Reaction of Sulfenes with Heterocyclic *N,N*-Disubstituted α-Aminomethyleneketones. XIII. Synthesis of 1,2-Oxathiino[6,5-*f*]quinazoline Derivatives

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The 1,4-cycloaddition of sulfene to *N,N*-disubstituted (*E*)-6-aminomethylene-7,8-dihydro-(2-methyl)-(2-phenyl)quinazolin-5(6*H*)-ones **I** gave *N,N*-disubstituted 4-amino-3,4,5,6-tetrahydro-(8-methyl)(8-phenyl)-1,2-oxathiino[6,5-*f*]quinazoline 2,2-dioxides **II**, which are derivatives of the new heterocyclic system 1,2-oxathiino[6,5-*f*]quinazoline. With 2-phenylenaminones **Id-h**, the cycloaddition occurred, generally in satisfactory yields, both in the case of aliphatic *N,N*-disubstitution and aromatic *N*-monosubstitution, whereas with 2-methyl enaminones **Ia-c** the reaction took place in low yields only in the case of aliphatic *N,N*-disubstitution. Also the reaction of 2-phenyl enaminones **Id-g** with chlorosulfene occurred as with sulfene, giving a mixture of cycloadducts which were dehydrochlorinated *in situ* with DBN to afford *N,N*-disubstituted 4-amino-5,6-dihydro-8-phenyl-1,2-oxathiino[6,5-*f*]quinazoline 2,2-dioxides **III** generally in satisfactory yields. Compounds **III** could not be dehydrogenated either by DDQ in boiling benzene or by palladium on carbon in boiling *p*-cymene.

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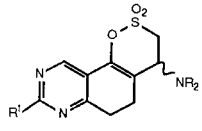
In pursuing our work on the polar 1,4-cycloaddition of sulfenes to heterocyclic *N,N*-disubstituted α-aminomethyleneketones [1], we now wish to report the reaction of *N,N*-disubstituted (*E*)-6-aminomethylene-7,8-dihydro-(2-methyl)(2-phenyl)quinazolin-5(6*H*)-ones **I** [2] with sulfene and (in part) with chlorosulfene to afford derivatives of a new heterocyclic system containing the 1,2-oxathiin ring fused with the quinazoline moiety, namely 1,2-oxathiino[6,5-*f*]quinazoline.

The reaction of enaminones **Id-h** (R′ = C_6H_5) with methanesulfonyl chloride and triethylamine (sulfene prepared *in situ*) occurred both in the case of aliphatic *N,N*-disubstitution and aromatic *N*-monosubstitution to give, in moderate to satisfactory yields, *N,N*-disubstituted 4-amino-3,4,5,6-tetrahydro-8-phenyl-1,2-oxathiino[6,5-*f*]quinazoline 2,2-dioxides **IId-g** (Table I), whose structure was confirmed by their ir and nmr spectral data (Table II). Only enaminone **Ih** (NR_2 = diphenylamino) did not react

Table I

N,N-Disubstituted 4-Amino-3,4,5,6-tetrahydro-(8-methyl)(8-phenyl)-1,2-oxathiino[6,5-*f*]quinazoline 2,2-Dioxides **IIa-b,d-g** [a]



Formula Number	R′	NR_2	Yield %	Mp °C	Molecular Formula	Analyses % Calcd./Found C	H	N
IIa	CH_3	$N(CH_3)_2$	23	206 dec [b]	$C_{13}H_{17}N_3O_3S$	52.86	5.80	14.23
						52.98	5.76	14.20
IIb	CH_3	1-Piperidinyl	35	147 [c]	$C_{16}H_{21}N_3O_3S$	57.29	6.31	12.53
						57.48	6.32	12.32
IId	C_6H_5	$N(CH_3)_2$	56	210 dec [b]	$C_{18}H_{19}N_3O_3S$	60.49	5.36	11.76
						60.31	5.48	11.56
IIe	C_6H_5	$N(C_2H_5)_2$	34	186 [b]	$C_{20}H_{23}N_3O_3S$	62.32	6.01	10.90
						62.45	6.01	11.07
IIf	C_6H_5	1-Piperidinyl	70	240 dec [b]	$C_{21}H_{23}N_3O_3S$	63.45	5.83	10.57
						63.76	5.92	10.58
IIg	C_6H_5	$N(CH_3)C_6H_5$	61	206 [b]	$C_{23}H_{21}N_3O_3S$	65.85	5.04	10.02
						66.06	4.92	9.98

[a] All compounds were prepared according to a previously described proceddure [1]. [b] From 95% ethanol. [c] From anhydrous diethyl ether.

