A Simple One-Pot Synthesis of 2-Substituted Quinazolin-4(3*H*)-ones from 2-Nitrobenzamides by Using Sodium Dithionite

Angel H. Romero, José Salazar, Simón E. López*

Laboratorio de Química Medicinal y Heterociclos, Departamento de Química, Edificio de Química y Procesos, Universidad Simón Bolívar, Valle de Sartenejas, Apartado 89000, Baruta, Caracas 1080-A, Venezuela
Fax +58(212)9063961; E-mail: slopez@usb.ve

Received: 29.01.2013; Accepted after revision: 19.04.2013

Abstract: A simple one-pot procedure for the preparation of 2-(het)arylquinazolin-4(3H)-ones starting from readily available 2-nitrobenzamides and (het)aryl aldehydes is described. Sodium dithionite is used as the reducing agent for the nitro group, and its decomposition in situ in aqueous N,N-dimethylformamide leads to the final oxidation step that gives the desired heterocyclic compounds.

Key words: heterocycles, oxidations, dehydrogenations, reductions, amides, aldehydes

The quinazolin-4(3*H*)-one system[1] has become an attractive core structure for the synthesis of new compounds that exhibit interesting pharmacological properties.[2–9] A number of natural products, such as the alkaloids tryptanthrin (**1**)[10] and deoxyvasicinone (**2**)[11] and the antimalarials febrifugine (**3**) and isofebrifugine (**4**),[12,13] contain a quinazolin-4(3*H*)-one moiety (Figure 1).

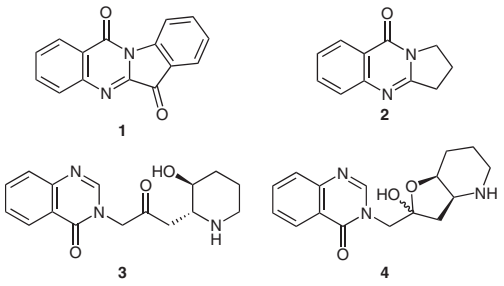


Figure 1

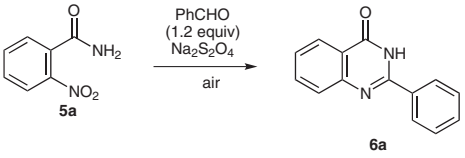
Several reports describe methods for the preparation of quinazolin-4(3*H*)-ones. These methods can be classified on the basis of the starting aromatic materials that form the A ring of the quinazolinone core. These include anthranilic acids,[14–18] 2-halobenzoic acids,[19,20] acyl anthranils or their derivatives,[21,22] isatoic anhydride [3,1-benzoxazine-2,4(1*H*)-dione],[23] 2-aminobenzamides,[24–26] acylanilides,[27] 2-iodoanilines,[28] or 2-halobenzamides[29,30] (Scheme 1). Some of these methods suffer from problems of low yields, long reaction times, harsh reaction conditions, difficulties in workup, the use of expensive or environmentally toxic catalysts, multistep procedures, or poor availability of starting materials, the preparation of which can be laborious and time-consuming.

2,3-Dihydroquinazolin-4(1*H*)-ones have also been synthesized by a number of methods,[31] but there are only a few reports on their synthesis by one-pot procedures.[31c,g,h,n,o] We therefore believed that it would be worthwhile developing a concise, practical, and convenient route to quinazolin-4(3*H*)-ones.

Sodium dithionite, a well-known reducing agent,[32] has been successfully used in the direct preparation of 2-arylbenzimidazoles by reduction of 2-nitroanilines in the presence of benzaldehydes.[33] This reaction is accelerated by the addition of water.[34]

We therefore sought a direct one-pot procedure for the synthesis of 2-substituted quinazolin-4(3*H*)-one deriva-

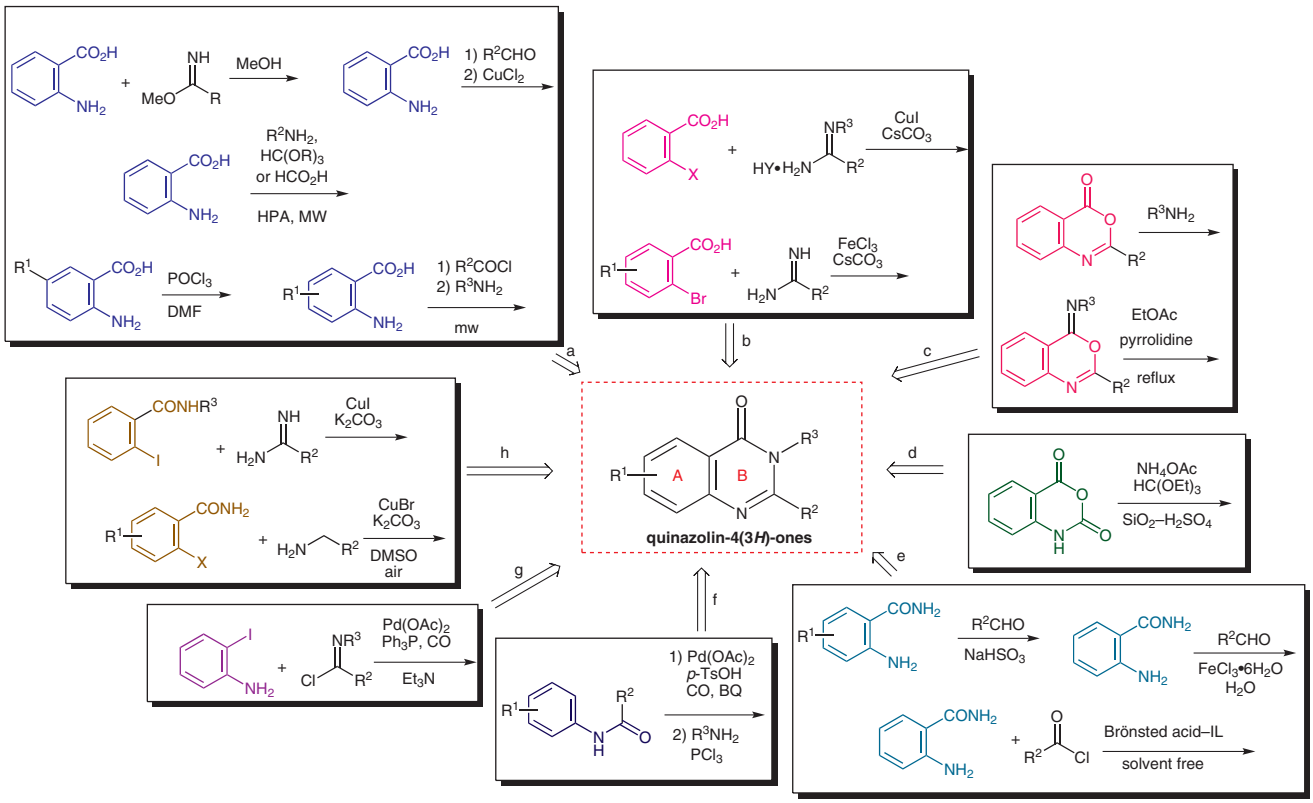
Table 1 Optimization of the Conditions for the Preparation of 2-Phenylquinazolin-4(3*H*)-one (**6a**) from 2-Nitrobenzamide by Using Sodium Dithionite



