Reaction of Sulfene with Heterocyclic α-Dialkylaminomethyleneketones II. Synthesis of 5*H*-1,2-Oxathiino[5,6-*c*][1]benzopyran Derivatives

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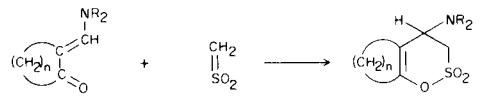
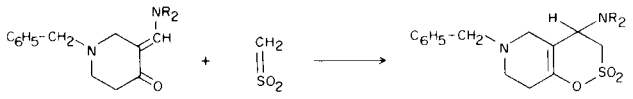
The reaction of sulfene with 3-dialkylaminomethylene-4-chromanone and 3-dialkylaminomethylene-6-methyl-4-chromanone gave 1,4-cycloadducts which are derivatives of a new heterocyclic system, *i.e.*, 5*H*-1,2-oxathiino[5,6-*c*][1]benzopyran. The structures of the adducts were determined by ir and nmr spectral data. Two new α-hydroxymethyleneketones (3-hydroxymethylene-4-chromanone and its 6-methyl analogue) as well as some of their derived enamines were prepared. During the preparation of *N,N*-diethylenamines a self-condensation occurs, which gives the byproducts Xa-b.

As part of our general investigation of *N,N*-disubstituted α-aminomethyleneketones we found that the reaction of sulfene with 2-dialkylaminomethylenecyclanones (I) occurs through a 1,4-cycloaddition to give 4-dialkylamino-5,6-polymethylene-3,4-dihydro-1,2-oxathiine 2,2-dioxides (II) (1,2):



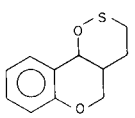
I, n = 4-6 II

This reaction was also applied to heterocyclic α-dialkylaminomethyleneketones, namely 1-benzyl-3-dialkylaminomethylene-4-piperidones (III) (3):



III

We have now extended this cycloaddition to include a variety of heterocyclic α-dialkylaminomethyleneketones in order to show the general usefulness of the reaction in synthesizing new polycondensed heterocyclic systems, in the present case 5*H*-1,2-oxathiino[5,6-*c*][1]benzopyran (IV):



IV

For this purpose 3-hydroxymethylene-4-chromanone (V) and its 6-methyl derivative (VI) were synthesized. From these we prepared the enamines (VII) by reaction with secondary amines in benzene solution at room temperature (see reaction scheme and Tables I, II and III).

During the preparation of the enamines a particular reaction course was noted when V and VI reacted with diethylamine.

In addition to the expected enamines (VII, NR_2 = diethylamino), other products of the general formula (X) were also obtained.

The uv, ir and nmr spectra are in good agreement with the proposed structure X and the mass spectrum of Xa shows the molecular ion at 306 m/e and two dominant peaks at 147 ($C_9H_7O_2^+$, base peak) and 160 ($C_{10}H_8O_2^+$).

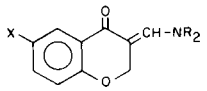
The uv data agree quite well with the chromone moiety present in the molecule (4,5). In the ir spectrum is found a strong CO absorption at 1682 (Xa) and 1678 (Xb) cm^{-1}, whereas the chromanone portion shows CO absorption at 1633 (Xa) and 1642 (Xb) cm^{-1}. Other typical chromone bands (1608, 1574, 1469 for Xa and 1616, 1575, 1484 cm^{-1} for Xb) are also present (6,7).

In the nmr spectra the signals from the two aromatic nuclei are clearly distinguished particularly in Xb; moreover, the chromone olefinic protons in both Xa and Xb appear at about 2.05 τ (8). The methylene group -O-C*H*$_2$- is found at 5.5 τ (9) and the -C*H*$_2$-C*H*< protons system as a complex multiplet at 7.0 τ.

The formation of X may be due to an aldol condensation between two molecules of V or VI in the β-dicarbonyl form, followed by dehydration and base induced elimination of the formyl group. The intermediates (IX) give

TABLE I

3-Dialkylaminomethylene-4-chromanones and 3-Dialkylaminomethylene-6-methyl-4-chromanones (VIIa-h).



