Reaction of Sulfene with Heterocyclic *N,N*-Disubstituted α-Aminomethyleneketones. X. Synthesis of Thieno[2,3-*h*]-1,2-benzoxathiin Derivatives.

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The polar 1,4-cycloaddition of sulfene to *N,N*-disubstituted (*E*)-5-aminomethylene-6,7-dihydrobenzo[*b*]-thiophen-4(5*H*)-ones II gave in excellent yield and only in the case of aliphatic *N*-substitution, *N,N*-disubstituted 4-amino-3,4,5,6-tetrahydrothieno[2,3-*h*]-1,2-benzoxathiin 2,2-dioxides III, which are derivatives of the new heterocyclic system thieno[2,3-*h*]-1,2-benzoxathiin. Dehydrogenation with DDQ of cycloadducts IIIa-d was successful only in the case of IIIa (NR_2 = dimethylamino) to give in low yield 4-dimethylamino-3,4-dihydrothieno[2,3-*h*]-1,2-benzoxathiin 2,2-dioxide.

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Part of our continuing study of sulfene 1,4-cycloaddition to *N,N*-disubstituted α-aminomethyleneketones is devoted to the synthesis of new heterocyclic systems derived from 1,2-oxathiin and incorporating potential pharmacologically active molecules (1). In this context, we now wish to report the reaction of *N,N*-disubstituted 5-aminomethylene-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-ones II with sulfene to afford derivatives of a new heterocyclic system incorporating the pharmacologically useful benzo[b]thiophene moiety (2), namely thieno[2,3-*h*]-1,2-benzoxathiin. The starting enaminones IIa-g (Table I) were prepared, generally in excellent yield, from 6,7-dihydro-5-hydroxymethylenebenzo[b]thiophen-4(5*H*)-one I and secondary amines, following previously described procedures (3,4). They are probably *E* isomers, at least as can be seen from the strong upfield shift of the CH_2-6 protons (*ca.* 0.5-0.8 ppm) caused by the phenyl group(s) in compounds IIf,g in comparison with IIa-e (Table II). Reac-

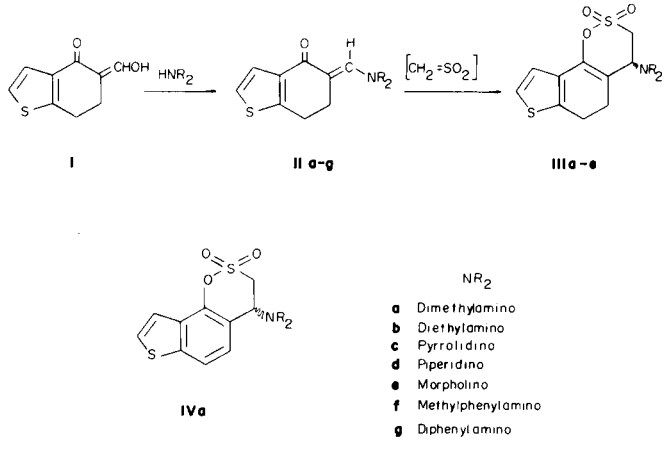
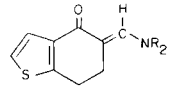


Table I

N,N-Disubstituted (*E*)-5-Aminomethylene-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-ones (IIa-g) (a)



Formula Number	NR_2	Yield %	Mp, °C or Bp/mm	Molecular Formula	Analyses % Calcd./Found C	H	N
IIa	$N(CH_3)_2$	95	106 (b)	$C_{11}H_{13}NOS$	63.73	6.32	6.76
					63.94	6.06	6.79
IIb	$N(C_2H_5)_2$	80	80 (b)	$C_{13}H_{17}NOS$	66.34	7.28	5.95
					66.05	7.58	5.94
IIc	Pyrrolidino	94	114 (c)	$C_{13}H_{15}NOS$	66.92	6.48	6.00
					66.74	6.20	6.05
IId	Piperidino	84	111 (c)	$C_{14}H_{17}NOS$	67.98	6.92	5.66
					67.78	6.96	5.73
IIe	Morpholino	89	134 (c)	$C_{13}H_{15}NO_2S$	62.62	6.06	5.61
					62.87	6.28	5.71
IIf	$N(CH_3)C_6H_5$	87	198/0.4 (d)	$C_{16}H_{15}NOS$	71.34	5.61	5.20
					71.30	5.41	5.20
IIg	$N(C_6H_5)_2$	42	189 (c)	$C_{21}H_{17}NOS$	76.10	5.17	4.22
					75.95	5.19	4.23

(a) Enaminones IIa-e were prepared according to (3) and IIf-g according to (4). (b) From anhydrous diethyl ether. (c) From ethyl acetate. (d) Lit (9), bp 150-155°/0.1.

