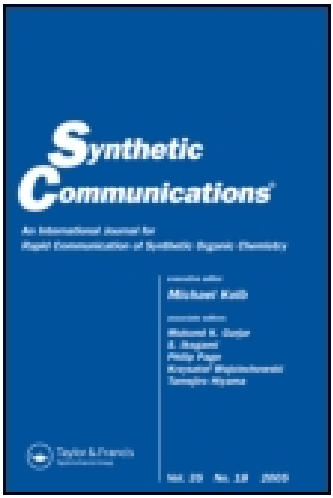


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Investigation of Chemoselective Reaction of 2-Amino-8-hydroxyquinoline with Arylsulfonylchloride Derivatives

Luiz Everson Da Silva [a] , Paulo Teixieira De Sousa Jr. [a] & Antonio Carlos Joussef [b]

[a] Department of Chemistry , Universidade Federal de Mato Grosso , Cuiabá, Brazil

[b] Department of Chemistry , Universidade Federal de Santa Catarina , Florianópolis, Brazil

Published online: 19 Mar 2009.

To cite this article: Luiz Everson Da Silva , Paulo Teixieira De Sousa Jr. & Antonio Carlos Joussef (2009) Investigation of Chemoselective Reaction of 2-Amino-8-hydroxyquinoline with Arylsulfonylchloride Derivatives, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 39:8, 1378-1388, DOI: 10.1080/00397910802527730

To link to this article: http://dx.doi.org/10.1080/00397910802527730

Synthetic Communications®, 39: 1378–1388, 2009

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910802527730

Taylor & Francis
Taylor & Francis Group

Investigation of Chemoselective Reaction of 2-Amino-8-hydroxyquinoline with Arylsulfonylchloride Derivatives

Luiz Everson Da Silva,[1] Paulo Teixieira De Sousa Jr.,[1] and Antonio Carlos Joussef[2]

[1]Department of Chemistry, Universidade Federal de Mato Grosso, Cuiabá, Brazil

[2]Department of Chemistry, Universidade Federal de Santa Catarina, Florianópolis, Brazil

Abstract: The reactions of 2-amino-8-hydroxyquinoline and 2-amino-4(1*H*)-quinolone with different sulfonyl chlorides have been investigated. The chemoselectivity was observed to afford exclusively the arylsulfonate ester derivatives. The mechanism of the reaction is also discussed.

Keywords: 2-Amino-4(1*H*)quinolone, 2-amino-8-hydroxyquinoline, arylsulfonate ester, chemoselectivity

INTRODUCTION

Historically, aromatic primary amines have been converted to the corresponding sulfonamides by reaction with appropriated sulfonylchloride in the presence of a base. The sulfonamides obtained have found many applications in organic synthesis to afford biologically active compounds.[1] On the other hand, aminoquinolines are pivotal constituents in a variety of pharmaceutically important compounds classes.[2] Moreover, 8-hydroxyquinoline derivatives show a wide spectrum of the properties as analytical reagents

Received July 5, 2008.

Address correspondence to Luiz Everson Da Silva, Department of Chemistry, Universidade Federal de Mato Grosso, Cuiabá, Cep 78060-900, MT, Brazil. E-mail: luiz_everson@yahoo.de

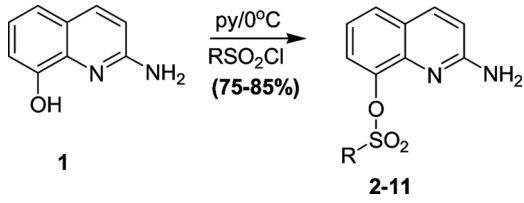
because of their ability to form stable complexes with many metallic ions.[3] Recently, nitrogen (N)/oxygen (O) alkyl derivatives have been investigated as protective agents against reactive oxygen species,[4] antiparasitic compounds,[5] and organic fluorophores in the optoelectronic industry[6] and in the treatment of neurodegenerative diseases.[7] We report now the synthesis of arylsulfonate ester derivatives starting from 2-amino-8-hydroxyquinoline (**1**) and 2-amino-4(1*H*)quinolone (**12**). In exploring potential applications of this method for polyfunctional substrates, we examined the chemoselectivity of esterification and its reaction mechanism.

