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Design of Chiral Derivatizing Agents for the Chromatographic Resolution of Optical Isomers. Asymmetric Synthesis of Some Chiral Fluoroalkylated Amines

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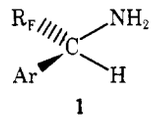
Received January 17, 1977

A general approach for the asymmetric synthesis of type 1 fluoroalkylated amines is described and an assignment of absolute configuration is made for 2,2,2-trifluoro-1-phenylethylamine (2). Amine 2 is obtained in high yield and >80% ee by reducing chiral imine 5 with sodium bis(2-methoxyethoxy)aluminum hydride with subsequent catalytic hydrogenolysis over palladium on charcoal. Catalytic hydrogenolysis of secondary amine 6 proceeds with complete regioselectivity owing to the retarding effect of the α-trifluoromethyl group upon the rate of hydrogenolysis of benzylamine. Fluoro amine 2 is evaluated as a chiral derivatizing agent (CDA) for the chromatographic resolution of racemic alcohols. Relative to the diastereomeric carbamates derived from menthol or 2-octanol and the nonfluorinated analogues of 2, those derived from 2 show greater chromatographic separability and an inverted elution order.

Recently, we reported the resolution of 2,2,2-trifluoro-1-(1-naphthyl)ethanol via the multigram chromatographic separation of diastereomeric carbamate derivatives[1] and in a subsequent paper elaborated a rationale which provides insight into the reasons underlying the chromatographic separability of diastereomeric carbamates.[2] On the basis of this rationale, we are endeavoring to design chiral derivatizing agents (CDA) that will confer still greater chromatographic separability upon the diastereomeric adducts of racemates. Although chiral type 1 fluoroalkylamines are of general interest in this context, we specifically desired 2,2,2-trifluoro-1-phenylethylamine (2), since the aforementioned chromatographic rationale suggests strongly that diastereomeric carbamates derived from this amine should show greater chromatographic separability and inverted elution order when compared to those derived from nonfluorinated analogues, such as 1-phenylethylamine (3) or 1-(1-naphthyl)ethylamine (3a).[3]



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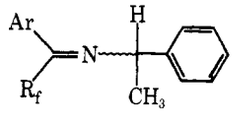
We presently describe the asymmetric synthesis, assignment of absolute configuration, and preliminary chromatographic evaluation of 2 as a CDA and demonstrate that the synthetic scheme utilized is applicable for a series of structurally related amines.

Initial efforts to prepare racemic 2 from phenyl trifluoromethyl ketone (4) by Leuckart reductive amination or through the use of sodium cyanoborohydride and ammonium acetate in methanol[4] were fruitless. While ammonia readily adds to this ketone to afford the carbinolamine, the latter is very resistant to dehydration to the imine. Nevertheless, lithium aluminum hydride converts the carbinolamine to racemic 2 in ca. 30% yield. In an alternate approach, the tosylate of 2,2,2-trifluoro-1-phenylethanol was found to react with ammonia at 130 °C and 6 kbar pressure although it is resistant to aminolysis at ordinary pressures. The Curtius sequence on 3,3,3-trifluoro-2-phenylpropionic acid also affords 2; however, the effort required, as well as the low overall yield (from 4), makes this route unattractive.

A more direct approach to chiral 2 is shown in Scheme I and involves asymmetric reduction of imine 5, derived from ketone 4 and the readily available chiral 1-phenylethylamine (3). This approach is similar to that of Overberger et al.,[5] who showed

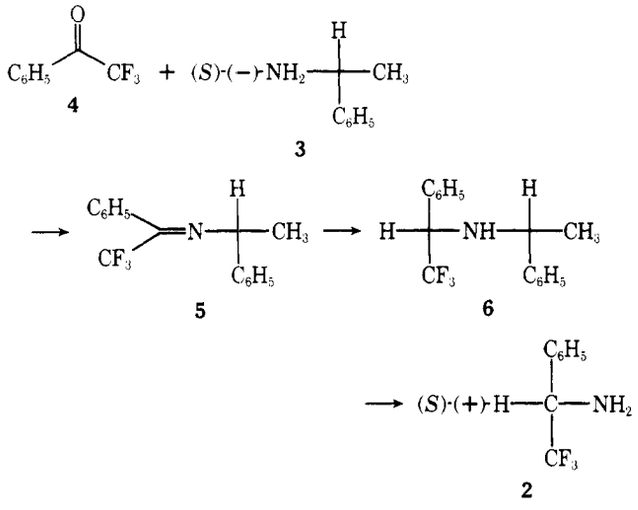
Table I. Asymmetric Reductions of Some Fluoroalkylated Imines