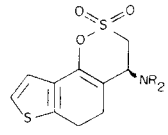
Table II

UV, IR and NMR Spectral Data of Compounds IIa-g

	UV λ max nm (log ε)	IR, cm^{-1} C=O	C=C	NMR, δ
IIa	220.5 (3.95) 253 (4.11) 265 sh (3.96) 365 (4.16)	1645	1550	3.00 (mc, CH_2-6 + CH_2-7), 3.10 (s, 2 CH_3N), 7.02 (d, J = 5.4, CH-3), 7.45 (d, J = 5.4, CH-2), 7.58 (near s, = CHN)
IIb	220 (3.94) 253 (4.10) 265 sh (3.95) 365 (4.18)	1640	1550	1.24 (t, J = 7.2, 2 CH_3), 2.96 (s, CH_2-6 + CH_2-7), 3.36 (q, J = 7.2, 2 CH_2N), 7.00 (d, J = 5.4, CH-3), 7.45 (d, J = 5.4, CH-2), 7.66 (near s, = CHN)
IIc	221 (3.91) 254.5 (4.05) 267 sh (3.90) 368 (4.13)	1642	1555	1.89 (mc, 2 CH_2 pyrr), 2.99 (mc, CH_2-6 + CH_2-7), 3.57 (mc, 2 CH_2N), 6.99 (d, J = 5.4, CH-3), 7.44 (d, J = 5.4, CH-2), 7.77 (near s, = CHN)
IId	221 (3.99) 253.5 (4.15) 267 sh (3.99) 368 (4.25)	1635	1548	1.64 (mc, 3 CH_2 pip), 2.95 (s, CH_2-6 + CH_2-7), 3.43 (mc, 2 CH_2N), 7.02 (d, J = 5.4, CH-3), 7.47 (d, J = 5.4, CH-2), 7.62 (near s, = CHN)
IIe	220 (3.60) 253.5(3.78) 266 sh (3.59) 364 (3.87)	1640	1550	2.96 (s, CH_2-6 + CH_2-7), 3.46 (mc, 2 CH_2N), 3.76 (mc, 2 CH_2O), 7.05, (d, J = 5.4, CH-3), 7.46 (d, J = 5.4, CH-2), 7.52 (s, = CHN)
IIf	230 sh (3.96) 256 (4.08) 378 (4.22)	1648	1552	2.42 (near t, J = 6, CH_2-6), 2.80 (mc, CH_2-7), 3.44 (s, CH_3N), 6.9-7.6 (m, C_6H_5), 7.02 (d, J = 5.4, CH-3), 7.49 (d, J = 5.4, CH-2), 7.75 (near s, = CHN)
IIg	230 (4.31) 263.5 (4.37) 280 sh (4.30 383 (4.45)	1645	1550	2.15 (near t, J = 6, CH_2-6), 2.81 (near t, J = 6.6, CH_2-7), 6.9-7.6 (m, 2 C_6H_5), 7.03 (d, J = 5.4, CH-3), 7.50 (d, J = 5.4, CH-2), 7.88 (near s, = CHN)

Table III

N,N-Disubstituted 4-Amino-3,4,5,6-tetrahydrothieno[2,3-*h*]-1,2-benzoxathiin 2,2-Dioxides (IIIa-e) (a)



Formula Number	NR_2	Yield %	Mp, °C	Molecular Formula	Analyses % Calcd./Found C	H	N
IIIa	$N(CH_3)_2$	83	145 (b)	$C_{12}H_{15}NO_3S_2$	50.50	5.29	4.90
					50.40	5.51	4.72
IIIb	$N(C_2H_5)_2$	89	141 (b)	$C_{14}H_{19}NO_3S_2$	53.65	6.11	4.47
					53.65	6.00	4.45
IIIc	Pyrrolidino	77	151 (c)	$C_{14}H_{17}NO_3S_2$	53.99	5.50	4.49
					53.90	5.60	4.50
IIId	Piperidino	82	161 (b)	$C_{15}H_{19}NO_3S_2$	55.36	5.88	4.30
					55.31	5.70	4.35
IIIe	Morpholino	80	165 (c)	$C_{14}H_{17}NO_4S_2$	51.35	5.23	4.27
					51.38	5.19	4.21

(a) All compounds were prepared according to (3), using anhydrous THF as the solvent. (b) From anhydrous diethyl ether. (c) From 95% ethanol.

tion of II with methanesulfonyl chloride and triethylamine (sulfene prepared *in situ*) occurred in excellent yield only in the case of aliphatic *N*-substitution to give 4-dialkylamino-3,4,5,6-tetrahydrothieno[2,3-*h*]-1,2-benzoxathiin 2,2-dioxides IIIa-e (Table III), whose structure was confirmed by ir and nmr spectral data (Table IV). Enaminones IIf,g (NR_2 = methylphenylamino and diphenylamino, respectively) did not react and were recovered un-