RESULTS AND DISCUSSION

This prompted us to consider the conversion of 2-amino-8-hydroxyquinoline (**1**) to 2-sulfonamide-8-hydroxyquinolines. However, the reaction showed a high chemoselectivity to afford the sulfonate esters **2**–**11**, confirmed by high-performance liquid chromatography (HPLC, Scheme 1). In this context, we study the regioselectivity of sulfonation of the heterocyclic amine toward phenolic hydroxyl or tautomeric pyridine/pyridine hydroxyl. In this procedure, besides the compound **1**, only the arylsulfonylchloride is dissolved in pyridine.

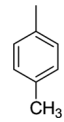
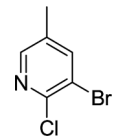
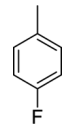
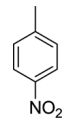
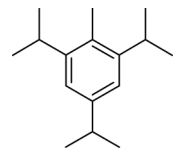
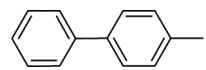
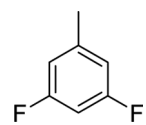
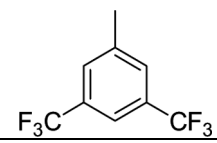
The reactions were carried out at low temperature (0 °C) and offered in most cases, generally within 1 h, the *O*-substituted aminoquinolines in good yields (75–85%). The products were isolated by addition of water, filtration, and subsequent crystallization with a methanol/dichloromethane mixture. The results of this study are summarized in Table 1.

The chemoselectivity can be attributed to the conjugation of the lone pair of electrons of the amino group nitrogen atom with the aromatic ring enhancing the nucleophilicity of the quinolinic nitrogen, which, in turn, plays the role of nucleophilic catalyst to transfer the arylsulfonyl moiety to the phenol oxygen atom via intramolecular nucleophilic attack. Pyridine in the sulfonylation reaction presented here acts as a base, and a mechanistic proposal is shown in Scheme 2. Moreover, the chemoselectivity is also observed when an excess of sulfonylchloride is used.



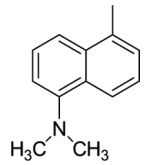
Scheme 1.

Table 1. Examples of selective *O*-sulfonylation products

Entry	(R)	Yield (%)
2		85
3		79
4		77
5		75
6		79
7		85
8		80
9		81
10		82

(*Continued*)

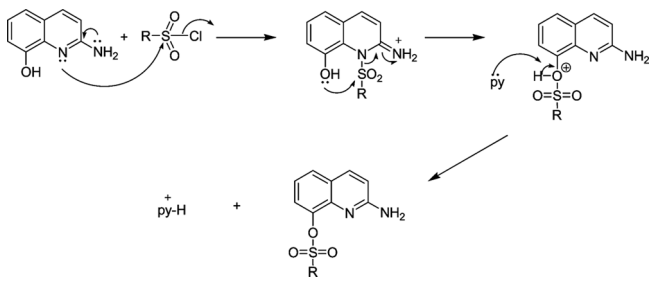
Table 1. Continued

Entry	(R)	Yield (%)
11		81

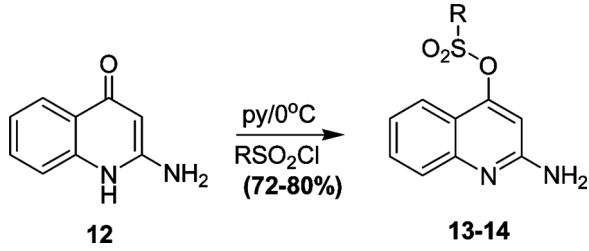
The compounds were characterized by ^{1}H NMR and mass spectrometry. The broad signal of NH_2 was assigned in the range of 5.39–5.83 ppm. The mass spectrometry gave two feature fragments: the base peak $m/z = 159$ related to the lost of RSO_2 [$M^+ - RSO_2$] and the peak $m/e = 131$ related to the elimination of HCN with the formation of the fragment $[C_6H_7N_2]^+$.[8] In addition, the arylsulfonates **2**, **4**, **6**, and **9** were characterized by x-ray analysis.[9]