Entry	$Na_2S_2O_4$ (equiv)	Solvent	Temp (°C)	Time (h)	Yield (%) of **6a**
1	3.5	DMF	100	5	12
2	2.0	DMF–H_2O (10:1)	100	5	10
3	3.0	DMF–H_2O (10:1)	100	5	70
4	3.5	DMF–H_2O (10:1)	80	5	40
5	3.5	DMF–H_2O (10:1)	90	5	79[a]
6	4.0	DMF–H_2O (10:1)	100	5	77
7	3.5	DMF–H_2O (10:1)	100	4	62[b]
8	3.5	DMF–H_2O (10:1)	100	3	47[b]
9	3.5	DMF–H_2O (10:1)	120	5	31[c]
10	3.5	DMF–H_2O (10:1)	100	5	78

[a] A similar yield (78%) was obtained when the reaction was carried out under N_2.
[b] The 2,3-dihydroquinazolin-4(1*H*)-one intermediate **8a** was detected as a byproduct and removed by recrystallization (EtOH).
[c] Unreacted 2-nitrobenzamide was recovered.

SYNTHESIS 2013, 45, 2043–2050
Advanced online publication: 14.06.2013
DOI: 10.1055/s-0033-1338854; Art ID: SS-2013-M0090-OP

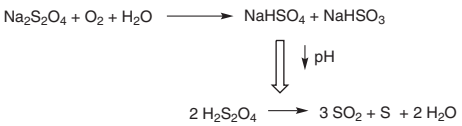


Scheme 1 General synthetic methods for the preparation of quinazolin-4(3*H*)-ones. a) Refs. 14–18; b) Refs. 19 and 20; c) Refs. 21 and 22; d) Ref. 23; e) Refs. 24–26; f) Ref. 27; g) Ref. 28; h) Refs. 29 and 30.

tives by the reaction of 2-nitrobenzamides with aldehydes in the presence of sodium dithionite. The reaction conditions were optimized by studying the model reaction of 2-nitrobenzamide with benzaldehyde (Table 1). As shown, water was required for optimal results at the temperatures tested. In the absence of water, the reaction gave a very low yield (12%) (entry 1). The chemical literature suggests that at least two equivalents of water are required during the reduction of 2-nitroaryl amines by sodium dithionite,[34] which clearly demonstrates that the reaction is accelerated by the presence of water. Higher yields were obtained with 3.5 equivalents of sodium dithionite at temperatures of 90–100 °C for five hours (entries 2, 3, 5, and 10). Lower yields of the quinazolin-4(3*H*)-one were obtained when the reaction time was reduced (entries 8 and 9). Higher temperatures probably led to decomposition of the sodium dithionite in solution in the presence of water, thereby diminishing its reducing power (entry 9).

Next we applied our optimized conditions in attempts to the synthesize a series of 2-substituted quinazolin-4(3*H*)-one derivatives **6a**–**w** (Table 2). Aromatic aldehydes with various electron-withdrawing or electron-donating groups gave good yields of the corresponding 2-arylquinazolin-4(3*H*)-ones (**6a**–**k**,**m**–**r**,**t**–**w**). The heteroaromatic 2-furyl substituent was also successfully introduced (entry 18; 87% yield), but the aliphatic aldehyde propanal (entry 19) failed to react, possibly because it might have been rapidly reduced to the corresponding alcohol before it could react with the 2-aminobenzamide intermediate.[35] Our method also proved to be useful for rapid and efficient synthesis of the 6-pyrrolidino-2-aryl-quinazolin-4(3*H*)-ones **6t**–**u**, which are important cytotoxic antitumor compounds.[24b,36]

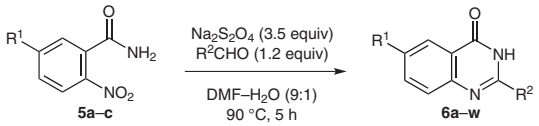
Under aerobic conditions, sodium dithionite decomposes in water. This decomposition, which is accelerated at lower pH values, generates sulfur dioxide (Scheme 2).[38]



Scheme 2 Decomposition of sodium dithionite in water under aerobic conditions with generation of sulfur dioxide in situ[38]

We therefore designed an experiment to examine the role of sulfur dioxide in the formation of the 2-substituted quinazolin-4(3*H*)-ones. An almost quantitative yield (99%) (Table 3, entry 1) of the oxidation product **6k** was obtained in two hours when sulfur dioxide was bubbled through a solution of the dihydro analogue **8k** in 9:1 *N*,*N*-dimethylformamide–water at 90 °C under aerobic conditions. Control experiments without bubbling sulfur dioxide were carried out under air or under nitrogen at atmospheric pressure. Virtually none of the compound **6k** was formed (entries 3 and 4). These experiments confirmed the role of sulfur dioxide as the dehydrogenating agent.

Table 2 Results for One-Pot Syntheses of 2-Substituted Quinazolin-4(3*H*)-ones from 2-Nitrobenzamides by Using Sodium Dithionite



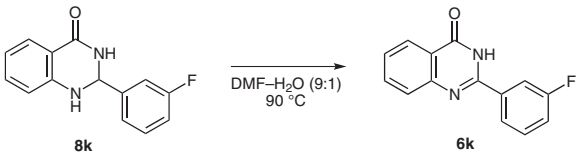
Entry	Product	R^1	R^2	Yield (%)	mp (°C) (Lit.)
1	**6a**	H	Ph	79	234–235 (236–237)19
2	**6b**	H	4-$MeOC_6H_4$	70	245–247 (247–248)30
3	**6c**	H	4-Tol	69	260–262 (261–263)30
4	**6d**	H	4-ClC_6H_4	75	295–297 (299–301)30
5	**6e**	H	4-FC_6H_4	84	264–266 (293–295)37a
6	**6f**	H	4-BrC_6H_4	92	>300 (296–297)37b
7	**6g**	H	3-BrC_6H_4	90	>300 (295–296)37b
8	**6h**	H	3-ClC_6H_4	82	292–294 (297–298)37c
9	**6i**	H	3-$MeOC_6H_4$	65	208–209 (209–210)37b
10	**6j**	H	3-Tol	72	209–211 (201–211)37b
11	**6k**	H	3-FC_6H_4	73	242–244 (222–224)37c
12	**6l**	H	2-ClC_6H_4	–[a]	–
13	**6m**	H	2-$MeOC_6H_4$	66	201–203 (202–203)31m
14	**6n**	H	2-HOC_6H_4	79	>300 (301–302)37d
15	**6o**	H	2,3-$(MeO)_2C_6H_3$	66	175–177 (177–179)37e
16	**6p**	H	3,4-$(MeO)_2C_6H_3$	70	240–242 (240–242)37f
17	**6q**	H	2-naphthyl	76	260–262 (212)37g
18	**6r**	H	2-furyl	87	218–220 (218–220)17
19	**6s**	H	Pr	–[b]	–
20	**6t**	pyrrolidin-1-yl	3-$MeOC_6H_4$	89	258–260 (261–263)24b
21	**6u**	pyrrolidin-1-yl	3,4-$(MeO)_2C_6H_3$	81	262–264 (263–264)24b
22	**6v**	Cl	Ph	72	299–300 (295–296)30
23	**6w**	Cl	4-ClC_6H_4	76	>300

[a] 2-(2-Chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (**8l**)37h was the sole product, even on extending the reaction time to 24 h.
[b] No quinazolinone product was detected; the reduced intermediate 2-aminobenzamide was recovered as the only product.

