a]indole-7-acetate, reacted in a different way with TFA, namely, via trifluoroacetylation of the aromatic ring.2 This result led us to investigate reactions of other pyrrolizines with TFA. We found that methyl 1,2,3,5,6,7,7a,8-octahydro-8-(methoxycarbonyl)cyclopenta[b]pyrrolizine-8-acetate (1, E = COOCH3)3 reacted smoothly with TFA at room temperature to give one product in 65% yield. According to the mass spectrum and elemental analysis, the elemental composition of the reaction product was C19H22F2NO5, indicating that trifluoroacetylation had taken place. In the 1H NMR spectrum, the characteristic NCH absorption at δ 4.74 (dd, J = 5 and 12 Hz) was still present. X-ray diffraction showed that the compound had the methyl 1,2,5,6,7,7a,8,9,10-tetrahydro-7-(methoxy carbonyl)-7H-benzo[g]pyrrolo[1,2-a]indole-7-acetate (1) structure (Figure 1). We assume that this reaction of 1 proceeds via its tautomeric form (Scheme I) in which trifluoroacetylation takes place at the β-eneamine carbon atom.

The surprising result of the reaction of 1, which possesses an enamine moiety, with TFA led us to study the reaction of other enamines with this reagent. To our knowledge such reactions have not been reported in the literature, although reactions with acetic anhydride4 and methanesulfonyl chloride5 were used.

Registry No.

MTBSTFA, 77377-52-7; MTBSA, 82112-20-7; MTBSF, 68844-33-2; MTBS, 82112-21-8; RO(CH2)2OR (R = tert-butyldimethylsilyl), 82112-22-9; ROCH2CH(OR)CH2OR (R = tert-butyldimethylsilyl), 82112-23-9; CH3OR (R = tert-butyldimethylsilyl), 18652-27-2; CH2=CH2CH=CHSR (R = tert-butyldimethylsilyl), 82112-24-7; RO-S(CH3)2SR (R = tert-butyldimethylsilyl), 82112-25-3; RSCH2CH(OR)2OR (R = tert-butyldimethylsilyl), 82112-27-4; ROCH2OR (R = tert-butyldimethylsilyl), 82112-28-5; RSCH2CH(OR)2OR (R = tert-butyldimethylsilyl), 82112-29-6; ROCH2OR (R = tert-butyldimethylsilyl), 82112-30-8; RO-m-C6H4CH2OR (R = tert-butyldimethylsilyl), 82112-31-0; RO-p-C6H4CH2OCOCOR (R = tert-butyldimethylsilyl), 82112-32-1; RO-o-C6H4CH2(NH2)COOR (R = tert-butyldimethylsilyl), 82112-33-2; RO-p-C6H4CH2(NH2)COOR (R = tert-butyldimethylsilyl), 82112-34-3; CH3CH(NH2)CH2OR (R = tert-butyldimethylsilyl), 82134-49-4; 2-(OR)-6-(RHN)=pyrimidine (R = tert-butyldimethylsilyl), 82125-34-5; C6H5CH2NR(CH3)2 (R = tert-butyldimethylsilyl), 82112-36-5; 1,3-propanediol, 504-63-2; glycerol, 56-81-5; phenol, 108-95-2; 1-propanethiol, 107-03-9; 2-propanethiol, 75-33-2; 1,3-propanedithiol, 109-80-8; 2-mercapto-1,2-propanediol, 96-27-5; 2-mercaptoethanol, 60-24-2; mercurcatoacetic acid, 68-11-1; 3-hydroxypropionic acid, 503-66-2; m-hydroxybenzyl alcohol, 99-06-9; 3-hydroxybenzyl alcohol, 90-01-7; p-hydroxyphenylpyruvic acid, 156-38-8; N,N-bis-(2-aminobutyric acid, 2853-81-6; 2-aminooctanoic acid, 2853-81-6; 2-aminooctanoic acid, 78-91-1; 4-amino-2,6-dihydroxypropionic acid, 873-83-6; benzylichemamine, 103-67-3; tert-butyldimethylsilyl chloride, 18162-48-6; N-methyltrifluoroacetamide, 815-06-5; N-methylacetamide, 79-16-3; N-methylformamide, 129-39-7; acetamide, 60-35-5.


(2) Verboom, W.; Visser, G. W.; Reinholdt, D. N. Tetrahedron 1982, 38, 1831.

Figure 1. Stereoscopic view of compound 3.

with trichloroacetic anhydride are known.

Reaction of 4-(1-cyclohepten-1-yl)morpholine (4) with 2.5 equiv of TFA in tetrahydrofuran (THF) at room temperature afforded the 4-[2,7-bis(trifluoroacetyl)-1-cyclohepten-1-yl]methylmorpholine (5), which after distillation was isolated in 57% yield (Scheme I). The mass spectrum and elemental analysis showed that two CF₃CO groups had been introduced.

