Nuclear Magnetic Resonance Determination of Enantiomeric Composition and Absolute Configuration of Amines, Alcohols, and Thiols with α-[1-(9-Anthryl)-2,2,2-trifluoroethoxy]acetic Acid as a Chiral Derivatizing Agent

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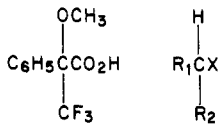
(*R*)-[1-(9-Anthryl)-2,2,2-trifluoroethoxy]acetic acid, easily prepared from commercially available (*R*)-2,2,2-trifluoro-1-(9-anthryl)ethanol, is a useful chiral reagent for the conversion of enantiomeric alcohols, thiols, or amines into diastereomeric derivatives. The resultant diastereomers typically have nonidentical NMR spectra, thus enabling NMR determination of the diastereomeric ratio, a ratio which reflects the original enantiomeric purity of the alcohol, thiol, or amine. A discussion of the conformational behavior of these derivatives is presented as is a conformational model for obtaining absolute configurations of the alcohol, thiol, or amine from the senses of the chemical shift differences noted between the diastereomeric derivatives.

During the last decade, determinations of enantiomeric purity and absolute configuration have been remarkably facilitated by the use of NMR techniques employing chiral solvating agents[1] (CSAs), chiral lanthanide shift reagents[2] (CLSRs), and chiral derivatizing agents[3] (CDAs). Although CDAs have several inherent disadvantages relative to CSAs or CLSRs, they nevertheless enjoy considerable use. The most widely used CDA, Mosher's acid, α-methoxy-α-(trifluoromethyl)phenylacetic acid (1),[4] affords diastereomeric



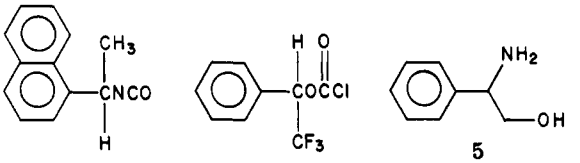
1 2, X = OH, NH_2, SH

derivatives from type 2 alcohols or amines that often show sufficient NMR chemical shift differences for diastereotopic nuclei to allow facile determination of the ratio of diastereomeric products. In general, this diastereomeric ratio will be the same as the original enantiomeric ratio of the alcohol or amine *provided* that (a) the CDA is optically pure, (b) the derivatives are configurationally stable, and (c) no asymmetric induction or fractionation has occurred during the synthesis or isolation of the diastereomers. All CDAs are subject to these limitations, which, in practice, tend to limit convenience rather than restrict usage. For example, the asymmetric induction/fractionation question can be answered through control experiments upon racemic substrates.

In principle, the absolute configurations of derivatized substrates can be deduced from the relative chemical shifts of the diastereomeric derivatives if one knows both the absolute configuration of the CDA and the solution conformations of its diastereomeric derivatives. The last requirement is generally the most difficult to meet.

Mosher and co-workers have concerned themselves with the conformational behavior of diastereomeric esters of 1 and have offered a conformational model for correlating NMR behavior with the absolute configurations of the diastereomers.[5] They carefully point out that the conformational model represents a weighted average of the effects of all conformations contributing to the diastereotopic nonequivalence and not the exclusive population of a single conformation. Since population of conformations giving rise to no nonequivalence dilutes the effects of those that do, Yamaguchi et al.[6] have advocated the use of lanthanide shift reagents to reduce the conformational mobility of diastereomeric derivatives of 1. The resultant chelatelike complexes also make more certain the assignment of absolute configurations to the derivatized solutes from NMR data. This approach might be avoided provided the diastereomeric derivatives were conformationally more rigid.

In addition of Mosher's acid, several other CDAs have been described. For example, isocyanates such as 3 (now



3 4 5

commercially available) or chloroformates such as 4 have been used to afford diastereomeric carbamates from type 2 alcohols or amines, respectively.[7] The absolute configurations of these CDAs are known, and the conformational behavior of the carbamate derivatives is well understood. Hence, NMR chemical shift differences between diastereomeric carbamates can be reliably and easily correlated to stereochemistry.[8] Similar correlations have been made by Helmchen for an extensive series of diastereomeric amides[9-11] derived from either chiral benzylamines or hydroxyamines such as 5.

One important difference between CDAs and either CSAs or CLSRs is that diastereomeric derivatives often prove to be chromatographically separable, thereby adding another dimension for analysis of diastereomeric ratios and absolute configurations. In many instances, differences in NMR or chromatographic behavior between a pair of diastereomers can be considered as different manifestations of the population of a particular set of conformations.

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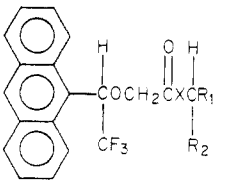
(2) (a) Whitesides, G. M.; Lewis, D. W. *J. Am. Chem. Soc.* **1971**, *93*, 5915. (b) Goering, H. L.; Eikenberry, J. N.; Koermen, G. S. *Ibid.* **1971**, *93*, 5913.
(3) Dale, J.; Dull, D.; Mosher, H. *J. Org. Chem.* **1969**, *34*, 2543.
(4) Kalyanam, N.; Lightner, D. *Tetrahedron Lett.* **1979**, 415.
(5) Dale, J.; Mosher, H. *J. Am. Chem. Soc.* **1973**, *95*, 512.
(6) Yamaguchi, S.; Yasuhara, F.; Kabuto, K. *Tetrahedron* **1976**, *32*, 1363.
(7) Pirkle, W. H.; Hoekstra, M. S. *J. Org. Chem.* **1974**, *39*, 3904.
(8) Pirkle, W. H.; Simmons, K. A.; Boeder, C. W. *J. Org. Chem.* **1979**, *44*, 4891.
(9) Helmchen, G.; Nill, G.; Flockerzi, D.; Schule, W.; Youssef, M. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 62.
(10) Helmchen, G.; Nill, G.; Flockerzi, D.; Youssef, M. *Ibid.* **1979**, *18*, 63.
(11) Helmchen, G.; Nill, G. *Ibid.* **1979**, *18*, 65.

0022-3263/81/1946-3239$01.25/0

Table I. ^1H and ^{19}F NMR Chemical Shift Differences for Diastereotopic Nuclei in ATEA Derivatives



				chemical shift differences, ppm					
						OCH_2CO			
compd	R_1	R_2	X	R_1	R_2	low	high	$CHCF_3$	CF_3
8	CH_3	CH_3	NH	0.20	0.20	0	0	0	
9	CH_3	CH_2CH_3	NH	0.25	0.24	0.01	0.02	0.03	
10	CH_3	cyclohexyl	NH	0.33		0.01	0.03	0.03	
11	CH_3	$C(CH_3)_3$	NH	0.43	0.08	0.09	0.06	0.02	
12	CH_3	$(CH_2)_5CH_3$	NH	0.15	0.09	0.03	0.02	0.02	
13	CH_3	CH_2Ph	NH	0.18	0.18	0	0	0.12	0.10
14	CH_3	Ph	NH	0.25					0.05
15	CH_2CH_3	Ph	NH	0.24				0.03	
16	CH_3	1-naphthyl	NH	0.25		0	0	0.11	0.10
17	CH_3	2-naphthyl	NH	0.25		0.07	0.12		0.13
18	phenyl	CH_2Ph	NH			0.09	0.02	0.11	
19	CH_3	CH_3	O	0.07	0.07	0	0	0	
20	CH_3	CH_2CH_3	O	0.09	0.07	0.02	0.02	0.02	
21	CH_3	cyclohexyl	O	0.11		0.03	0.05	0.06	0.13
22	CH_3	$CH_2C(CH_3)_3$	O	0.13	0.12	0.01	0.15	0.09	
23	CH_3	$C(CH_3)_3$	O	0.14	0.05	0.02	0.06	0.03	
24	CH_3	$(CH_2)_5CH_3$	O	0.12	0.03	0.02	0.08	0.01	0.10
25	CH_3	C≡CH	O	0.02	0.10	0.02	0.03	0	
26	CH_2CH_3	C≡CH	O	0.03	0.10	0.02	0.04	0	
27	$(CH_2)_3CH_3$	C≡CH	O	0.03	0.10	0.02	0.05	0.03	
28	CH_3	Ph	O	0.07		0	0.01	0.03	0.05
29	CH_3	CH_2Ph	O	0.06				0.14	
30	$C(CH_3)_3$	Ph	O	0.07		0.01	0.03	0.05	
31	CH_3	CH_2SPh	O	0.03		0.02	0.15	0.03	0
32	CH_3	$CH_2CH_2CH=C(CH_3)_2$	O	0.10	0.11/0.05	0.02	0.05	0.05	
33	CH_3	Ph	S	0.05		0	0.02	0.03	

However, diastereomers showing dissimilar NMR properties need not differ in their chromatographic properties and vice versa. In this paper, we address ourselves solely to the NMR behavior of diastereomers.

