longation effect of the peptide. The frogs used in these studies were obtained from Lemberger Co., Germantown, WI, and the lizards were from the Snake Farm, La Place, LA.

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Registry No. II, 117499-47-5; III, 117499-48-6; IV, 117499-49-7; V, 117499-50-0; VI, 117499-52-2; VII, 117499-51-1; VIII, 117499-53-3; IX, 117499-54-4; X, 117499-55-5; XI, 117526-36-0; XII, 117499-56-6; XIII, 117499-57-7; XIV, 117603-86-8; XV, 117603-87-9; BOC-Val-OH, 13734-41-3; BOC-Pro-OH, 15761-39-4; BOC-Gly-OH, 4530-20-5; BOC-Lys(2-Clz)-OH, 54613-99-9; BOC-Trp(For)-OH, 47355-10-2; BOC-Arg(Tos)-OH, 13836-37-8; BOC-D-Phe-OH, 18942-49-9; BOC-His(Tos)-OH, 35899-43-5; BOC-Glu(OBzl)-OH, 13574-13-5; BOC-Nle-OH, 6404-28-0; BOC-Ser(Bzl)-OH, 23680-31-1; BOC-Tyr(2-BrZ)-OH, 47689-67-8; BOC-Asp(OBzl)-OH, 7536-58-5; BOC-Orn(Z)-OH, 2480-93-5; BOC-Dab(Z)-OH, 3350-20-7; BOC-Dpr(Z)-OH, 65710-57-8; BOC-Phe-OH, 13734-34-4.

Synthesis and α_2-Adrenoceptor Antagonist Activity of Some Disulfonamidobenzoquinolizines

Terence J. Ward,*[†] Graham J. Warrellow,[†] John A. Stirrup,[†] Norman Lattimer,[‡] and Keith F. Rhodes[‡]

Departments of Chemistry and Biomedical Research, Wyeth Research (UK), Taplow, Maidenhead, England.
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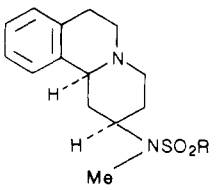
A series of disulfonamidobenzo[*a*]quinolizines were synthesized and evaluated for their α_2- and α_1-adrenoceptor antagonist activity on the rat vas deferens and anococcygeus muscle, respectively. *N*-((2β,11bα)-1,3,4,6,7,11b-Hexahydro-2*H*-benzo[*a*]quinolizin-2-yl)-*N*-[2-[(methylsulfonyl)amino]ethyl]methanesulfonamide (**4**) and its *N*-[2-[(methylsulfonyl)amino]ethyl]ethanesulfonamide (**22**), *N*-[2-[(ethylsulfonyl)amino]ethyl]ethanesulfonamide (**27**), and *N*-[2-[(methylsulfonyl)amino]ethyl]-4-methylbenzenesulfonamide (**30**) analogues showed 400-fold or greater selectivity in favor of α_2- over α_1-adrenoceptor blockade.

The therapeutic potential of agents which selectively block α_2-adrenoceptors has prompted the search for such agents in a number of laboratories, and selective agents from a variety of chemical classes have been reported in recent years.[1] In a previous publication we described the chemistry and biological activity of a series of 2-sulfonamidobenzoquinolizines of general structure **1** possessing selective α_2-adrenoceptor antagonist activity.[2]



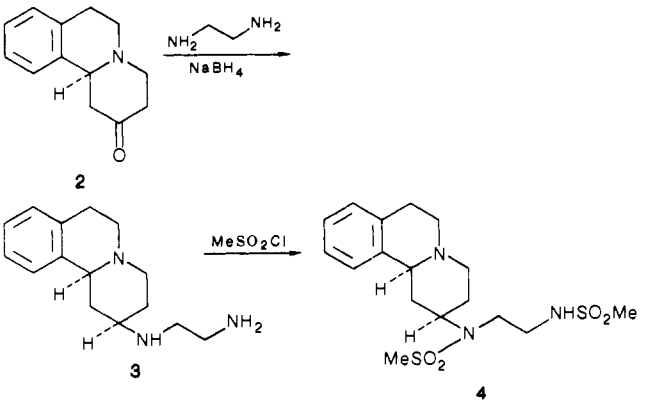
1

The importance of the *N*-methyl substituent for activity in this series, observed in our previous study, prompted us to investigate further modifications at this site in detail and led to the discovery of further analogues having enhanced selectivity in favor of the α_2-adrenoceptor. These new analogues differ from our earlier series in that they bear a second sulfonamide group on the nitrogen-linked side chain.