A possible mechanism for the one-pot reaction is shown in Scheme 3. The 2-nitro group of benzamide **5** is reduced by the action of sodium dithionite in aqueous *N*,*N*-dimethylformamide to produce the 2-aminobenzamide intermediate **7**. This reacts with the aldehyde (or more probably its bisulfite adduct formed in situ) to give an imine-like intermediate that undergoes cyclization to the corresponding 2,3-dihydro 4(1*H*)-quinazolinone **8**. The sulfur dioxide that is generated in situ might form the adduct **9** with the 2,3-dihydroquinazolin-4(1*H*)-one. Finally, this adduct eliminates hyposulfurous acid to give the desired quinazolin-4(3*H*)-one **6**. A similar dehydrogenation process has been observed in syntheses of several other heterocycles by using sodium hydrogen sulfite.[40,41]

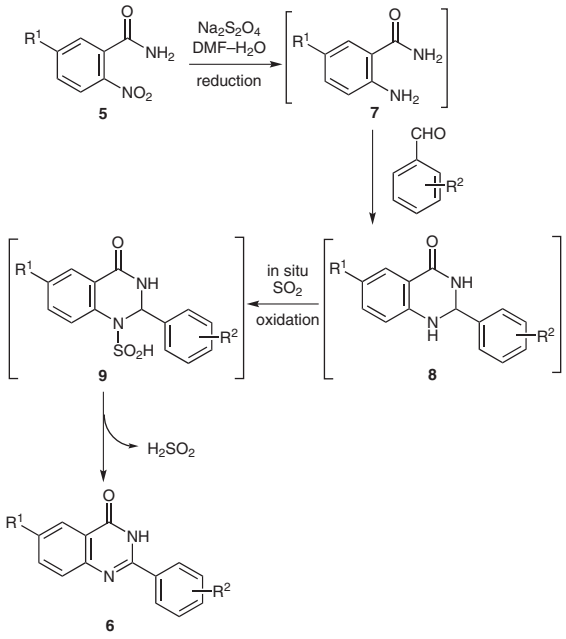
In conclusion, we have developed an easy, practical, and useful one-pot procedure for the preparation of 2-(het)arylquinazolin-4(3*H*)-one derivatives starting from readily available 2-nitrobenzamides and aldehydes in the presence of sodium dithionite. The method readily gives the corresponding quinazolin-4(3*H*)-ones in good yields.

Table 3 Study of the Dehydrogenation Reaction of a 2,3-Dihydroquinazolin-4(1*H*)-one Intermediate



Entry	Conditions	Time (h)	Yield (%) of **6k**
1	SO_2, DMF–H_2O (9:1), air [a]	2	99
2	SO_2, DMF–H_2O (9:1), N_2 [a]	3	99
3	DMF–H_2O (9:1), air	3	–
4	DMF–H_2O (9:1), N_2	3	–

[a] SO_2 gas was generated by the reaction of Cu turnings with concd H_2SO_4 in a separate vessel and continuously bubbled into the reaction flask.39



Scheme 3 Postulated pathway for the generation of 2-substituted quinazolin-4(3*H*)-ones **6** by the reaction of 2-nitrobenzamide **5** with (het)aryl aldehydes in the presence of sodium dithionite in aqueous *N*,*N*-dimethylformamide

Melting points were determined in duplicate using a Fischer-Johns micro hot-stage apparatus and are uncorrected. IR spectra were recorded as KBr discs by using an FT-IR Nicolet Magna spectrometer. ^{1}H NMR spectra were recorded at 400 MHz on a JEOL Eclipse spectrometer, and ^{13}C NMR spectra were recorded at 68 MHz on an Eclipse Plus spectrometer. DMSO-d_6 was used as the solvent for all NMR studies. Chemical shifts are reported in ppm relative to TMS as an internal standard. Elemental analyses of synthesized compounds were performed on a PerkinElmer 2400 CHN analyzer; results were within ±0.4% of the theoretical values. Silica gel plates (ALUGRAM SIL G/UV254; Macherey-Nagel GmbH, Germany) were used for TLC. Reagents were obtained from Aldrich (Milwaukee, MI, USA) or Merck (Darmstadt, Germany) and used without further purification. 2-nitro-5-pyrrolidin-1-ylbenzamide (**5b**) and 2-(3-fluorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (**8k**) were synthesized according to the procedures described in the literature.[24b,37c]

2-Substituted Quinazolin-4(3*H*)-ones (6a–k,m–r,t–x); General Procedure

A soln of the appropriate 2-nitrobenzamide **5** (1.0 mmol), substituted aldehyde (1.2 mmol), and $Na_2S_2O_4$ (3.5 mmol) in 9:1 DMF–H_2O (3 mL) was stirred at 90 °C for 5 h then cooled to r.t. The mixture was then poured into ice-water (10 mL) and the precipitated that formed was collected by filtration, washed with cold water, dried under vacuo, and crystallized (EtOH) when necessary.

2-Phenylquinazolin-4(3*H*)-one (6a)

Pale-yellow solid; yield: 175 mg (79%); mp 234–235 °C (Lit.[19] 236–237 °C).

IR (KBr): 3310 (NH), 1660 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.55 (br s, 1 H, NH), 8.18 (m, 3 H, Ar-H), 7.85 (ddd, *J* = 1.5, 7.3, 7.7 Hz, 1 H, Ar-H), 7.75 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.56 (m, 4 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 163.0, 153.1, 149.1, 135.3, 133.2, 132.0, 129.2, 128.3, 127.8, 127.2, 126.4, 121.3.

Anal. Calcd for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.72; H, 4.49; N, 12.68.

2-(4-Methoxyphenyl)quinazolin-4(3*H*)-one (6b)

Pale-yellow solid; yield: 177 mg (70%); mp 245–247 °C (Lit.[30] 247–248 °C).