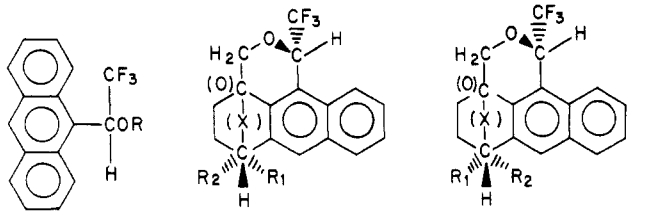
If one set out to design an efficient CDA for the NMR determination of enantiomeric purity and absolute configuration, a prime goal would be to attain extensive population of well-defined conformations capable of placing diastereotopic nuclei in substantially different magnetic environments. This clearly requires a stereochemically dependent placement of diastereotopic groups relative to a powerful chemical shift perturber.

We now describe the synthesis of α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetic acid (6, ATEA) demonstrate its usefulness as a CDA, address the question of solution conformations of its derivatives, and discuss those cases in which it may be used to assign absolute configurations to derivatives of unknown stereochemistry.

Results and Discussion

Williamson alkylation of 2,2,2-trifluoro-1-(9-anthryl)-ethanol (7) with ethyl bromoacetate followed by saponification leads to ATEA in high yield. Either enantiomer of ATEA can be obtained from the corresponding enantiomer of 7. After carboxyl activation, ATEA was allowed to react with enantiomeric primary amines, alcohols, and mercaptans to afford diastereomeric derivatives 8–33. No measurable asymmetric induction[12] was noted during the course of this study. The resulting derivatives typically exhibit chemical shift differences between most of the diastereotopic nuclei as shown in Table I, although these differences are usually greatest for the groups designated R_1 and R_2. In general, amides show more diastereotopic nonequivalence than do the analogous esters or thioesters. Note that for the derivatives of 2-aminooctane **12** and 2-octanol **24**, the terminal methyl groups exhibit 0.09 and 0.03 ppm of diastereotopic nonequivalence even though these groups are *twelve* bonds removed from the chiral center of ATEA.

Chart I[a]



6, R = CH_2CO_2H
7, R = H

34a 34b

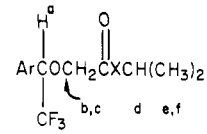
[a] X = O, NH, S, and NR.

Conformational Behavior of ATEA Derivatives

Without preamble, we will assert that **34a,b** are the conformational representations of diastereomeric derivatives 8–33 which best account for the observed time-average chemical shift nonequivalence of these diastereomers. The basis for this assertion follows in the next few paragraphs.

(12) When optically pure ATEA was allowed to react with several racemic amines and the reaction stopped before completion, there was a 50:50 mixture of diastereomers, as determined by NMR integration, indicating no asymmetric induction had occurred.

Table II. Isopropyl Derivatives of ATEA Analogues



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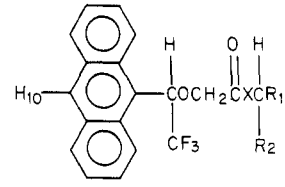
compd	Ar	X	^{1}H NMR chemical shift, ppm a	b,c	d	e	f	e,f
35a	phenyl	O	4.96	4.08	5.07	1.24	1.24	0
35b	phenyl	NH	4.64	3.75	4.14	1.20	1.16	0.04
35c	1-naphthyl	O	5.97	4.15	5.12	1.19	1.15	0.04
35d	3-pyrenyl	O	6.23	4.25	5.05	1.09	1.06	0.03
19	9-anthryl	O	6.65	3.96	4.97	1.16	1.09	0.07
8	9-anthryl	NH	6.24	4.02	3.98	1.03	0.82	0.21

The anthryl group of ATEA is directly involved in the generation of diastereomeric nonequivalence; neither the phenyl nor the 1-naphthyl analogues of ATEA are as efficacious in producing diastereomeric nonequivalence (see Table II). Moreover, because of the greater diamagnetic anisotropy of the anthryl group, the R_1 and R_2 resonances occur at higher field in the ATEA derivatives than for the phenyl or 1-naphthyl analogues.

In a series of aryl trifluoromethyl carbinols, the carbinyl proton resonance is found progressively further downfield on going from the phenyl (4.93 ppm) to the 1-naphthyl (5.62 ppm) to the 9-anthryl (6.57 ppm) analogue. In the last instance, the trifluoromethyl and hydroxyl groups must "straddle" one of the two peri hydrogens, placing the carbinyl hydrogen in close proximity to the remaining peri hydrogen. In this preferentially populated conformation, the carbinyl hydrogen is deshielded both by steric crowding and by its "in plane" relationship to the anthryl group. An important consequence of this conformation is that the hydroxyl group is positioned above the plane of and offset toward one end of the anthryl system. Analogously, the carbonyl of ATEA and its derivatives is similarly offset, making it possible to readily achieve an orientation such that the carbonyl is above and perpendicular to the terminal ring of the anthryl system, the positive end of the carbonyl dipole being "buried" in the aromatic π cloud. This type of solvation is responsible for most benzene induced solvent shifts in amides and esters.[13] In the case of ATEA derivatives, this solvation is particularly favorable since not only is it intramolecular but there also are three intervening atoms (C–O–C) between the interacting groups, a geometrically favorable arrangement for such an interaction.[14]

Finally, in esters, amides, and thioesters derived from ATEA, the conformation placing the methine hydrogen near and essentially in the plane of the carbonyl group is preferentially populated. This conformational preference is responsible for the acylation shifts (for the methine proton) that occur when a type **2** alcohol, amine, or thiol is acetylated. It is pertinent to point out that lanthanide-induced shift gradients (LIS) for several ATEA derivatives are consistent with this conformational picture. Note from Table III that the large, similar LIS gradients observed for the OCH_2CO and XCH protons suggest that these protons are near the coordination site for $Eu(fod)_3$ (i.e., the carbonyl oxygen). Just such a relationship is depicted in conformations **34a,b**. The much smaller gradients observed for the $CHCF_3$ proton and the proton on the 10-position of the anthryl system indicate that these protons are remote from the coordination site.

Table III. LIS Gradients for ATEA Derivatives in $CDCl_3$



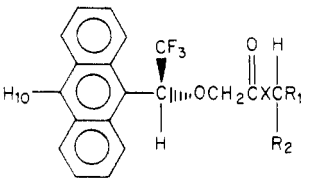
R_2[a]	X	^{1}H obsd LIS gradients,[b] ppm/equiv of LSR R_1	R_2	XCH	OCH_2-CO	$CHCF_3$
CH_2Ph	NH	8.7	9.3	22.7	22.1	4.9
$C(CH_3)_3$	NH	9.0	6.9	27.3	27.7	5.4
Ph	O	5.0		14.0	12.0	6.4

[a] R_1 is CH_3 in all cases. [b] H-10 value was 1.0 ppm/equiv of LSR in all cases.

A more rigorous test of the solution conformation responsible for the observed diastereotopic nonequivalences is provided by examining the NMR properties of a series of stereochemically known diastereomerically enriched ATEA derivatives.[15] One notes that the R_1 resonance should occur at higher field in **34a** than in **34b** owing to greater shielding by the anthryl group in the former instance. The converse is expected for R_2. The diastereomers indicated in Table IV were prepared from ATEA and from amines or alcohols of known absolute configuration. In each instance where the sense of nonequivalence could be discerned, the observed sense was in accord with the conformational representations shown in **34a,b**. Accordingly, we presume that derivatives **8–33** all show NMR behavior in accord with that demonstrated for the ATEA derivatives in Table IV. We hasten to point out that only the senses of nonequivalence for R_1 and/or R_2 should be used in assigning relative/absolute configurations to type **2** amines, alcohols, or thiols, since the diastereotopic nonequivalence for these groups stems predominantly from differential exposure to the ring current effects of the anthryl system. The senses of nonequivalence noted for the remaining diastereotopic nuclei show no clear nor consistent pattern. This is not especially surprising since these diastereotopic groups, being further removed from the face of the anthryl system and experiencing weakened effects from this system, may experience additional chemical shift perturbations from other sources, these

(13) Ronayne, J.; Williams, D. *J. Chem. Soc., Chem. Commun.* **1966**, 712.
(14) Leonard, N. J. *Acc. Chem. Res.* **1979**, *12*, 423.
(15) Diastereomeric enrichment facilitates assignment of NMR signals to each diastereomer.