Chemistry

Reductive amination of the 2-oxohexahydrobenzoquinolizine (**2**) with ethylenediamine gave the key intermediate **3** (Scheme I).[3] Interestingly, reductive amination of **2** with ethylenediamine, or its homologues, did not require the use of sodium cyanoborohydride[4] as generally employed for reductive aminations, but was readily achieved by simple treatment of the ketone with ethylenediamine and sodium borohydride in ethanol. Symmetrical disulfonamide derivatives of **3** were prepared by treatment of **3** with slightly over 2 equiv of a sulfonyl chloride. The primary and secondary amine centers

Scheme I



present in **3** differ sufficiently in their reactivity to allow their differential sulfonation (Scheme II). Accordingly, although reaction of **3** with 1 equiv of methanesulfonyl chloride gave an intractable mixture of mono- and disulfonamides, the use of the more sterically demanding reagent methanesulfonic anhydride gave monosulfonamide **5**. Selective sulfonation was also achieved with the more bulky ethane-, propane-, and benzenesulfonyl chlorides. Intermediates monosulfonated on the secondary amine function of **3** were prepared following protection of the primary amine group. Accordingly, **3** was reacted with methyl acetate to form monoacetamide **6**, which was then sulfonated and deacetylated to yield monosulfonamide **7**. Monosulfonamides derived from **3** enabled the synthesis of unsymmetrical disulfonamides by reaction with a second equivalent of a sulfonyl chloride. Intermediate amines

[†] Department of Chemistry.
[‡] Department of Biomedical Research.

(1) Clark, R. D.; Michel, A. D.; Whiting, R. L. In *Progress in Medicinal Chemistry*; Ellis, G. P., West, G. B., Eds.; Elsevier: Amsterdam, 1986; Vol. 23, p 1.
(2) Ward, T. J.; White, J. F.; Lattimer, N.; Rhodes, K. F.; Sharma, S.; Waterfall, J. F. *J. Med. Chem.* 1988, *31*, 1421.
(3) All of the compounds reported are racemic; structural formulae depict relative stereochemistry only.
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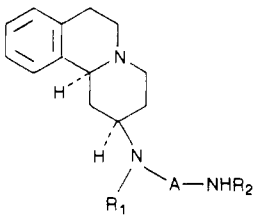
0022-2623/89/1832-0179$01.50/0

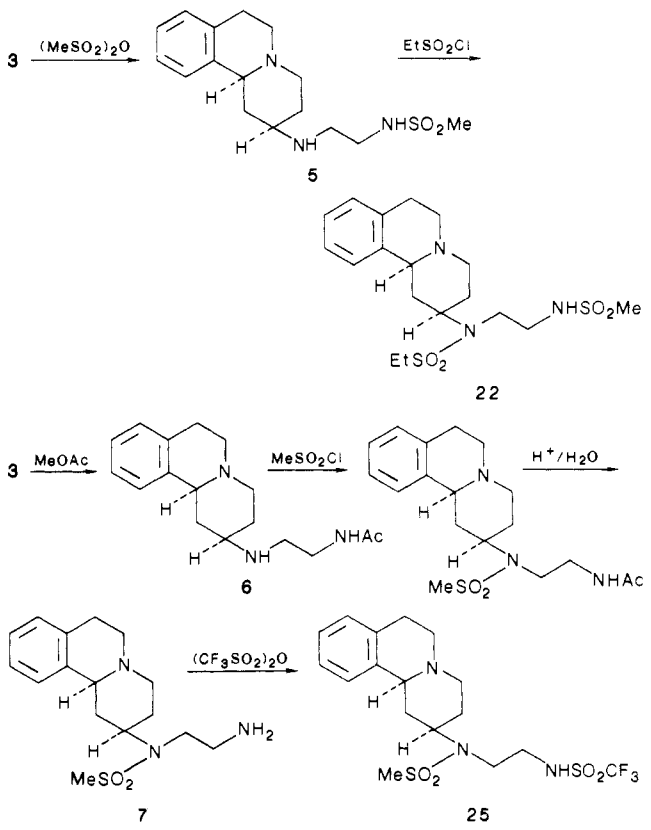
Table I. Intermediates[a]