The same trend was also observed in the reaction of 2-amino-4(1*H*)-quinolone **12** with sulfonyl chloride derivatives (Scheme 3 and Table 2). The exclusive formation of sulfonyl esters products **13** and **14** can be attributed by low nucleophilicity of aminic nitrogen that is conjugate to the π-deficient system. In addition, the driving force for the chemoselectivity of the reaction at the oxygen atom can be attributed to the attack at the oxygen, which is preferred because the ring nitrogen belongs to a π-deficient system. Moreover, the arylsulfonate **13** was also characterized by x-ray analysis.[10]

After establishing the general principle, it was then decided to investigate the reactivity of this class of compounds by subjecting **2** to a reaction with Meldrum's acid (**15**) in trimethyl ortoformate to give the Michael addition product **16**,[11] a precursor of diazaheterocycles[12] (Scheme 4). The conversion of **16** in the tricycle **17** is under studies.



Scheme 2.



12 13-14

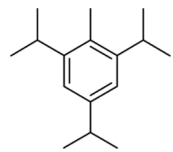
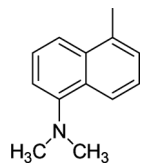
Scheme 3.

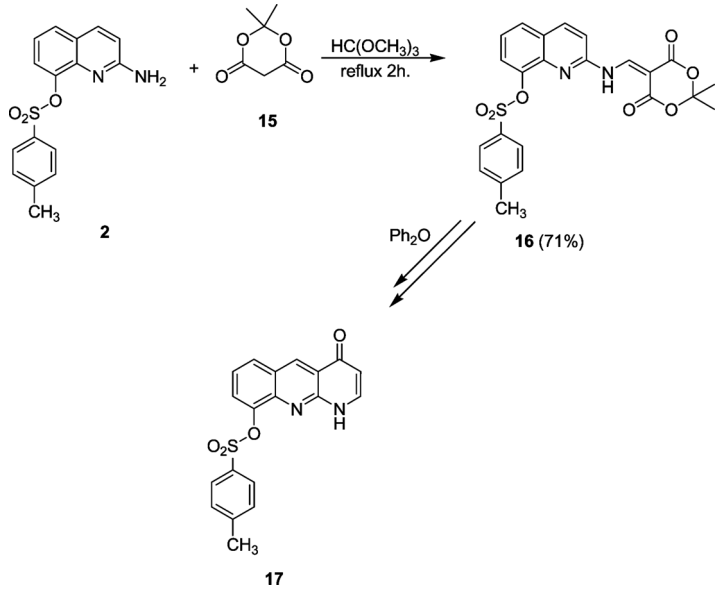
A short and efficient route toward the synthesis of 2-aminoquinolin-8-ylarylsulfonate ester derivatives has been developed. The reaction tolerates a wide range of functional groups. In addition, the reaction with Meldrum's acid in trimethyl orthoformate gave the Michael addition product **16**. The transformation of the 2-amino-8-hydroxyquinoline to the corresponding 2-aminoquinoline-8-yl-arylsulfonate ester derivatives is novel and might well prove useful as an important precursor for the synthesis of more complex structures with biological significance.