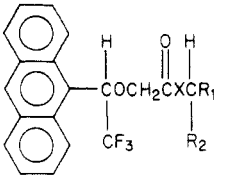
Table IV. Observed ^1H and ^{19}F Diastereotopic Nonequivalences for Enriched ATEA Derivatives



			^1H nonequivalences[a]				
compd[b]	R_2[c]	X	R_2	OCH_2CO	$CHCF_3$	CF_3	H-10
13	CH_2Ph	NH	L	none	H	L	H
14	Ph	NH		none	none	L	L
16	1-naphthyl	NH		none	H	H	L
17	2-naphthyl	NH		both H		L	H
24	$(CH_2)_5CH_3$	O	L	both L	H	H	none
32	$CH_2CH_2CH{=}C(CH_3)_2$	O	both L	both L	H		none

[a] H means the major diastereomer's NMR signal was found to higher field (lower chemical shift) than the minor diastereomer. L means the converse of H. The nonequivalence was H for R_1 in all cases. [b] Excess diastereomer was *RS* in all cases. [c] R_1 was CH_3 in all cases.

Table V. ^1H NMR Nonequivalences for Additional ATEA Derivatives



				nonequivalence, ppm[a]				
compd	R_1	R_2	X	R_1	R_2	XCH	OCH_2CO	$CHCF_3$
36	Ph	CO_2CH_3	O		0.09	0.01	0.07, 0.11	0.12
37	CH_3	$CONH_2$	O	0.18		0.04		0
38	CH_3	CO_2CH_3	O	0.11	0.13	0.02	0.03, 0.07	0.02
39	CH_3	CO_2CH_3	S	0.03	0.06	0		0
40	H	Ph	O	0.04		0.04		
41	H	Ph	S	0		0		
42	H	Ph	NH	0.02		0.02		
43	H	4-NO_2Ph	O	0		0		

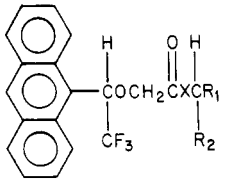
[a] The nonequivalences reported for compounds 41-43 were obtained at low temperature (−45 °C).

latter effects actually determining the observed nonequivalence senses. For example, small differences in steric or electronic interactions between R_1 or R_2 and the anthryl system when these groups are disposed over the aromatic system (shown in **34a** and **34b**, respectively) could result in minor conformational differences between the diastereomers. Diastereotopic nonequivalence of the OCH_2CO protons may result from different dihedral angles between these hydrogens and the anisotropic carbonyl. Similarly, nonequivalence of the $CHCF_3$ hydrogens may result from different dihedral angles with respect to the anthryl ring. Contemplation of the possibility that interactions between the anthryl system and R_1 and R_2 might alter the conformations depicted in **34a,b** led us to search for such interactions. Toward this end, ATEA derivatives **36–43** were prepared, **36** and **38** being diastereomerically enriched and of known absolute configuration (see Table V). In compounds **36–39**, R_2 contains a carbonyl group that conceivably might provide an additional bonding dipole–π electron interaction in the conformation depicted in **34b**. The nonequivalence magnitudes noted for diastereomers **36–39** are not notably different than those reported in Table I, and the senses of nonequivalence observed for R_1 and R_2 in configurationally known **36** and **38** are those expected from the previously discussed conformational model. Compounds **40–43** are single compounds rather than mixtures of diastereomers. However, R_1 and XCH are diastereotopic benzylic hydrogens and can, in principle, have different chemical shifts. A possible origin of this chemical shift difference might stem from interaction between the anthryl group and the aromatic R_2 group, leading to population of rotamers (about the X–CH bond) that place XCH and R_1 in different average positions with respect to the anthryl system. The modest chemical shift differences noted for the diastereotopic benzylic hydrogens could be observed only at low temperature (−40 °C). This suggests that no significant interactions occur between the anthryl and the aryl R_2 groups that lead to selective population of the aforementioned rotamers.

The apparent lack of strong interactions between R_1 or R_2 and the anthryl system so as to perturb conformations **34a,b** supports the notion that ATEA should be a reliable CDA for NMR determinations of absolute/relative configurations for type **2** amines, alcohols, and thiols.

In the preceding discussions of amides derived from ATEA and type **2** amines, we have implicitly assumed that the proton on nitrogen is directed toward the anthryl π cloud. That is, the configuration about the rotationally hindered amide bond is *Z* rather than *E*. This intuitively seems reasonable in consideration of the acidity of amide protons and the basicity of aromatic π clouds. Moreover, steric factors should also favor population of the *Z* rotamer. Efforts to determine the *Z*/*E* ratio for ATEA amide **8** by low-temperature (−50 °C) NMR measurements led to the

Table VI. Diastereomeric Nonequivalence Magnitudes for Some ATEA Derivatives in Various Solvents



R_2[a]	X	^{1}H NMR nonequivalence for R_1[a] (ppm) in $(CD_3)_2CO$	$CDCl_3$	CCl_4
Ph	NH		0.25	0.25
1-naphthyl	NH		0.25	0.25
$C(CH_3)_3$	NH	0.41	0.43	0.43
CH_2Ph	NH	0.19	0.18	0.15
CH_3	NH	0.16	0.20	0.21
CH_3	O	0.03	0.07	0.09
CH_2Ph	O	0.07	0.05	0.07
cyclohexyl	O	0.12	0.11	0.14
Ph	O	0.12	0.07	

[a] R_1 was CH_3 in all cases.

observation of neither a second conformational species nor line broadening attributable to the significant population of such a species. Since we presume that the magnitude of the rotational barrier and the chemical shift difference between rotamers would allow observation of the second rotamer, we infer that the equilibrium concentration of the *E* rotamer is too low to detect by NMR. Low-temperature NMR measurements upon esters **23** and **25** gave similar results. Importantly, the nonequivalence magnitudes noted for **8**, **23**, and **25** are the same at −50 °C as at 25 °C, indicating that conformation **34a,b** is quite stable and *heavily populated at 25 °C*. However, in the case of the ATEA amide **44** of the secondary amine *N*-methyl-1-phenylethylamine, population of the *E* rotamer is significant. At 25 °C, the 220-MHz NMR spectrum of **44** shows additional (and severely broadened) resonances for the NCH_3 and CCH_3 groups attributed to slow rotation about the carbonyl–nitrogen bond. At 62 °C, the NCH_3 signal is a relatively sharp singlet, coalescence occurring near 40 °C (line width ca. 15 Hz). At −20 °C, the ratio of *Z* to *E* rotamers is 70:30. The NCH_3 signal in the major *Z* rotamer is 0.42 ppm upfield of that in the *E* rotamer, consistent with the NCH_3 of the *Z* rotamer being thrust into the anthryl π cloud in **34a,b**. Ideally, one could use the senses of nonequivalences for the CCH_3 to assign configuration in the slow-exchange limit, but, practically, this could not be done owing to overlapping of the requisite NMR signals. In general, the significant population of both the *Z* and *E* rotamers will complicate the NMR determinations of enantiomeric purity and configuration for secondary amines. In some cases, this complication might be overcome through variable-temperature NMR techniques.

Finally, insofar as conformations **34a,b** represent an intramolecular solvation, we investigated the extent to which solvent polarity would alter such conformations. Table VI lists nonequivalence magnitudes for several diastereomeric ATEA derivatives in the more common NMR solvents. As a rule, there is no great change or trend evident in observed nonequivalence magnitudes, consistent with the view that conformations **34a,b** are quite stable and not easily disrupted by solvent polarity.

Experimental Section

Melting points were taken on Büchi apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 237B or Beckman IR-12 spectrophotometer. NMR spectra were obtained with a Varian Associates EM-390 or HR-220 spectrometer. Mass spectra were determined by using a Varian MAT CH-5 spectrometer, and microanalyses were performed by J. Nemeth and associates at the University of Illinois.

