Studies on Isocyanides and Related Compounds. Synthesis of 3-Substituted 2-Arylsulfonylamino-3,4-dihydro-4-oxoquinazolines *via* a Novel Three-Component Reaction

Ricardo Bossio, Stefano Marcaccini*, and Roberto Pepino

CNR, Centro di Studio sulla Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni,
Dipartimento di Chimica Organica "Ugo Schiff", Università di Firenze,
via Gino Capponi 9, I-50121 Firenze, Italy

Received March 22, 1995

The reaction between isocyanides **1**, methyl anthranilate (**2**) and chloramine T (**3a**) or chloramine B (**3b**) occurred easily, in the presence of benzyltriethylammonium chloride to give the guanidines **4** which, upon heating, underwent a ring-closure reaction to afford the title compounds **5**.

J. Heterocyclic Chem., **32**, 1115 (1995).

Recently [1], we have found that isocyanides react with anilines and chloramine T to give *N,N'*-disubstituted *N''*-tosylguanidines. Since our interest is focused on the synthesis of heterocyclic compounds [2-6], we attempted the synthesis of quinazoline derivatives by reacting isocyanides **1**, methyl anthranilate (**2**), and chloramine T (**3a**) or B (**3b**) in the presence of triethylbenzylammonium chloride. This reaction took place easily, under mild conditions, to give the expected *N*-substituted *N'*-(2-methoxycarbonylphenyl)-*N''*-arylsulfonylguanidines **4** in good yields. The structure of compounds **4** appeared to be suitable to give a ring-closure reaction to 3-substituted 2-arylsulfonylamino-3,4-dihydro-4-oxoquinazolines **5** [7]. In fact, upon heating at 240°, compounds **4** underwent loss of methanol to give the desired compounds **5** in good yields.

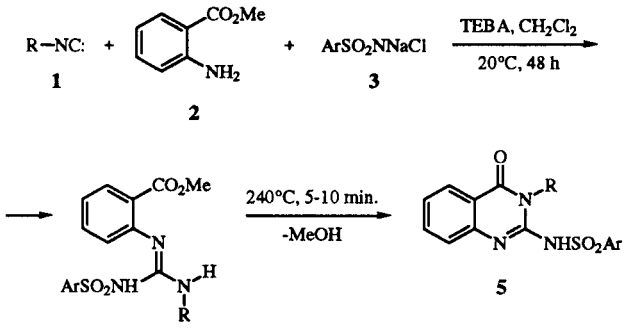
Evidence for the structure of the hitherto unknown 3-substituted 2-arylsulfonylamino-3,4-dihydro-4-oxoquinazolines **5** was provided by their ir and ^{1}H nmr spectra. In the ir spectra of compounds **5**, besides the strong absorption at 1693-1703 cm^{-1}, due to the cyclic amide CO group, two absorptions at 3224-3299 and 1130-1159 cm^{-1} were detected, due to the NH and SO_2 groups, respectively. In the ^{1}H nmr spectra of compounds **5**, the singlet signal of the methyl belonging to the ester group was never detected and this confirmed the cyclization of compounds **4**. Furthermore, a singlet signal at about 11.04 δ, which dis-

Table 1

Physical, Analytical and IR Spectral Data for Compounds **4a-f** and **5a-f**

Compound	Mp (°C)	Yield %	IR (cm^{-1})	Molecular Formula	Analysis % Calcd./Found C	H	N
4a	127-128	72	3327 (NH), 1692 (CO), 1134 (SO_2)	$C_{22}H_{27}N_3O_4S$	61.52 61.31	6.34 6.47	9.78 10.01
4b	104-105	68	3317 (NH), 1696 (CO), 1127 (SO_2)	$C_{22}H_{29}N_3O_4S$	61.23 61.32	6.78 6.97	9.74 9.60
4c	105-106	79	3338 (NH), 1694 (CO), 1136 (SO_2)	$C_{23}H_{29}N_3O_4S$	62.28 62.03	6.59 6.71	9.48 9.59
4d	105-106	65	3308 (NH), 1693 (CO), 1147 (SO_2)	$C_{21}H_{25}N_3O_4S$	60.71 60.66	6.07 6.27	10.11 10.02
4e	98-99	65	3333 (NH), 1697 (CO), 1134 (SO_2)	$C_{21}H_{27}N_3O_4S$	60.41 60.35	6.52 6.78	10.07 10.27
4f	114-115	75	3343 (NH), 1694 (CO), 1153 (SO_2)	$C_{22}H_{27}N_3O_4S$	61.52 61.66	6.34 6.30	9.78 9.60
5a	207-208	81	3224 (NH), 1693 (CO) 1133 (SO_2)	$C_{21}H_{23}N_3O_3S$	63.46 63.40	5.83 5.99	10.57 10.41
5b	113-115	70	3299 (NH), 1696 (CO) 1159 (SO_2)	$C_{21}H_{25}N_3O_3S$	63.14 63.03	6.31 6.49	10.52 10.70
5c	187-189	85	3281 (NH), 1703 (CO) 1130 (SO_2)	$C_{22}H_{25}N_3O_3S$	64.21 64.39	6.13 6.28	10.21 10.11
5d	176-177	79	3222 (NH), 1693 (CO) 1134 (SO_2)	$C_{20}H_{21}N_3O_3S$	62.65 62.41	5.52 5.77	10.96 10.90
5e	117-118	72	3288 (NH), 1697 (CO) 1143 (SO_2)	$C_{20}H_{23}N_3O_3S$	62.32 62.33	6.02 6.25	10.90 10.82
5f	144-145	88	3240 (NH), 1693 (CO) 1130 (SO_2)	$C_{21}H_{23}N_3O_3S$	63.46 63.40	5.83 5.98	10.57 10.42