no.	R_1	R_2	A	crystn solv	mp, °C	yield, %	formula[b]
3	H	H	$(CH_2)_2$	EtOH	250[c]	86.4	$C_{15}H_{23}N_3 \cdot 3HCl \cdot H_2O$
8	H	H	$(CH_2)_3$	EtOH	>250[c]	96.0[d]	
9	H	H	$(CH_2)_4$	EtOAc		40.3[d]	
10	H	H	CH_2CMe_2	EtOH	285–290	77.2	$C_{17}H_{27}N_3 \cdot 3HCl \cdot 0.25H_2O$
11	H	Me	$(CH_2)_2$	EtOH	245–248	68.1	$C_{16}H_{25}N_3 \cdot 3HCl$
5	H	$MeSO_2$	$(CH_2)_2$	MeOH	238–245	54.4	$C_{16}H_{25}N_3O_2S \cdot 2HBr$
12	H	$EtSO_2$	$(CH_2)_2$	EtOH	>200[d]	22.5	$C_{17}H_{27}N_3O_2S \cdot 2HCl$
13	H	n-$PrSO_2$	$(CH_2)_2$	EtOH	190–192	44.8	$C_{18}H_{29}N_3O_2S \cdot 2HBr \cdot 0.5H_2O$
14	H	$PhSO_2$	$(CH_2)_2$	$MeOH/H_2O$	245–247	49.3	$C_{21}H_{27}N_3O_2S \cdot 2HBr$
7	$MeSO_2$	H	$(CH_2)_2$	IPA	174–177	88	$C_{16}H_{25}N_3O_2S \cdot 2HCl \cdot 0.25H_2O$

[a] All compounds exhibited IR and ^1H NMR spectra consistent with the assigned structure. [b] C, H, and N analysis were within 0.4% of the theoretical values for the formula given. [c] Melts with decomposition. [d] These amines were used in their crude partially carbonated form.

Scheme II



prepared by the general methods are listed in Table I.

Results and Discussion

Compounds were examined for α_1- and α_2-adrenoceptor antagonism with the rat anococcygeus muscle and vas deferens, respectively, as described previously.[2] Test results are listed in Table II together with values for the α_2-adrenoceptor antagonists idazoxan[5] and Wy 26392 (1, R = n-Pr).[2]

The prototypical compound in this series (4) showed similar antagonist potency at the α_2-adrenoceptor to that observed in our earlier series of compounds, exemplified by Wy 26392 (Table I). However, the presence of the second sulfonamide function greatly reduced potency at the α_1-adrenoceptor, resulting in enhanced selectivity for the α_2 site. The nature of the carbon chain linking the two sulfonamide nitrogens was critical for activity and extension beyond two carbons (**15**, **16**) or branching (**17**) reduced potency. N-Methylation (**18**) also reduced activity. Accordingly further studies concentrated on analogues which retained the two-carbon A chain and secondary sulfonamide group present in **4**. α_2-Antagonist potency and selectivity declined as the alkyl loading (R_3) on the secondary sulfonamide group increased (**4**, **19**, and **20**) and the secondary benzenesulfonamide (**21**) showed only modest activity, indicating an unfavorable steric interaction for the R_3 side chain. By contrast α_2-adrenoceptor potency was relatively insensitive to the degree of alkyl loading on the tertiary sulfonamide group (R_1). Among the dialkyl sulfonamides, the diethanesulfonamide **27** was the most selective compound in our series. Chlorine substituents on the alkylsulfonyl groups were tolerated, but trifluoromethanesulfonamide **25** showed poor activity, perhaps reflecting an unfavorable pK_a value for this secondary sulfonamide. A number of tertiary aromatic sulfonamides (**29–36**) showed good potency and selectivity, although only p-toluenesulfonamide **31** rivalled the selectivity shown by the dialkyl sulfonamides. Interestingly, the monosulfonamides **5** and **7** (Table I) were without significant activity.