ATEA Amides. ATEA amides were prepared by the following procedure. ATEA **6** (1.0 mmol), 5 mL of $CHCl_3$, and 1.1 mmol of *N*-(ethoxycarbonyl)-2-ethoxy-1,2-dihydroquinoline (EEDQ) were stirred for 10 min, the amine (1.0 mmol) was added in 1 mL of $CHCl_3$, and the reaction was stirred for 8 h. The reaction was washed with 3 N HCl, H_2O, saturated $NaHCO_3$, and H_2O, dried, and concentrated under vacuum to give the amides as very viscous oils which were purified by liquid chromatography (silica gel, CH_2Cl_2–hexane (1:1)) followed by molecular distillation at 150 °C and 0.10 torr.

ATEA Esters and Thioesters. ATEA esters were prepared by the following procedure. ATEA **6** (1.1 mmol), 3 g (14 mmol) of trifluoroacetic anhydride (TFAA), and 2 mL of CH_2Cl_2 were stirred under nitrogen for 2 h, and the excess TFAA, TFA, and CH_2Cl_2 was distilled under reduced pressure to give the mixed anhydride of TFA and **6** as a pale, yellow solid: IR ($CHCl_3$) 1850, 1780 cm^{-1}. To a THF solution of this anhydride (5 mL) was added a solution of 1.0 mmol of alcohol (or thiol) and ca. 3 mmol of pyridine in 5 mL of THF. The reaction was heated at reflux for 2 h and then washed with 1 N HCl, H_2O, saturated $NaHCO_3$, and H_2O. Evaporation of the solvent (after drying) afforded the esters (thioesters) as very viscous oils which were purified by molecular distillation at 130 °C and 0.10 torr.

Alternately, ATEA **6** can be activated by use of oxalyl chloride. ATEA **6** (0.5 mmol), 0.26 g (2 mmol) of oxalyl chloride, and 3 mL of benzene were heated to reflux for 5 h. Removing the volatiles under reduced pressure gives the acid chloride as an oil, IR ($CHCl_3$) 1795 cm^{-1}.

Since the ATEA diastereomeric derivatives would not separate on silica gel, all reaction products were characterized as the diastereomeric mixture unless otherwise noted.

α-[1-(9-Anthryl)-2,2,2-trifluoroethoxy]acetic Acid (6). NaH (1.72 g, 72 mmol) in 30 mL of dry THF was cooled to 0 °C, 18.0 g (65 mmol) of racemic 1-(9-anthryl)-2,2,2-trifluoroethanol in 80 mL of THF was added slowly, and the mixture was stirred 3 h at 0 °C. Then, 12.1 g (72 mmol) of ethyl bromoacetate in 25 mL of THF was slowly added, and the reaction was stirred at room temperature for 8 h, washed with water, dried, and concentrated under reduced pressure to give the ethyl ester of ATEA as a yellow solid: mp 79–81 °C (hexane); 93% yield; NMR ($CDCl_3$) δ 1.13 (t, 3 H), 3.86–4.20 (AB pattern, 2 H), 4.07 (dq, 2 H), 6.70 (q, 1 H), 7.36–7.59 (m, 4 H), 7.95 (t, 2 H), 8.11 (d, 1 H), 8.48 (s, 1 H), 8.91 (d, 1 H); IR ($CHCl_3$) 3065, 3020, 1755, 1455, 1380, 1280, 1180, 1135, 1065, 890 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 362 (M^+, 66), 294 (20), 293 (100), 259 (27), 239 (12), 206 (36), 205 (17), 191 (11), 179 (10), 178 (61), 177 (11), 176 (12).

Anal. Calcd for $C_{20}H_{17}F_3O_3$: C, 66.30; H, 4.73; F, 15.73. Found: C, 66.74; H, 4.79; F, 15.51.

This ester was saponified (KOH, 90% EtOH) to give ATEA **6** as white needles: mp 182–183 °C (CCl_4–CH_2Cl_2); 90% yield; NMR (acetone-d_6) δ 4.18–4.39 (AB pattern, 2 H), 6.96 (q, 1 H), 7.36–7.73 (m, 4 H), 7.98–8.18 (m, 2 H), 8.37 (d, 1 H), 8.73 (s, 1 H), 9.01 (d, 1 H); IR (KBr) 3500, 3030, 1750, 1640, 1455, 1380, 1275, 1190, 1150, 1070, 1040, 890 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 334 (M^+, 92), 266 (21), 265 (100), 259 (19), 239 (11), 207 (16), 206 (58), 205 (24), 178 (34), 177 (13), 176 (10). When prepared from *R*-**7**, the resultant *R*-**6** was found to melt at 155–160 °C; $[\alpha]^{27}_D$ −91.0° (*c* 3.0, EtOH).

***N*-(2-Propyl)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamide (8)**: pale yellow glass; 90% yield; NMR ($CDCl_3$) δ 0.85 (d, CH_3), 1.05 (d, CH_3), 3.7–4.2 (AB pattern and m, OCH_2CO, NCH), 6.0–6.3 (q and br s, $CHCF_3$, NH), 7.25–7.65 (m, 4 H), 7.8–8.2 (m, 3 H), 8.50 (s, 1 H), 8.75 (d, 1 H); IR ($CHCl_3$) 3400, 3030, 2970, 1670, 1530, 1450, 1380, 1260, 1180, 1130 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 375 (M^+, 34), 293 (12), 259 (33), 239 (11), 238 (11), 209 (10), 205 (14), 189 (10), 178 (15), 101 (100), 100 (18), 86 (46), 73 (11).

***N*-(2-Butyl)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (9)**: viscous oil; 80% yield; NMR ($CDCl_3$) δ 0.65 (t, CH_3), 0.88 (d, CH_3), 0.91 (t, CH_3), 1.15 (d, CH_3), 1.2–1.6 (m, 4 H, CH_2), 3.80 (m, 2 H), 3.91–4.20 (AB pattern, 4 H, OCH_2CO), 6.25 (q and br s, 4 H), 7.32–7.59 (m, 8 H), 7.95 (d, 4 H), 8.06 (d, 2 H), 8.50

(s, 2 H), 8.80 (d, 2 H); IR ($CHCl_3$) 3400, 3025, 2970, 1675, 1530, 1450, 1375, 1260, 1180, 1125 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 389 (M^+, 45), 259 (52), 239 (14), 209 (15), 208 (24), 180 (23), 152 (18), 149 (18), 115 (100), 91 (25), 86 (39), 60 (79), 57 (29).

***N*-(1-Cyclohexylethyl)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (10)**: pale orange glass; 95% yield; NMR ($CDCl_3$) δ 0.5–1.77 (m, cyclohexyl H), 0.67 (d, CH_3), 1.00 (d, CH_3), 3.63–3.86 (m, 2 H), 3.93–4.27 (AB pattern, 4 H, OCH_2CO), 6.27 (dq and br s, 4 H), 7.32–7.59 (m, 8 H), 7.97 (d, 4 H), 8.05 (d, 2 H), 8.50 (s, 2 H), 8.77 (d, 2 H); IR ($CHCl_3$) 3400, 3150, 3050, 2945, 1670, 1520, 1460, 1370, 1275, 1180, 1120 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 443 (M^+, 33), 260 (15), 259 (76), 169 (45), 149 (24), 110 (16), 87 (27), 86 (100), 69 (21), 60 (44), 55 (29), 44 (21).

Anal. Calcd for $C_{26}H_{28}NO_2F_3$: C, 70.41; H, 6.36; N, 3.16; F, 12.86. Found: C, 70.52; H, 6.41; N, 3.27; F, 12.57.

***N*-(3,3-Dimethylbut-2-yl)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (11)**: pale orange solid; mp 105–118 °C (hexane); 80% yield; NMR ($CDCl_3$) δ 0.65 (d, CH_3), 0.72 (s, 9 H), 0.80 (s, 9 H), 1.08 (d, CH_3), 3.77 (dq, 2 H), 3.93–4.25 (AB pattern, 4 H, OCH_2CO), 6.27 (dq, 2 H), 6.45 (br s, 2 H), 7.41–7.61 (m, 8 H), 7.91–8.09 (m, 6 H), 8.52 (s, 2 H), 8.77 (d, 2 H); IR ($CHCl_3$) 3400, 3150, 3050, 2950, 1670, 1520, 1465, 1380, 1265, 1180, 1120 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 417 (M^+, 26), 259 (69), 143 (29), 86 (100), 57 (14), 44 (18).

Anal. Calcd for $C_{24}H_{26}NO_2F_3$: C, 69.05; H, 6.28; N, 3.36. Found: C, 69.47; H, 6.37; N, 2.99.