More reactive enamines, such as 4-(1-cyclopenten-1-yl)morpholine and 1-(1-cyclohexen-1-yl)pyrrolidine, reacted even at low temperature, to give very complicated reaction mixtures. It has been reported that these types of enamines react with an excess of acetic anhydride to produce only monoacetylation.4

4-(3,4-Dihydro-1-naphthalenyl)morpholine (6a) and 1-(1H-inden-3-yl)pyrrolidine (6b) reacted with TFA in THF to give, after distillation, the trifluoroacetylated compounds 7a,b in yields of 83 and 82%, respectively (Scheme III). Isolation of 7a,b by column chromatography of the crude reaction mixture on silica gel or alumina was not possible because of decomposition.

Reaction of 1-(3,4-dihydro-1-naphthalenyl)pyrrolidine (6c) with TFA in THF, however, afforded, after distillation, a mixture of products, of which the minor compound was the trifluoroacetylated compound 7c. After column chromatography (alumina), the major reaction product, a white crystalline compound, was isolated in a yield of 53%. Mass spectrometry and elemental analysis exhibited that a CF₃CO moiety had been introduced, but the absence of a carbonyl group (IR and ¹³C NMR spectroscopy) ruled out a structure like 7c. The ¹H NMR spectrum showed characteristic absorptions at δ 5.05 (br d, J = 4.2 Hz, 1 H) and 4.54 (q, J = 7.8 Hz, 1 H), and the ¹³C NMR spectrum showed characteristic absorptions at δ 86.5 (d) and 72.8 (dq, J = 29.6 Hz). On the basis of these and other spectroscopic data, we concluded that the reaction product was 1,2,3,3a,6,7-hexahydro-5H-(1,2-d)pyrrolo[2,1-b][1,3]oxazine (8c). TLC of the crude reaction mixture revealed that 6c had reacted possibly to 7c. However, 8c was not present, so that further reaction must have occurred during the distillation.

1-(3,4-Dihydro-1-naphthalenyl)piperidine (6d) reacted similarly to give, after distillation, the 2,3,4,4a,7,8-hexahydro-6-(trifluoromethyl)-1H,6H-naphtho[1,2-d]pyrrolo[2,1-b][1,3]oxazine (8d) in 44% yield as a mixture of two isomers.

Reaction of 1-(6,7-dihydro-5H-benzocyclohepten-9-yl)pyrrolidine (6e) with TFA afforded, after distillation, 7e, slightly contaminated with the 1,3-oxazine 8e in a yield of 87%. Compound 7e could not be isolated in a pure state on account of decomposition on silica gel and alumina. Heating of 7e in toluene in the presence of trifluoroacetic acid for 3 days yielded, after column chromatography, the 1,2,3,3a,5,6,7,8-octahydro-5-trifluoromethyl)benzo[6,7]cyclohepta[1,2-d]pyrrolo[2,1-b][1,3]oxazine (8e) in a yield of 30% as a mixture of isomers. This experiment demonstrated that the 1,3-oxazine formation takes place via the trifluoroacetylated compounds 7. Starting from 7, the formation of 8 can be rationalized as depicted in Scheme IV. Protonation of 7c–e will give the stabilized carboca-

tion 9, in which a hydride transfer takes place to 10. Subsequently, intramolecular addition of the hydroxy group to the iminium double bond gives rise to compounds 8c-e. An intermediate such as 10 has also been proposed in order the formation of dihydrobenzimidazoles by reaction of anils of ortho-substituted amines in the presence of acid as described by Meth-Cohn et al.; the conversion of 10 into 8c-e represents the well-known reaction of alcohols with iminium salts.

**Experimental Section**

Met helyl 1,2,5,6,7,8a,8a-Octahydro-5-(methoxy- carbonyl)-1-cyclohepten-1-yl)morpholine (5).

To a stirred solution of 410 (3.6 g, 20 mmol) in 15 mL of THF was added TFA at room temperature for 45 min. The TFA was removed under reduced pressure, and the residue was dissolved in 25 mL of CHCl₃. This solution was stirred for 30 min with K₂CO₃ (6 g). After filtration, the CHCl₃ was evaporated to give an oil, which after crystallization from Et₂O gave 65% of m: mp 126-129°C; IR (KBr) 1730 (C=O, esters), 1685 (O=C=O) cm⁻¹; ¹H NMR δ 4.74 (dd, J = 5 and 12 Hz, NCH₃), 4.0-3.9 (m, 2 H, NCH₃), 3.72 and 3.67, OCH₃, 3.25 and 2.65 (ABq, J = 18 Hz, CH₂), 3.3-3.1 (m, 1 H, CH₃), 3.0-2.7 (m, 2 H, H₂C=CH₂), 2.2-1.1 (m, 6 H, CH₃). ¹³C NMR δ 172.3 and 171.3 (s, C=O), 117.5 (q, J = 291 Hz, CF₃), 79.7 (d, NCH₃), 52.4 and 51.9 (q, OCH₃), 48.5 (t, NCH₃), 47.4 [s, (CH₂)CH=CH₂], 38.4 (t, CH₃), 33.2, 26.2, and 25.5 (t, 2 CH₃), mass spectrum, m/e 375.130 (M⁺; calcld 375.129).


