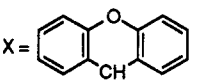
Single Electron Transfer versus Nucleophilic Ring Opening in Reactions of Cis–Trans Pairs of Activated 2-Phenylaziridines. Strong Influence of Nitrogen Pyramid for *N*-Benzoylaziridines[1]

Reinhard Falkenstein, Thomas Mall, Dieter Speth, and Helmut Stamm*

Faculty of Pharmacy, University of Heidelberg, Neuenheimer Feld 346, D-69120 Heidelberg, Germany

Received August 10, 1993•

Activated 2-phenylaziridines with a second substituent R in position 3 were made to react with xanthyl anion X^-. Nucleophilic ring opening is the only reaction that occurs with sulfonyl activation. The analogous N-benzoylaziridines 1 undergo this type of ring opening when the two substituents Ph and R are trans. The cis isomers (*cis*-1, Ph and R cis) react in this manner to a negligible extent if any. The (nearly) exclusive ring cleavage reaction of *cis*-1 is C–N homolysis of an intermediate ketyl formed by single electron transfer (SET) from X^-. This cis–trans phenomenon is in accordance with the hypothesis that the two competing reactions depend in an opposite manner on the steepness of the nitrogen pyramid. A predominant or exclusive final result of SET is reductive aziridine opening and dimerization of the xanthyl radical $X^•$. Formation of both diastereomers of the



XH = xanthene
X–X = 9,9'-bixanthyl
X^- = xanthyl anion
$X^•$ = xanthyl radical

amidoethylated xanthene in one case (R = Me) is evidence for a cross combination of $X^•$ with the radical formed by homolytic ring opening. Cross combination is also a likely path for R = H (no cis–trans isomerism), in addition to reductive ring opening. *cis*-Aziridines with dimethylcarbamoyl on nitrogen do not react via SET since the ketyl is not stabilized and therefore difficult to generate. Carbonyl attack on both types of acylaziridines competes more or less successfully with the two ring cleavage reactions.

Introduction

Ham[4] coined the term activated aziridines for aziridines that undergo S_N2-like nucleophilic ring opening even in the absence of a positive charge on nitrogen. A suitable substituent Y enhances the leaving group tendency of the nitrogen by stabilization of the negative charge that develops in the transition state. This stabilization should be inversely reflected in the basicity of the displaced nitranion. This reasoning can explain why sulfonyl is superior to acyl activation.[5] Moreover, arguments have been presented, supported by experiments and calculations,[6,3] that nucleophilic ring opening of an acylaziridine may require a flat nitrogen pyramid except when induced by extremely strong nucleophiles. A flat pyramid gives the acyl function more amide character. Flat pyramids are rather easily attained when the barrier of nitrogen inversion is low, i.e. when the inversion is rapid.

On the other hand, sufficient steric shielding of the aziridine carbon atoms may slow down the nucleophilic ring opening in favor of an alternative single electron transfer (SET) reaction. A sulfonylaziridine[7] requires stronger shielding than an acylaziridine.[8] For instance, reactions of trityl anion with 2,2-dimethylaziridines proceed with acyl activation almost exclusively via SET[8] and with sulfonyl activation via S_N2 (49% at 74% conversion)[9] with a maximal SET contribution of 25%, if any. SET is indicated by cleavage of the N–S bond of a sulfonylaziridine[7] and normally (for an exception see ref 2) by homolytic ring opening of an acylaziridine.[2,8,10]

Attachment of an electron to an acylaziridine initially forms a ketyl-like radical anion. This step will profit both from spin delocalization by R in the acyl group RCO and from a steep nitrogen pyramid that causes the acyl group to resemble a ketone. Thus, as regards the reactivity of acylaziridines, one may expect opposing effects on the mechanism from steepness and inversion rate of the nitrogen pyramid. Both properties depend on the substitution of the aziridine ring. Any reactivity difference should be rather distinct for diastereomers of the cis–trans type. A *trans*-aziridine has two rapidly inverting, flat inversional ground states; a *cis*-aziridine exists nearly

• Abstract published in *Advance ACS Abstracts*, November 15, 1993.

(1) Aziridines. 63. Part 62: Bentz, G.; Werry, J.; Stamm, H. *J. Chem. Soc., Perkin Trans. 1*, in press. Part 61: Buchholz, B.; Lin, Y.-P.; Onistschenko, A.; Stamm, H. *Z. Naturforsch.* **1993**, *48b*, 483–487. For parts 60 and 59, see refs 2 and 3.

(2) Lin, P.-Y.; Werry, J.; Stamm, H. *J. Chem. Soc., Perkin Trans. 1*, **1993**, 1139–1145.

(3) Lin, P.-Y.; Bentz, G.; Stamm, H. *J. Prakt. Chem.* **1993**, *335*, 23–34.

(4) Ham, G. E. *J. Org. Chem.* **1964**, *29*, 3052–3055.

(5) cf. e.g.: Stamm, H.; Gerster, G.; Baumann, T. *Chem. Ber.* **1983**, *116*, 2936–2957.

(6) Lin, P.-Y.; Bellos, K.; Stamm, H.; Onistschenko, A. *Tetrahedron* **1992**, *48*, 2359–2372.

(7) Bellos, K.; Stamm, H.; Speth, D. *J. Org. Chem.* **1991**, *56*, 6846–6849.