IR (KBr): 3315 (NH), 1665 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.41 (br s, 1 H, NH), 8.19 (dd, *J* = 2.0, 7.0 Hz, 2 H, Ar-H), 8.13 (dd, *J* = 1.1, 8.1 Hz, 1 H, Ar-H), 7.82 (ddd, *J* = 1.5, 7.7, 7.7 Hz, 1 H, Ar-H), 7.70 (dd, *J* = 1.1, 8.1 Hz, 1 H, Ar-H), 7.48 (ddd, *J* = 1.5, 7.7, 7.7 Hz, 1 H, Ar-H), 7.09 (dd, *J* = 1.9, 7.0 Hz, 2 H, Ar-H), 3.85 (s, 3 H, OCH_3).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 163.0, 162.5, 152.7, 149.2, 135.2, 130.0, 127.6, 126.8, 126.4, 125.3, 121.1, 114.6.

Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.36; H, 4.72; N, 11.18.

2-(4-Tolyl)quinazolin-4(3*H*)-one (6c)

Pale-yellow solid; yield: 163 mg (69%); mp 260–262 °C (Lit.[30] 261–263 °C).

IR (KBr): 3308 (NH), 1667 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.47 (br s, 1 H, NH), 8.14 (d, *J* = 7.7 Hz, 1 H, Ar-H), 8.09 (d, J_{AB} = 8.1 Hz, 2 H, Ar-H), 7.83 (dd, *J* = 7.3, 7.3 Hz, 1 H, Ar-H), 7.72 (d, *J* = 7.7 Hz, 1 H, Ar-H), 7.51 (dd, *J* = 7.3, 7.3 Hz, 1 H, Ar-H), 7.35 (d, J_{AB} = 8.1 Hz, 2 H, Ar-H), 2.39 (s, 3 H, CH_3).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 152.9, 149.4, 142.1, 135.1, 130.5, 129.8, 128.2, 127.8, 127.0, 126.4, 121.4, 21.5.

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.28; H, 5.15; N, 11.90.

2-(4-Chlorophenyl)quinazolin-4(3*H*)-one (6d)

Pale-yellow solid; yield: 193 mg (75%); mp 295–297 °C (Lit.[30] 299–301 °C).

IR (KBr): 3316 (NH), 1657 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.59 (br s, 1 H, NH), 8.16 (m, 3 H, Ar-H), 7.85 (ddd, *J* = 1.4, 7.5, 7.9 Hz, 1 H, Ar-H), 7.34 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.62 (dd, *J* = 1.8, 8.4 Hz, 2 H, Ar-H), 7.54 (ddd, *J* = 1.4, 7.4, 8.0 Hz, 1 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 162.8, 152.0, 151.3, 149.0, 136.9, 135.2, 132.1, 130.2, 129.2, 127.9, 127.4, 126.4, 121.5.

Anal. Calcd for $C_{14}H_9ClN_2O$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.95; H, 4.60; N, 12.52.

2-(4-Fluorophenyl)quinazolin-4(3*H*)-one (6e)
Pale-yellow solid; yield: 202 mg (84%); mp 264–266 °C (Lit.[37a] 293–295 °C).

IR (KBr): 3318 (NH), 1654 (C=O) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 12.58 (br s, 1 H, NH), 8.25 (m, 2 H, Ar-H), 8.15 (dd, *J* = 1.5, 8.0 Hz, 1 H, Ar-H), 7.85 (ddd, *J* = 1.4, 7.5, 7.7 Hz, 1 H, Ar-H), 7.74 (d, *J* = 7.7 Hz, 1 H, Ar-H), 7.53 (ddd, *J* = 1.4, 7.5, 7.7 Hz, 1 H, Ar-H), 7.39 (m, 2 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 166.5, 162.9, 152.1, 149.0, 135.2, 130.9 (d, *J* = 8.8 Hz, 1 C), 129.7, 127.8, 127.2, 126.4, 121.3, 116.1 (d, *J* = 22 Hz, 1 C).

Anal. Calcd for $C_{14}H_9FN_2O$: C, 69.99; H, 3.78; N, 11.66. Found: C, 70.09; H, 3.84; N, 11.71.

2-(4-Bromophenyl)quinazolin-4(3*H*)-one (6f)
Pale-yellow solid; yield: 277 mg (92%); mp >300 °C (Lit.[37b] 296–297 °C).

IR (KBr): 3316 (NH), 1667 (C=O) cm^{-1}.

^1H NMR (270 MHz, DMSO-d_6): δ = 12.47 (br s, 1 H, NH), 8.14 (m, 3 H, Ar-H), 7.83 (ddd, *J* = 1.2, 7.2, 7.2 Hz, 1 H, Ar-H), 7.74 (m, 3 H, Ar-H), 7.53 (ddd, *J* = 1.2, 7.2, 7.2 Hz, 1 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 162.7, 152.0, 149.1, 135.2, 132.5, 132.1, 130.3, 128.0, 127.3, 126.4, 125.7, 121.6.

Anal. Calcd for $C_{14}H_9BrN_2O$: C, 55.84; H, 3.01; N, 9.30. Found: C, 55.96; H, 2.95; N, 9.35.

2-(3-Bromophenyl)quinazolin-4(3*H*)-one (6g)
Pale-yellow solid; yield: 195 mg (65%); mp >300 °C (Lit.[37b] 295–296 °C).

IR (KBr): 3315 (NH), 1665 (C=O) cm^{-1}.

^1H NMR (270 MHz, DMSO-d_6): δ =12.49 (br s, 1 H, NH), 8.38 (s, 1 H, Ar-H), 8.17 (dd, *J* = 8.1, 8.1 Hz, 1 H, Ar-H), 7.79 (m, 3 H, Ar-H), 7.51 (m, 3 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ =162.6, 151.5, 149.0, 135.5, 135.2, 134.6, 131.3, 130.9, 128.1, 127.4, 127.3, 126.4, 122.4, 121.7.

Anal. Calcd for $C_{14}H_9BrN_2O$: C, 55.84; H, 3.01; N, 9.30. Found: C, 55.94; H, 2.96; N, 9.38.

2-(3-Chlorophenyl)quinazolin-4(3*H*)-one (6h)
Pale-yellow solid; yield: 210 mg (82%); mp 292–294 °C (Lit.[37c] 297–298 °C).

IR (KBr): 3312 (NH), 1670 (C=O) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 12.58 (br s, 1 H, NH), 8.24 (m, 1 H, Ar-H), 8.16 (m, 2 H, Ar-H), 7.85 (m, 1 H, Ar-H), 7.76 (m, 1 H, Ar-H), 7.65 (d, *J* = 8.8 Hz, 1 H, Ar-H), 7.57 (m, 2 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 162.7, 151.6, 148.9, 135.3, 135.2, 134.1, 131.7, 131.1, 128.1, 128.0, 127.5, 126.9, 126.4, 121.7.

Anal. Calcd for $C_{14}H_9ClN_2O$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.57; H, 4.47; N, 12.68.

2-(3-Methoxyphenyl)quinazolin-4(3*H*)-one (6i)
Pale-yellow solid; yield: 184 mg (73%); mp 208–209 °C (Lit.[37b] 209–210 °C).