***N*-(2-Octyl)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (12)**: viscous oil; 76% yield; NMR ($CDCl_3$) δ 0.80 (t, CH_3), 0.89 (t, CH_3), 0.77–1.36 (m, 20 H, $(CH_2)_5$), 1.01 (d, CH_3), 1.16 (d, CH_3), 3.82 (m, 2 H), 3.91–4.23 (AB pattern, 4 H, OCH_2CO), 6.23 (q, 2 H), 7.32–7.61 (m, 8 H), 7.95 (d, 4 H), 8.05 (d, 2 H), 8.50 (s, 2 H), 8.76 (d, 2 H); IR ($CHCl_3$) 3380, 3090, 2960, 1670, 1520, 1460, 1370, 1270, 1180, 1120 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 445 (M^+, 61), 260 (20), 259 (95), 239 (22), 209 (16), 205 (19), 191 (16), 178 (18), 171 (40), 156 (24), 142 (25), 137 (17), 128 (29), 125 (22), 123 (32), 111 (43), 110 (16), 109 (38), 100 (29), 97 (49), 95 (46), 87 (54), 86 (84), 85 (44), 83 (52), 81 (40), 71 (66), 69 (64), 60 (100), 57 (94), 55 (63), 43 (66).

***N*-(1-Phenylprop-2-yl)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (13)**: light yellow solid; mp 113–115 °C (EtOAc–hexane); 71% yield; NMR ($CDCl_3$) δ 0.90 (d, CH_3), 1.08 (d, CH_3), 2.3–2.7 (m, 4 H), 3.7–4.3 (AB pattern and quintet, 6 H), 5.9–6.5 (dq and br s, 4 H), 6.7–7.6 (m, 18 H), 7.7–8.1 (m, 6 H), 8.5 (s, 2 H), 8.65 (br d, 2 H); IR ($CHCl_3$) 3350, 3100, 2950, 1665, 1520, 1460, 1370, 1270, 1180, 1120 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 451 (M^+, 31), 360 (6), 260 (14), 259 (83), 177 (11), 118 (26), 91 (22), 86 (100), 44 (14), 43 (10).

***N*-(1-Phenylethyl)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (14)**: pale yellow solid; mp 110–121 °C ($CHCl_3$–hexane); 80% yield; NMR ($CDCl_3$) δ 1.12 (d, CH_3), 1.36 (d, CH_3), 3.90–4.23 (AB pattern, 4 H, OCH_2CO), 4.98 (q, 2 H), 6.20 (q, 2 H), 6.68 (br s, 2 H), 6.88–7.34 (m, 10 H), 7.34–7.61 (m, 8 H), 7.89–8.34 (m, 6 H), 8.52 (s, 2 H), 8.75 (d, 2 H); IR ($CHCl_3$) 3350, 3100, 2950, 1660, 1520, 1460, 1370, 1270, 1180, 1120 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 437 (M^+, 28), 259 (17), 208 (11), 180 (10), 163 (44), 106 (12), 105 (100), 104 (14), 84 (15), 59 (18).

***N*-(1-Phenylprop-1-yl)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (15)**: yellow glass; 74% yield; NMR ($CDCl_3$) δ 0.60 (t, CH_3), 0.84 (t, CH_3), 0.8–1.0 (m, 2 H), 1.2–1.5 (m, 2 H), 3.8–4.3 (AB pattern, 4 H, OCH_2CO), 4.78 (q, 2 H), 6.27 (dq, 2 H), 6.6–6.8 (br m, 2 H), 7.0–7.4 (m, 10 H), 7.4–7.6 (m, 8 H), 7.9–8.2 (m, 6 H), 8.59 (d, 2 H), 8.85 (br d, 2 H); IR ($CHCl_3$) 3360, 3100, 2955, 1600, 1520, 1465, 1370, 1270, 1175, 1120 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 451 (M^+, 4), 293 (26), 279 (13), 259 (12), 206 (11), 178 (12), 167 (41), 150 (12), 149 (100), 113 (13), 91 (16), 83 (8), 71 (26), 70 (19), 57 (35), 55 (12).

***N*-[1-(1-Naphthyl)ethyl]-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (16)**: viscous oil; 86% yield; NMR ($CDCl_3$) δ 1.30 (d, CH_3), 1.53 (d, CH_3), 3.8–4.3 (AB pattern, 4 H, OCH_2CO), 5.6–6.0 (quintet, 2 H), 5.9–6.4 (dq, 2 H), 6.5–6.8 (br s, 2 H), 6.8–8.0 (m, 28 H), 8.4 (s, 1 H), 8.5 (s, 1 H), 8.5–8.6 (br d, 2 H); IR ($CHCl_3$) 3350, 3100, 2950, 1660, 1520, 1450, 1370, 1260, 1180, 1120 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 487 (M^+, 2), 259 (1), 213 (2), 155 (12), 91 (7), 88 (11), 86 (84), 84 (100), 47 (19), 42 (7).

***N*-[1-(2-Naphthyl)ethyl]-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (17)**: yellow glass; 80% yield; NMR ($CDCl_3$) δ 1.36 (d, CH_3), 1.54 (d, CH_3), 3.82–4.32 (AB patterns, 4 H, OCH_2CO), 5.23 (quintet, 2 H), 6.69 (q, 2 H), 6.82 (br d, 2 H), 7.23–7.57 (m, 18 H), 7.61–7.77 (m, 6 H), 7.80–7.95 (m, 2 H), 8.04 (d, 2 H), 8.44 (s, 2 H), 8.72 (br d, 2 H); IR ($CHCl_3$) 3345, 3100, 2990, 2950, 1670, 1520, 1450, 1365, 1260, 1175, 1120 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 487 (M^+, 4), 259 (5), 213 (2), 155 (15), 91 (5), 88 (10), 86 (85), 84 (100), 47 (19), 42 (6).

***N*-(1,2-Diphenylethyl)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (18)**: light yellow solid; mp 154–164 °C (CH_2Cl_2–hexane); 85% yield; NMR ($CDCl_3$) δ 2.59–3.11 (7, 4 H, CH_2), 3.82–4.16 (AB pattern, 4 H, OCH_2CO), 5.02–5.30 (dq, 2 H), 6.02–6.27 (dq, 2 H), 6.6–6.73 (m, 20 H), 7.3–7.5 (m, 8 H), 7.8–8.0 (m, 6 H), 8.48 (d, 2 H), 8.73 (m, 2 H); IR ($CHCl_3$) 3350, 3100, 2950, 1660, 1520, 1460, 1370, 1270, 1180, 1120 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 513 (M^+, 3), 422 (7), 259 (32), 101 (21), 86 (100), 58 (35), 57 (17), 56 (10), 44 (13).

2-Propyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetate (19): light yellow solid; mp 62–63 °C (hexane); 85% yield; NMR ($CDCl_3$) δ 1.08 (d, CH_3), 1.15 (d, CH_3), 3.9–4.2 (AB pattern, 2 H, OCH_2CO), 4.97 (septet, 1 H), 6.67 (q, 1 H), 7.28–7.70 (m, 4 H), 7.8–8.2 (m, 3 H), 8.48 (s, 1 H), 8.91 (d, 1 H).

Anal. Calcd for $C_{21}H_{19}F_3O_3$: C, 67.02; H, 5.09. Found: C, 67.33; H, 5.00.

2-Butyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (20): light yellow viscous oil; 75% yield; NMR ($CDCl_3$) δ 0.68 (t, CH_3), 0.76 (t, CH_3), 1.03 (d, CH_3), 1.13 (d, CH_3), 1.3–1.5 (m, 4 H), 3.8–4.2 (AB patterns, 4 H), 4.8–4.9 (m, 2 H), 6.6–6.8 (dq, 2 H), 7.4–7.6 (m, 8 H), 7.95 (dd, 4 H), 8.12 (d, 2 H), 8.49 (s, 2 H), 8.91 (d, 2 H); mass spectrum (70 eV), m/e (relative intensity) 390 (M^+, 4), 199 (16), 173 (27), 172 (17), 155 (68), 91 (100), 65 (27), 56 (45), 43 (20).