1-[2-8-(trifluoroacetyl)-1-cyclohepten-1-yl)morpholine (6). To a stirred solution of 410 (3.6 g, 20 mmol) in 15 mL of THF was added TFA (10.5 g, 50 mmol), the temperature being kept between 15 and 25 °C. After 1.5 h of stirring, the solvent was removed under reduced pressure. Distillation of the resulting oil afforded 57% of an oil, bp 137-139 °C (2 mm). After crystallization from Et₂O gave yellow crystals: mp 167-169 °C; IR (KBr) 3290 (s), 3090 (s), 2910 (m), 1622 (s), 1517 (m), 1452 (s), 1375 (s), 1363 (s), 1231 (m), 1175 (s), 1148 (s), 1091 (s, (NCH₃), 85.6 and 84.6 (d, NCH₃), 72.8 (dq, J = 29.6 Hz, CF₃), 50.7 (t, NCH₃), 31.9, 28.0, 24.1, and 23.2 (t, CH₃), mass spectrum, m/e 295.119 (M⁺; calcld 295.118).


5d: mp 87-90 °C dec (MeOH); IR (KBr) 1646 (C=O) cm⁻¹; ¹H NMR δ 7.5-7.0 (m, 4 H, Ar H), 4.5-4.0 (m, 2 H, NCH₃, 0.1-0.7 (m, 4 H, Ar H), 4.5-3.9 (m, 2 H, NCH₃), 3.0-1.7 (m, 2 H, CH₂), 2.2-1.1 (m, 6 H, CH₃). ¹³C NMR δ 164.7 (s, (NCH₃), 138.7 (s, 136.3 (s), 129.6 (s), 127.4 (d), 126.1 (d), 122.6 (d) and 122.2 (d) (Ar C), 124.3 (q, J = 288 Hz, CF₃), 113.5 (s, NCH₃), 82.9 and 81.7 (d, NCH₃), 75.0 and 73.2 (d, J = 29 Hz, CF₃), 46.1 (t, NCH₃), mass spectrum, m/e 309.134 (M⁺; calcld 309.134).

Anal. Calcld for C₂₂H₂₄F₁₄N₂O: C, 66.01; H, 5.87; N, 4.53. Found: C, 66.02; H, 5.90; N, 4.41.

1,2,5,6,7,8a-Octahydro-5-(trifluoroacetyl)-1H-benzo[6,7]cyclohept[a][1,2-d][1,3]oxazone (8e). Reaction of 6e (2.1 g, 10 mmol) with TFA (4.2 g, 20 mmol) gave, after distillation [bp 145-150 °C (0.7 mm)], 7e in 87% yield in an impure state. This reaction containing compound 7e (1.0, 3.2 mmol) was heated in 15 mL of toluene in the presence of 2 mL of trifluoroacetic acid for 3 days. The reaction mixture was washed with sodium bicarbonate solution and then dried (MgSO₄). Column chromatography [alumina (V), petroleum ether (bp 60-80 °C) with 5% CHCl₃], yield 8e and 8d in 53 and 44% yield, respectively.

8c: mp 85-86.5 °C (MeOH); IR (KBr) 1638 (C=O) cm⁻¹; ¹H NMR δ 7.5-7.0 (m, 4 H, Ar H), 4.5-4.0 (m, 2 H, NCH₃, 0.1-0.7 (m, 4 H, Ar H), 4.5-3.9 (m, 2 H, NCH₃), 3.0-1.7 (m, 2 H, CH₂), 2.2-1.1 (m, 6 H, CH₃). ¹³C NMR δ 164.7 (s, (NCH₃), 138.7 (s, 136.3 (s), 129.6 (s), 127.4 (d), 126.1 (d), 122.6 (d) and 122.2 (d) (Ar C), 124.3 (q, J = 288 Hz, CF₃), 113.5 (s, NCH₃), 82.9 and 81.7 (d, NCH₃), 75.0 and 73.2 (d, J = 29 Hz, CF₃), 46.1 (t, NCH₃), mass spectrum, m/e 309.134 (M⁺; calcld 309.134).