IR (KBr): 3310 (NH), 1663 (C=O) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 12.39 (br s, 1 H, NH), 8.16 (d, *J* = 8.3 Hz, 1 H, Ar-H), 7.82 (m, 2 H, Ar-H), 7.75 (m, 2 H, Ar-H), 7.53 (dd, *J* = 7.7, 7.7 Hz, 1 H, Ar-H), 7.46 (dd, *J* = 7.7, 7.7 Hz, 1 H. Ar-H), 7.15 (dd, *J* = 2.2, 7.7 Hz, 1 H, Ar-H), 3.87 (s, 3 H, OCH_3).

^{13}C NMR (68 MHz, DMSO-d_6): δ =159.9, 135.1, 134.6, 130.3, 128.1, 127.1, 126.2, 125.7, 121.4, 120.7, 118.2, 114.4, 113.3, 56.0.

Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.50; H, 4.70; N, 11.04.

2-(3-Tolyl)quinazolin-4(3*H*)-one (6j)
Pale-yellow solid; yield: 153 mg (65%); mp 209–211 °C (Lit.[37b] 201–211 °C).

IR (KBr): 3307 (NH), 1662 (C=O) cm^{-1}.

^1H NMR (270 MHz, DMSO-d_6): δ = 12.35 (br s, 1 H, NH), 8.15 (d, *J* = 7.7 Hz, 1 H, Ar-H), 8.03 (s, 1 H, Ar-H), 7.97 (d, *J* = 6.7 Hz, 1 H, Ar-H), 7.84 (dd, *J* = 7.5, 7.5 Hz, 1 H, Ar-H), 7.74 (d, *J* = 8.1 Hz, 1 H, Ar-H), 7.52 (dd, *J* = 7.5, 7.5 Hz, 1 H, Ar-H), 7.43 (m, 2 H, Ar-H), 2.41 (s, 3 H, CH_3).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 162.8, 153.0, 149.3, 138.5, 135.1, 133.3, 132.5, 129.0, 128.8, 127.9, 127.0, 126.4, 125.4, 121.5, 21.5.

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.12; H, 5.07; N, 11.79.

2-(3-Fluorophenyl)quinazolin-4(3*H*)-one (6k)
Pale-yellow solid; yield: 182 mg (76%); mp 222 °C (Lit.[37c] 267 °C).

IR (KBr): 3315 (NH), 1671 (C=O) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 12.55 (br s, 1 H, NH), 8.16 (d, *J* = 7.3 Hz, 1 H, Ar-H), 8.03 (d, *J* = 7.3 Hz, 1 H, Ar-H), 7.98 (d, *J* = 10.2 Hz, 1 H, Ar-H), 7.86 (dd, *J* = 7.3, 8.0 Hz, 1 H, Ar-H), 7.76 (d, *J* = 8.4 Hz, 1 H, Ar-H), 7.58 (m, 2 H, Ar-H), 7.44 (ddd, *J* = 2.6, 8.4, 8.8 Hz, 1 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ =162.8, 151.8, 148.8, 144.9, 139.1, 135.6, 135.4 (d, *J* = 7.3 Hz), 131.3 (d, *J* = 29.5 Hz), 128.1, 127.5, 126.4, 124.5, 121.6, 118.9, 118.6, 115.2, 114.9.

Anal. Calcd for $C_{14}H_9FN_2O$: C, 69.99; H, 3.78; N, 11.66. Found: C, 70.07; H, 3.84; N, 11.58.

2-(2-Methoxyphenyl)quinazolin-4(3*H*)-one (6m)
Pale-yellow solid; yield: 166 mg (66%); mp 201–203 °C (Lit.[31m] 202–203 °C).

IR (KBr): 3308 (NH), 1657 (C=O) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 12.04 (br s, 1 H, NH), 8.15 (d, *J* = 7.7 Hz, 1 H, Ar-H), 7.83 (ddd, *J* = 1.4, 7.7, 7.7 Hz, 1 H, Ar-H), 7.72 (m, 2 H, Ar-H), 7.54 (m, 2 H, Ar-H), 7.20 (d, *J* = 8.4, 1 H), 7.10 (dd, *J* = 7.7, 7.7 Hz, 1 H, Ar-H), 3.87 (s, 3 H, CH_3).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 183.0, 161.8, 157.8, 152.8, 149.5, 135.0, 132.9, 127.9, 127.1, 126.3, 123.1, 121.5, 121.1, 112.6, 56.5.

Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.33; H, 4.86; N, 11.03.

2-(2-Hydroxyphenyl)quinazolin-4(3*H*)-one (6n)
Pale-yellow solid; yield: 188 mg (79%); mp >300 °C (Lit.[37d] 301–302 °C).

IR (KBr): 3400 (OH), 1633 (C=O) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 8.37 (s, 1 H, OH), 8.10 (m, 2 H, Ar-H), 7.83 (dd, *J* = 7.0, 8.0 Hz, 1 H, Ar-H), 7.71 (d, *J* = 7.0 Hz, 1 H, Ar-H), 7.52 (dd, *J* = 7.0, 8.0 Hz, 1 H, Ar-H), 7.43 (dd, *J* = 7.0, 8.0 Hz, 1 H, Ar-H), 6.97 (m, 2 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 159.9, 134.6, 135.7, 134.3, 128.1, 127.7, 126.6, 126.3, 123.5, 120.8, 119.9, 118.4, 118.3, 114.5.

Anal. Calcd for $C_{14}H_{10}N_2O_3$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.45; H, 4.16; N, 11.65.

2-(2,3-Dimethoxyphenyl)quinazolin-4(3*H*)-one (6o)
Pale-yellow solid; yield: 186 mg (66%); mp 175–177 °C (Lit.[37e] 177–179 °C).

IR (KBr): 3305 (NH), 1656 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.06 (br s, 1 H, NH), 8.16 (d, J = 7.7 Hz, 1 H, Ar-H), 7.83 (dd, J = 7.0, 8.0 Hz, 1 H, Ar-H), 7.70 (d, J = 8.0 Hz, 1 H, Ar-H), 7.53 (dd, J = 7.3, 7.7 Hz, 1 H, Ar-H), 7.23 (m, 3 H, Ar-H), 3.88 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3).

^{13}C NMR (68 MHz, DMSO-d_6): δ =162.0, 153.0, 152.6, 149.3, 147.5, 135.2, 128.5, 127.9, 127.4, 126.3, 124.8, 121.9, 121.4, 115.9, 61.6, 56.6.

Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92. Found: C, 68.04; H, 4.97; N, 9.95.

2-(3,4-Dimethoxyphenyl)quinazolin-4(3*H*)-one (6p)
Pale-yellow solid; yield: 198 mg (70%); mp 240–242 °C (Lit.[37f] 240–242 °C).