In conclusion, optimum selectivity and antagonist potency for the α_2-adrenoceptor was observed in this series for compounds in which R_3 is methyl or ethyl, R_1 is alkyl, and A is an ethylene chain. These compounds were about 10-fold more selective for the α_2-adrenoceptor than analogous compounds in our earlier series or idazoxan; this enhanced selectivity arose from reduced potency at the α_1-adrenoceptor. Compounds **4** and **27** were selected for more detailed studies which have confirmed their potency and selectivity. The results of these studies on **4** have been reported elsewhere.[6]

Experimental Section

Melting points were obtained on a Reichert microscope heating stage and are uncorrected. IR spectra were obtained with a

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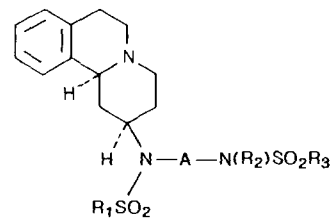
Table II[a]



no.	R_1	R_2	R_3	A	starting material	crystn solv	mp, °C	yield, %	formula[b]	pA_2 (n)[e] α_2 (95% limits)	pA_2 (n)[e] α_1 (95% limits)	selectivity[f] ratio
4	Me	H	Me	$(CH_2)_2$	3	MeOH	197–198	44.2	$C_{17}H_{27}N_3O_4S_2{\cdot}C_4H_4O_4$[g]	7.93[h] (4) (7.7–8.3)	5.32[h] (8) (5.1–5.8)	410
15	Me	H	Me	$(CH_2)_3$	8	*i*-PrOH	141–143	27.6	$C_{18}H_{29}N_3O_4S_2{\cdot}HCl{\cdot}0.5H_2O$	5.7 (4)	5.7 (4)	1
16	Me	H	Me	$(CH_2)_4$	9	EtOH	151–153	45.6	$C_{19}H_{31}N_3O_4S_2{\cdot}C_4H_4O_4$	5.66 (3) (5.0–6.3)	NT	
17	Me	H	Me	CH_2CMe_2	10	EtOH	175–180	68.9	$C_{19}H_{31}N_3O_4S_2{\cdot}C_4H_4O_4$	6.14[h] (4)	NT	
18	Me	Me	Me	$(CH_2)_2$	11	$EtOH/H_2O$	235–237	44.3	$C_{18}H_{29}N_3O_4S_2{\cdot}HBr$	6.03[h] (4)	5.5 (3)	3
19	Me	H	Et	$(CH_2)_2$	12	EtOH	168–172	40.5	$C_{18}H_{29}N_3O_4S_2{\cdot}C_4H_4O_4$	7.73[h] (5) (7.6–8.0)	5.65[h] (4)	120
20	Me	H	*n*-Pr	$(CH_2)_2$	13	MeOH/EtOH	155–157	77	$C_{19}H_{31}N_3O_4S_2{\cdot}C_4H_4O_4$	6.7[h] (2)	5.7 (2)	10
21	Me	H	Ph	$(CH_2)_2$	14	PhMe	146–147	55.5	$C_{22}H_{29}N_3O_4S_2$	5.9 (2)	5.9 (2)	1
22	Et	H	Me	$(CH_2)_2$	5	H_2O	193–194	30.1	$C_{18}H_{29}N_3O_4S_2{\cdot}C_4H_4O_4$	8.34[h] (6) (7.8–9.55)	5.65 (4) (5.3–6.0)	490
23	Me	H	$ClCH_2$	$(CH_2)_2$	7	EtOH	176–178	40.0	$C_{17}H_{26}ClN_3O_4S_2{\cdot}C_4H_4O_4$	8.1[h] (6) (7.8–8.5)	6.2[h] (6)	79