1-Cyclohexylethyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (21): pale yellow glass; 94% yield; NMR ($CDCl_3$) δ 1.01 (d, CH_3), 1.11 (d, CH_3), 1.20–1.90 (m, cyclohexyl H), 3.8–4.2 (two AB patterns, 4 H), 4.78 (d of quintets, 2 H), 6.70 (dq, 2 H), 7.3–7.7 (m, 8 H), 7.9 (dd, 4 H), 8.15 (d, 2 H), 8.50 (s, 2 H), 8.91 (d, 2 H); mass spectrum (70 eV), m/e (relative intensity) 444 (M^+, 0), 334 (12), 266 (18), 265 (100), 260 (11), 259 (57), 239 (17), 238 (10), 209 (10), 206 (25), 178 (23), 97 (78), 55 (60).

Anal. Calcd for $C_{26}H_{27}F_3O_3$: C, 70.26; H, 6.12; F, 12.82. Found: C, 70.49; H, 5.96; F, 12.84.

4,4-Dimethylpent-2-yl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (22): pale yellow viscous oil; 70% yield; NMR ($CDCl_3$) δ 0.64 (s, 9 H), 0.71 (s, 9 H), 0.93 (d, CH_3), 1.06 (d, CH_3), 1.0–1.5 (m, 4 H, CH_2), 3.5–4.1 (two AB patterns, 4 H), 5.8 (m, 2 H), 6.45 (dq, 2 H), 6.95–7.3 (m, 8 H), 7.6 (d, 4 H), 7.8 (d, 2 H), 8.12 (s, 2 H), 8.56 (d, 2 H); mass spectrum (70 eV), m/e (relative intensity) 432 (M^+, 45), 334 (11), 293 (9), 265 (69), 259 (58), 206 (21), 178 (13), 99 (11), 83 (27), 57 (100), 55 (11), 43 (15).

3,3-Dimethylbut-2-yl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (23): light yellow solid; mp 75–81 °C (hexane); 70% yield; NMR ($CDCl_3$) δ 0.75 (s, 9 H), 0.80 (s, 9 H), 0.97 (d, CH_3), 1.11 (d, CH_3), 3.8–4.2 (two patterns, 4 H), 4.7 (m, 2 H), 6.68 (dq, 2 H), 7.4–7.6 (m, 8 H), 7.95 (dd, 4 H), 8.12 (d, 2 H), 8.49 (s, 2 H), 8.91 (d, 2 H); mass spectrum (70 eV), m/e (relative intensity) 418 (M^+, 64), 266 (19), 265 (98), 260 (30), 259 (82), 239 (18), 206 (24), 191 (32), 189 (15), 178 (17), 85 (100), 73 (20), 71 (16), 69 (23), 57 (72), 55 (25), 44 (23), 43 (99), 41 (54).

2-Octyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (24): pale yellow oil; 90% yield; NMR ($CDCl_3$) δ 0.83 (t, CH_3), 0.86 (t, CH_3), 1.0–1.5 (m, 20 H, CH_2), 1.02 (d, CH_3), 1.11 (d, CH_3), 3.8–4.2 (two AB patterns, 4 H), 4.91 (m, 2 H), 6.73 (dq, 2 H), 7.3–7.6 (m, 8 H), 7.93 (m, 4 H), 8.12 (d, 2 H), 849 (s, 2 H), 8.91 (d, 2 H); mass spectrum (70 eV), m/e (relative intensity) 446 (M^+, 24), 378 (27), 377 (100), 265 (16), 97 (16), 95 (14), 83 (15), 71 (37), 70 (16), 69 (33), 57 (80), 56 (22), 55 (45).

But-1-yn-3-yl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]-acetates (25): pale yellow solid; mp 53–63 °C; 76% yield; NMR ($CDCl_3$) δ 1.28 (d, CH_3), 1.30 (d, CH_3), 2.24 (d, 1 H), 2.34 (d, 1 H), 3.74–4.17 (two AB patterns, 4 H), 5.31 (dq, 2 H), 6.60 (q, 2 H), 7.3–7.5 (m, 8 H), 7.9 (dd, 4 H), 8.05 (d, 2 H), 8.42 (s, 2 H), 8.80 (d, 2 H); mass spectrum (70 eV), m/e (relative intensity) 386 (M^+, 52), 355 (20), 317 (23), 281 (16), 265 (16), 259 (33), 221 (18),

209 (18), 208 (30), 206 (29), 180 (28), 178 (19), 152 (26), 147 (29), 85 (26), 83 (27), 73 (86), 71 (44), 69 (36), 57 (100), 55 (54), 44 (87), 43 (62).

Anal. Calcd for $C_{22}H_{17}F_3O_3$: C, 68.39; H, 4.43. Found: C, 68.10; H, 4.74.

Pent-1-yn-3-yl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (26): pale yellow oil; 77% yield; NMR ($CDCl_3$) δ 0.86 (t, CH_3), 0.90 (t, CH_3), 1.68 (quintet, 4 H), 2.33 (d, 1 H), 2.43 (d, 1 H), 3.9–4.3 (two AB patterns, 4 H), 5.3 (m, 2 H), 6.70 (m, 2 H), 7.3–7.5 (m, 8 H), 7.9 (dd, 4 H), 8.05 (d, 2 H), 8.42 (s, 2 H), 8.80 (d, 2 H); mass spectrum (70 eV), *m/e* (relative intensity) 400 (M^+, 47), 331 (19), 265 (39), 259 (44), 208 (27), 206 (27), 180 (23), 178 (22), 152 (22), 97 (23), 85 (22), 83 (25), 81 (19), 73 (23), 71 (40), 69 (38), 67 (46), 57 (100), 56 (25), 55 (73), 44 (39), 43 (63), 41 (71).

Hept-1-yn-3-yl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (27): pale yellow viscous oil; 73% yield; NMR ($CDCl_3$) δ 0.75 (t, CH_3), 0.79 (t, CH_3), 0.98–1.36 (m, 8 H), 1.47–1.70 (m, 4 H), 2.31 (d, 1 H), 2.41 (d, 1 H), 3.8–4.3 (two AB patterns, 4 H), 5.3 (m, 2 H), 6.75 (dq, 2 H), 7.2–7.5 (m, 8 H), 7.85 (d, 4 H), 8.14 (d, 2 H), 8.39 (s, 2 H), 8.93 (d, 2 H); mass spectrum (70 eV), *m/e* (relative intensity) 428 (M^+, 100), 359 (23), 293 (15), 266 (15), 265 (77), 260 (17), 259 (88), 239 (28), 238 (20), 209 (19), 207 (16), 206 (41), 205 (28), 191 (17), 189 (16), 178 (35), 67 (17), 55 (24).

1-Phenylethyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (28): pale yellow viscous oil; 60% yield; NMR ($CDCl_3$) δ 1.35 (d, CH_3), 1.41 (d, CH_3), 3.8–4.3 (two AB patterns, 4 H), 5.85 (q, 2 H), 6.60 (dq, 2 H), 7.0–7.3 (m, 10 H), 7.3–7.5 (m, 8 H), 7.92 (d, 4 H), 8.02 (d, 2 H), 8.45 (s, 2 H), 8.91 (m, 2 H); mass spectrum (70 eV), *m/e* (relative intensity) 438 (M^+, 27), 334 (9), 333 (16), 265 (20), 259 (17), 206 (9), 179 (10), 178 (55), 176 (11), 105 (100).

1-Phenylprop-2-yl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (29): viscous oil; 77% yield; NMR ($CDCl_3$) δ 1.04 (d, CH_3), 1.10 (d, CH_3), 2.5–2.8 (m, 4 H), 3.7–4.2 (two AB patterns, 4 H), 5.10 (hextet, 2 H), 6.55 (q, 1 H), 6.69 (q, 1 H), 6.9–7.3 (m, 10 H), 7.3–7.6 (m, 8 H), 7.8–8.0 (m, 4 H), 8.06 (d, 2 H), 8.45 (s, 2 H), 8.91 (d, 2 H); mass spectrum (70 eV), *m/e* (relative intensity) 452 (M^+, 12), 383 (3), 265 (8), 178 (65), 119 (18), 92 (97), 91 (100), 71 (33), 58 (17), 45 (28), 43 (62).

1-Phenyl-2,2-dimethylprop-1-yl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (30): white solid; mp 88–98 °C; 83% yield; NMR ($CDCl_3$) δ 0.80 (s, 9 H), 0.87 (s, 9 H), 3.8–4.4 (two AB patterns, 4 H), 5.50 (s, 1 H), 5.56 (s, 1 H), 6.5–6.8 (dq, 2 H), 7.0–7.3 (m, 10 H), 7.3–7.6 (m, 8 H), 7.9–8.1 (m, 6 H), 8.50 (s, 2 H), 8.95 (br d, 2 H); mass spectrum (70 eV), *m/e* (relative intensity) 480 (M^+, 3), 259 (8), 178 (11), 147 (10), 108 (11), 107 (100), 105 (13), 91 (16), 79 (43), 77 (17), 57 (32), 43 (12).

