Reaction of Ketenes with *N,N*-Disubstituted α-Aminomethyleneketones VII. Synthesis of 2*H*,5*H*-[1]Benzothiopyrano[4,3-*b*]pyran and 2*H*,5*H*-Thiopyrano[4,3-*b*]pyran Derivatives

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The dipolar 1,4-cycloaddition of dichloroketene to *N,N*-disubstituted 3-aminomethylene-2,3-dihydro-4-thiochromanones and 3-aminomethylenetetrahydro-4-thiopyranones gave *N,N*-disubstituted 4-amino-3,3-dichloro-3,4-dihydro-2*H*,5*H*-[1]benzothiopyrano[4,3-*b*]pyran-2-ones and 4-amino-3,3-dichloro-3,4,7,8-tetrahydro-2*H*,5*H*-thiopyrano[4,3-*b*]pyran-2-ones, respectively, only in the case of aromatic or strong hindering aliphatic *N*-substitution. The adducts gave *N,N*-disubstituted 4-amino-3-chloro-2*H*,5*H*-[1]benzothiopyrano[4,3-*b*]pyran-2-ones and 4-amino-3-chloro-7,8-dihydro-2*H*,5*H*-thiopyrano[4,3-*b*]pyran-2-ones, respectively, by dehydrochlorination with DBN. By chromatography on neutral alumina, 3-(2,2-dichloroethylidene)-2,3-dihydro-4-thiochromanone was isolated as an unstable liquid from the reaction between dichloroketene and 3-diethylaminomethylene-2,3-dihydro-4-thiochromanone.

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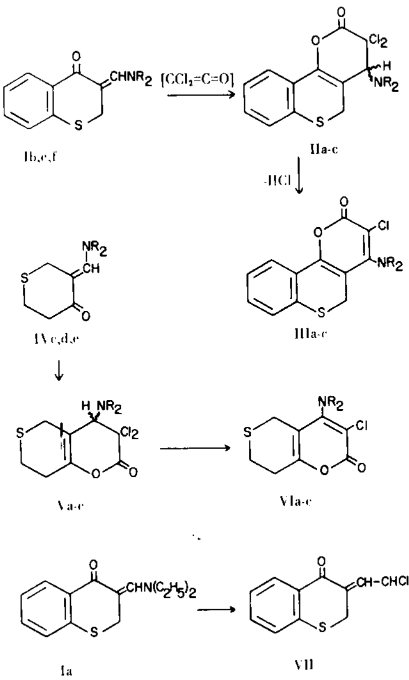
In a previous publication we described the reaction of *N,N*-disubstituted 3-aminomethylene-2,3-dihydro-4-thiochromanones I and 3-aminomethylene-tetrahydro-4-thiopyranones IV with sulfene to give new polycondensed sulfur heterocycles (1).

As part of our continuing study of the cycloadditions of *N,N*-disubstituted α-aminomethyleneketones to dichloroketene (2-6), we wish to report the synthesis of 2*H*,5*H*-[1]benzothiopyrano[4,3-*b*]pyran and 2*H*,5*H*-thiopyrano[4,3-*b*]pyran derivatives starting from I and IV. For this purpose, we reacted enamines Ib,e,f,IVc (1), IVd,e (the last two are new compounds, see Experimental) with dichloroacetyl chloride and triethylamine (dichloroketene prepared *in situ*). As in similar cases, *ie.*, aromatic or strong hindering aliphatic *N*-substitution of the α-aminomethyleneketone (2-6), the dipolar 1,4-cycloaddition occurred readily to give *N,N*-disubstituted 4-amino-3,3-dichloro-3,4-dihydro-2*H*,5*H*-[1]benzothiopyrano-[4,3-*b*]pyran-2-ones IIa-c and 4-amino-3,3-dichloro-3,4,7,8-tetrahydro-2*H*,5*H*-thiopyrano[4,3-*b*]pyran-2-ones Va-c. The structures of II and V were supported by uv, ir, and nmr spectral data (Tables I and III).

Refluxing IIa-c and Va-c with 1,5-diazabicyclo[4.3.0]-non-5-ene (DBN) in benzene (4) gave the dehydrochlorinated products, namely *N,N*-disubstituted 4-amino-3-chloro-2*H*,5*H*-[1]benzothiopyrano[4,3-*b*]pyran-2-ones IIIa-c and 4-amino-3-chloro-7,8-dihydro-2*H*,5*H*-thiopyrano[4,3-*b*]-pyran-2-ones VIa-c (Tables II and IV).