No.	R_F	Ar	Reducing agent	Solvent	Temp, °C	Time, h	Ratio of[a] amines	%
5	CF_3	Phenyl	$LiAlH_4$	Et_2O	25	24	60:40	90
5	CF_3	Phenyl	$LiAlH_4$	Et_2O	−78	24	70:30	95
5	CF_3	Phenyl	$LiAlH_4$	THF	25	24	65:35	90
5	CF_3	Phenyl	$LiAlH_4$	THF	−78	24	80:20	95
11	CF_3	Benzyl	$LiAlH_4$	Et_2O	25	24	65:35	80
11	CF_3	Benzyl	$LiAlH_4$	THF	−10	5	69:31	70
11	CF_3	Benzyl	$LiAlH_4$	THF	−78	36	85:15	95
5	CF_3	Phenyl	Red-Al	THF	25	18–20	70:30	65
5	CF_3	Phenyl	Red-Al	THF	−78	72	92:08	95
12	C_3F_7	Phenyl	Red-Al	THF	25	18–20	65:35	60
12	C_3F_7	Phenyl	Red-Al	THF	−78	72	90:10	80
5	CF_3	Phenyl	$NaBH_3CN$	THF	25	24	83:17	70
5	CF_3	Phenyl	$NaBH_3CN$	THF	0	72	96:04	67
5	CF_3	Phenyl	$NaBH_3CN$	THF	−78	72		*b*
5	CF_3	Phenyl	BH_3	THF	25	3–5	55:45	95
5	CF_3	Phenyl	BH_3	THF	−78	6–10	57:43	90
5	CF_3	Phenyl	$NaBH_4$	Et_2O	25	72		*b*
5	CF_3	Phenyl	$NaBH_4$	THF	25	72		*b*
5	CF_3	Phenyl	$LiAl(O\text{-}t\text{-}Bu)_3H$	Et_2O	25	72		*b*
5	CF_3	Phenyl	$LiAl(O\text{-}t\text{-}Bu)_3H$	THF	25	72		*b*
5	CF_3	Phenyl	9-BBN	Et_2O	25	72		*b*
5	CF_3	Phenyl	9-BBN	THF	25	72		*b*
5	CF_3	Phenyl	H_2/Pd[c]	Cyclohexane	55	48	*d*	*d*
5	CF_3	Phenyl	H_2/Pd	THF	25	0.3	63:37	10
5	CF_3	Phenyl	H_2/Pd	THF	25	10	64:36	90

[a] The diastereomeric ratios were determined by examination of the nonequivalent ^1H or ^{19}F NMR spectra of these diastereomers. [b] No reaction. [c] Catalytic amount of dry HCl. [d] Racemic 2 is obtained in 95% yield.

Scheme I



that catalytic hydrogenation of the imine derived from acetophenone and chiral **3** preferentially affords the chiral rather than the meso diastereomer of the resultant secondary amine. Catalytic hydrogenation of fluoroalkylated imine **5** does not proceed as stereoselectively as might be desired; however, the ratio of the resultant diastereomeric secondary amines **6** can be more strongly biased by appropriate choice of other reducing agents as shown in Table I. Note that for all cases considered, reductions conducted in tetrahydrofuran give greater asymmetric induction than those similarly conducted in ether. From the standpoint of expense, degree of asymmetric induction, and overall yield, Red-Al[6] seems the optimum reducing agent among those surveyed.