24	$ClCH_2$	H	$ClCH_2$	$(CH_2)_2$	3	Me_2CO	135–136	9.4	$C_{17}H_{25}N_3Cl_2O_4S_2{\cdot}C_4H_4O_4$	8.0[h] (4) (7.8–8.3)	6.33 (4)	47
25	Me	H	CF_3	$(CH_2)_2$	7	MeOH/EtOH	99–101	35.9	$C_{17}H_{24}F_3N_3O_4S_2{\cdot}C_4H_4O_4$	6.4[h] (4) (6.1–6.8)	NT	
26	*n*-Pr	H	Me	$(CH_2)_2$	5	EtOH	180–182	19.7	$C_{19}H_{31}N_3O_4S_2{\cdot}C_4H_4O_4$	8.29[h] (6) (8.05–8.6)	5.8 (4) (5.65–5.9)	310
27	Et	H	Et	$(CH_2)_2$	3	MeOH	156–157	57.0	$C_{19}H_{31}N_3O_4S_2{\cdot}C_4H_4O_4$	8.27[h] (5) (7.8–9.25)	5.54 (4) (5.1–6.0)	540
28	*n*-Pr	H	Et	$(CH_2)_2$	12	EtOH	175–176	50.3	$C_{20}H_{33}N_3O_4S_2{\cdot}C_4H_4O_4$	8.1[h] (6) (7.9–8.4)	NT	
29	Ph	H	Me	$(CH_2)_2$	5	EtOH	197–198	63.6	$C_{22}H_{29}N_3O_4S_2{\cdot}C_4H_4O_4$	8.12[h] (4) (7.9–8.3)	6.16 (4)	91
30	4-MeC_6H_4	H	Me	$(CH_2)_2$	5	EtOAc	125–127	45.6	$C_{23}H_{31}N_3O_4S_2{\cdot}C_4H_4O_4{\cdot}0.5H_2O$	8.4[h] (6) (8.0–9.3)	5.8 (4)	400
31	4-MeC_6H_4	H	Et	$(CH_2)_2$	12	EtOH	186–188	74.1	$C_{24}H_{33}N_3O_4S_2{\cdot}C_4H_4O_4$	7.62[h] (4) (7.3–8.5)	6.6[h] (2)	
32	3-MeC_6H_4	H	Me	$(CH_2)_2$	5	MeOH/*i*-PrOH	218–220	37.0	$C_{23}H_{31}N_3O_4S_2{\cdot}HCl{\cdot}0.5H_2O$	8.0[h] (16) (7.9–8.2)	6.4[h] (12) (6.2–6.6)	40
33	4-$MeOC_6H_4$	H	Me	$(CH_2)_2$	5	EtOAc	121–123	65.2	$C_{23}H_{31}N_3O_5S_2{\cdot}C_4H_4O_4{\cdot}0.5H_2O$	8.1[h] (6) (7.9–8.3)	6.1 (4)	100
34	4-ClC_6H_4	H	Me	$(CH_2)_2$	5	EtOH	218–219	43.0	$C_{22}H_{28}ClN_3O_4S_2{\cdot}HCl{\cdot}H_2O$	8.04[h] (6)	NT	
35	4-FC_6H_4	H	Me	$(CH_2)_2$	5	EtOH	183–185	54.4	$C_{22}H_{28}FN_3O_4S_2{\cdot}C_4H_4O_4$	7.7[h] (2)	5.7 (2)	100
36	2-$NO_2C_6H_4$	H	Me	$(CH_2)_2$	5	EtOH	159–163	36.0	$C_{22}H_{28}N_4O_6S_2$	7.69[h] (2)	6.7[h] (3)	10
idazoxan										8.04[h] (4) (7.9–8.3)	6.16[h] (4) (5.9–6.5)	76
WY 26392										8.08[h] (6) (7.8–8.4)	6.34[h] (6) (6.2–6.5)	55

[a,b] See footnotes to Table I. [e] n = number of determinations. [f] Antilog ($\alpha_2 pA_2 - \alpha_1 pA_2$), rounded to two significant figureds. [g] Maleate. [h] pA_2 values calculated from Schild plots; other values calculated from results at one antagonist concentration assuming a Schild plot slope of unity. NT = not tested.