IR (KBr): 3316 (NH), 1664 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.39 (br s, 1 H, NH), 8.14 (dd, J = 1.5, 8.1 Hz, 1 H, Ar-H), 7.81 (m, 2 H, Ar-H), 7.87 (dd, J = 2.2, 8.4 Hz, 1 H, Ar-H), 7.81 (ddd, J = 1.5, 7.5, 7.9 Hz, 1 H, Ar-H), 7.72 (d, J = 8.1 Hz, 1 H, Ar-H), 7.49 (ddd, J = 0.8, 7.3, 7.7 Hz, 1 H, Ar-H), 7.12 (d, J = 8.8 Hz, 1 H, Ar-H), 3.89 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3).

^{13}C NMR (68 MHz, DMSO-d_6): δ =162.9, 152.4, 149.3, 147.1, 141.0, 134.9, 126.6, 126.4, 125.4, 121.8, 121.0, 112.1, 111.5, 56.4.

Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92. Found: C, 68.01; H, 4.97; N, 9.95.

2-(2-Naphthyl)quinazolin-4(3*H*)-one (6q)
Pale-yellow solid; yield: 207 mg (76%); mp 260–262 °C (Lit.[37g] 212 °C).

IR (KBr): 3308 (NH), 1666 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.62 (br s, 1 H, NH), 8.23 (d, J = 7.7 Hz, 1 H, Ar-H), 8.16 (dd, J = 1.8, 8.0 Hz, 1 H, Ar-H), 8.13 (d, J = 8.0 Hz, 1 H, Ar-H), 8.05 (dd, J = 1.8, 8.0 Hz, 1 H, Ar-H), 7.87 (dd, J = 6.6, 7.7 Hz, 1 H, Ar-H), 7.80 (d, J = 7.0 Hz, 1 H, Ar-H), 7.74 (d, J = 8.0 Hz, 1 H, Ar-H), 7.60 (m, 4 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 162.4, 154.3, 149.3, 135.1, 133.8, 132.3, 130.9, 130.8, 128.9, 128.2, 128.0, 127.6, 127.3, 126.9, 126.4, 125.7, 125.6, 121.8.

Anal. Calcd for $C_{18}H_{12}N_2O$: C, 79.39; H, 4.44; N, 10.29. Found: C, 79.30; H, 4.37; N, 10.21.

2-(2-Furyl)quinazolin-4(3*H*)-one (6r)
Pale-yellow solid; yield: 184 mg (87%); mp 218–220 °C (Lit.[17] 218–220 °C).

IR (KBr): 3401 (NH), 1664 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.38 (br s, 1 H, NH), 8.12 (dd, J = 1.10, 8.1 Hz, 1 H, Ar-H), 7.99 (d, J = 0.7 Hz, 1 H, furan-H), 7.82 (ddd, J = 1.4, 7.3, 7.7 Hz, 1 H, Ar-H), 7.69 (d, J = 8.1 Hz, 1 H, Ar-H), 7.62 (d, J = 3.3 Hz, 1 H, furan-H), 7.50 (ddd, J = 1.4, 7.3, 7.7 Hz, 1 H, Ar-H), 6.75 (dd, J = 1.4, 3.3 Hz, 1 H, furan-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ =162.1, 149.1, 147.0, 146.6, 144.9, 135.1, 127.6, 127.2, 126.4, 121.9, 114.9, 113.1.

Anal. Calcd for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.80; N, 13.20. Found: C, 67.85; H, 3.73; N, 13.12.

2-(3-Methoxyphenyl)-6-pyrrolidin-1-ylquinazolin-4(3*H*)-one (6t)
Pale-yellow solid; yield: 286 mg (89%); mp 258–260 °C (Lit.[24b] 261–263 °C).

IR (KBr): 3417 (NH), 1666 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.00 (br s, 1 H, NH), 7.74 (d, J = 8.1 Hz, 1 H, Ar-H), 7.71 (d, J = 1.8 Hz, 1 H, Ar-H), 7.41 (dd, J = 7.9, 8.1 Hz, 1 H, Ar-H), 7.15 (dd, J = 2.6, 8.9 Hz, 1 H, Ar-H), 7.07 (m, 3 H, Ar-H), 3.86 (s, 3 H, OCH_3), 3.40 (m, 4 H, pyrrolid-H), 2.01 (m, 4 H, pyrrolid-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 162.8, 160.0, 147.7, 146.9, 139.5, 135.0, 130.2, 129.2, 122.6, 120.8, 120.1, 117.3, 112.6, 104.6, 55.9, 48.1, 25.6.

Anal. Calcd for $C_{19}H_{19}N_3O_2$: C, 71.01; H, 5.96; N, 13.08. Found: C, 70.91; H, 5.99; N, 13.14.

2-(3,4-Dimethoxyphenyl)-6-pyrrolidin-1-ylquinazolin-4(3*H*)-one (6u)
Pale-yellow solid; yield: 284 mg (81%); mp 262–264 °C (Lit.[24b] 263–264 °C).

IR (KBr): 3390 (NH), 1670 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.81 (br s, 1 H, NH), 7.78 (dd, J = 1.8, 8.4 Hz, 1 H, Ar-H), 7.76 (d, J = 1.8 Hz, 1 H, Ar-H), 7.58 (d, J = 9.1 Hz, 1 H, Ar-H), 7.14 (dd, J = 2.6, 8.9 Hz, 1 H, Ar-H), 7.08 (d, J = 8.4 Hz, 1 H, Ar-H), 7.05 (d, J = 2.9 Hz, 1 H, Ar-H), 3.88 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 3.35 (m, 4 H, pyrrolid-H), 2.02 (m, 4 H, pyrrolid-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 162.9, 151.4, 149.3, 147.6, 146.6, 141.9, 139.9, 128.8, 125.9, 122.1, 120.9, 120.8, 112.2, 111.1, 104.6, 56.3, 48.1, 25.6.

Anal. Calcd for $C_{20}H_{21}N_3O_3$: C, 68.36; H, 6.02; N, 11.96. Found: C, 68.47; H, 5.97; N, 11.90.

6-Chloro-2-phenylquinazolin-4(3*H*)-one (6v)
White solid; yield: 185 mg (72%); mp 299–300 °C (Lit.[30] 295–296 °C).

IR (KBr): 3385 (NH), 1668 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.73 (br s, 1 H), 8.15 (d, J = 7.0 Hz, 2 H, Ar-H), 8.08 (d, J = 2.6 Hz, 1 H Ar-H), 7.84 (dd, J =2.6, 8.8 Hz, 1 H, Ar-H), 7.76 (d, J = 8.8 Hz, 1 H, Ar-H), 7.61–7.54 (m, 3 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 161.8, 153.6, 148.0, 135.1, 133.2, 132.0, 131.5, 130.1, 129.1, 128.4, 125.4, 122.8.

Anal. Calcd for $C_{14}H_9ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.48; H, 3.55; N, 10.95.

6-Chloro-2-(4-chlorophenyl)quinazolin-4(3*H*)-one (6w)
White solid; yield: 221 mg (76%); mp >300 °C.

IR (KBr): 3390 (NH), 1665 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.18 (d, J = 8.8 Hz, 2 H, Ar-H), 8.09 (d, J =2.6 Hz, 1 H, Ar-H), 7.83 (dd, J =2.6, 8.8 Hz, 1 H, Ar-H), 7.76 (d, J =8.8 Hz, 1 H, Ar-H), 7.60 (d, J = 8.8 Hz, 2 H, Ar-H).

^{13}C NMR (68 MHz, DMSO-d_6): δ = 161.8, 152.6, 147.9, 137.2, 135.2, 132.0, 131.7, 130.2, 130.1, 129.2, 125.5, 122.9.

Anal. Calcd for $C_{14}H_8Cl_2N_2O$: C, 57.76; H, 2.77; N, 9.62. Found: C, 57.80; H, 2.74; N, 9.65.

Dehydrogenation of 2-(3-Fluorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (8k) by Sulfur Dioxide
A soln of dihydroquinazolinone **8k** (0.242 g; 1.0 mmol) in 9:1 DMF–H_2O (3 mL) was continuously stirred at 90 °C and bubbled with SO_2 gas for the indicated time under air or N_2 (see Table 3). The flow of the SO_2 gas was stopped and the mixture was allowed to cool to r.t then poured into ice-water (10 mL). The precipitate was collected by filtration and washed with H_2O to give 2-(3-fluorophenyl)quinazolin-4(3*H*)-one (**6k**) almost quantitatively; yield: 0.237 g (99%).

Acknowledgement

We thank Professor Jaime E. Charris (Faculty of Pharmacy, Universidad Central de Venezuela) and TSU Noelani Cigüela (NMR Laboratory, Universidad Simón Bolívar) for the NMR spectra; we also thank Dr. Ajoy Banerjee (Centro de Química, IVIC, Venezuela) and Professor William R. Dolbier Jr. (Department of Chemistry, Uni-

versity of Florida, USA) for their careful revision of the manuscript. S.L. and J.S. also thank Decanato de Investigación y Desarrollo (Universidad Simón Bolívar) and Programa de Estímulo a la Investigación e Innovación (PEII) for financial aid. A.H.R. thanks the Department of Chemistry of the Universidad Simón Bolívar for a teaching assistantship and Decanato de Estudios de Postgrado, Universidad Simón Bolívar, for a fellowship.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

References

(1) (a) Rewcastle, G. W. In *Comprehensive Heterocyclic Chemistry III*; Vol. 8; Katritzky, A. R.; Ramsden, C. A.; Scriven, E. F. V.; Taylor, R. J. K., Eds.; Elsevier: Oxford, **2008**, Chap. 2, 11. (b) Undheim, K.; Benneche, T. In *Comprehensive Heterocyclic Chemistry II*; Vol. 6; Katritzky, A. R.; Rees, C. W.; Scriven, E. V. F., Eds.; Pergamon: Oxford, **1996**, Chap. 2, 9.
(2) Ozaki, K.; Yamada, Y.; Oine, T.; Ishizuka, T.; Iwasawa, Y. *J. Med. Chem.* **1985**, *28*, 568.
(3) Cao, S. L.; Feng, Y. P.; Jiang, Y. Y.; Liu, S. Y.; Ding, G. Y.; Li, R. T. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1915.
(4) Wolfe, J. F.; Rathman, T. L.; Sleevi, M. C.; Campbell, J. A.; Greenwood, T. D. *J. Med. Chem.* **1990**, *33*, 161.
(5) (a) Hussain, M. A.; Chiu, A. T.; Price, W. A.; Timmermans, P. B.; Shefter, E. *Pharm. Res.* **1988**, *5*, 242. (b) Hess, H. J.; Cronin, T. H.; Scriabine, A. *J. Med. Chem.* **1968**, *11*, 130.
(6) Terashima, K.; Shimamura, H.; Kawase, A.; Tanaka, Y.; Tanimura, T.; Kamisaki, T.; Ishizuka, Y.; Sato, M. *Chem. Pharm. Bull.* **1995**, *43*, 2021.
(7) Kurogi, Y.; Inoue, Y.; Tsutsumi, K.; Nakamura, S.; Nagao, K.; Yohsitsugu, H.; Tsuda, Y. *J. Med. Chem.* **1996**, *39*, 1433.
(8) Jiang, S.; Zeng, Q.; Gettayacamin, M.; Tungtaeng, A.; Wannaying, S.; Lim, A.; Hansukjariya, P.; Okunji, C. O.; Zhu, S.; Fang, D. *Antimicrob. Agents Chemother.* **2005**, *49*, 1169.
(9) Kunes, J.; Bazant, J.; Pour, M.; Waisser, K.; Slosárek, M.; Janota, J. *Farmaco* **2000**, *55*, 725.
(10) (a) Witt, A.; Bergman, J. *Curr. Org. Chem.* **2003**, *7*, 659. (b) Mitscher, L. A.; Wong, W. C.; De Meulenere, T.; Sulko, J.; Drake, S. *Heterocycles* **1981**, *15*, 1017.
(11) (a) Amin, A. H.; Mehta, D. R. *Nature (London)* **1959**, *184*, 1317. (b) Chatterjee, A.; Ganguly, M. *Phytochemistry* **1968**, *7*, 307. (c) Joshi, B. S.; Newton, M. G.; Lee, D. W.; Barber, A. D.; Pelletier, S. W. *Tetrahedron: Asymmetry* **1996**, *7*, 25. (d) Ghosal, S.; Chauhan, P. S. R. B.; Mehta, R. *Phytochemistry* **1975**, *14*, 830.
(12) (a) Jang, C. S.; Fu, F. Y.; Wang, C. Y.; Huang, K. C.; Lu, G.; Thou, T. C. *Science* **1946**, *103*, 59. (b) Koepfli, J. B.; Mead, J. F.; Brockman, J. A. Jr. *J. Am. Chem. Soc.* **1947**, *69*, 1837.
(13) Kobayashi, S.; Ueno, M.; Suzuki, R.; Ishitani, H. *Tetrahedron Lett.* **1999**, *40*, 2175.
(14) Connolly, D. J.; Guiry, P. J. *Synlett* **2001**, 1707.
(15) Majo, V. J.; Perumal, P. T. *Tetrahedron Lett.* **1996**, *37*, 5015.
(16) Liu, J.-F.; Lee, J.; Dalton, A. M.; Bi, G.; Yu, L.; Baldino, C. M.; McElory, E.; Brown, M. *Tetrahedron Lett.* **2005**, *46*, 1241.
(17) Abdel-Jalil, R. J.; Voelter, W.; Saeed, M. *Tetrahedron Lett.* **2004**, *45*, 3475.
(18) Ighilahriz, K.; Boutemeur, B.; Chami, F.; Rabia, C.; Hamdi, M.; Hamdi, S. M. *Molecules* **2008**, *13*, 779.
(19) Liu, X.; Fu, H.; Jiang, Y.; Zhao, Y. *Angew. Chem. Int. Ed.* **2009**, *48*, 348.
(20) Yang, D.; Fu, H.; Hu, L.; Jiang, Y.; Zhao, Y. *J. Comb. Chem.* **2009**, *11*, 653.
(21) Errede, L. A.; McBrady, J. J.; Oien, H. T. *J. Org. Chem.* **1977**, *42*, 656.
(22) Snider, B. B.; Zeng, H. *Heterocycles* **2003**, *61*, 173.
(23) Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Baghbanzadeh, M. *Tetrahedron Lett.* **2005**, *46*, 7051.
(24) (a) Imai, Y.; Sato, S.; Takasawa, R.; Ueda, M. *Synthesis* **1981**, 35. (b) López, S. E.; Rosales, M. E.; Urdaneta, N.; Godoy, M. V.; Charris, J. E. *J. Chem. Res., Synop.* **2000**, 258.
(25) Wang, G.-W.; Miao, C.-B.; Kang, H. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1426.
(26) Heravi, M. M.; Tavakoli-Hoseini, N.; Bamoharram, F. F. *Synth. Commun.* **2011**, *41*, 707.
(27) Giri, R.; Lam, J. K.; Yu, J. Q. *J. Am. Chem. Soc.* **2010**, *132*, 686.
(28) Zheng, Z.; Alper, H. *Org. Lett.* **2008**, *10*, 829.
(29) Zhou, J.; Fu, L.; Lv, M.; Liu, J.; Pei, D.; Ding, K. *Synthesis* **2008**, 3974.
(30) Xu, W.; Jin, Y.; Liu, H.; Jiang, Y.; Fu, H. *Org. Lett.* **2011**, *13*, 1274.
(31) (a) Khurana, J. K.; Kukreja, G. *J. Heterocycl. Chem.* **2003**, *40*, 677. (b) Rao, V. B.; Ratnam, C. V. *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1979**, *18*, 409. (c) Yoo, C. L.; Fettinger, J. C.; Kurth, M. J. *J. Org. Chem.* **2005**, *70*, 6941. (d) Moore, J. A.; Sutherland, G. J.; Sowerby, R.; Kelly, E. G.; Palermo, S.; Webster, W. *J. Org. Chem.* **1969**, *34*, 887. (e) Yale, H. L. *J. Heterocycl. Chem.* **1977**, *14*, 1357. (f) Böhme, H.; Böing, H. *Arch. Pharm. (Weinheim, Ger.)* **1960**, *293*, 1011. (g) Cai, G.; Xu, X.; Li, Z.; Weber, W. P.; Lu, P. *J. Heterocycl. Chem.* **2002**, *39*, 1271. (h) Shi, D.; Rong, L.; Wang, J.; Zhuang, Q.; Wang, X.; Hu, H. *Tetrahedron Lett.* **2003**, *44*, 3199. (i) Chen, J. X.; Wu, H. Y.; Su, W. K. *Chin. Chem. Lett.* **2007**, *18*, 536. (j) Shaabani, A.; Maleki, A.; Mofakham, H. *Synth. Commun.* **2008**, *38*, 3751. (k) Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Baghbanzadeh, M. *Synlett* **2005**, 1155. (l) Dabiri, M.; Salehi, P.; Otokesh, S.; Baghbanzadeh, M.; Kozehgary, G.; Mohammadi, A. A. *Tetrahedron Lett.* **2005**, *46*, 6123. (m) Gao, L.; Ji, H.; Rong, L.; Tang, D.; Zha, Y.; Shi, Y.; Tu, S. *J. Heterocycl. Chem.* **2011**, *48*, 957. (n) Su, W.; Yang, B. *Aust. J. Chem.* **2002**, *55*, 695. (o) Bunce, R. A.; Nammalwar, B. *J. Heterocycl. Chem.* **2011**, *48*, 991.
(32) (a) Balasubramanian, M.; Keay, J. G. In *e-EROS Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: New York, **2010–2013**, DOI: 10.1002/047084289X. (b) Makarov, S. V.; Silaghi-Dumitrescu, R. *J. Sulfur Chem.* **2012**, DOI: 10.1080/17415993.2012.749878.
(33) (a) Yang, D.; Fokas, D.; Li, J.; Yu, L.; Baldino, C. M. *Synthesis* **2005**, 47. (b) Surpur, M. P.; Singh, P. R.; Patil, S. B.; Samant, S. D. *Synth. Commun.* **2007**, *37*, 1375.
(34) Oda, S.; Shimizu, H.; Aoyama, Y.; Ueki, T.; Shimizu, S.; Osato, H.; Takeuchi, Y. *Org. Process Res. Dev.* **2012**, *16*, 96.
(35) De Vries, J. G.; Kellogg, R. M. *J. Org. Chem.* **1980**, *45*, 4126.
(36) Hour, M. J.; Huang, L. J.; Kuo, S. C.; Xia, Y.; Bastow, K.; Nakanishi, Y.; Hamel, E.; Lee, K. H. *J. Med. Chem.* **2000**, *43*, 4479.
(37) (a) Heravi, M. M.; Montazeri, N.; Rahimizadeh, M.; Bakavoli, M.; Ghassemzadeh, M. *Pol. J. Chem.* **2004**, *78*,

2101. (b) Zhou, J.; Fang, J. *J. Org. Chem.* **2011**, *76*, 7730. (c) Chen, J.; Wu, D.; He, F.; Liu, M.; Wu, H.; Ding, J.; Su, W. *Tetrahedron Lett.* **2008**, *49*, 3814. (d) Petridou-Fischer, J.; Papadopoulos, E. P. *J. Heterocycl. Chem.* **1983**, *20*, 1159. (e) Wang, X.-S.; Yang, K.; Zhang, M.-M.; Yao, C.-S. *Synth. Commun.* **2010**, *40*, 2633. (f) Bhat, B. A.; Sahu, D. P. *Synth. Commun.* **2004**, *34*, 2169. (g) Mohamed, M. M.; El-Khamry, A. A.; El-Nagdy, S.; Shoshaa, S. W. *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1986**, *25*, 207. (h) Rostamizadeh, S.; Amani, A. M.; Aryan, R.; Ghaieni, H. R.; Shadjou, N. *Synth. Commun.* **2008**, *38*, 3567.

(38) International Programme on Chemical Safety, INCHEM database. http://www.inchem.org/documents/sids/sids/7775146.pdf (accessed Jan. 2013).

(39) Ghosh, P.; O'Driscoll, K. F. *J. Polym. Sci., Part B: Polym. Lett.* **1966**, *4*, 519.

(40) López, S. E.; Restrepo, J.; Pérez, B.; Ortiz, S.; Salazar, J. *Bull. Korean Chem. Soc.* **2009**, *30*, 1628.

(41) Restrepo, J.; Salazar, J.; López, S. E. *Phosphorus, Sulfur Silicon Relat. Elem.* **2011**, *186*, 2311.