1-(Phenylthio)prop-2-yl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (31): viscous oil; 80% yield; NMR ($CDCl_3$) δ 1.14 (d, CH_3), 1.17 (d, CH_3), 2.6–3.1 (m, 4 H), 3.6–4.1 (two AB patterns, 4 H), 5.02 (hextet, 2 H), 6.68 (dq, 2 H), 6.8–7.5 (m, 18 H), 7.86 (d, 4 H), 8.09 (br t, 2 H), 8.39 (s, 2 H), 8.86 (d, 2 H); mass spectrum (70 eV), *m/e* (relative intensity) 484 (M^+, 4), 179 (16), 178 (100), 176 (18), 168 (58), 151 (22), 124 (82), 123 (30), 110 (16), 109 (20), 91 (33), 89 (15), 78 (29), 76 (16), 71 (21); mass spectrum (10 eV), *m/e* (relative intensity) 486 (M + 2, 8.1), 484 (M^+, 83.4).

6-Methyl-5-hepten-2-yl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetate (32): pale yellow oil; 90% yield; NMR (*RS* diastereomer, $CDCl_3$) δ 1.05 (d, CH_3), 1.1–1.5 (m, 2 H), 1.55 (s, CH_3), 1.67 (s, CH_3), 1.85 (br q, 2 H), 3.8–4.4 (AB pattern, 2 H), 4.9 (q and m, 2 H), 6.71 (q, 1 H), 7.4–7.7 (m, 4 H), 7.9–8.3 (m, 3 H), 8.56 (s, 1 H), 8.93 (br d, 1 H); MS (70 eV), *m/e* (relative intensity) 444 (M^+, 48), 334 (42), 266 (11), 261 (56), 259 (31), 206 (19), 178 (14), 111 (24), 110 (15), 95 (17), 69 (100), 55 (16), 41 (25).

1-Phenylethyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]thioacetates (33): pale yellow oil; 79% yield; NMR ($CDCl_3$) δ 1.52 (d, CH_3), 1.57 (d, CH_3), 3.8–4.2 (two AB patterns, 4 H), 4.73 (q, 2 H), 6.50 (2 q, 2 H), 7.0–7.6 (m, 18 H), 7.7–8.2 (m, 3 H), 8.43 (s, 2 H), 8.90 (br d, 2 H); mass spectrum (70 eV), *m/e* (relative intensity) 456 (M + 2, 1.4), 454 (M^+, 16.7), 349 (10), 259 (25), 239 (6), 119 (8), 117 (13), 106 (11), 105 (100), 103 (9), 79 (12), 77 (13), 44 (12).

(Methoxycarbonyl)phenylmethyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (36): white solid; mp 123–130 °C; 66% yield; NMR ($CDCl_3$) δ 3.60 (s, CH_3), 3.89 (s, CH_3), 3.95–4.5 (two AB patterns, 4 H), 5.94 (s, 1 H), 5.95 (s, 1 H), 6.80 (dq, 2 H), 7.2–7.6 (m, 18 H), 7.95 (br d, 4 H), 8.20 (d, 2 H), 8.48 (s, 2 H), 8.90 (br d, 2 H); mass spectrum (70 eV), *m/e* (relative intensity) 482 (M^+, 100), 414 (12), 413 (42), 353 (10), 333 (13), 260 (11), 259 (57), 239 (14), 209 (12), 205 (16), 181 (15), 178 (17), 149 (67), 121 (44), 77 (11), 44 (10).

1-(Aminocarbonyl)ethyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (37): clear viscous oil; 82% yield; NMR ($CDCl_3$) δ 1.20 (d, CH_3), 1.38 (d, CH_3), 3.8–4.4 (two AB patterns, 4 H), 5.1 (dq, 2 H), 6.1 (br s, 4 H), 6.55 (q, 2 H), 7.3–7.7 (m, 8 H), 7.8–8.3 (m, 6 H), 8.48 (s, 2 H), 8.8 (br d, 2 H); IR ($CHCl_3$) 3350, 3200, 2970, 1720, 1660, 1420, 1320, 1110, 1050, 700 cm^{-1}.

1-(Methoxycarbonyl)ethyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetates (38): pale yellow oil; 75% yield; NMR ($CDCl_3$) δ 1.25 (d, CH_3), 1.36 (d, CH_3), 3.55 (s, CH_3), 3.68 (s, CH_3), 3.7–4.5 (two AB patterns, 4 H), 5.1 (dq, 2 H), 6.7 (dq, 2 H), 7.3–7.7 (m, 8 H), 7.8–8.3 (m, 6 H), 8.5 (s, 2 H), 8.9 (br d, 2 H); mass spectrum (70 eV), *m/e* (relative intensity) 420 (M^+, 61), 352 (19), 351 (79), 259 (41), 208 (27), 206 (32), 189 (34), 180 (22), 178 (16), 172 (32), 157 (43), 153 (25), 152 (23), 145 (30), 137 (20), 129 (100), 128 (33), 127 (23), 121 (21), 119 (62), 117 (62), 109 (17), 107 (42), 105 (18), 91 (18), 89 (23), 79 (26), 78 (20), 77 (63), 76 (22), 63 (16), 57 (17), 51 (30), 50 (15).

1-(Methoxycarbonyl)ethyl α-[1-(9-Anthryl)-2,2,2-trifluoroethoxy]thioacetates (39): pale yellow oil; 42% yield; NMR ($CDCl_3$) δ 1.47 (d, CH_3), 1.50 (d, CH_3), 3.67 (s, CH_3), 3.73 (s, CH_3), 4.2 (AB patterns, 4 H), 4.23 (q, 2 H), 6.50 (q, 2 H), 7.3–7.7 (m, 8 H), 7.9–8.3 (m, 6 H), 8.56 (s, 2 H), 8.9 (br d, 2 H); mass spectrum (70 eV), *m/e* (relative intensity) 438 (M + 2, 2.1), 436 (M^+, 25.2), 259 (30), 189 (43), 172 (34), 157 (42), 137 (19), 129 (100), 128 (35), 127 (23), 119 (43), 117 (44), 109 (22), 107 (33), 100 (18), 91 (18), 77 (26), 44 (18).

Benzyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetate (40): pale yellow solid; mp 53–55 °C; 80% yield; NMR ($CDCl_3$) δ 3.7–4.3 (AB pattern, 2 H), 5.0 (s, 2 H), 6.72 (q, 1 H), 7.15 (br s, 5 H), 7.3–7.5 (m, 4 H), 7.7–8.2 (m, 3 H), 8.4 (s, 1 H), 8.87 (br d, 1 H); mass spectrum (70 eV), *m/e* (relative intensity) 424 (M^+, 42), 333 (7), 293 (6), 259 (13), 219 (25), 178 (9), 119 (6), 117 (6), 92 (8), 91 (100), 87 (13), 44 (7).

Benzyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]thioacetate (41): pale yellow solid; mp 70–72 °C; 71% yield; NMR ($CDCl_3$) δ 4.1 (AB pattern and m, 4 H), 6.50 (q, 1 H), 7.2 (s, 5 H), 7.3–7.7 (m, 4 H), 7.8–8.2 (m, 3 H), 8.5 (s, 1 H), 8.9 (br d, 1 H); mass spectrum (70 eV), *m/e* (relative intensity) 442 (M + 2, 6), 440 (M^+, 78), 371 (23), 274 (16), 260 (14), 259 (69), 239 (16), 238 (11), 209 (10), 207 (15), 205 (14), 191 (10), 137 (10), 103 (17), 91 (100), 65 (8).

***N*-Benzyl-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamide (42)**: pale yellow solid; mp 65–67 °C; 72% yield; NMR ($CDCl_3$) δ 3.9–4.1 (AB pattern, 2 H), 4.35 (d, 2 H), 6.22 (q, 1 H), 6.7 (br s, 1 H), 7.0–7.6 (m, 9 H), 7.8–8.1 (dd, 3 H), 8.48 (s, 1 H), 8.7 (br d, 1 H).

Anal. Calcd for $C_{25}H_{20}NO_2F_3$: C, 70.91; H, 4.76; F, 13.46. Found: C, 70.91; H, 5.12; F, 13.19.

4-Nitrobenzyl α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetate (43): pale yellow solid; mp 137–138 °C (benzene–hexane); 74% yield; NMR ($CDCl_3$) δ 3.9–4.4 (AB pattern, 2 H), 5.16 (s, 2 H), 5.66 (q, 1 H), 7.2–7.4 (m, 2 H), 7.4–7.7 (m, 4 H), 7.9–8.2 (m, 5 H), 8.56 (s, 1 H), 8.8–9.1 (m, 1 H).

Anal. Calcd for $C_{25}H_{18}NO_5F_3$: C, 63.97; H, 3.87; N, 2.98; F, 12.14. Found: C, 63.75; H, 3.83; N, 2.85; F, 12.02.

***N*-Methyl-*N*-(1-phenylethyl)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetamides (44)**: pale yellow viscous oil; 85% yield; NMR ($CDCl_3$) δ 1.13 (br d, CH_3), 1.30 (br d, CH_3), 2.3 (br s, NCH_3), 2.6 (br s, NCH_3), 3.9–4.5 (AB pattern, 4 H, OCH_2CO), 5.9 (m, 2 H), 6.85 (q, 2 H), 6.9–7.7 (m, 18 H), 7.95 (d, 4 H), 8.2 (d, 2 H), 8.5 (s, 2 H), 8.95 (d, 2 H); IR ($CHCl_3$) 3000, 2990, 1650, 1470, 1420, 1260, 1150, 1120, 900 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 451 (M^+, 17), 259 (19), 239 (10), 208 (17), 180 (14), 178 (16), 177 (100), 176 (23), 162 (24), 152 (12), 120 (21), 119 (33), 117 (32), 105 (77), 104 (34), 86 (45), 82 (21), 77 (13), 72 (10), 58 (10).

Acknowledgment. This work has been supported by a grant from the National Science Foundation.

Registry No. (±)-**6**, 77507-13-2; (±)-**6** ethyl ester, 77507-14-3; (±)-**7**, 65487-67-4; (±)-**8**, 77507-15-4; **9**, 77507-16-5; **10**, 77507-17-6;

11, 77507-18-7; 12, 77507-19-8; 13, 77507-20-1; 14, 77507-21-2; 15, 77507-22-3; 16, 77507-23-4; 17, 77507-24-5; 18, 77507-25-6; (±)-19, 77507-26-7; 20, 77507-27-8; 21, 77507-28-9; 22, 77507-29-0; 23, 77507-30-3; 24, 77507-31-4; 25, 77507-32-5; 26, 77520-25-3; 27, 77507-33-6; 28, 77507-34-7; 29, 77507-35-8; 30, 77507-36-9; 31, 77507-37-0; 32, 77507-38-1; 33, 77507-39-2; (±)-35a, 77507-40-5; (±)-35b, 77507-41-6; (±)-35c, 77507-42-7; (±)-35d, 77507-43-8; 36, 77507-44-9; 37, 77507-45-0; 38, 77507-46-1; 39, 77507-47-2; (±)-40, 77507-48-3; (±)-41, 77507-49-4; (±)-42, 77507-50-7; (±)-43, 77507-51-8.

Some Novel Transformations of 1,4-Dithiafulvenes

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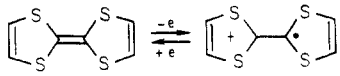
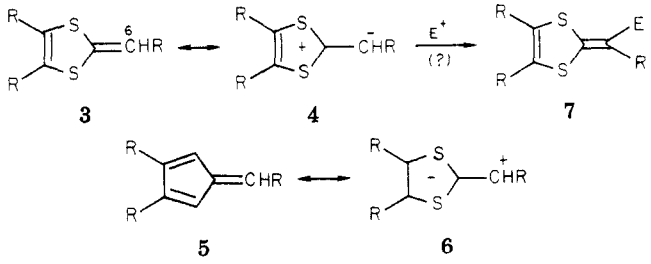
6-Phenyl-1,4-dithiafulvenes have been substituted at the 6-position by bromo, phenylazo, and nitroso groups; cation radical intermediates are proposed in these reactions. The 6-nitroso derivatives are deoxygenated by phosphines to give products derived from the fragmentation of intermediary nitrenes.

The chemistry of tetrathiafulvalene (1, TTF) and its derivatives has been the object of intense interest during the past decade, as a result of the ability of TTF to undergo a reversible one-electron oxidation to give a stable cation–radical (2), many salts of which show unusual electrical conductivity in the solid state.[1]



1 2

The rather closely related 1,4-dithiafulvene system 3 should be stabilized by the 1,3-dithiolium ylide contributor 4, in contrast to carbocyclic fulvenes 5 in which the cyclopentadienide form 6 is the important charge-separated contributor. It might be predicted, therefore, that 1,4-dithiafulvenes would undergo attack by electrophiles at the exocyclic carbon to give 6-substituted derivatives of the type 7. In this paper, we report the results of a study initiated by a search for such substitution reactions.[2]



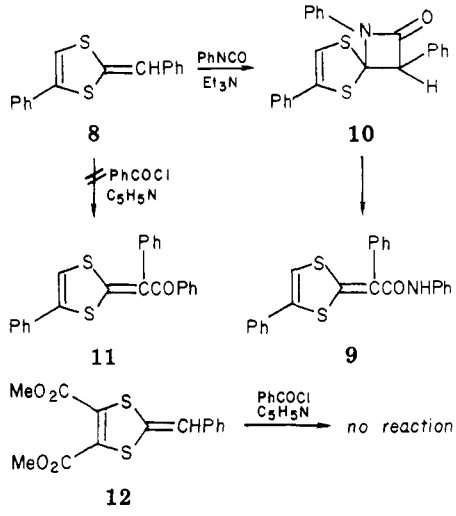
3 4 7

5 6

Results and Discussion

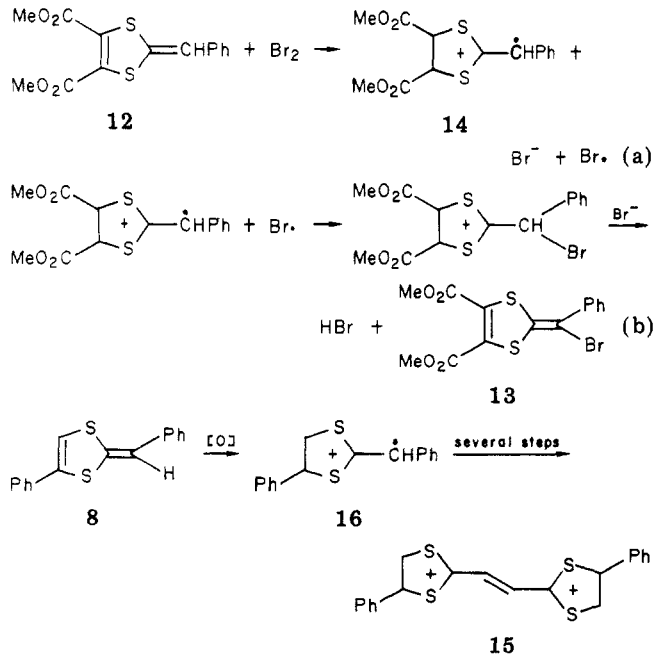
Substitution Reactions of 1,4-Dithiafulvenes. The first 1,4-dithiafulvenes which were reported in 1958 were obtained by the photolysis of 1,2,3-thiadiazoles.[3] One of these compounds, the trans isomer of 2,6-diphenyl-1,4-dithiafulvene (8) was later found to react slowly with hot phenyl isocyanate in the presence of triethylamine to give the 6-carboxamide derivative 9[4] (Scheme I). The conversion of 8 to 9, which represents the only reported substitution reaction of a 1,4-dithiafulvene, at first appears

Scheme I



8 10 11 9 12

Scheme II



12 14 13 8 16 15

(1) For general reviews on this subject see: (a) A. F. Garito and A. G. Heeger, *Acc. Chem. Res.*, 7, 232 (1974); (b) E. M. Engler, *CHEM TECH*, 6, 274 (1976); (c) M. Narita and C. U. Pittman, Jr., *Synthesis*, 489 (1976).

(2) A preliminary account of this work was presented in a Plenary Lecture delivered at the 7th International Heterocyclic Conference held in Tampa, FL, Aug 1979 [M. P. Cava and M. V. Lakshmikantham, *J. Heterocycl. Chem.*, 17, S-39 (1980)].

(3) W. Kirmse and L. Horner, *Justus Liebigs Ann. Chem.*, 614, 4 (1958).

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