Table IV

IR and NMR Spectral Data of Compounds IIIa-e

	IR, cm^{-1}			NMR, δ
	C=C	O=S=O		
IIIa (a)	1657	1377	1178	2.34 (s, 2 CH_3N), 2.55-3.10 (m, CH_2-5 + CH_2-6), 3.27-3.57 (m, CH_2-3), 3.8-4.2 (m, CH-4), 7.08 (s, CH-8 + CH-9)
IIIb	1655	1375	1178	1.10 (t, J = 7.2, 2 CH_3), 2.49 (q, J = 7.2, 2 CH_2N), 2.40-3.05 (m, CH_2-5 + CH_2-6), 3.20-3.55 (m, CH_2-3), 3.90-4.25 (m, CH-4), 7.06 (s, CH-8 + CH-9)
IIIc	1655	1375	1182	1.79 (mc, 2 CH_2 pyrr), 2.40-3.15 (m, 2 CH_2N + CH_2-5 + CH_2-6), 3.25-3.80 (m, CH_2-3), 4.1-4.5 (m, CH-4), 7.07 (s, CH-8 + CH-9)
IIId	1657	1377	1183	1.54 (mc, 3 CH_2 pip), 2.54 (mc, 2 CH_2N), 2.81 (mc, CH_2-5 + CH_2-6), 3.3-3.6 (m, CH_2-3), 3.8-4.2 (m, CH-4), 7.08 (s, CH-8 + CH-9)
IIIe	1655	1377	1187	2.62 (mc, 2 CH_2N), 2.84 (mc, CH_2-5 + CH_2-6), 3.2-4.3 (m, CH_2-3 + CH-4), 3.75 (mc, 2 CH_2O), 7.08 (s, CH-8 + CH-9)

(a) Uv: λ max nm (log ϵ) 226.5 (4.32), 232 sh (4.29), 282 (3.72).

changed from the reaction mixtures, according to a well established trend of this reaction (1,5,6). Dehydrogenation of adducts III was attempted in the case of IIIa-d with DDQ in refluxing benzene (7). A low yield of the corresponding 4-dialkylamino-3,4-dihydrothieno-[2,3-*h*]-1,2-benzoxathiin 2,2-dioxide IV was obtained after 12 hours reflux only in the case of IIIa (NR_2 = dimethylamino), whereas IIIb,d gave inseparable mixtures of the starting and final products (evidenced by nmr spectra) even after 15-23 hours reflux, and IIIc was recovered unchanged. Thus it seems that compounds III are more reluctant even to an incomplete aromatization than the corresponding oxygen isosteric compounds, namely 4-dialkylamino-3,4,5,6-tetrahydrofuro[2,3-*h*]-1,2-benzoxathiin 2,2-dioxides (6).

EXPERIMENTAL

The uv spectra were measured in 95% ethanol with a Hitachi-Perkin-Elmer Model EPS-3T spectrophotometer. The ir spectra were taken in chloroform on a Perkin-Elmer Model 398 spectrophotometer; the nmr spectra were recorded in deuteriochloroform on a Perkin-Elmer Model R12 instrument (60 MHz, TMS as internal standard, J in Hz). Melting points were determined with a Fisher-Johns apparatus.

6,7-Dihydro-5-hydroxymethylenebenzo[b]thiophen-4(5*H*)-one (I).

This compound, whose synthesis has been already described (8,9), was prepared from 6,7-dihydrobenzo[b]thiophen-4(5*H*)-one (9) (10 mmoles), ethyl formate (15 mmoles) and sodium methoxide (15 mmoles) in benzene following a previously described procedure (10), yield, 78%, bp 120°/0.5 mm [lit (8) 180°/20 mm]; mp 43-44° [lit (8,9) mp 45°]; uv: λ max nm (log ϵ) 234 (4.13), 257.5 (4.02), 309 (3.95); ir (neat): ν max 1725, 1632, 1585 cm^{-1}; nmr (deuteriochloroform): δ 2.65 (mc, CH_2-7), 2.99 (mc, CH_2-6), 7.12 (d, J = 5.4, CH-3), 7.43 (d, J = 5.4, CH-2), 7.52 (s, =CH-O), 10.04 and 13.75 (2 broad s, OH, disappear with deuterium oxide).

ed procedure (7), reflux time, 12 hours, yield, 0.68 g (24%), mp 147-148° (from anhydrous diethyl ether); ir (chloroform): ν max 1615, 1548, 1383, 1163 cm^{-1}; nmr (deuteriochloroform): δ 2.36 (s, 2 CH_3N), 3.45-3.75 (m, CH_2-3), 4.55-4.85 (m, CH-4), 7.51 (s, CH-5 + CH-6), 7.73 (s, CH-8 + CH-9).

Anal. Calcd. for $C_{12}H_{13}NO_3S_2$: C, 50.86; H, 4.62; N, 4.94. Found: C, 50.88; H, 4.58; N, 5.03.

4-Dimethylamino-3,4-dihydrothieno[2,3-*h*]-1,2-benzoxathiin 2,2-dioxide (IVa).

This compound was prepared from IIIa (2.85 g, 10 mmoles) and DDQ (2.27 g, 10 mmoles) in anhydrous benzene following a previously describ-

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