The reaction of I and IV bearing aliphatic *N,N*-disubstitution with dichloroketene was tried only in the case of Ia and IVa [$NR_2 = N(C_2H_5)_2$]. Whereas IVa led to inconclusive results, Ia apparently gave the same reaction as in another case previously described by us (5). By chromatography on neutral alumina, an unstable liquid was obtained in a low yield, which was identified as 3-(2,2-dichloroethylidene)-2,3-dihydro-4-thiochromanone VII by its ir and nmr spectral data.



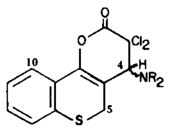
In conclusion, as a survey of the literature revealed, few derivatives of 2*H*,5*H*-[1]benzothiopyrano[4,3-*b*]-pyran (7,8) and especially of 2*H*,5*H*-thiopyrano[4,3-*b*]-pyran (9) are known. This new example of dipolar cycloaddition of heterocyclic α-aminomethyleneketones to dichloroketene seems to open another route to the synthesis of the above-mentioned sulfur heterocycles.

EXPERIMENTAL

Uv spectra were measured in 95% ethanol with a Hitachi-Perkin-Elmer Model EPS-3T spectrophotometer. Ir spectra

Table I

N,N-Disubstituted 4-Amino-3,3-dichloro-3,4-dihydro-2*H*,5*H*-[1]benzothiopyrano[4,3-*b*]pyran-2-ones IIa-c



Compound No.	NR_2	Yield %	M.p., °C	Molecular Formula	Analyses % Calcd./Found C	H	N
IIa	$N[CH(CH_3)_2]_2$	83	151 (a)	$C_{18}H_{21}Cl_2NO_2S$	55.96 56.05	5.48 5.60	3.62 3.60
IIb	$N(CH_3)C_6H_5$	81	149 (a)	$C_{19}H_{15}Cl_2NO_2S$	58.17 58.02	3.85 4.04	3.57 3.40
IIc	$N(C_6H_5)_2$	86	177 (a)	$C_{24}H_{17}Cl_2NO_2S$	63.44 63.45	3.77 3.93	3.08 2.93

Uv, Ir and Nmr Spectral Data

	Uv λ max nm (log ε)	Ir, cm^{-1} C=O	C=C	Nmr, δ
IIa	236 (4.25), 255 sh (4.13), 340 (3.38)	1787	1667 (b)	1.15 (d, J = 6.6, $4CH_3$), 3.11 (h, J = 6.6, 2NCH), 3.59 and 3.79 (2d, J = 15, CH_2-5), 3.86 (near s, H-4), 7.28 (m, $3H_{ar}$), 7.65 (m, H_{ar}-10) (d)
IIb	242 (4.48), 350 (3.22)	1788	1678 (c)	2.80 (s, NCH_3), 3.36 and 3.67 (2d, J = 15, CH_2-5), 5.00 (near s, H-4), 7.34 (m, $8H_{ar}$), 7.72 (m, H_{ar}-10) (d)
IIc	240 (4.45), 262 sh (4.27), 290 sh (4.06), 340 (3.42)	1794	1680 (b)	3.54 and 3.91 (2d, J = 14.4, CH_2-5), 5.20 (near s, H-4), 7.15 (mc, $14H_{ar}$) (b)

(a) From ethyl acetate. (b) In tetrachloromethane. (c) In potassium bromide. (d) In deuteriochloroform.

were taken on a Perkin-Elmer Model 257 spectrophotometer; nmr spectra were recorded on a Perkin-Elmer Model R12 instrument. Chemical shifts are reported as δ (ppm) relative to TMS as an internal standard; J in Hz. Melting points were determined with a Mettler FP1 apparatus.

Compounds IIa-c and Va-c were prepared according to (2) and were dehydro chlorinated with DBN according to (4).

3-Diisopropylaminomethylenetetrahydro-4-thiopyranone (IVd) and 3-Diphenylaminomethylenetetrahydro-4-thiopyranone (IVe).

These compounds were synthesized by a previously described procedure (10).

Compound IVd.