Subsequent catalytic hydrogenolysis of **6** proceeds smoothly and in essentially quantitative yield to give exclusively fluoroalkylated amine **2** of the same enantiomeric composition as the diastereomeric composition of **6**. Although catalytic hydrogenolysis of benzylic carbon–nitrogen bonds is well known, we are unaware of prior reports concerning the retarding effect of α-perfluoroalkyl groups upon the rate of such hydrogenolyses. In the present instances, this retarding effect affords complete regioselectivity of hydrogenolysis of **6**.

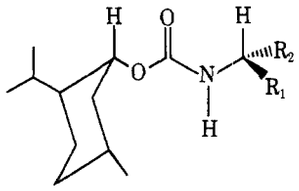
Obtained in enantiomeric purities ≥80%, amine **2** was totally resolved through recrystallization of the natural tartaric acid salt. When totally resolved, (*S*)-(+)-**2** exhibits $[\alpha]^{25}_D$ +24.11° (*c* 12.0, ethanol). The enantiomeric composition and absolute configuration of fluoro amine **2** were determined by NMR[7] using (*S*)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol[8] as a chiral solvating agent.

This sequence of reactions is readily applicable to other fluorinated amines. For example, chiral 2,2,3,3,4,4,4-heptafluoro-1-phenylpentylamine (**7**) and 2,2,2-trifluoro-1-(1-benzyl)ethylamine (**8**) have been similarly prepared. Racemic fluoro amines **2**, **7**, and **8** may be conveniently prepared from the imines of benzylamine by concomitant catalytic hydrogenation and hydrogenolysis.

Chromatographic Evaluation. Samples of (*S*)-(+)-enriched (80% ee) fluoro amine **2** were treated with the chloroformates derived from (*R*)-(−)-menthol and (*R*)-(−)-2-octanol, respectively. The diastereomeric ratios of the resulting carbamates were determined by ^{19}F NMR and corresponded closely with the initial enantiomeric composition of amine **2**. These diastereomeric carbamates were chromatographed upon silica gel with 1:1 methylene chloride–hexane and exhibited the expected inversion of elution order and improvement in chromatographic separability relative to the nonfluorinated analogues. Chromatographic data for these carbamates appear in Table II.[3]

It should be noted that incorporation of perfluoroalkyl

Table II. Comparative Data for Fluorinated vs. Nonfluorinated Carbamates



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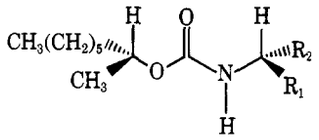

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Compd	R_2	R_1	K'	α
9a	α-Naph	CH_3	2.0	1.4
9b	CH_3	α-Naph	1.4	
9c	Ph	CF_3	1.6	1.5
9d	CF_3	Ph	2.4	
10a	α-Naph	CH_3	3.3	1.2
10b	CH_3	α-Naph	2.8	
10c	Ph	CF_3	2.3	1.4
10d	CF_3	Ph	3.1	

groups into CDA does not automatically confer great chromatographic separability upon diastereomeric derivatives. Although not originally described as chromatographic resolving agent, α-methoxy-α-trifluoromethylphenylacetic acid has found such application.[9] We have found that, for a given alcohol, diastereomeric esters derived from this acid are considerably more difficult to separate chromatographically than are the diastereomeric carbamates derived from amines 2 or 3. We ascribe this to a lesser degree of conformational preference in the esters than in the carbamates.[2,10] Although more extensive appraisal of fluoro amines is still underway, these initial results suggest that these amines will be quite useful for the chromatographic resolution of racemic alcohols. We also note that the carbamates derived from fluoro amine 2 and menthol (or 2-octanol) are rather more crystalline than their nonfluorinated counterparts, thus serendipitally enhancing the separability of these diastereomers by the classical approach.

Experimental Section

Melting points were taken on a Buchi apparatus and are uncorrected. Infrared spectra were obtained with a Beckman IR-12 or a Perkin-Elmer 237B spectrophotometer. ^1H and ^{19}F NMR spectra were obtained with Varian Associates A-60A, EM-390, HA-100, or HR-220 instruments. Mass spectra were determined using a Varian MAT CH-5 spectrometer. Microanalyses were performed by J. Nemeth and his colleagues.