Table II

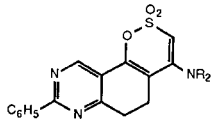
IR and NMR Spectral Data of Compounds **IIa-b,d-g**

Compound	IR, cm^{-1} C=C	IR, cm^{-1} O=S=O	NMR, δ
IIa	1665	1383 1180	2.36 (s, $(CH_3)_2N$), 2.6-3.1 (m, CH_2-5 + CH_2-6), 2.71 (s, CH_3-8), 3.3-3.7 (m, CH_2-3), 3.8-4.2 (m, CH-4), 8.58 (s, CH-10)
IIb	1665	1383 1185	1.57 (mc, 3 CH_2 pip), 2.0-3.2 (m, CH_2-5 + CH_2-6 + 2 CH_2N), 2.72 (s, CH_3-8), 3.35-3.75 (m, CH_2-3), 3.8-4.2 (m, CH-4), 8.58 (s, CH-10)
IId	1657	1378 1177	2.32 (s, $(CH_3)_2N$), 2.80 and 3.00 (2 mc, CH_2-5 + CH_2-6), 3.30-3.65 (m, CH_2-3), 3.80-4.25 (m, CH-4), 7.49 (mc, 2 H ar *m* + 1 H ar *p*), 8.47 (mc, 2 H ar *o*), 8.73 (s, CH-10)
IIe	1657	1378 1175	1.11 (t, J = 6.6, 2 CH_3), 2.57 (q, J = 6.6, 2 CH_2N), 2.81 and 3.00 (2 mc, CH_2-5 + CH_2-6), 3.50 (mc, CH_2-3), 4.0-4.4 (m, CH-4), 7.50 (mc, 2 H ar *m* + 1 H ar *p*), 8.46 (mc, 2 H ar *o*), 8.72 (s, CH-10)
IIf	1657	1380 1183	1.48 (mc, 3 CH_2 pip), 2.51 (mc, 2 CH_2N), 2.81 and 2.99 (2 mc, CH_2-5 + CH_2-6), 3.20-3.75 (m, CH_2-3), 3.80-4.25 (m, CH-4), 7.55 (mc, 2 H ar *m* + 1 H ar *p*), 8.42 (mc, 2 H ar *o*), 8.67 (s, CH-10) [a]
IIg	1658	1385 1182	2.60 (mc, CH_2-5), 2.87 (s, CH_3N), 3.10 (mc, CH_2-6), 3.4-3.7 (m, CH_2-3), 5.17 (mc, CH-4), 6.90 (mc, 2 H ar *m* + 1 H ar *p*), 7.28 (mc, 2 H ar *o*), 7.49 (mc, 2 H ar *m* + 1 H ar *p*), 8.48 (mc, 2 H ar *o*), 8.78 (s, CH-10)

[a] In DMSO-d_6.

Table III

N,N-Disubstituted 4-Amino-5,6-dihydro-8-phenyl-1,2-oxathiino[6,5-*f*]quinazoline 2,2-Dioxides **IIId-g**



Formula Number	NR_2	Yield %	Mp °C [a]	Molecular Formula	Analyses % Calcd./Found C	H	N
IIId	$N(CH_3)_2$	70	220	$C_{18}H_{17}N_3O_3S$	60.83 60.63	4.82 4.66	11.82 11.80
IIIe	$N(C_2H_5)_2$	72	187	$C_{20}H_{21}N_3O_3S$	62.64 62.65	5.52 5.53	10.96 10.88
IIIf	1-Piperidinyl	57	228	$C_{21}H_{21}N_3O_3S$	63.78 63.63	5.35 5.42	10.62 10.52
IIIg	$N(CH_3)C_6H_5$	40	179	$C_{23}H_{19}N_3O_3S$	66.17 66.12	4.59 4.60	10.06 10.07

IR and NMR Spectral Data

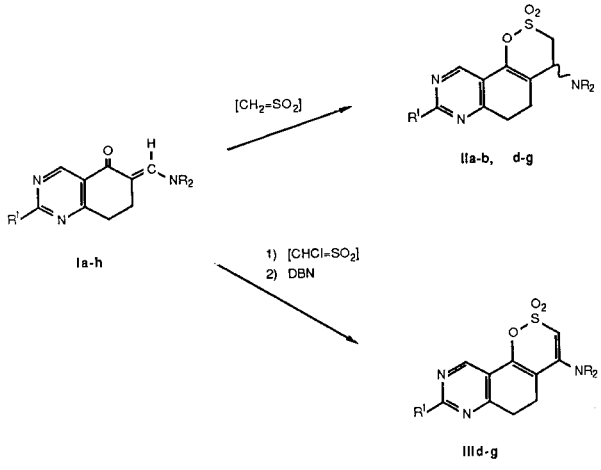
	IR, cm^{-1} C=C	IR, cm^{-1} O=S=O	NMR, δ
IIId	1627 1548	1365 1182	2.84 (s, $(CH_3)_2N$), 2.5-3.5 (m, CH_2-5 + CH_2-6), 5.68 (s, CH-3), 7.2-7.7 (m, 2 H ar *m* + 1 H ar *p*), 8.45 (mc, 2 H ar *o*), 8.90 (s, CH-10)
IIIe	1626 1530	1362 1177	1.17 (t, J = 6.6, 2 CH_3), 2.5-3.4 (m, CH_2-5 + CH_2-6 + 2 CH_2N), 5.76 (s, CH-3), 7.50 (mc, 2 H ar *m* + 1 H ar *p*), 8.48 (mc, 2 H ar *o*), 8.89 (s, CH-10)
IIIf	1627 1532	1365 1168	1.68 (mc, 2 CH_2N), 2.5-3.8 (m, CH_2-5 + CH_2-6 + 2 CH_2N), 5.77 (s, CH-3), 7.46 (mc, 2 H ar *m* + 1 H ar *p*), 8.47 (mc, 2 H ar *o*), 8.88 (s, CH-10)
IIIg	1626 1530	1370 1168	2.10 (mc, CH_2-5), 2.70 (mc, CH_2-6), 3.27 (s, CH_3N), 6.03 (s, CH-3), 7.0-7.6 (m, 2 H ar *m* + 1 H ar *p* + C_6H_5), 8.40 (mc, 2 H ar *o*), 8.87 (s, CH-10)