(8) Werry, J.; Lin, P.-Y.; Bellos, K.; Assithianakis, P.; Stamm, H. *J. Chem. Soc., Chem. Commun.* **1990**, 1389–1390.

(9) Assithianakis, P.; Stamm, H., unpublished results.

(10) Stamm, H.; Assithianakis, P.; Weiss, R.; Bentz, G.; Buchholz, B. *J. Chem. Soc., Chem. Commun.* **1984**, 753–754. Archier-Jay, D.; Besbes, N.; Laurent, A.; Laurent, E.; Lesniak, S.; Tardivel, R. *Bull. Soc. Chim. Fr.* **1989**, 537–543.

0022-3263/93/1958-7377$04.00/0

Table I. Reactions of X^- with Aziridines 1, 2, and 3 in THF[a] at Room Temperature

	mmol of reagents			% yields of products (yields in parentheses are calculated from ^1H NMR)				
run	X^-	aziridine	time[b]	4, 5	6, 7, 8	9	X–X	1–3
1	4	2.85 *trans*-**1a**	7 d	(54) **4**	(30) ϵ-**6a**	0 **9a**	0	
2	3	1.9 *cis*-**1a**	7 d	(33) **4**	0 **6a**	(50) **9a**	(22)	
3	8	2.1 *cis*-**1a**	6 d	(53) **4**	0 **6a**	(44) **9a**	(39)	
4	4	2.3 *trans*-**1b**	8 d	(17) **4**	61 ϵ-**6b**	0 **9b**	0	
5	4	2.3 *cis*-**1b**	8 d	(4) **4**	(7) ϵ-**6b**, (7) ϑ-**6b**	(56) **9b**	(49)	16 *cis*-**1b**
6	4	2.8 *cis*-**1b**	5 d	0 **4**	(7) ϵ-**6b**, (8) ϑ-**6b**	(41) **9b**	(46)	39 *cis*-**1b**
7	8	5 *cis*-**1c**	8 d	40 **4**	1 ϑ-**6c**	(52) **9c**	(31)	6 *cis*-**1c**
8	4	2.7 **1d**	8 d	(11) **4**	55 **6d**	(30) **9d**	(29)	
9	4.4	2.3 *cis*-**2a**	4 h	(80) **5**	(18) ϑ-**7a**			
10	4.4	2.3 *cis*-**2b**	4 h	(19) **5**	(68) ϑ-**7b**			
11	5.2	1.0 *trans*-**3a**	5 min		79 ϵ-**8a**			
12	5.2	1.0 *cis*-**3a**	5 min		98 ϑ-**8a**			
13	5.0	1.0 *trans*-**3b**	3 min		99 ϵ-**8b**			
14	3.0	0.5 *cis*-**3b**	3 min		92 ϑ-**8b**			
15	3.0	2.0 **3d**	3 min		91 **8d**			

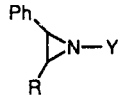
[a] X^- was generated from xanthene (10–30% excess) with BuLi in 60–70 mL (100 mL in run 7) of THF. The solution of the aziridine (1–3) in 15 mL of THF (30 mL in runs 1–2, 50 mL in run 7) was added within 2–3 min (5 min in runs 1–2; 10–15 s in runs 12–15). [b] The reactions were quenched with acetic acid.

exclusively as the anti invertomer with a steep pyramid of low energy.

Results

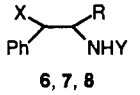
We carried out reactions of the xanthyl anion X^- with some 2-phenylaziridines. The activating group Y was sulfonyl or acyl, the latter with and without the possibility of stabilizing the ketyl.

Our investigation started with the cis–trans pair of **1a**. Configurational inversion in the S_N2-like nucleophilic ring opening of *trans*-**1a** by X^- should yield *erythro*-**6a** while *cis*-**1a** would produce *threo*-**6a** in the analogous process. In order to have a simple and homogeneous differentiation of the diastereomeric products **6–8**, we gave the prefix ϵ (ϑ) to all products that can be derived from *erythro*-**6** (from *threo*-**6**) by exchange of R and/or Y.

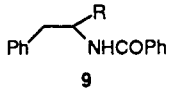


1, 2, 3

X–COPh
4
X–CONMe$_2$
5

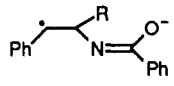


6, 7, 8



9

	Y	R
1a, 6a, 9a	COPh	Ph
1b, 6b, 9b	COPh	Me
1c, 6c, 9c	COPh	CH_2Ph
1d, 6d, 9d	COPh	H
2a, 7a	$CONMe_2$	Ph
2b, 7b	$CONMe_2$	Me
3a, 8a	SO_2Ph	Ph
3b, 8b	Ts	Me
3d, 8d	Ts	H



10

The benzoylaziridine *trans*-**1a** provided two products (run 1, Table I) of nucleophilic attack: benzoylxanthene **4** and ϵ-**6a**, the product of nucleophilic ring opening. Nucleophilic attack on the carbonyl group of an acylaziridine (forming **4** in the present case) is a common reaction (cf. e.g. ref 11) that often accompanies or precedes (cf. ref 12 and preceding papers) the ring opening. Reaction of the isomeric *cis*-**1a** (runs 2 and 3) yielded **4** in sizable amounts but no **6a**. The remainder of the *cis*-**1a** had undergone reductive ring opening, furnishing the xanthene-free *N*-(diphenylethyl)benzamide **9a**. This reduction of **1a** to **9a** proceeds in three or four steps. SET forms the ketyl of *cis*-**1a**. Homolytic ring opening generates the amidatoalkyl radical **10**. This benzylic radical has two possible ways to form the saturated benzyl group: immediate abstraction of a hydrogen atom from excess xanthene XH or reduction to the benzylic carbanion, which then abstracts a proton from excess XH. The electron required for the reduction may be provided by the carbanion X^- or[2] by the ketyl. The overall process from *cis*-**1a** to the N-anion of **9a** always generates 2 equiv of xanthyl radical X• that dimerize. The yields of bixanthyl X–X in Table I were calculated on this basis.