Imines. All imines used in this study were prepared in the following manner. To a 100-mL round-bottom flask fitted with a Dean-Stark water trap and reflux condenser were added 10.6 mmol of fluoroalkylated ketone and (*S*)-(−)-α-Phenylethylamine (10.7 mmol, 1.29 g), along with 30 mL of dry toluene and ca. 3% by weight of *p*-toluenesulfonic acid. The mixture was refluxed until the theoretical amount of water had collected in the trap. The imine was collected and purified by distillation at reduced pressure; isolated yields ranged between 80 and 91%.

Imine 5 from phenyl trifluoromethyl ketone and (*S*)-(−)-1-phenylethylamine is a very pale yellow liquid: bp 99–101 °C (0.5 mm); NMR ($CDCl_3$) δ 1.40 (d, CCH_3), 4.59 (quartet, CH), 7.18–7.35 ppm (multiplet, $C_{12}H_{10}$); IR (neat) 3090, 3000, 1670 (C=N), 1500, 1460, 1380, 1340, 1220, 1150, 1020, 970 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 277 (5.4, M^+), 106 (8.7), 105 (100.0), 104 (4.6), 79 (9.6), 78 (4.3), 77 (14.2).

Anal Calcd for $C_{16}H_{14}F_3N$: C, 69.33; H, 5.05; N, 5.05. Found: C, 69.42; H, 5.06; N, 5.12.

Imine 11 from benzyl trifluoromethyl ketone and (*S*)-(−)-1-phenylethylamine is a very pale yellow liquid that was purified by molecular distillation: NMR ($CDCl_3$) δ 1.38 (d, CCH_3), 3.73 (AB multiplet, $=CCH_2$), 4.81 (quartet, CH), 7.00–7.46 ppm (multiplet, $C_{12}H_{10}$); IR (neat) 3095, 3000, 1670 (C=N), 1500, 1465, 1380, 1365, 1275, 1210, 1130, 925 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 291 (13.4, M^+), 107 (14.7), 106 (5.7), 105 (100.0), 104 (4.2), 79 (15.4), 78 (7.0), 77 (23.8).

Anal. Calcd for $C_{17}H_{16}F_3N$: C, 70.09; H, 5.54: N, 4.81. Found: C, 69.97: H, 5.42; N, 4.68.

Imine 12 from 1,1,2,2,3,3,3-heptafluoropropyl phenyl ketone and (*S*)-(−)-1-phenylethylamine is a very pale yellow liquid: bp 129–131 °C (1.5 mm); NMR ($CDCl_3$) δ 1.45 (d, CCH_3), 4.55 (quartet, CH), 7.13–7.78 ppm (multiplet, $C_{12}H_{10}$); IR (neat) 3070, 3000, 1655 (C=N), 1500, 1460, 1380, 1350, 1240, 1170, 1120, 980 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 377 (12.3, M^+), 107 (10.6), 106 (18.7), 105 (100.0), 104 (5.3), 103 (6.7), 79 (14.3), 78 (5.1), 77 (26.8).

Anal. Calcd for $C_{18}H_{14}F_7N$: C, 57.30; H, 3.74; N, 3.71. Found: C, 57.28; H, 3.71; N, 3.67.

Asymmetric Reductions. Diastereomeric secondary amines were produced by asymmetric reduction of imines in the following manner. A solution of 2.7 mmol of imine in 50 mL of dry tetrahydrafuran was placed in a three-necked 100-mL round-bottom flask equipped with overhead stirrer, vented dropping funnel, and nitrogen inlet. The reaction vessel was cooled in a −78 °C bath and Red-Al[6] (2.7 mmol) in 30 mL of dry tetrahydrofuran was slowly added over a 4-h period with continuous stirring. After addition was completed, stirring was continued for 72–96 h at −78 °C. The mixture was then slowly warmed to room temperature and hydrolyzed with cold, aqueous ammonium chloride and the entire mixture was extracted with three 25-mL portions of ether. The ether extracts were dried over magnesium sulfate prior to solvent evaporation. NMR data are given for the major diastereomer.