EXPERIMENTAL

Melting points were measured using a Kofler hot-stage apparatus (Microquímica APF-301) and are uncorrected. Each analytical sample

Table 2. Examples of selective *O*-sulfonylation products with 2-amino-4(1*H*)quinolone **12**

Entry	(R)	Yield (%)
13		72
14		80



Scheme 4.

was homogeneous as confirmed by thin-layer chromatography (TLC) performed on silica-gel (Kieselgel 60 F 254-Merck) plates, which were visualized with ultraviolet (UV) light. Flash chromatography was performed with Merck silica gel 60 (230–400 mesh). ^{1}H NMR spectra were determined on a Bruker DRX-300 (300-MHz) instrument, with tetramethylsilane (TMS) as the internal standard, and ^{13}C NMR spectra were recorded on a Bruker (75.5-MHz) spectrometer. Mass spectra were obtained with on a Shimadzu GC-MS-2000A instrument. Microanalyses were carried out with a Carlo Erba EA 1110 instrument.

Typical Experimental Procedure for Compounds 2–11 and 16–17

2-Amino-8-hydroxyquinoline (1 mmol) or 2-amino-4(1*H*)quinolone was added to a stirred solution of the arylsulfonyl choride (1.1 mmol) in pyridine (2 ml) at 0 °C. The mixture was stirred for 1 h, and 5 ml of water were added. A colored solid immediately appeared, which was filtered and washed with water until no pyridine was present in the filtrate. Purification by crystallization from a methanol/dichloromethane solution (1:1) gave the desired products.

Data

2-Aminoquinolin-8-yl-4-methylbenzenesulfonate (**2**)

Colorless crystalline solid (85%). Mp 205 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.37 (s, 3H), 5.83 (s, br, 2H), 6.76 (d, $J = 8.9$ Hz, 1H), 7.47–7.26 (m, 4H), 7.49 (dd, $J = 8$ Hz, 1H), 7.84 (t, $J = 8$ Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 29.94, 113.00, 115.09, 121.99, 123.33, 125.04, 126.79, 129.13, 129.43, 133.46, 138.19, 143.03, 145.16, 157.38. MS m/z: 314 ($M^{+\bullet}$; 100), 250 (25), 159 (100), 131 (60). $C_{16}H_{14}N_2O_3S$ requires C, 61.13; H, 4.49; N, 8.91; S, 10.20. Found: C, 61.09; H, 4.26; N, 8.80; S, 10.06.

2-Aminoquinolin-8-yl-5-bromo-6-chloropyridin-3-yl-sulfonate (**3**)

Brown solid (79%). Mp: 183–185 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.32 (s, br, 2H), 6.70 (d, $J = 8.5$ Hz, 1H), 7.23 (t, $J = 8.5$ Hz, 1H), 7.57 (dd, $J = 8.5$ Hz, 1H), 7.60 (d, $J = 8$ Hz, 1H), 7.80 (d, $J = 8$ Hz, 1H), 8.55 (s, 1H), 8.72 (s, 1H). MS m/z: 415 ($M^{+\bullet} + 2$), 187 (55), 160 (100). $C_{14}H_9BrClN_3O_3S$ requires C, 40.55; H, 2.19; N, 10.13; S, 7.73. Found: C, 40.52; H, 2.23; N, 10.06; S, 7.56.

2-Aminoquinolin-8-yl-4-fluorobenzenesulfonate (**4**)

Brown solid (77%). Mp: 194–196 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.32 (s, br, 2H), 6.70 (d, $J = 9$ Hz, 1H), 6.99 (t, $J = 9$ Hz, 1H), 7.11 (t, $J = 8$ Hz, 1H), 7.19 (dd, $J = 8$ Hz, 2H), 7.49 (dd, $J = 8$ Hz, 1H), 7.71 (d, $J = 8.5$ Hz, 1H), 7.89 (dd, $J = 8$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 113.10, 115.80, 116.10, 121.61, 123.23, 127.05, 125.17, 131.97, 132.10, 137.88, 140.62, 143.07, 157.65, 164.34, 167.74. MS m/z: 318 ($M^{+\bullet}$; 18), 159 (100), 131 (35). $C_{15}H_{11}FN_2O_3S$ requires C, 56.60; H, 3.48; N, 8.80; S, 10.07. Found: C, 56.71; H, 3.52; N, 8.75; S, 9.95.