Perkin-Elmer Model 521 spectrophotometer. NMR spectra were determined on a Brucker WP200 instrument. C, H, and N analysis were within ±0.4% of theoretical values.

***N*-((2α,11bα)-1,3,4,6,7,11b-Hexahydro-2*H*-benzo[*a*]quinolizin-2-yl)ethylenediamine Trihydrochloride (3).** A solution of 2-oxo-1,3,4,6,7,11bα-hexahydrobenzoquinolizine hydrochloride (38.4 g, 0.16 mol) and ethylenediamine (53.4 mL, 0.8 mol) in 160 mL of EtOH was heated at reflux for 1.5 h. The solution was then ice-cooled and stirred while sodium borohydride (8 g) was added below 35 °C. The mixture was stirred overnight and the solvent was removed by rotary evaporation. The residue was diluted with water and extracted into $CHCl_3$. The extract was dried (Na_2SO_4) and evaporated, and the residue was dissolved in 240 mL of EtOH and acidified with ethanolic HCl to precipitate the title compound: 49.1 g (86.4%); mp 250 °C dec; IR (Nujol) 1580, 1375, 1055, 755 cm^{-1}; NMR (CD_3OD) δ 2.1–3.85 (14 H, m, $(CH_2)_7$), 3.90 (1 H, tt, H-2), 4.75 (1 H, dd, H-11b), 7.25–7.55 (4 H, m, aromatics).

***N*-((2β,11bα)-1,3,4,6,7,11b-Hexahydro-2*H*-benzo[α]quinolizin-2-yl)-*N*-[2-[(methylsulfonyl)amino]ethyl]methanesulfonamide Maleate (4).** Compound **3**·3HCl (28.4 g, 0.08 mol) was basified with excess aqueous 2 M NaOH and extracted in $CHCl_3$. The extract was dried and evaporated. The residue obtained was dissolved in 200 mL of CH_2Cl_2 together with Et_3N (24 g, 0.24 mol). The solution was then ice-cooled and stirred while methanesulfonyl chloride (19.15 g, 5% excess) was added dropwise over 5 min. After addition was complete, the mixture was stirred for a further 0.5 h, washed with aqueous Na_2CO_3 solution, dried (Na_2SO_4), and evaporated. The residue was crystallized from 140 mL of EtOH to give 20.3 g (63%) of 4 base. The base was dissolved in 240 mL of hot MeOH and maleic acid (5.86 g) added. On cooling, 4 maleate separated and was recrystallized from a mixture of 250 mL of MeOH and 30 mL of H_2O to give 19.3 g (48%): mp 196–197 °C; IR (Nujol) 3310, 1580, 1150, 1000, 760 cm^{-1}; NMR (CD_3OD) δ 2.0–3.8 (14 H, m, $(CH_2)_7$), 2.94 (3 H, s, Me), 3.08 (3 H, s, Me), 4.10 (1 H, tt, H-2), 4.52 (1 H, dd, H-11b), 7.25–7.45 (4 H, m, aromatics).

***N*-[2-((2β,11bα)-1,3,4,6,7,11b-Hexahydro-2*H*-benzo[*a*]quinolizin-2-ylamino)ethyl]methanesulfonamide Dihydrobromide (5).** Methanesulfonic anhydride (11.3 g, 0.065 mol) was added over 2–3 min to a vigorously stirred, ice-cooled mixture of **3**·3HCl (17.7 g, 0.05 mol), K_2CO_3 (27.6 g, 0.2 mol), 200 mL of CH_2Cl_2, and 100 mL of H_2O. After addition was complete, the mixture was stirred for a further 0.5 h. Water was then added to dissolve precipitated potassium methanesulfonate and the organic phase separated, dried, and evaporated to give an oil. The oil was dissolved in 100 mL of methanol and hydrogen bromide gas passed into the solution to precipitate the title compound: 13.2 g (54.4%); mp 238–245 °C; IR (Nujol) 3150, 1570, 1315, 1140, 1095, 750 cm^{-1}; NMR (CD_3OD) δ 2–3.9 (14 H, m, $(CH_2)_7$), 3.06 (3 H, s, Me), 3.90 (1 H, tt, H-2), 4.78 (1 H, dd, H-11b), 7.25–7.5 (4 H, m, aromatics).