***N*-2,2,2-Trifluoro-1-phenylethyl-*N*-1′-(phenyl)ethylamine (6)** is a colorless liquid: bp 82–83 °C (0.4 mm); NMR ($CDCl_3$) δ 1.36 (d, CCH_3), 1.99 (broad s, NH), 4.01 (quartet, CH_3CH), 4.09 (quartet, CF_3CH), 7.16–7.45 ppm (multiplet, $C_{12}H_{10}$); IR (neat) 3500 (NH), 3180, 3060, 1495, 1480, 1380, 1255, 1175, 1130, 880 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 279 (3.3, M^+), 265 (16.4), 264 (100.0), 210 (6.6), 159 (58.1), 120 (2.3), 109 (34.5), 107 (31.1), 106 (15.6), 105 (35.3), 70 (31.1), 78 (7.3), 77 (29.5), 69 (2.2).

Anal. Calcd for $C_{16}H_{16}F_3N$: C, 68.80; H, 5.77; N, 5.02. Found: C, 68.71; H, 5.67; N, 4.97.

***N*-1,1,1-Trifluoro-3-phenylpropyl-*N*-1′-(phenyl)ethylamine (14)** is a colorless liquid: bp 119–121 °C (1.0 mm); NMR ($CDCl_3$) δ 1.20 (d, CCH_3), 2.01 (broad s, NH), 2.48 [doublet of doublets (J = 15, 10 Hz), CCH_2], 2.98 [doublet of doublets (J = 15, 5 Hz), CCH_2], 3.01 (multiplet, CF_3CH), 3.94 (quartet, CH_3CH), 7.06–7.38 ppm (multiplet, $C_{12}H_{10}$); IR (neat) 3490 (NH), 3080, 3000, 1490, 1460, 1375, 1270, 1200, 1150, 940 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 293 (8.2 (8.2, M^+), 278 (19.0), 202 (17.3), 109 (7.4), 106 (9.2), 105 (100.0), 103 (7.1), 91 (26.2), 79 (10.8), 77 (14.6).

Anal. Calcd for $C_{17}H_{18}F_3N$: C, 69.61; H, 6.19; N, 4.78. Found: C, 69.53; H, 6.07; N, 4.53.

***N*-4,4,4,3,3,2,2-Heptafluoro-1-phenylbutyl-*N*-1′-phenylethylamine (15)** is a colorless liquid, which was molecularly distilled; NMR ($CDCl_3$) δ 1.28 (d, CCH_3), 3.94 (quartet, CH_3CH), 4.14 (broad s, NH), 4.35 [doublet of doublets (J = 20, 10 Hz), CF_3CH], 7.08–7.43 ppm (multiplet, $C_{12}H_{10}$); IR (neat) 3495 (NH), 3090, 3005, 1492, 1475, 1380, 1240, 1180, 1130, 1095, 875 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 379 (5.4, M^+), 364 (100.0), 259 (61.7), 133 (2.7), 120 (4.5), 109 (31.4), 107 (30.4), 106 (10.1), 105 (41.4), 79 (27.7), 78 (4.3), 77 (34.6).

Anal. Calcd for $C_{18}H_{16}F_7N$: C, 56.99; H, 4.25; N, 3.69. Found: C, 56.74; H, 4.15; N, 3.52.

Hydrogenolysis. The following general procedure was utilized to conduct all hydrogenolysis. A solution of 1.5 mmol of secondary amine in 50 mL of absolute ethanol containing a trace of dry HCl was hydrogenated in a Parr shaker at ca. 60 °C and 40 psi for 24–48 h over ca. 3–5% by weight of 5% Pd on charcoal. After removal of the catalyst and evaporation of the ethanol, the mixture of amine–amine hydrochloride was treated with dilute aqueous sodium hydroxide. This mixture was extracted with three 25-mL portions of methylene chloride and the combined extracts were dried over magnesium sulfate prior to evaporation of the solvent and distillation of the primary amines, generally obtained in close to quantitative yields.