Scheme



1	R
a	c-C_6H_{11}
b	n-C_6H_{13}
c	c-C_7H_{13}

3	Ar
a	4-$CH_3C_6H_4$
b	C_6H_5

4,5	R	Ar
a	c-C_6H_{11}	4-$CH_3C_6H_4$
b	n-C_6H_{13}	4-$CH_3C_6H_4$
c	c-C_7H_{13}	4-$CH_3C_6H_4$
d	c-C_6H_{11}	C_6H_5
e	n-C_6H_{13}	C_6H_5
f	c-C_7H_{13}	C_6H_5

appeared quickly upon treatment with deuterium oxide, was in agreement with the presence of a $NHSO_2$ group.

EXPERIMENTAL

Melting points were obtained in open capillary tubes with a Büchi 512 apparatus and are uncorrected. The ir spectra were measured on a Perkin-Elmer 881 spectrophotometer for potassium bromide discs. Proton nuclear magnetic resonance (^1H nmr) spectra were recorded on a Varian Gemini 200 spectrometer for deuteriochloroform saturated solutions.

Isocyanide **1a** is commercially available. Isocyanides **1b** [8] and **1c** [9] were prepared according to literature procedures. Compounds **3** were purchased from Fluka and employed without further purification.

General Procedure for the Preparation of *N*-Substituted *N'*-(2-Methoxycarbonylphenyl)-*N''*-arylsulfonylguanidines **4a-f**.

Caution: In some runs, after an induction period, the reaction took place violently. A suspension of **1** (11 mmoles), **2** (1.66 g, 11 mmoles), **3** (11 mmoles), and TEBA (70 mg) in ethanol free dichloromethane (30 ml) was stirred for 48 hours at room temperature. The reaction mixture was treated with water (30 ml) and the phases separated. The organic layer was dried over sodium sulfate, and then evaporated to dryness to give **4**. Analytical samples were obtained from ethanol (Table 1).

Table 2

^1H NMR Spectral Data for Compounds **5a-f**

Compound	Chemical Shifts (δ, ppm)
5a	1.03-2.61 (m, 10 H, cyclohexyl), 2.41 (s, 3 H, CH_3), 4.89-5.12 (m, 1 H, 1-H cyclohexyl), 7.08-8.16 (m, 8 H, benzenoid), 11.04 (s, 1 H, NH)
5b	0.78-1.68 (m, 11 H, hexyl), 2.42 (s, 3 H, CH_3), 4.04-4.16 (m, 2 H, NCH_2), 7.17-8.20 (m, 8 H, benzenoid), 11.05 (s, 1 H, NH)
5c	1.36-2.44 (m, 12 H, cycloheptyl), 2.42 (s, 3 H, CH_3), 5.06-5.26 (m, 1 H, 1-H cycloheptyl), 7.13-8.18 (m, 8 H, benzenoid), 11.03 (s, 1 H, NH)
5d	1.07-2.58 (m, 10 H, cyclohexyl), 4.92-5.16 (m, 1 H, 1-H cyclohexyl), 7.10-8.18 (m, 9 H, benzenoid), 11.05 (s, 1 H, NH)
5e	0.68-1.72 (m, 11 H, hexyl), 4.00-4.10 (m, 2 H, NCH_2), 7.12-8.13 (m, 9 H, benzenoid), 11.06 (s, 1 H, NH)
5f	1.32-2.48 (m, 12 H, cycloheptyl), 5.07-5.33 (m, 1 H, 1-H cycloheptyl), 7.10-8.18 (m, 9 H, benzenoid), 11.02 (s, 1 H, NH)

General Procedure for the Preparation of 3-Substituted 2-Arylsulfonylamino-3,4-dihydro-4-oxoquinazolines **5a-f.**

A small flask containing **4** (6 mmoles) was poured into an oil bath preheated at 240°. When the effervescence ceased (5-10 minutes) the flask was removed and allowed to cool at room temperature. The glass-like residue was stirred with a little cold ethanol to give a suspension of **5** which was collected by filtration. Analytical samples were obtained from ethanol (Tables 1 and 2).

REFERENCES AND NOTES

[1] R. Bossio, S. Marcaccini, and R. Pepino, *Tetrahedron Letters*, in press.

[2] Review: S. Marcaccini and T. Torroba, *Org. Prep. Proced. Int.*, **25**, 141 (1993).

[3] R. Bossio, S. Marcaccini, S. Papaleo, and R. Pepino, *J. Heterocyclic Chem.*, **31**, 397 (1994).

[4] R. Bossio, S. Marcaccini, R. Pepino, and P. Paoli, *J. Heterocyclic Chem.*, **31**, 729 (1994).

[5] R. Bossio, S. Marcaccini, and R. Pepino, *Liebigs Ann. Chem.*, 527 (1994).

[6] R. Bossio, S. Marcaccini, and R. Pepino, *Synthesis*, 765 (1994).

[7] W. L. F. Armarego, The Chemistry of Heterocyclic Compounds, Vol **24**, Part **1**, D. J. Brown, ed, Interscience, New York, 1967, p 326.

[8] M. Lipp, F. Dallacker, and I. M. Köcker, *Monatsh. Chem.*, **90**, 48 (1959).

[9] R. Bossio, S. Marcaccini, R. Pepino, P. Paoli, and C. Polo, *Synthesis*, 999 (1991).