Formula number	NR_2	X	Yield, %	M.p., °C	Molecular formula	Analyses % – Calcd. (Found) C	H	N
VIIa	$N(C_2H_5)_2$	H	12	80-81 (a)	$C_{14}H_{17}NO_2$	72.70 (72.54	7.41 7.66	6.06 6.28)
VIIb	$N(C_2H_5)_2$	CH_3	23	84 (a)	$C_{15}H_{19}NO_2$	73.44 (73.32	7.81 7.72	5.71 5.77)
VIIc		H	71	145-146 (b)	$C_{14}H_{15}NO_2$	73.34 (73.29	6.59 6.71	6.11 6.29)
VIId		CH_3	81	164-165 (b)	$C_{15}H_{17}NO_2$	74.05 (73.83	7.04 7.10	5.76 5.96)
VIIe		H	50	111-112 (a)	$C_{15}H_{17}NO_2$	74.05 (73.87	7.04 6.83	5.76 5.80)
VIIf		CH_3	68	104-106 (a)	$C_{16}H_{19}NO_2$	74.68 (74.40	7.44 7.35	5.44 5.46)
VIIg		H	81	141-142 (b)	$C_{14}H_{15}NO_3$	68.55 (68.41	6.16 6.13	5.71 5.79)
VIIh		CH_3	83	147-148 (b)	$C_{15}H_{17}NO_3$	69.48 (69.51	6.61 6.40	5.40 5.46)

(a) From diethyl ether; (b) From ethanol 95°.

TABLE II

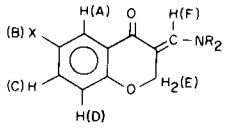
Uv and ir Spectral Data of Compounds VIIa-h

	uv λ max, nm (log ε)					ir (cm^{-1}) C=O	C=C
VIIa	215(4.16),	236(4.09),	260(3.94)(a),	319(3.93),	370(4.27)	1663	1564
VIIb	219(4.12),	236(4.15),	260(3.92)(a),	328(4.02),	374(4.27)	1661	1564
VIIc	215(4.16),	241(4.07),	263(3.93)(a),	321(3.91),	374(4.30)	1651(b)	1545(b)
VIId	219(4.13),	237(4.13),	260(3.94)(a),	330(3.98),	377(4.28)	1651(b)	1545(b)
VIIe	216(4.14),	239(4.05),	256(3.98)(a),	317(3.92),	375(4.30)	1658	1554
VIIf	219(4.17),	237(4.16),	260(3.96)(a),	324(4.01),	378(4.30)	1658	1562
VIIg	215(4.12),	236(4.05),	260(3.90)(a),	318(3.96),	372(4.27)	1652(b)	1549(b)
VIIh	218(4.15),	236(4.16),	260(3.91)(a),	325(4.04),	376(4.26)	1661	1567

(a) Shoulder; (b) In chloroform.