(*S*)-(+)-2,2,2-Trifluoro-1-phenylethylamine (2) is a colorless liquid: bp 88 °C (20 mm); NMR ($CDCl_3$) δ 1.80 (broad s, NH), 4.34 (quartet, CH), 7.23–7.41 ppm (multiplet, C_6H_5); IR (neat) 3390 (NH), 3000, 1595, 1500, 1460, 1340, 1255, 1170, 1120, 860 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 175 (13.2, M^+), 136 (4.2), 112 (4.8), 109 (11.7), 108 (4.9), 107 (64.4), 106 (100.0), 105 (7.1), 104 (8.5), 83 (6.4), 80 (5.7), 79 (85.1), 78 (12.2), 77 (56.4), 69 (7.4); $[\alpha]^{25}_D$ +24.11° (*c* 12.0, ethanol).

Anal. Calcd for $C_8H_8F_3N$: C, 54.86; H, 4.60; N, 8.00. Found: C, 54.69; H, 4.52; N, 7.95.

Carbamates. The diastereomeric carbamates employed were prepared by a previously described method.[2]

Menthyl *N*-[1-(phenyl)-2,2,2-trifluoroethyl]carbamate (9c) and 9d as a 1:9 diastereomeric mixure is a colorless solid: mp 93–105 °C.

After separation of the carbamate diastereomers **9c** and **9d**, NMR, IR, and elemental analysis of each are consistent with the assigned structure.

9c: NMR ($CDCl_3$) δ 0.80–1.00 [multiplet, $C(CH_3)_2$ and $-CHCH_3$], 1.19–2.20 (multiplet, C_6H_8), 2.25 [heptet of doublets, $(CH_3)_2CH$], 4.69 (triplet of doublets, OCH), 7.38 ppm (broad s, C_6H_5); IR ($CDCl_3$) 1705 cm^{-1} (C=O).

Anal. Calcd for $C_{19}H_{26}F_3NO_2$: C, 63.85; H, 7.33; N, 3.92. Found: C, 63.92; H, 7.19; N, 3.85.

9d: NMR ($CDCl_3$) δ 0.80–1.00 [multiplet, $C(CH_3)_2$ and $-CHCH_3$], 1.19–2.20 (multiplet, C_6H_8), 2.25 [heptet of doublets, $(CH_3)_2CH$], 4.69 (triplet of doublets, OCH), 7.38 ppm (broad s, C_6H_5); IR ($CDCl_3$) 1715 cm^{-1} (C=O).

Anal. Calcd for $C_{19}H_{26}F_3NO_2$: C, 63.85; H, 7.33; N, 3.92. Found: C, 63.81; H, 7.24; N, 3.88.

2-Octyl *N*-[1-(phenyl)-2,2,2-trifluoroethyl]carbamate (10c) and 10d as a 1:9 diastereomeric mixture is a colorless solid: mp 105–106 °C.

After separation of **10c** and **10d**, NMR, IR, and elemental analysis of each were consistent with the assigned structure.

10c: NMR ($CDCl_3$) δ 0.91 [t, $(CH_2)_5CH_3$], 1.20–1.83 [multiplet, $CH_3C(CH_2)_5$], 4.85 (sextet, OCH), 5.40 (quintet, NCH), 5.53 (broad doublet, NH), 7.35 ppm (broad s, C_6H_5); IR ($CDCl_3$) 1705 cm^{-1} (C=O).

Anal. Calcd for $C_{17}H_{24}F_3NO_2$: C, 61.62; H, 7.30; N, 4.23. Found: C, 61.55; H, 7.24; N, 4.18.

10d: NMR ($CDCl_3$) δ 0.91 [t, $(CH_2)_5CH_3$], 1.20–1.83 [multiplet, $CH_3C(CH_2)_5$], 4.85 (sextet, OCH), 5.40 (quintet, NCH), 5.53 (broad doublet, NH), 7.35 ppm (broad s, C_6H_5); IR ($CDCl_3$) 1715 cm^{-1} (C=O).