An analogous reactivity difference for a cis–trans pair was observed with the benzoylaziridine **1b** (R = Me). *trans*-**1b** (run 4) provided a high yield of ϵ-**6b** and some ketone **4**. The *cis*-aziridine (runs 5 and 6) gave (nearly) no ketone **4**, about 50% of reductive opening (**9b**), similar yields of X–X, and a 1:1 mixture of diastereomeric substitution products ϵ-**6b** and ϑ-**6b**. The yields of both diastereomers in run 6 can be considered equal within the limits of precision, since these yields have been determined by ^1H NMR analysis of a mixture whose main component was **9b**. Chromatographic separation in run 5 provided exactly equal amounts of both diastereomers from a portion of the analogous mixture. There can be little doubt that the diastereomers (or at least ϵ-**6b** and the major part of ϑ-**6b**) arise from the cross combination of radicals **10** and X•. However, we cannot exclude the possibility that a small amount of ϑ-**6b** arises from the S_N2 path (cf. run 7). The excess of X^- in runs 5 and 6 was insufficient for the complete conversion of *cis*-**1b**, which was recovered in 16 and 39% yield, respectively.

The benzoylaziridine *cis*-**1c** (R = benzyl) reacted via SET (run 7) in a manner similar to *cis*-**1a**: 40% of **4** and 52% of **9c** (reductive opening). However, 1% of the substitution product **6c** was also found. Since only one diastereomer could be detected, **6c** was assumed to be an S_N2 product and was assigned the configuration ϑ. The monosubstituted benzoylaziridine **1d** (run 8) provided all possible products: **4**, **6d**, **9d**, and X–X. The latter two indicated an SET reaction even for R = H.

The carbamoylaziridines *cis*-**2a,b** (runs 9 and 10) did not react in an SET manner despite their cis configuration. Only the carbamoylxanthene **5** and the substitution products ϑ-**7a,b** were obtained. All sulfonylaziridines **3**

(11) Kascheres, A.; Hassner, A. *Tetrahedron Lett.* **1970**, 4623–4626.
(12) Stamm, H.; Mall, T.; Falkenstein, R.; Werry, J.; Speth, D. *J. Org. Chem.* **1989**, *54*, 1603–1607.

reacted exclusively in an S_N2 manner providing high yields of the respective diastereomer of 8 (runs 11–15).

Discussion

No indication of SET was detected in any run with 2 (carbamoyl activation) or with 3 (sulfonyl activation). The carbamoyl group does not allow a spin delocalization in its ketyl, while the sulfonyl group increases the S_N2 reactivity of the aziridines enormously as was already shown by the reaction times of runs 11–15. One would expect the carbamoyl group to decrease rather than increase the S_N2 reactivity relative to the benzoyl group. This stresses the importance of spin delocalization. As for the regioselectivity of nucleophilic ring opening, it is remarkable that only the phenyl-bearing aziridine carbon is ever attacked. This regioselectivity is independent of the kind of activation, in contrast to the behavior[6] of 2,2-dimethylaziridines. Rate enhancement due to a benzylic effect had not been found in the ring opening of oxiranes.[13] The respective stereoelectronic effect (King and Tsang[14]) should generally be weak in the ring opening of three-membered rings since the transition state cannot be linear, to say nothing of the unfavorable conformations.[13] Thus, one or more other effects must significantly influence the regioselectivity in the reactions of Table I. This may, for instance, include steric hindrance of the attack on the unsubstituted or methyl-substituted carbon when the direction of this attack is largely determined by the p orbital of this carbon (Walsh model). The analogous, orbital-dependent attack on a phenyl-bearing carbon may in the same manner suffer from steric hindrance by R depending on its size. This could provide an explanation for the surprising finding that the competition between nucleophilic attack on the ring carbon and on the carbonyl group is remarkably influenced by the size of R: run 1 vs run 4, run 9 vs run 10.

There is a trend indicated in Table I and in some additional experiments with crude **1a**, that the yield of 4 is higher the greater the excess of X^- is. This would be expected from a weakly reversible carbonyl attack. Consecutive reactions should become very slow for very low concentrations of **1a**. This tendency should be small or even be absent for *cis*-**1a** when an essential part of the dissociation of the anionic carbonyl adduct is homolytic, resulting in $X^\bullet$ and the ketyl. More evidence against an essential contribution from this inner-sphere SET path comes from previous results[15] with the unsubstituted benzoylaziridine: ring-cleaving substitutions of X^- and reductive ring cleavage proceeded in the same ratio (7.7:1) within 20 h (74% of 4 isolated) and within 14 days (0% of 4), when the counterion was lithium, as in the present work.