2-Aminoquinolin-8-yl-4-nitrobenzenesulfonate (**5**)

White solid (75%). Mp 243–244 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.49 (s, br, 2H), 6.67 (d, $J = 9$ Hz, 1H), 7.13 (t, $J = 6$ Hz, 1H), 7.40 (d, $J = 6$ Hz, 1H), 7.42 (d, $J = 6$ Hz,1H), 7.60 (d, $J = 9$ Hz, 1H), 7.86 (d, $J = 9$ Hz, 1H), 8.23 (d, $J = 9$ Hz, 2H), 8.34 (d, $J = 9$ Hz, 2H); MS m/z: 345 ($M^{+\bullet}$; 18); 159 (100); 131 (28). $C_{15}H_{11}N_3O_5S$ requires C, 52.17; H, 3.21; N, 12.17; S, 9.29. Found: C, 52.14; H, 3.28; N, 12.11; S, 9.02.

2-Aminoquinolin-8-yl-2,4,6-triisopropylbenzenesulfonate (**6**)

Colorless crystalline solid (79%). Mp 173–176 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.08 (s, 18 H), 2.78 (m, 1H), 4.59 (m, 2H), 6.86 (s, 2H), 7.10 (d, $J = 9$ Hz, 1H), 7.21–7.37 (m, 3H), 8.33 (d, $J = 9$ Hz, 1H), 8.42 (t, $J = 9$ Hz, 1H), 8.85 (d, $J = 6$ Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 23.90, 24.80, 30.10, 34.51, 112.99, 121.42, 122.11, 123.87, 125.45, 126.58, 132.54, 137.71, 141.62, 144.15, 151.03, 153.77, 157.55. MS m/z: 428 ($M^{+\bullet}-2$), 363 (30), 159 (100). $C_{24}H_{30}N_2O_3S$ requires C, 67.58; H, 7.09; N, 6.57; S, 7.52. Found: C, 67.54; H, 7.08; N, 6.51; S, 7.48.

2-Aminoquinolin-8-yl-4-biphenylsulfonate (**7**)

Colorless crystalline solid (85%). Mp 210–211 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.59 (s, br, 2H), 6.75 (d, $J = 6$ Hz, 1H), 7.18 (t, $J = 6$ Hz, 1H), 7.42 (d, $J = 6$ Hz, 1H), 7.49–7.62 (m; 6H), 7.77 (dd, $J = 9$ Hz, 1H), 7.90 (dd, $J = 9$ Hz, 1H), 8.02 (d, $J = 8$ Hz, 2H); MS m/z: 376 ($M^{+\bullet}$), 312 (40), 159 (100), 131 (25). $C_{21}H_{16}N_2O_3S$ requires C, 67.00; H, 4.28; N, 7.44; S, 8.52. Found: C, 67.02; H, 4.25; N, 7.43; S 8.50.

2-Aminoquinolin-8-yl-4,5-dibromothiophene-2-sulfonate (**8**)

Pale crystalline solid (80%). Mp 269–270 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.54 (s, br, 2H), 6.74 (d, $J = 8.9$ Hz, 1H), 7.18 (t, $J = 8.0$ Hz, Hz, 2H), 7.32 (s, 1H), 7.50 (d, $J = 7.9$, 1H), 7.78 (d; $J = 8.9$ Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 113.04, 114.80, 121.92, 123.85, 125.17, 127.55, 137.25, 138.10, 136.32, 140.65, 142.90, 153.21, 157.52. MS m/z: 464 ($M^{+\bullet}$), 400 (15), 159 (100), 131 (35). $C_{13}H_8Br_2N_2O_3S_2$ requires C, 33.64; H, 1.74; N, 6.04; S,13.82. Found: C, 33.62; H, 1.71; N, 6.04; S, 13.84.