This compound was obtained in a yield of 65%, m.p. 100° from anhydrous diethyl ether; uv λ max nm (log ε): 334 (4.29); ir (tetrachloromethane) ν max: 1642, 1525 cm^{-1}; nmr (tetrachloromethane): δ 1.28 (d, J = 6.6, $4CH_3$), 2.65 (m, CH_2-5 + CH_2-6), 3.59 (near s, CH_2-2), 3.86 (h, J = 6.6, 2CHN), 7.50 (near s, =CHN).

Anal. Calcd. for $C_{12}H_{21}NOS$: C, 63.39; H, 9.31; N, 6.16. Found: C, 63.20; H, 9.38; N, 6.05.

Compound IVe.

This compound was obtained in a yield of 78%, m.p. 94° from anhydrous diethyl ether; uv λ max nm (log ε): 232 (3.99), 281.5 (3.99), 354 (4.30): ir (tetrachloromethane) ν max: 1660, 1545 cm^{-1}; nmr (tetrachloromethane): δ 2.78 (m, $3CH_2$), 7.19 (mc, $2NC_6H_5$), 7.57 (near s, =CHN).

Anal. Calcd. for $C_{18}H_{17}NOS$: C, 73.19; H, 5.80; N, 4.74. Found: C, 73.32; H, 6.08; N, 5.02.

This enamine is an E-isomer, as can be seen from the strong upfield shift of CH_2-2 protons (~0.8 ppm) caused by the phenyl groups [compare (1)].

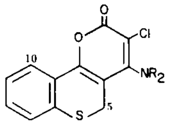
3-(2,2-Dichloroethylidene)-2,3-dihydro-4-thiochromanone (VII).

This compound was obtained starting from Ia (1), dichloroacetyl chloride and triethylamine in anhydrous benzene, by a previously described procedure (5). Chromatography on neutral alumina grade I followed by elution with petroleum ether (b.p. 40-70°) gave VII (36%) as an unstable liquid; further elution with benzene and diethyl ether gave no results. Because VII decomposed by attempted distillation *in vacuo* and even by standing at 0°, becoming deep-green coloured, it was purified by chromatography; ir (tetrachloromethane) ν max: 1627, 1674 cm^{-1} [*cf.* (5)]; nmr (tetrachloromethane): δ 3.88 (near s, CH_2-2), 6.56 and 6.89 (2d, J = 9.6, $=CH\text{-}CHCl_2$), 7.30 (m, $3H_{ar}$), 7.95-8.30 (m, H_{ar}-5) [*cf.* (5)].

Anal. Calcd. for $C_{11}H_8Cl_2OS$: C, 50.98; H, 3.11. Found: C, 51.06; H, 3.19.

Table II

N,N-Disubstituted 4-Amino-3-chloro-2*H*,5*H*-[1]benzothiopyrano[4,3-*b*]pyran-2-ones IIIa-c



Compound No.	NR_2	Yield %	M.p., °C	Molecular Formula	Analyses % Calcd./Found C	H	N
IIIa	$N[CH(CH_3)_2]_2$	81	122 (a)	$C_{18}H_{20}ClNO_2S$	61.79 62.11	5.76 5.61	4.00 4.27
IIIb	$N(CH_3)C_6H_5$	96	142 (a)	$C_{19}H_{14}ClNO_2S$	64.13 64.17	3.97 4.05	3.94 3.80
IIIc	$N(C_6H_5)_2$	74	190 (a)	$C_{24}H_{16}ClNO_2S$	68.98 68.94	3.86 3.90	3.35 3.30

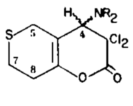
Uv, Ir and Nmr Spectral Data

	Uv λ max nm (log ε)	Ir, cm^{-1} (b) C=O	C=C		Nmr, δ
IIIa	241.5 (4.36), 270 (3.60), 340 (3.99), 380 (3.97)	1738	1618	1510	1.22 (2 superimposed d, J = 6.6, 4CH_3), 3.77 (near h, J = 6.6, 2NCH), 3.87 (near s, CH_2-5), 7.25 (m, 3H_{ar}), 7.85 (m, H_{ar}-10) (b)
IIIb	243 (4.51), 274 (3.87), 301 sh (3.70), 344 (4.05), 387 (4.11)	1738	1623	1515	3.42 (near s, CH_2-5 + NCH_3), 7.31 (mc, 8H_{ar}), 7.90 (m, H_{ar}-10) (c)
IIIc	244.5 (4.44), 272 (4.29), 307 sh (3.85), 345 (4.04), 390 (4.13)	1738 1732	1622	1512	3.32 (near s, CH_2-5), 7.20 (mc, 13H_{ar}), 7.92 (m, H_{ar}-10) (b)

(a) From ethyl acetate. (b) In tetrachloromethane. (c) In deuteriochloroform.