The ketyl of an acylaziridine, especially that of an aroylaziridine, is a true intermediate, and reveals a certain lifetime in some experiments.[2,10] This excludes an in-cage combination of radicals **10** and $X^\bullet$. The main or exclusive reaction of the benzylic radical **10** is the above-mentioned conversion to a saturated benzyl group, while the more stable $X^\bullet$ dimerizes. The lack of any cross combination of **10a** (**10**, R = Ph) and **10c** (**10**, R = benzyl) in contrast to some cross combination of **10b** (**10**, R = Me) with $X^\bullet$ is probably due to steric effects. Since **1d** (R = H) underwent SET at least to an extent of 30% (**9d** in run 8), we extrapolate from the cis isomers of **1a–c** that the majority of **6d** was formed by cross combination of **10d** (**10**, R = H). It is not surprising that **1d** seems to resemble the cis isomers of **1a–c** with regard to the nitrogen pyramid and its inversion.

This study clearly shows the strong dependence of the reactivity of some acylaziridines on the nitrogen pyramid.

Experimental Section

General Methods and Materials. ^1H NMR spectra ($CDCl_3$) were recorded on a Bruker W 250 (250 MHz) instrument. Chemical shifts are recorded in δ (ppm) downfield from internal TMS followed in parentheses by signal multiplicity (s, d, t, q, m, m_c), coupling constants J, number of protons if necessary for clarity, and assignment. IR spectra (KBr unless otherwise stated) were recorded on a Perkin-Elmer 283 spectrometer.

All reactions were performed in dry THF with continuous stirring under dry nitrogen (for the technique see ref 17). Details are given in Table I. All reactions were quenched with acetic acid. Subsequent evaporation provided a residue that was taken up in dichloromethane and washed with water. Evaporation of the organic layer yielded a residue that was subjected to chromatography. Column chromatography was performed with 0.063–0.2-mm silica gel (Merck); column dimensions (thickness × length, cm) are given for the specific workup.

The activated aziridines **1b**,[16] **1c,d**,[17] **3a**,[18] and **3d**[19] are known. The other activated aziridines were prepared from the respective aziridine base (**1–3**, Y = H) and the chloride **YCl** of the respective acid using the technique of refs 16–19. For **1d** and for both **1b** the benzoyl chloride was replaced by benzoic anhydride.

***cis*-1-Benzoyl-2,3-diphenylaziridine (*cis*-1a)**: yield 92%; mp 141–142 °C (recryst from petroleum ether); IR 1675 cm^{-1} (C=O); ^1H NMR δ 3.98 (s, 2 CH), 7.22–7.31 (m, 2 Ph and 2 meta H of PhCO), 7.37–7.43 (m, para H of PhCO), 7.88–7.91 (m, 2 ortho H of PhCO). Anal. Calcd for $C_{21}H_{17}NO$: C, 84.25; H, 5.73; N, 4.68. Found: C, 84.19; H, 5.70; N, 4.45.

***trans*-1-Benzoyl-2,3-diphenylaziridine (*trans*-1a)**: yield 90%; mp 98–99 °C (recryst from petroleum ether); IR 1651 cm^{-1} (C=O); ^1H NMR δ 4.08 (s, 2 CH), 7.14–7.38 (m, 2 Ph and 2 meta H of PhCO), 7.47–7.52 (m, para H or PhCO), 8.03–8.07 (m, 2 ortho H of PhCO). Anal. Calcd for $C_{21}H_{17}NO$: C, 84.25; H, 5.73; N, 4.68. Found: C, 84.07; H, 5.78; N, 4.59.

***cis*-1-(Dimethylcarbamoyl)-2,3-diphenylaziridine (*cis*-2a)**: yield: yield 90%; mp 135–136 °C; IR 1670 cm^{-1} (C=O); ^1H NMR δ 3.02 (s, 1 Me), 3.03 (s, 1 Me), 3.91 (s, 2 CH), 7.11–7.17 (m, 2 Ph). Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.49; H, 6.79; N, 10.28.

***cis*-1-(Dimethylcarbamoyl)-2-methyl-3-phenylaziridine (*cis*-2b)**: yield 94%; mp 33–35 °C; IR 1675 cm^{-1} (C=O); ^1H NMR δ 1.04 (d, J = 5.7 Hz, CMe), 2.82–2.90 (m, 2-H), 2.97 (s, 1 NMe), 3.05 (s, 1 NMe), 3.53 (d, J = 6.7 Hz, 3-H), 7.28–7.35 (m, Ph). Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.55; H, 7.89; N, 13.71. Found: C, 70.32; H, 7.86; N, 13.39.

***cis*-2-Methyl-3-phenyl-1-tosylaziridine (*cis*-3b)**: yield 85%; mp 75–76 °C (recryst from tetrachloromethane); IR 1370, 1115 cm^{-1} (both SO_2); ^1H NMR δ 1.02 (d, J = 5.8 Hz, NCMe), 2.43 (s, Me of Ts), 3.14–3.24 (m, 2-H), 3.76 (d, J = 6.7 Hz, 3-H), 7.18–7.22 (m, 2 metal H of Ts), 7.23–7.35 (m, Ph), 7.86–7.90 (m, 2 ortho H of Ts). Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.86; H, 5.96; N, 4.87. Found: C, 66.89; H, 5.93; N, 4.81.