***N*-((2β,11bα)-1,3,4,6,7,11b-Hexahydro-2*H*-benzo[*a*]quinolizin-2-yl)-*N*-[2-[(methylsulfonyl)amino]ethyl]-4-methylbenzenesulfonamide Maleate (30).** A solution of 4-methylbenzenesulfonyl chloride (1 g, 5.24 mmol) in 50 mL of CH_2Cl_2 was added over 5 min to a stirred, ice-cooled solution of **5**·HBr (2.0 g, 4.12 mmol) and Et_3N (1.9 mL, 13.5 mmol) in 50 mL of CH_2Cl_2. The solution was allowed to stand overnight, washed with aqueous Na_2CO_3, dried (Na_2SO_4), and evaporated. The residue was chromatographed on neutral alumina with $CHCl_3$ as eluent to give the title product which was crystallized from ethanol to give 0.7 g (35.6%), mp 150–154 °C. Treatment of a solution of the base in EtOAC with maleic acid gave the maleate: mp 125–127 °C; IR (Nujol) 3280, 1110, 975, 915, 720 cm^{-1}; NMR (CD_3OD) δ 1.8–3.8 (14 H, m, $(CH_2)_7$), 2.50 (3 H, s, Me), 2.95 (3 H, s, Me), 4.23 (1 H, tt, H-2), 4.50 (1 H, dd, H-11b), 7.70 (1 H, m, H-11), 7.2–7.35 (3 H, m, H-8,9,10), 7.47 (2 H, d, H-3′,5′), 7.85 (2 H, d, H-2′,6′).

***N*-[2-((2β,11bα)-1,3,4,6,7,11b-Hexahydro-2*H*-benzo[*a*]quinolizin-2-yl)ethyl]acetamide Dihydrochloride (6).** A solution of **3**·3HCl (88.5 g, 0.25 mol) in 200 mL of H_2O was basified with NaOH (40 g) and extracted into $CHCl_3$. The extract was dried (Na_2SO_4) and evaporated. The residue obtained was dissolved in 300 mL of MeOAc and heated at reflux for 3 days. The solution was evaporated, and the residue was dissolved in 200 mL of EtOH and acidified with ethanolic HCl to precipitate the title compound: 72.9 g (80.9%); mp 227–230 °C; IR (Nujol) 3245, 1680, 1570, 740 cm^{-1}; NMR (CD_3OD) δ 2.0 (3 H, s, Me), 2.0–3.9 (14 H, m, $(CH_2)_7$), 3.87 (1 H, tt, H-2), 4.75 (1 H, dd, H-11b), 7.25–7.5 (4 H, m, aromatics).

***N*-((2β,11bα)-1,3,4,6,7,11b-Hexahydro-2*H*-benzo[*a*]quinolizin-2-yl)-*N*-(2-aminoethyl)methanesulfonamide Dihydrochloride (7).** Methanesulfonyl chloride (25.4 g, 0.22 mol) was added dropwise over 1 h to a stirred, ice-cooled mixture of **6**·2HCl (72.5 g, 0.2 mol), Et_3N (98.2 mL, 0.7 mol), and 350 mL of CH_2Cl_2. After addition was complete the mixture was stirred for a further 1 h and then washed with aqueous Na_2CO_3 solution, dried (Na_2SO_4), and evaporated. The residue obtained above was then heated at reflux in a mixture of concentrated hydrochloric acid (60 mL) and 350 mL of H_2O for 20 h. The solution was then cooled, basified with aqueous sodium hydroxide, and extracted with CH_2Cl_2. The extract was dried and evaporated, and the residue was dissolved in 2-propanol and acidified with 2-propanol–HCl to precipitate the title compound: 70.2 g (88%); mp 174–177 °C; IR (Nujol) 1605, 1375, 1180, 950, 770 cm^{-1}; NMR (CD_3OD) δ 2–3.9 (14 H, m, $(CH_2)_7$), 3.12 (3 H, s, Me), 4.25 (1 H, tt, H-2), 4.65 (1 H, dd, H-11b), 7.25–7.45 (4 H, m, aromatics).

***N*-((2β,11bα)-1,3,4,6,7,11b-Hexahydro-2*H*-benzoquinolizin-2-yl)-*N*-[2-[[(trifluoromethyl)sulfonyl]amino]ethyl]methanesulfonamide Maleate (25).** Trifluoromethanesulfonic anhydride (3.67 g, 0.013 mol) was added dropwise over 5 min to a vigorously stirred, ice-cooled mixture of **7**·2HCl (4 g, 0.01 mol), K_2CO_3 (2.76 g, 0.02 mol), 10 mL of H_2O, and 20 mL of CH_2Cl_2. After addition was complete, the solution was stirred for a further 1 h, and the organic phase was then separated, washed with water, dried, and evaporated. The residue was chromatographed on neutral alumina (act. I) with 4% MeOH in $CHCl_3$ as eluent. The major product band was collected and treated with maleic acid in ethanol to precipitate the title compound, 2.05 g. Recrystallization from 1:1 MeOH/EtOH gave 1.5 g (26%): mp 99–101 °C; IR (Nujol) 1700, 1580, 1190, 1150, 865, 605 cm^{-1}; NMR (CD_3OD) δ 2–3.8 (14 H, m, $(CH_2)_7$), 3.1 (3 H, s, Me), 4.13 (1 H, tt, H-2), 4.55 (1 H, dd, H-11b), 7.2–7.4 (4 H, m, aromatics).

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Registry No. **3**, 95669-34-4; **4**, 95669-35-5; **4**·$C_4H_4O_4$, 117145-07-0; **5**, 95669-52-6; **6**, 117145-08-1; **7**, 117145-09-2; **8**, 95669-05-9; **9**, 117145-10-5; **10**, 117145-11-6; **11**, 95669-36-6; **12**, 117145-12-7; **13**, 95669-42-2; **14**, 95669-46-8; **15**, 95669-08-2; **15**·HCl, 95693-51-9; **16**, 117145-13-8; **17**, 117145-15-0; **16**·$C_4H_4O_4$, 117145-14-9; **17**·$C_4H_4O_4$, 117145-16-1; **18**, 95669-38-8; **18**·HBr, 95669-39-9; **19**, 117145-17-2; **19**·$C_4H_4O_4$, 117145-18-3; **20**, 95669-43-5; **20**·$C_4H_4O_4$, 117145-19-4; **21**, 95669-47-9; **22**, 95668-97-6; **22**·$C_4H_4O_4$, 95693-49-5; **23**, 117145-20-7; **23**·$C_4H_4O_4$, 117145-21-8; **24**, 95668-98-7; **24**·$C_4H_4O_4$, 117145-22-9; **25**, 117145-23-0; **25**·$C_4H_4O_4$, 117145-24-1; **26**, 95669-53-7; **26**·$C_4H_4O_4$, 117145-25-2; **27**, 95669-57-1; **27**·$C_4H_4O_4$, 117145-26-3; **28**, 117145-27-4; **28**·$C_4H_4O_4$, 117145-28-5; **29**, 95669-55-9; **29**·$C_4H_4O_4$, 117145-29-6; **30**, 95669-02-6; **30**·$C_4H_4O_4$, 117145-30-9; **31**, 117145-31-0; **31**·$C_4H_4O_4$, 117145-32-1; **32**, 117145-38-7; **32**·HCl, 117145-33-2; **33**, 95669-03-7; **33**·$C_4H_4O_4$, 117145-34-3; **34**, 117145-39-8; **34**·HCl, 117145-35-4; **35**, 95669-00-4; **35**·$C_4H_4O_4$, 117145-36-5; **36**, 117145-37-6; $H_2N(CH_2)_3NH_2$, 109-76-2; $H_2N(CH_2)_4NH_2$, 110-60-1; $H_2NCH_2C(Me)_2NH_2$, 811-93-8; $H_2NCH_2CH_2NHMe$, 109-81-9; $H_2N(CH_2)_2NH_2$, 107-15-3; 2-oxo-1,3,4,6,7,11bα-hexahydrobenzoquinolizine hydrochloride, 20821-40-3.