[a] From anhydrous diethyl ether-acetone 2:1.

and was recovered unchanged from the reaction mixture, according to a well established trend of this reaction (*cf.* [1]).

The reaction of enaminones **Ia-c** (R′ = CH_3) with sulfene occurred only in the case of aliphatic *N,N*-disubstitution to give in low yields the corresponding cycloadducts **IIa-b** (Tables I and II); moreover, the reaction did not occur with enaminone **Ic** (NR_2 = methylphenylamino). Thus, the reaction of quinazoline enaminones **Ia-h** with sulfene confirmed the lower reactivity of the compounds bearing the 2-methyl group as substituent in comparison with those bearing the 2-phenyl group, a fact already found by us in the cycloaddition of **I** with dichloroketene [1].

The reaction of **I** with chloromethanesulfonyl chloride and triethylamine (chlorosulfene prepared *in situ* [1]) was tried only with enaminones **Id-g** (R′ = C_6H_5) to give an unseparable mixture of cycloadducts which were dehydrochlorinated *in situ* with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in refluxing benzene [1] to afford in moderate to satisfactory yields *N,N*-disubstituted 4-amino-5,6-dihydro-8-phenyl-1,2-oxathiino[6,5-*f*]quinazoline 2,2-dioxides **IIId-g**, showing CH-3 as a singlet at δ 5.7-6.0 (Table III) (*cf.* [1]). Thus, the reactivity of the above enaminones with chlorosulfene was qualitatively the same as with sulfene.



	R^1	NR_2
a	CH_3	$N(CH_3)_2$
b	CH_3	1-Piperidinyl
c	CH_3	$N(CH_3)C_6H_5$
d	C_6H_5	$N(CH_3)_2$
e	C_6H_5	$N(C_2H_5)_2$
f	C_6H_5	1-Piperidinyl
g	C_6H_5	$N(CH_3)C_6H_5$
h	C_6H_5	$N(C_6H_5)_2$

A full dehydrogenation of compounds **IIId-g** was attempted both with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in boiling toluene and with palladium on carbon in refluxing *p*-cymene [3], but without appreciable results. With DDQ, the above compounds remained unchanged also after 48 hours of reflux; with palladium on carbon, the compounds decomposed on prolonged reflux and little amounts of a mixture consisting of the starting and dehydrogenated product were recovered. For example, in the case of **IIIe** the final product showed in the nmr spectrum two singlets at δ 5.76 and 6.00 (CH-3) and the other two at δ 8.88 and 9.88 (CH-10).

The reluctance of compounds **III** to completely aromatize could be due to the non-aromatic nature of 6 π-electron system present in the 1,2-oxathiin-2,2-dioxide ring [4], therefore the driving force to complete aromatization of the 1,2-oxathiino[6,5-*f*]quinazoline system could be decreased.

EXPERIMENTAL

The ir spectra were taken in chloroform on a Perkin-Elmer Model 398 spectrophotometer and the nmr spectra were recorded in deuteriochloroform on a Perkin-Elmer Model R-600 instrument (60 MHz, TMS as internal standard, J in Hz). Melting points were determined with a Fisher-Johns apparatus.

General Procedure for *N,N*-Disubstituted 4-Amino-5,6-dihydro-8-phenyl-1,2-oxathiino[6,5-*f*]quinazoline 2,2-Dioxides **IIId-g** (Table III).

The procedure was the same already described in the literature [1], but using 0.15 g (15 mmoles) of triethylamine and a temperature of 80° for **Id**. The reaction mixture was stirred at room temperature for 20 minutes, filtered and the solution was evaporated under reduced pressure. The oily residue was chromatographed on neutral alumina (grade I) using as eluant acetone-chloroform 3:1. The thick oils so obtained were dehydrochlorinated with DBN according to a previously described procedure [1] (reflux time, 2 hours; purification by chromatography on neutral alumina (grade I) as above).

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