***trans*-2-Methyl-3-phenyl-1-tosylaziridine (*trans*-3b)**: yield 83%; mp 77–79 °C (recryst from tetrachloromethane); IR 1320, 1155 cm^{-1} (both SO_2); ^1H NMR δ 1.84 (d, J = 6.0 Hz, NCMe), 2.38 (s, Me of Ts), 2.86–2.95 (m, 2-H), 3.79 (d, J = 4.3 Hz, 3-H),

(13) Lynas-Gray, J. L.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1984**, 483–484.
(14) King, J. F.; Tsang, C. T. Y. *J. Chem. Soc., Chem. Commun.* **1979**, 1131–1132.
(15) Mall, T.; Stamm, H. *Chem. Ber.* **1988**, *121*, 1349–1352.
(16) Werry, J.; Stamm, H.; Lin, P.-Y.; Falkenstein, R.; Gries, S.; Irngartinger, H. *Tetrahedron* **1989**, *45*, 5015–5028.
(17) Stamm, H.; Woderer, A.; Wiesert, W.; Mall, T.; Assithianakis, P. *J. Org. Chem.* **1985**, *50*, 4946–4955.
(18) Mall, T.; Stamm, H. *J. Org. Chem.* **1987**, *52*, 4812–4814.
(19) Buchholz, B.; Stamm, H. *Isr. J. Chem.* **1967**, *27*, 17–23.

7.12–7.20 (m, 2 meta H of Ts), 7.21–7.29 (m, Ph), 7.80–7.84 (m, 2 ortho H of Ts). Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.86; H, 5.96; N, 4.87. Found: C, 66.89; H, 6.03; N, 4.85.

Experiments of Table I. Run 1. Chromatography (1.5 × 90, toluene) provided 378 mg of XH and 437 mg (54%) of 4.[17] Elution with dichloromethane yielded a few milligrams of unknown products. Dichloromethane/ethyl acetate (10:1) gave 411 mg (30%) of ϵ-**6a**.

ϵ-9-[2-(Benzoylamino)-1,2-diphenylethyl]xanthene (ϵ-6a): mp 221–222 °C (recryst from petroleum ether); IR 3400 (NH), 1649 (amide I), 1524 (amide II), 1262 cm^{-1} (C–O–C); ^1H NMR δ 3.58 (dd, J = 11.4/2.8 Hz, NCCH), 4.22 (d, J = 2.8 Hz, NCCCH), 5.73 (dd, J = 11.3/8.3 Hz, NCH), 6.13 (d br, J = 8.2 Hz, NH), 6.38–6.41 (m, 2 ortho H of NCCPh), 6.75–6.82 (m, 2 arom H), 6.92–6.98 (m, 2 arom H), 7.08–7.29 (m, 11 arom H), 7.36–7.41 (m, 2 arom H), 7.49–7.55 (m, 2 arom H), 7.71–7.74 (m, 2 ortho H or PhCO). Anal. Calcd for $C_{34}H_{27}NO_2$: C, 84.80; H, 5.65; N, 2.90. Found: C, 84.57; H, 5.66; N, 2.69.

Run 2. Chromatography (1.5 × 90, toluene) provided 712 mg of a mixture consisting (^1H NMR) of 306 mg (44%) of X–X[21] and 406 mg XH. This was followed by 182 mg (33%) of 4. Elution with dichloromethane/ethyl acetate (2:1) yielded 287 mg (50%) of **9a**.

***N*-(1,2-Diphenylethyl)benzamide (9a):** mp 177–179 °C; IR 3360 (NH), 1635 (amide I), 1526 cm^{-1} (amide II); ^1H NMR δ 3.24 (d, J = 7.0 Hz, CH_2), 5.51 (dt, J = 7.4/7.0 Hz, NCH), 6.41 (d br, J = 7 Hz, NH), 7.09–7.12 (m, 2 arom H), 7.19–7.51 (m, 11 arom H), 7.66–7.70 (m, 2 ortho H of PhCO). Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.78; H, 6.39; N, 4.58.

Run 3. Chromatography (1.5 × 50, dichloromethane) provided 942 mg of XH and 614 mg of a mixture consisting (^1H NMR) of 318 mg (53%) of 4 and 296 mg (39%) of X–X. Elution with ethyl acetate yielded 65 mg of xanthone and 278 mg (44%) of **9a**.

Run 4. Chromatography (1.5 × 50, dichloromethane) provided 615 mg of a mixture consisting (^1H NMR) of 557 mg of XH and 58 mg of 4. Further elution yielded 54 mg (total 112 mg corresponding to 17%) of 4. Dichloromethane/ethyl acetate (10:1) gave 592 mg (61%) of ϵ-**6b**.

ϵ-9-[2-(Benzoylamino)-2-methyl-1-phenylethyl]xanthene (ϵ-**6b**): mp 212–214 °C; IR 3300 (NH), 1630 (amide I), 1550 (amide II), 1265 cm^{-1} (C–O–C); ^1H NMR δ 1.51 (d, J = 6.4 Hz, Me), 2.91 (q, J = 8.7 Hz, NCCH), 4.51 (d, J = 5.3 Hz, NCCCH), 4.68 (m_c, NCH), 5.63 (d, br, J = 8.2 Hz, NH), 6.45–6.48 (m, 2 ortho H of NCCPh), 6.83–6.92 (m, 2 arom H), 6.95–7.07 (m, 3 arom H), 7.08–7.23 (m, 5 arom H), 7.24–7.45 (m, 6 arom H); MS (80 eV, 138 °C) m/e (rel inten) 419 (0.1, $M^{\bullet+}$), 271 (0.1, M – PhCONHCHPh), 238 (11, M – xanthyl), 181 (xanthyl), 105 (10, PhCO). Anal. Calcd for $C_{29}H_{25}NO_2$: C, 83.03; H, 6.01; N, 3.34. Found: C, 82.93; H, 6.17; N, 3.21.