2-Aminoquinolin-8-yl-3,5-difluorobenzenesulfonate (**9**)

Brown solid (81%). Mp 167–168 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.72 (s, br, 2H), 6.68 (d, $J = 8.9$ Hz, 1H), 6.92 (t, $J = 7$ Hz, 2H), 7.20 (d, $J = 9$ Hz, 1H), 7.29 (s, 1H), 7.53 (s, 2H), 8.08 (d, $J = 9$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 109.65, 109.99, 112.70, 113.08, 121.83, 123.40, 125.32, 127.37, 138.03, 140.53, 142.89, 157.49, 160.81, 164.17, 164.02. MS m/z: 336 ($M^{+\bullet}$;18), 159 (100), 131 (80). MS m/z: 336 ($M^{+\bullet}$;18), 159 (100), 131 (80). $C_{15}H_{10}F_2N_2O_3S$ requires C, 53.57; H, 3.00; N, 8.33; S, 9.53. Found: C, 53.55; H, 3.08; N, 8.38; S, 9.55.

2-Aminoquinolin-8-yl-3,5-bis(trifluoromethyl)benzenesulfonate (**10**)

Yellow solid (82%). Mp 177–179 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.71 (s, 2H), 6.60 (d, $J = 8.7$ Hz, 1H), 7.26 (t, $J = 6.6$ Hz, 1H), 7.58 (d, $J = 8$ Hz, 1H), 7.67 (d, $J = 8$ Hz, 1H), 7.80 (d, $J = 8$ Hz, 1H), 8.01 (s, 1H), 8.36 (s, 2H). MS m/z: 436 ($M^{+\bullet}$; 20), 159 (100), 131 (22). $C_{17}H_{10}F_6N_2O_3S$ requires C, 46.80; H, 2.31; N, 6.42; S, 7.35. Found: C, 46.74; H, 2.30; N, 6.40; S, 7.36.

2-Aminoquinolin-8-yl-5-(dimethylamino)naphthalen-1-yl-sulfonate (**11**)

Yellow solid (81%). Mp 205–206 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.91 (s, 6H), 4.46 (s, 2H), 6.53 (d,$J = 8.7$ Hz, 1H), 7.12 (t, $J = 7.8$ Hz, 1H), 7.26–7.39 (m, 4H), 7.66 (d, $J = 8.7$ Hz, 1H), 7.73 (t, $J = 8.7$ Hz, 1H), 8.08 (d, $J = 6$ Hz, 1H), 8.56 (d, $J = 8.4$ Hz, 1H), 8.78 (d, $J = 8.7$ Hz, 1H). MS m/z: 393 ($M^{+\bullet}$; 39), 329 (45), 170 (75), 159 (100), 131 (90). $C_{21}H_{19}N_3O_3S$ requires C, 64.10; H, 4.87; N, 10.68; S, 8.15. Found: C, 64.08; H, 4.88; N, 10.66; S, 8.15.

2-Aminoquinolin-4-yl-2,4,6-triisopropylbenzenesulfonate (**13**)

Yellow solid: 97 mg (72%). Mp: 207–209 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.28 (s, 18H), 2.99 (m,1H), 4.16 (m, 2H), 4.76 (s, 2H), 6.49 (s, 1H), 7.20 (d, $J = 6$ Hz, 1H), 7.26 (s, 2H), 7.54 (d, $J = 7.5$ Hz, 1H), 7.64 (d, $J = 7.8$ Hz, 1H), 7.79 (d, $J = 7.2$ Hz, 1H). EM m/z (relative intensity): 426 (M^+, 100), 267 (70), 160 (45), 91 (42), 43 (39). $C_{24}H_{30}N_2O_3S$ requires C, 67.58; H, 7.09; N, 6.57; S, 7.52. Found: C, 67.54; H, 7.10; N, 6.59; S, 7.55.