TABLE III

Nmr Spectral Data of Representative Compounds VII

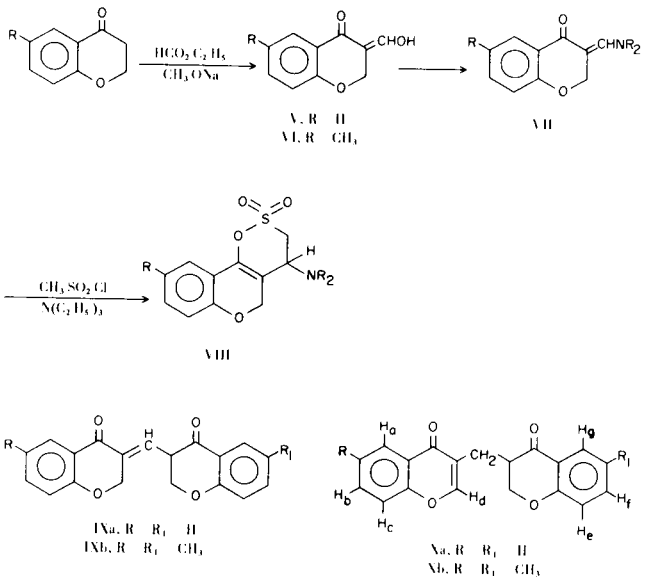


	X	NR_2	Chemical Shifts (τ) (a) (A)	(B)	(C)	(D)	(E)	(F)	NR_2
VIIb (b)	CH_3	diethylamino	2.38 (near d) J ~2	7.69 (s)	2.92 (d,d) $J_{'}$ = 8.4 $J_{''}$ ~2	3.33 (d) J = 8.4	4.98 (near s)	2.63 (near s)	6.72 (q, J = 7, 2 NCH_2) 8.75 (t, J = 7, 2 CH_3)
VIIe (b)	H	piperidino	2.20 (d,d) $J_{'}$ = 7 $J_{''}$ ~2		2.60-3.40 (m)		4.89 (near s)	2.71 (near s)	6.61 (m, 2 NCH_2) 8.34 (m, 3 CH_2)
VIIf (b)	CH_3	piperidino	2.38 (near d) J ~2	7.69 (s)	2.91 (d,d) $J_{'}$ = 8 $J_{''}$ ~2	3.32 (d) J = 8	4.92 (near s)	2.68 (near s)	6.63 (m, 2 NCH_2) 8.36 (m, 2 NCH_2)
VIIg	H	morpholino	2.04 (d,d) $J_{'}$ = 7 $J_{''}$ ~2		2.40-3.25 (m)		4.84 (near s)	2.48 (near s)	6.30 (m, 2 OCH_2) 6.53 (m, 2 NCH_2)

(a) s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, mc = multiplet center. (b) In carbon tetrachloride.

rise to the more stable chromone derivatives (X) by shift of the double bond.

Finally, the reaction of the enamines (VII) with sulfene, generated *in situ* by dehydrochlorination of methanesulfonyl chloride with triethylamine, gave 3,4-dihydro-4-dialkylamino-5*H*-1,2-oxathiino[5,6-c][1]benzopyran 2,2-dioxides (VIII, Tables IV, V and VI).



These compounds show in the ir spectrum (Table V) the strong SO_2 stretching vibrations of cyclic sulfonates at 1389-1393, 1188-1192 cm^{-1} and a medium-strong olefin band at 1669-1674 cm^{-1} (1,2,10).

In the nmr spectrum (Table VI) the signal of the protons alpha to sulfur (-CH_2-SO_2-O-) appears at 6.46-6.63 τ whereas the signal of the methine proton (>CH-NR_2) is at 5.87-6.07 τ.

The methylene and methine protons give rise to a typical pattern due to an AB_2 system with higher-order splittings of both the central member of the triplet and the high field part of the doublet. In the spectrum of VIIIc the scan from 5.6 to 6.7 τ approximately matches the theoretical pattern for J/δ = 0.25 reported by Corio (11).

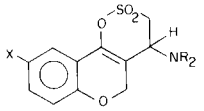
It can thus be concluded that 3-hydroxymethylene-4-chromanones (V) and (VI) show a different behaviour from other α-hydroxymethylenecyclanones already examined by us (1-3). On the other hand the enamines (VII) undergo 1,4-cycloaddition with sulfene to give derivatives of 5*H*-1,2-oxathiino[5,6-c][1]benzopyran.

EXPERIMENTAL

Ir spectra were measured, except when otherwise specified, in carbon tetrachloride solution with a Perkin-Elmer Model 257 spectrophotometer; uv spectra were taken in ethanol solution,

TABLE IV

3,4-Dihydro-4-dialkylamino-5*H*-1,2-oxathiino[5,6-c][1]benzopyran 2,2-Dioxides (VIIIa-f).



Formula number	NR_2	X	Yield, %	M.p., °C	Solvent for the reaction	Molecular formula	Analyses % - Calcd. (Found) C	H	N
VIIIa		H	30	124-125 (a)	Dioxane	$C_{15}H_{17}NO_4S$	58.61 (58.61	5.57 5.75	4.56 4.47)
VIIIb		CH_3	26	129-130 (b)	Ether	$C_{16}H_{19}NO_4S$	59.79 (59.64	5.96 5.99	4.36 4.24)
VIIIc		H	30	148-149 (c)	Ether + + Dioxane	$C_{16}H_{19}NO_4S$	59.79 (59.62	5.96 5.78	4.36 4.43)
VIIId		CH_3	70	145-146 (d)	Ether	$C_{17}H_{21}NO_4S$	60.87 (60.86	6.31 6.30	4.18 4.25)
VIIIe		H	45	171-172 (b)	Ether + + Tetrahydro= furane	$C_{15}H_{17}NO_5S$	55.71 (55.83	5.30 5.48	4.33 4.16)
VIIIf		CH_3	33	157 (b)	Ether	$C_{16}H_{19}NO_5S$	56.96 (56.77	5.68 5.72	4.15 3.91)

(a) From ethanol 95°. (b) From methanol. (c) From ether. (d) From petroleum ether (b.p. 40-70°).

TABLE V

Uv and ir Spectral Data of Compounds VIIIa-f

	uv λ max, nm (log ε)	ir (cm^{-1}) C=C	O=S=O	
VIIIa	222(4.40), 266(3.83), 276(3.73)(a), 312(3.67)	1674	1391	1189
VIIIb	223(4.43), 267(3.86), 276(3.76)(a), 320(3.68)	1674	1390	1188
VIIIc	222(4.40), 266(3.83), 276(3.73)(a), 312(3.67)	1672	1389	1189
VIIId	223(4.41), 267(3.83), 276(3.73)(a), 320(3.62)	1670	1390	1191
VIIIe	221(4.39), 266(3.83), 275(3.73)(a), 313(3.64)	1670	1393	1191
VIIIf	223(4.42), 267(3.84), 277(3.73)(a), 321(3.62)	1669	1393	1192

(a) Shoulder.

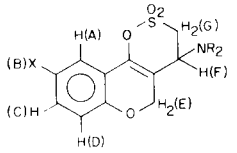
in concentrations of about 7-9 mg./l, with a Hitachi-Perkin Elmer Model EPS-3T spectrophotometer.

Nmr spectra were recorded on a Perkin-Elmer Model R12 (60 Mc/s) instrument in deuteriochloroform solution, except when otherwise specified. Chemical shifts are reported as τ (ppm) relative to tetramethylsilane as an internal standard; J in Hz.

The mass spectrum was obtained from a Perkin-Elmer RMS4 mass spectrometer.

TABLE VI

Nmr Spectral Data of Representative Compounds VIII



			Chemical shifts (τ) (a)							
	X	NR_2	(A)	(B)	(C)	(D)	(E)	(F)	(G)	NR_2
VIIIc	H	piperidino		2.50-3.30 (m)			5.06 (near s)	5.87 (near q) J = 9	6.46 (near t) J = 9	7.41 (m, 2 NCH_2) 8.43 (m, 3 CH_2)
VIIId (b)	CH_3	piperidino	2.90 (m)	7.74 (s)	3.06 (d,d) $J_{\prime} = 8$ $J_{\prime\prime} \sim 2$	3.40 (d) J = 8	5.22 (near s)	6.07 (near q) J = 9	6.63 (near t) J = 9	7.49 (m, 2 NCH_2) 8.47 (m, 3 CH_2)
VIIIe	H	morpholino		2.50-3.30 (m)			5.11 (near s)	5.97 (near q) J = 9	6.50 (near t) J = 9	6.31 (m, 2 OCH_2) 7.40 (m, 2 NCH_2)
VIIIf	CH_3	morpholino	2.87 (m)	7.72 (s)	2.98 (d,d) $J_{\prime} \sim 8$ $J_{\prime\prime} \sim 2$	3.29 (d) J = 7.6	5.14 (near s)	5.95 (near q) J ~9	6.49 (near t) J ~9	6.30 (m, 2 OCH_2) 7.40 (m, 2 NCH_2)

(a) See note to Table III; (b) In carbon tetrachloride.

Melting points were determined with a Mettler FP1 apparatus.

3-Hydroxymethylene-4-chromanone (V) and 3-Hydroxymethylene-6-methyl-4-chromanone (VI).

To a suspension of freshly prepared sodium methoxide (10.8 g., 0.2 mole) in anhydrous benzene (30 ml.) was added a solution of ethyl formate (15.2 g., 0.205 mole) in anhydrous benzene (70 ml.).

The ice-cooled mixture was treated with a solution of the corresponding 4-chromanone (0.1 mole) in anhydrous benzene (100 ml.) with stirring. A precipitate gradually appeared, and after 4 hours at room temperature it was hydrolyzed with water (100 ml.). The benzene layer was extracted with 10% sodium hydroxide and then with water.

The aqueous fractions were combined, washed with ether and acidified at 0° with hydrochloric acid.

The separated oil was extracted with ether, the extracts were washed with water, dried (magnesium sulfate) and concentrated. Distillation *in vacuo* of the crude product gave a light yellow oil.

3-Hydroxymethylene-4-chromanone.