Table III

N,N-Disubstituted 4-Amino-3,3-dichloro-3,4,7,8-tetrahydro-2*H*,5*H*-thiopyrano[4,3-*b*]pyran-2-ones Va-c



Compound No.	NR_2	Yield %	M.p., °C	Molecular Formula	Analyses % Calcd./Found C	H	N
Va	$N[CH(CH_3)_2]_2$	40	144 (a)	$C_{14}H_{21}Cl_2NO_2S$	49.71 49.53	6.26 6.22	4.14 4.00
Vb	$N(CH_3)C_6H_5$	36	156 (b)	$C_{15}H_{15}Cl_2NO_2S$	52.33 52.17	4.39 4.21	4.07 4.35
Vc	$N(C_6H_5)_2$	42	184 (a)	$C_{20}H_{17}Cl_2NO_2S$	59.12 59.11	4.21 4.48	3.44 3.40

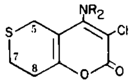
Uv, Ir and Nmr Spectral Data

	Uv λ max nm (log ε)	Ir, cm^{-1} C=O	 C=C	Nmr, δ
Va	230 (3.52)	1792	1700 (c)	1.09 and 1.15 (2d, J = 6.6, 4CH_3), 2.80 (mc, CH_2-7 + CH_2-8 + 2NCH), 3.28 (m, CH_2-5), 3.63 (m, CH-4) (c)
Vb	244.5 (4.15), 292 (3.32)	1795	1708 (c)	2.70 (near s, NCH_3), 2.84 (mc, 3CH_2), 4.69 (m, CH-4), 6.91 (mc, 5H_{ar}) (c)
Vc	250 (4.15), 293 sh (3.60)	1787	1712 (d)	2.27 and 2.72 (2m, CH_2-7 + CH_2-8), 3.22 and 3.55 (2d, J = 15, CH_2-5), 5.08 (m, CH-4), 7.08 and 7.25 (2m, 2NC_6H_5) (e)

(a) From ethyl acetate. (b) From anhydrous diethyl ether. (c) In tetrachloromethane. (d) In chloroform. (e) In deuteriochloroform.

Table IV

N,N-Disubstituted 4-Amino-3-chloro-7,8-dihydro-2*H*,5*H*-thiopyrano[4,3-*b*]pyran-2-ones VIa-c



Compound No.	NR_2	Yield %	M.p., °C	Molecular Formula	Analyses % Calcd./Found C	 H	 N
VIa	$N[CH(CH_3)_2]_2$	71	114 (a)	$C_{14}H_{20}ClNO_2S$	55.71 55.96	6.68 6.38	4.64 4.60
VIb	$N(CH_3)C_6H_5$	85	151 (a)	$C_{15}H_{14}ClNO_2S$	58.53 58.40	4.58 4.60	4.55 4.44
VIc	$N(C_6H_5)_2$	51	150 (a)	$C_{20}H_{16}ClNO_2S$	64.95 65.08	4.36 4.71	3.79 3.80

Uv, Ir and Nmr Spectral Data

	Uv λ max nm (log ε)	Ir, cm^{-1} C=O	 C=C	Nmr, δ
VIa	237.5 sh (3.30), 316 (3.79)	1735	1633 1510 (b)	1.21 (2 superimposed d, J = 6.6, 4CH_3), 2.85 (near s, CH_2-7 + CH_2-8), 3.46 (near s, CH_2-5), 3.70 (h, J = 6.6, 2NCH) (b)
VIb	241.5 (4.11), 318 (3.87) 360 (3.79)	1710	1632 1520 (c)	2.86 (m, CH_2-7 + CH_2-8), 3.08 (m, CH_2-5), 3.33 (near s, NCH_3), 6.82 (mc, NC_6H_5) (d)
VIc	253 (4.02), 279.5 (4.19), 320 (3.84), 374 (3.83)	1710	1633 1517 (c)	2.84 (m, CH_2-7 + CH_2-8), 2.98 (m, CH_2-5), 7.10 and 7.23 (2m, 2NC_6H_5) (d)

(a) From ethyl acetate. (b) In tetrachloromethane. (c) In chloroform. (d) In deuteriochloroform.

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