Run 5. When the residue was dissolved in a small quantity of dichloromethane, 114 mg of X–X slowly precipitated. The filtered solution was put on a column (1.5 × 50). Elution with dichloromethane provided 748 mg of a mixture consisting (^1H NMR) of 294 mg (total 408 mg corresponding to 49%) of X–X, 27 mg (4%) of 4, and 427 mg of XH. Further elution gave 142 mg of a mixture consisting (^1H NMR) of 87 mg (16%) of *cis*-**1b** and 55 mg of xanthone. Elution with ethyl acetate yielded 443 mg of a mixture consisting (^1H NMR) of 67 mg (7%) of ϵ-**6b**, 68 mg (7%) of ϑ-**6b**, and 308 mg (56%) of **9b**.[17] These analytically calculated yields were confirmed as follows. Chromatography (1.5 × 50, dichloromethane/ethyl acetate 50:1) of 190 mg of the latter mixture yielded 131 mg of **9b** and 28 mg each of ϵ-**6b** and ϑ-**6b**.

ϑ-9-[2-(Benzoylamino)-2-methyl-1-phenylethyl]xanthene (ϑ-6b): mp 227–229 °C; IR 3300 (NH), 1635 (amide I), 1535 (amide II), 1260 cm^{-1} (C–O–C); ^1H NMR δ 1.02 (d, J = 6.4 Hz, Me), 2.89 (dd, J = 3.4/10.8 Hz, NCCH), 4.58 (d, J = 3.4 Hz, NCCCH), 4.73–4.89 (m, NCH), 6.23–6.30 (m, NH, 2 ortho H of NCCPh), 6.75–6.85 (m, 2 arom H), 6.91–7.02 (m, 2 arom H), 7.06–7.38 (m, 6 arom H), 7.45–7.60 (m, 4 arom H), 7.86–7.95 (m, 2 ortho H of PhCO); MS (80 eV, 143 °C), m/e (rel inten) 419 (0.2, $M^{\bullet+}$), 271 (0.1, M – PhCONHCHPh), 238 (8, M – xanthyl), 181 (100, xanthyl), 105 (20, PhCO); molecular mass calcd for M^+ of $C_{29}H_{25}NO_2$ m/e 419.1887, found m/e 419.1886.

Run 6. Chromatography (1.5 × 50, dichloromethane) provided 986 mg of a mixture consisting (^1H NMR) of 468 mg of XH, 465 mg (46%) of X–X, and 53 mg of *cis*-**1b**. Further elution yielded 205 mg (total 258 mg corresponding to 39%) of *cis*-**1b**. Elution with ethyl acetate gave 462 mg of a mixture consisting (^1H NMR) of 274 mg (41%) of **9b**, 88 mg (7%) of ϵ-**6b**, and 100 mg (8%) of ϑ-**6b**.

Run 7. Chromatography (3 × 15, toluene) provided 1.216 g of a mixture consisting (^1H NMR) of 663 mg of XH and 553 mg (31%) of X–X. Further elution yielded 575 mg (40%) of 4, 98 mg (6%) of *cis*-**1c**, and 30 mg (1%) of ϑ-**6c**. Elution with dichloromethane provided 744 mg of **9c**. Elution with ethyl acetate yielded 481 mg of a mixture consisting (^1H NMR) of 403 mg (38%) of *cis*-2-benzyl-3-phenylaziridine and 78 mg (total 822 mg corresponding to 52%) of **9c**.[17]

ϑ-9-[2-(Benzoylamino)-2-benzyl-1-phenylethyl]xanthene (ϑ-6c): mp 223–226 °C; IR 3320 (NH), 1640 (amide I), 1544 (amide II), 1260 cm^{-1} (C–O–C); ^1H NMR δ 2.61 (dd, J = 14.2 Hz, J = 6.6 Hz, 1 H of CH_2), 2.88 (dd, J = 14.0/4.5 Hz, 1H of CH_2), 3.07 (dd, J = 11.7/2.4 Hz, NCCH), 4.53 (d, J = 2.5 Hz, NCCCH), 4.83–5.01 (m, NCH), 6.08 (d br, J = 9.4 Hz, NH), 6.24–6.31 (m, 2 ortho H of NCHCHPh), 6.72–6.80 (m, 2 arom H), 6.90–6.96 (m, 2 arom H), 6.98–7.31 (m, 10 arom H), 7.46–7.61 (m, 5 arom H), 7.77–7.84 (m, 2 ortho H of PhCO). Anal. Calcd for $C_{35}H_{29}NO_2$: C, 84.82; H, 5.90; N, 2.83. Found: C, 84.61; H, 5.72; N, 2.99.