This compound had b.p. of 105-110°/0.5; yield 11.5 g. (65%). uv λ max (log ε) nm 218 (4.24), 259 (3.84), 300 (3.86), 349 (3.85); ir ν max cm^{-1} 1657 (con. C=O), 1610 (con. C=C).

Anal. Calcd. for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 67.96; H, 4.56.

3-Hydroxymethylene-6-methyl-4-chromanone.

This compound had b.p. of 100-105°/0.3; yield 13.9 g. (73%); uv λ max (log ε) nm 223 (4.28), 265 (3.90), 295 (3.92), 354 (3.84); ir ν max cm^{-1} 1657 (con. C=O), 1622 (con. C=C).

Anal. Calcd. for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.41; H, 5.56.

General Procedure for Enamines VIIa-h (Table I); Compounds Xa-b.

3-Hydroxymethylene-4-chromanone (V) or 3-hydroxymethylene-6-methyl-4-chromanone (VI) (16 mmoles) was added to a solution of the secondary amine (18 mmoles) in anhydrous benzene (50 ml.).

After standing 24 hours at room temperature the benzene layer was separated and the benzene evaporated. The residue was crystallized from a suitable solvent.

In the case of enamine VIIa the residue was dissolved in excess ether: by slow evaporation at room temperature a white solid was obtained (Xa, 0.6 g., 15%, m.p. 138-139° from ether), whereas from the concentrated solution red crystals of the enamine were separated.

Compound Xa.

This compound had uv λ max (log ε) nm 216 (4.54), 249 (4.26), 307 (3.97); ir (potassium bromide) ν max cm^{-1} 1682, 1633, 1608, 1574, 1469, 1228, 1033; nmr τ 1.74 (dd, 1H, $J_{\prime} = 8$; $J_{\prime\prime} = 2$, H_a), 2.03 (near s, 1H, H_d), 2.10-3.20 (m, 7H, ar. H), 5.6 (mc, 2H, $-CH_2-O-$), 7.0 (mc, 3H, $>C=C(H)-CH_2-CH-$); Mass spectrum: m/e 306 (1.7), 185 (14.9), 171 (4.7), 160 (52.7), 147 (100), 121 (14.3), 92 (14.6), 77 (8.7), 75 (11), 28 (46.8).

Anal. Calcd. for $C_{19}H_{14}O_4$: C, 74.50; H, 4.61. Found: C, 74.47; H, 4.73.

In the case of enamine VIIb the crude residue was recrystallized from methanol yielding a white product (Xb, 0.75 g., 16%, m.p. 152° after several recrystallizations).

The enamine was obtained from methanolic mother liquors by concentration and several recrystallizations from ether.

Compound Xb.

This compound had uv λ max (log ε) nm 223 (4.57), 252

(4.29), 315 (3.95); ir (potassium bromide) ν max cm^{-1} 1678, 1642, 1616, 1575, 1484, 1218, 1022; nmr τ 1.98 (d, 1H, J ~2, Ha), 2.05 (near s, 1H, Hd), 2.31 (d, 1H, J = 2, Hg), 2.62 (m, 2H, Hb and Hc), 2.73 (dd, 1H, $J_{'}$ = 8; $J_{''}$ = 2, Hf), 3.16 (d, 1H, J = 8, He), 5.55 (mc, 2H, -CH_2-O-), 7.05 (mc, 3H, >C=C(-)-CH_2-CH-), 7.55 (s, 3H, R), 7.71 (s, 3H, $R_{'}$).

Anal. Calcd. for $C_{21}H_{18}O_4$: C, 75.43; H, 5.43. Found: C, 75.27; H, 5.64.

General Procedure for 3,4-Dihydro-4-dialkylamino-5*H*-1,2-oxathiino[5,6-*c*][1]benzopyran 2,2-Dioxides (VIIIa-f) (Table IV).

A solution of methanesulfonyl chloride (10-25 mmoles) in a suitable anhydrous solvent (20 ml.; see Table IV) was added dropwise with stirring to an ice-cooled solution of enamine (10-25 mmoles) and triethylamine (12-27 mmoles) in the same solvent (100 ml.).

After the addition was complete the reaction mixture was stirred for 4 hours at room temperature, filtered and the precipitate washed several times with ether. The filtrate and the washing liquors were combined, evaporated and the residue was recrystallized from a suitable solvent.

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