Anal. Calcd for $C_{17}H_{24}F_3NO_2$: C, 61.62; H, 7.30; N, 4.23. Found: C, 61.82; H, 7.34; N, 4.28

Acknowledgment. This work has been partially supported by grants from the National Science Foundation and the National Institutes of Health.

Registry No.—**2**, 62197-94-8; **3**, 2627-86-3; **4**, 434-45-7; **5**, 62197-91-5; **6** isomer 1, 62197-92-6; **6** isomer 2, 62197-93-7; **9a**, 17397-46-5; **9b**, 17397-45-4; **9c**, 62197-95-9; **9d**, 62197-96-0; **10a**, 62197-97-1; **10b**, 62197-98-2; **10c**, 62197-99-3; **10d**, 62198-00-9; **11**, 62198-01-0; **12**, 62198-02-1; **14** isomer 1, 62198-03-2; **14** isomer 2, 62198-04-3; **15** isomer 1, 62198-05-4; **15** isomer 2, 62198-06-5; benzyl trifluorometrhyl ketone, 350-92-5; 1,1,2,2,3,3,3-heptafluoropropyl phenyl ketone, 559-91-1.

References and Notes

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Photolysis and Thermolysis of 2,4,4-Trisubstituted Δ^2-Oxazolin-5-ones. Activation and Control by a Trifluoromethyl Group

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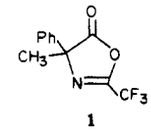
Received December 21, 1976

The photochemical and thermal reactivity of 4-methyl-4-phenyl-2-trifluoromethyl-Δ^2-oxazolin-5-one (1) and 2,4-dimethyl-4-phenyl-Δ^2-oxazolin-5-one (2) have been investigated. Photolysis of 1 in the presence of dipolarophiles gives Δ^1-pyrrolines presumably via carbon dioxide expulsion from 1 to give trappable nitrile ylides. However, photolysis of 2 (with or without dipolarophiles) gives *N*-(1-methylbenzylidene)acetamide (6) presumably via carbon monoxide expulsion. Thermally (refluxing xylene), 1 loses carbon monoxide to form *N*-(1-phenylvinyl)trifluoroacetamide (10); however, 2 is unreactive. A rationalization of the trifluoromethyl group's effect on the thermolysis of 1 is presented, and some points in possible photochemical reaction sequences at which a trifluoromethyl group may control photoreactivity are discussed.

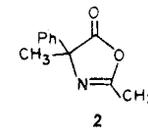
One of the most troublesome aspects of synthetic photochemistry is the capriciousness of many photorearrangements. Therefore, the investigation and development of possible photodirecting, photoactivating, or photoprotecting groups which may make photoreactions more predictable or even controllable are worthwhile, if difficult, goals.

A substituent which may show promise at directing the course of photoreactions is the trifluoromethyl group. For example, Wexler and Swenton[1] have recently reported that the acetone sensitized cycloaddition of 5-trifluoromethyluracil to isobutylene occurs with greater than 95% regioselectivity.

In connection with work to photochemically synthesize β-lactam systems,[2] we have synthesized 4-methyl-4-phenyl-2-trifluoromethyl-Δ^2-oxazolin-5-one (**1**).[3] Because the photochemistry of Δ^2-oxazolin-5-ones has been studied only to a limited extent[4] (see below), and because a comparison of the photoreactivity of **1** with that of 2,4-dimethyl-4-phenyl-Δ^2-oxazolin-5-one (**2**)[5] would test the effect of the trifluoromethyl group, we have explored the photolytic and thermal behavior of **1** and **2**. The results of the study will follow a brief discussion of pertinent published work.



1



2

There are two reports of Δ^2-oxazolin-5-one photolysis.[4a,b] Padwa and Wetmore[4a] report that no Δ^1-pyrroline product is formed when a Δ^2-oxazolin-5-one is photolyzed in the presence of electron-deficient olefin dipolarophiles, but the products formed, if any, are not described.[6] The photolysis of one 2,4,4-trialkyl-Δ^2-oxazolin-5-one followed by acidic hydrolysis is reported by Slates et al.[4b] to yield a ketone de-