Run 8. Chromatography (1.5 × 50, dichloromethane) provided 598 mg of a mixture consisting (^1H NMR) of 230 mg of XH, 283 mg (29%) of X–X, and 85 mg of 4. Elution with dichloromethane/ethyl acetate (5:1) yielded 431 mg of **6d** and 272 mg of a mixture consisting (^1H NMR) of 170 mg (total 601 mg corresponding to 55%) of **6d** and 102 mg of **9d**. Further elution gave 91 mg (total of 193 mg corresponding to 30%) of **9d**.[17]

9-[2-(Benzoylamino)-1-phenylethyl]xanthene (6d): mp 151–153 °C; IR 3310 (NH), 1635 (amide I), 1540 (amide II), 1260 cm^{-1} (C–O–C); ^1H NMR δ 3.16–3.24 (m, NCCH), 3.65 (ddd, J = 13.9/5.6/4.5 Hz, 1 H of NCH_2), 4.00 (ddd, J = 13.9/6.8/5.3 Hz, 1 H of NCH_2), 4.28 (d, J = 5.3 Hz, NCCCH), 5.74 (s br, NH), 6.62–6.66 (m, 2 ortho H of NCCPh), 6.92–7.47 (m, 16 arom H). Anal. Calcd for $C_{28}H_{23}NO_2$: C, 82.93; H, 5.71; N, 3.45. Found: C, 82.98; H, 5.98; N, 3.77.

Run 9. Chromatography (1.5 × 50) with dichloromethane removed 418 mg of XH. Elution with ethyl acetate provided 652 mg of a mixture consisting (^1H NMR) of 466 mg (80%) of 5 and 186 mg (18%) of ϑ-**7a**. A solution of the mixture in dichloromethane precipitated 27 mg of pure ϑ-**7a**. Slow evaporation at atmospheric pressure precipitated several fractions of impure ϑ-**7a**. The final residue provided pure 5 on recrystallization from methanol.

***N,N*-Dimethylxanthene-9-carboxamide (5):** mp 140–141 °C (lit.[20] 140 °C); IR 1650 (amide), 1270 cm^{-1} (C–O–C); ^1H NMR δ 2.76 (s, 1 Me), 2.93 (s, 1 Me), 5.44 (s, O=CCH), 7.03–7.24 (m, 8 arom H).

ϑ-9-[2-[(Dimethylcarbamoyl)amino]-1,2-diphenylethyl]xanthene (ϑ-7a): mp 233–235 °C; IR 3360 (NH), 1630 (amide I), 1520 (amide II), 1265 cm^{-1} (C–O–C); ^1H NMR δ 3.00 (s, 2 Me), 3.31 (dd, J = 12.0/2.4 Hz, NCCH), 4.81 (d, J = 2.4 Hz, NCCCH), 4.78 (d br, J = 9.6 Hz, NH), 5.56 (dd, J = 12.0/9.6 Hz, NCH), 6.01–6.04 (m, 2 ortho H of NCCPh), 6.66–6.81 (m, 3 arom H), 6.85–6.93 (m, 1 arom H), 6.96–7.26 (m, 10 arom H), 7.34–7.41 (m, 1 arom H), 7.76–7.85 (m, 1 arom H); MS (80 eV, 148 °C) m/e (rel inten) 448 (0.04, $M^{\bullet+}$), 267 (30, M – xanthyl), 181 (100, xanthyl); molecular mass calcd for M^+ of $C_{30}H_{28}N_2O_2$ 448.2106, found m/e 448.2146.

Run 10. Chromatography (1.5 × 50, dichloromethane/ethyl acetate 5:1) provided 568 mg of XH and 208 mg of a mixture consisting (^1H NMR) of 110 mg (19%) of 5 and 98 mg of ϑ-**7b**. Further elution yielded 495 mg (total 593 mg corresponding to 68%) of ϑ-**7b**.

ϑ-9-[2-[(Dimethylcarbamoyl)amino]-2-methyl-1-phenylethyl]xanthene (ϑ-7b): mp 228–230 °C; IR 3310 (NH), 1625 (amide I), 1535 (amide II), 1265 cm^{-1} (C–O–C); ^1H NMR δ 0.92 (d, J = 6.3 Hz, CMe), 2.72 (dd, J = 10.7/3.4 Hz, NCCH), 3.03 (s, 2 NMe), 4.29 (d br, J = 9.4 Hz, NH), 4.41–4.56 (m, NCH), 4.63

(20) Acheson, R. M.; MacPhee, K. E.; Philpott, P. G.; Barltrop, J. A. *J. Chem. Soc.* **1956**, 698–705.

(21) Werry, J.; Stamm, H.; Sommer, A. *Chem. Ber.* **1990**, *123*, 1553–1562.

(d, J = 3.4 Hz, NCCCH), 6.19–6.23 (m, 2 ortho H of Ph), 6.74–6.82 (m, 2 arom H), 6.90–6.96 (m, 2 arom H), 7.06–7.27 (m, 6 arom H), 7.50–7.53 (m, 1 arom H). Anal. Calcd for $C_{25}H_{28}N_2O_2$: C, 77.68; H, 6.78; N, 7.25. Found: C, 77.83; H, 6.79; N, 7.25.

Run 11. Chromatography (2 × 20) with toluene removed 880 mg of XH. Elution with ethyl acetate yielded 405 mg (77%) of **ϵ-8a**.