2-Aminoquinolin-4-yl-5-(dimethylamino)naphthalene-1-sulfonate (**14**)

Crystalline solid: 97 mg (80%). Mp: 191–193 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.82 (s, 6H), 4.80 (s, 2H), 6.51 (s, 1H), 7.02 (t, $J = 7.2$ Hz, 1H), 7.19 (d, $J = 7.5$ Hz, 1H), 7.50 (t, $J = 8.4$ Hz, 1H), 7.51 (d, $J = 8.4$ Hz, 1H), 7.60 (t, $J = 4.2$ Hz, 1H), 8.18 (d, $J = 7.5$ Hz, 2H), 8.44 (d, $J = 8.7$ Hz, 2H), 8.55 (d, $J = 8.4$ Hz, 1H).^{13}C NMR ($CDCl_3$) δ 45.65, 101.93, 116.04, 117.94, 119.37, 121.89, 123.22, 123.25, 125.81, 129.54, 130.11, 130.23, 131.04, 131.33, 132.80, 142.76, 149.28, 152.23, 154.75, 157.17. EM m/z (relative intensity): 393 (M^+, 20), 170 (100), 28 (50). $C_{21}H_{19}N_3O_3S$ requires C, 64.10; H, 4.87; N, 10.68; S, 8.15. Found: C, 64.14; H, 4.88; N, 10.65; S, 8.16.

2,2-Dimethyl-5-[8-(4-methylbenzenesulfonate)quinolin-2-ylamino)]-methylene-1,3-dioxane-4,6-dione (**16**)

White solid (71%). Mp 223–225 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.73 (s, 6H), 2.29 (s, 3H), 7.15 (d, $J = 8.7$ Hz, 2H), 7.25 (d, $J = 8.1$ Hz, 2H), 7.56 (t, $J = 8$ Hz, 1H), 7.69 (d, $J = 6$ Hz, 1H), 7.77 (d, $J = 6$ Hz, 1H), 7.86 (d, $J = 8$ Hz, 2H), 8.13 (d, $J = 13$ Hz, 1H), 9.25 (d, $J = 13$ Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 27.43, 90.07, 105.74, 112.65, 113.25, 118.39, 127.18, 127.62, 136.58, 140.41, 146.81, 151.39, 151.62, 163.46, 165.69. MS m/z: 468 ($M^{+\bullet}$), 239 (50), 211 (45), 195 (100), 155 (40), 91 (35). $C_{23}H_{20}N_2O_7S$ requires C, 58.97; H, 4.30; N, 5.98; S, 6.84. Found: C, 58.96; H, 4.31; N, 5.97; S, 6.82.

ACKNOWLEDGMENTS

This work was supported by grants from the Brazilian agency Coordination for the Improvement of Higher Education Service (CAPES) and from DAAD (German Academic Exchange Service).

REFERENCES

1. Supuran, C. T.; Mincione, F.; Scozzafava, A.; Briganti, F.; Mincione, G.; Ilies, M. A. Carbonic anhydrase inhibitors, part 52: Metal complexes of heterocyclic sulfonamides: A new class of strong topical intraocular pressure-lowering agents in rabbits. *Eur. J. Med. Chem.* **1998**, *33*, 247–254.
2. (a) Inglis, S. R.; Stojkoski, C.; Branson, K. M.; Cawthray, J. F.; Fritz, D.; Wiadrowski, E.; Pyke, S. M.; Booker, G. W. Identification and specificity studies of small-molecule ligands for SH3 protein domains. *J. Med. Chem.* **2004**, *47*, 5405–5417; (b) Storz, T. First safe and practical synthesis of 2-amino-8-hydroxyquinoline. *Org. Process Res. Dev.* **2004**, *8*, 663–665.
3. Song, K. C.; Kim, J. S.; Park, S. M.; Chung, K.-C.; Ahn, S.; Chang, S.-K. Fluorogenic Hg^{2+}-selective chemodosimeter derived from 8-hydroxyquinoline. *Org. Lett.* **2006**, *8*, 3413–3416.
4. González-Álvarez, M.; Alzuet, G.; Borrás, J.; Agudo, L. C.; Garcia-Granda, S.; Montejo-Bernardo, J. M. Comparison of protective effects against reactive oxygen species of mononuclear and dinuclear Cu(II) complexes with N-substituted benzothiazolesulfonamides. *Inorg. Chem.* **2005**, *44*, 9424–9433.
5. Da Silva, L. E.; Joussef, A. C.; Pacheco, L. K.; Da Silva, D. G.; Steindel, M.; Rebelo, R. A. Synthesis and in vitro evaluation of leishmanicidal and trypanocidal activities of N-quinolin-8-yl-arylsulfonamides. *Bioorg. Med. Chem.* **2007**, *15*, 7553–7560.
6. Mishra, A.; Periasamy, N.; Patankar, M. P.; Narasimhan, K. L. Synthesis and characterisation of soluble aluminium complex dyes based on

5-substituted-8-hydroxyquinoline derivatives for OLED applications. *Dyes Pigm.* **2005**, *66*, 89–97.

7. (a) Papazian, V.; Jackson, T.; Pham, T.; Liu, X.; Greguric, I.; Loc'h, C.; Rowe, C.; Villemagne, V.; Masters, C. L.; Katsifis, A. The preparation of $^{123/125}$I-clioquinol for the study of a β protein in Alzheimer's disease. *J. Label Compd. Radiopharm.* **2005**, *48*, 473–484; (b) Zheng, H.; Weiner, L. M.; Bar-Am, O.; Epsztejn, S.; Cabantchik, Z. I.; Warshawsky, A.; Youdim, M. B. H.; Fridkin, M. Design, synthesis, and evaluation of novel bifunctional iron-chelators as potential agents for neuroprotection in Alzheimer's, Parkinson's, and other neurodegenerative diseases. *Bioorg. Med. Chem.* **2005**, *13*, 773–783.
8. Brown, E. V.; Palsz, A. C.; Mitchell, S. R. Mass spectra of some aminonaphthyridines and aminoquinolines. *J. Heterocycl. Chem.* **1970**, *7*, 661–665.
9. (a) Da Silva, L. E.; Joussef, A. C.; Foro, S.; Schmidt, B. 2-Aminoquinolin-8-yl-p-toluenesulfonate. *Acta Cryst.* **2007**, *E63*, o72–74; (b) Da Silva, L. E.; Joussef, A. C.; Foro, S.; Schmidt, B. 2-Aminoquinolin-8-yl-4-fluorobenzenesulfonate. *Acta Cryst.* **2007**, *E63*, o407–408; (c) Da Silva, L. E.; Foro, S.; Schmidt, B. 2-Aminoquinolin-8-yl-2,4,6-triisopropylbenzenesulfonate. *Acta Cryst.* **2007**, *E63*, o409–411; (d) Da Silva, L. E.; Foro, S.; Schmidt, B. 2-Aminoquinolin-8-yl-3,5-difluorobenzenesulfonate. *Acta Cryst.* **2007**, *E63*, o829–830.
10. Cassis, R.; Tapia, R.; Valderrama, J. A. Synthesis of 4(1H)-quinolones by thermolysis of arylaminomethylene Meldrum's acid derivatives. *Synth. Commun.* **1985**, *15*, 125–129.
11. (a) Hermecz, I.; Mészáros, Z.; Debreczy-Vasvári, L.; Horváth, A.; Horváth, G.; Pongor-Csákvári, M. Nitrogen bridgehead compounds, part 4:1→3 N→C-acyl migration, part 2. *J. Chem. Soc., Perkin Trans.* **1977**, 789–795; (b) Graf, G. I.; Hastreiter, D.; Da Silva, L. E.; Rebelo, R. A.; Montalban, A. G.; McKillop, A. The synthesis of aromatic diazatricycles from phenylenediamine-bis(methylene Meldrum's acid) derivatives. *Tetrahedron* **2002**, *58*, 9095.
12. Da Silva, L. E.; Joussef, A. C.; Foro, S.; Rebelo, R. A.; Schmidt, B. 2-Aminoquinolin-4-yl-2,4,6-triisopropylbenzenesulfonate. *Acta Cryst.* **2006**, *E62*, o5421–5422.