Anal. Calcld for C₂₂H₂₄F₁₄N₂O: C, 66.01; H, 5.87; N, 4.53. Found: C, 66.02; H, 5.90; N, 4.41.

**Notes**


scan width (deg) 3.3 ± 1.0 tg θ. The total number of reflections measured was 3315, of which 2648 had an intensity greater than the standard deviation estimated from counting statistics. The solution and refinement of the crystal structure are based on the latter reflections. The structure was solved by direct methods and refined by full-matrix least squares to a final R factor of 5.5%. All hydrogen atoms were found from Fourier difference syntheses. The number of parameters refined in the last cycles was 316 (scale factor, extinction parameter, positional parameters of all atoms, anisotropic thermal parameters for non-hydrogen atoms, isotropic thermal parameters for hydrogen atoms). The figure was produced by ORTEP.

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Registry No. 1, 67395-20-4; 3, 82281-38-7; 4, 7185-08-3; 5, 82281-39-8; 6a, 31401-28-2; 6b, 31554-37-7; 6c, 7007-34-3; 6d, 31401-27-1; 6e, 25579-44-6; 7a, 82281-40-1; 7b, 82281-41-2; 7c, 82281-42-3; 8c, 82281-43-4; 8d (isomer 1), 82281-44-5; 8d (isomer 2), 82281-45-6; 8e (isomer 1), 82281-46-7; 8e (isomer 2), 82281-47-8.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond distances, and bond angles (6 pages). Ordering information is given on any current masthead page.

Cope and 1,3-Allyl Rearrangements and Ring Closure of the 1,5-Hexadiene Radical Cation Prior to Decomposition in the Gas Phase

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The chemistry of neutral 1,5-hexadiene (1) has been studied extensively. It undergoes the well-known (degenerate) Cope rearrangement under thermal conditions. Facile transformations occur upon irradiation, and depending on the photochemical conditions allylcyclop propane and bicyclo[2.1.1]-2-hexane may be formed. Isotopic separation of deuterated 1 in favor of deuterium situated in the external vinyl sites has been demonstrated with infrared laser deuterium in the allylic positions, however, is favored under thermal conditions. In contrast, recent electron impact studies indicate a chemical inertness of the radical cation of 1+(+). It was shown by photodissociation spectroscopy that 1+ remains as an unconjugated diene at low internal energies.

Comparison of the heat of formation of C6H5+ ions formed by CH3+ loss from isomeric C6H10 radical cations (ions of m/z 67 give rise to base peak in the normal mass spectra of C6H10 isomers) and the kinetic energy release (T) associated therewith showed that 1+ among its linear isomers forms the cyclopentenyl cation with the lowest excess energy and smallest T value. This result is in accord with the photodissociation results insofar as 1+ cannot isomerize to another linear diene prior to decomposition. The collisional activation mass spectra of C6H10 isomers confirmed that nondecomposing 1+ has no or only little resemblance with the radical cations of 1,3-, 1,4-, and 2,4-hexadiene, cyclohexene, and 1-methylcyclopentene.

In light of the apparent retention of structure of 1+, this work is concerned with how the cyclopentenyl cation is formed therefrom.

It is necessary to consider which isomeric C6H10+ ions have heats of formation lying below the energy required for fragmentation of 1+ by CH3+ loss and which can display similar kinetic energy release characteristics. From our previous studies, these can be reduced to cyclohexene, 2-methyl-1,4-pentadiene, and methylcyclopentene (and methylene cyclopentene).

Isomerization of 1+ to the cyclohexene radical cation is not likely to occur, because it would involve the formation of bicyclo[2.2.0]hexane+ in the first step, a process having an energy barrier of 16 kcal mol−1 (see Table I). Loss of ethylene is an abundant process of the cyclohexene radical cation (RDA elimination), while it is nearly absent in the normal mass spectrum and in the metastable time frame of 1+, thus further disfavoring an isomerization.

Isomerized 2-methyl-1,4-pentadiene also cannot be involved in the behavior of 1+, because the kinetic energy release for the random statistical losses of the deuterium-labeled methyl radicals from 2-methyl-1,4-pentadiene-1-d was twice as large as that observed for the unlabeled compound, while this is not the case with labeled 1,5-hexadienes (see also note 23).

(14) (10) and (13) above.
(15) The CA mass spectra were measured on a ZAB-2F mass spectrometer using He as a collision gas. The spectra were averaged and corrected for unimolecular decomposition.
(17) Comparison of the data obtained for losses of deuterated methyl from cyclohexene-5,6,6-d3 with those from 1,5-hexadiene-1,5,5,6-d4 (2, see Table II) clearly show a dissimilarity in disfavor of an isomerization; in particular note the absence of CD3+ loss from the former.