ϵ-9-[2-[(Phenylsulfonyl)amino]-1,2-diphenylethyl]xanthene (ϵ-8a): mp 251–253 °C; IR 3270 (NH), 1325 (SO_2), 1265 (C–O–C), 1160 cm^{-1} (SO_2); ^{1}H NMR δ 3.18 (dd, J = 10.4/3.4 Hz, NCCH), 4.05 (d, J = 3.5 Hz, NCCCH), 4.43 (d, J = 3.9 Hz, NH), 4.85 (dd, J = 10.4/4.0 Hz, NCH), 6.19–6.23 (m, 2 ortho H of NCCPh), 6.71–6.80 (m, 2 arom H), 6.93–7.10 (m, 5 arom H), 7.12–7.38 (m, 13 arom H). Anal. Calcd for $C_{33}H_{27}NO_3S$: C, 76.57; H, 526; N, 2.71. Found: C, 76.28; H, 5.47; N, 3.00.

Run 12. Workup as in run 11 provided 851 mg of XH and 509 mg (98%) of **ϑ-8a**.

ϑ-9-[2-[(Phenylsulfonyl)amino]-1,2-diphenylethyl]xanthene (ϑ-8a): mp 276 °C; IR 3250 (NH), 1325 (SO_2), 1262 (C–O–C), 1158 cm^{-1} (SO_2); ^{1}H NMR δ 3.25 (dd, J = 11.7/2.5 Hz, NCCH), 4.95 (dd, J = 11.7/10.2 Hz, NCH), 5.16 (d, J = 2.4 Hz, NCCCH), 5.84–5.87 (m, 2 ortho H of NCCPh), 6.58–6.88 (m, 10 arom H, NH), 6.91–6.94 (m, 1 arom H), 7.01–7.14 (m, 3 arom H), 7.20–7.26 (m, 4 arom H), 7.62–7.70 (m, 2 arom H), 8.02–8.11 (m, 1 arom H). Anal. Calcd for $C_{33}H_{27}NO_3S$: C, 76.57; H, 526; N, 2.71. Found: C, 76.39; H, 5.55; N, 2.96.

Run 13. Chromatography (3 × 22) with toluene removed 943 mg of XH. Elution with ethyl acetate yielded 463 mg (99%) of **ϵ-8b**.

ϵ-9-[2-Methyl-1-phenyl-2-(tosylamino)ethyl]xanthene (ϵ-8b): mp 185–187 °C; IR 3280 (NH), 1320 (SO_2), 1260 (C–O–C), 1155 cm^{-1} (SO_2); ^{1}H NMR δ 1.33 (d, J = 6.3 Hz, NCMe), 2.39 (s, Me of Ts), 2.64 (dd, J = 7.6/5.9 Hz, NCCH), 3.69 (m_c, NCH), 3.92 (d br, J = 6.3 Hz, NH), 4.46 (d, J = 5.9 Hz, NCCCH), 6.12–6.24 (m, 2 ortho H of NCCPh), 6.79–6.92 (m, 5 arom H), 6.97–7.21 (m, 7 arom H), 7.41–7.45 (m, 1 arom H), 7.52–7.55 (m, 2 arom H). Anal. Calcd for $C_{29}H_{27}NO_3S$: C, 74.17; H, 5.79; N, 2.98. Found: C, 74.01; H, 5.84; N, 2.93.

Run 14. Workup as in run 13 provided 604 mg of XH and 206 mg (92%) of **ϑ-8b**.

ϑ-9-[2-Methyl-1-phenyl-2-(tosylamino)ethyl]xanthene (ϑ-8b): mp 91–93 °C; IR 3280 (NH), 1325 (SO_2), 1260 (C–O–C), 1160 cm^{-1} (SO_2); ^{1}H NMR δ 0.78 (d, J = 6.5 Hz, NCMe), 2.44 (s, Me of Ts), 2.56 (dd, J = 8.9/4.8 Hz, NCCH), 3.78–3.91 (m, NCH), 4.48 (d br, J = 10.0 Hz, NH), 4.68 (d, J = 4.8 Hz, NCCCH), 6.21–6.24 (m, 2 ortho H of NCCPh), 6.73–6.90 (m, 2 arom H), 6.91–6.99 (m, 3 arom H), 7.03–7.44 (m, 8 arom H), 7.73–7.81 (m, 2 arom H). Anal. Calcd for $C_{29}H_{27}NO_3S$: C, 74.17; H, 5.79; N, 2.98. Found: C, 73.76; H, 5.79; N, 2.68.

Run 15. Workup as in run 13 provided 364 mg of XH and 811 mg (91%) of **8d**.

9-[1-Phenyl-2-(tosylamino)ethyl]xanthene (8d): mp 184–186 °C; IR 3260 (NH), 1320 (SO_2), 1250 (C–O–C), 1165 cm^{-1} (SO_2); ^{1}H NMR δ 2.43 (s, Me), 2.77–2.85 (m, NCCH), 3.12 (ddd, J = 12.8/9.6/3.2 Hz, 1 H of NCH_2), 3.41 (ddd, J = 12.8/9.1/2.9 Hz, 1 H of NCH_2), 4.14 (d, J = 5.4 Hz, NCCCH), 4.26 (dd br, J = 9/3 Hz, NH), 6.33–6.36 (m, 2 H ortho H of Ph), 6.89–7.06 (m, 7 arom H), 7.13–7.27 (m, 6 arom H), 7.54–7.58 (m, 2 arom H). Anal. Calcd for $C_{28}H_{25}NO_3S$: C, 73.82; H, 5.53; N, 3.07. Found: C, 73.49; H, 5.59; N, 3.00.

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie.