

Tetrahedron 54 (1998) 2607-2618

TETRAHEDRON

# Silane-Mediated Direct Condensation of Nitroarenes with Cinnamyl-type Sulfones. The way to 2-Aryl-4-X-quinolines and Their Hetero Analogs.

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Received 3 November 1997; revised 22 December 1997; accepted 8 January 1998

*Abstract*: DBU/silane mediated double condensation of nitroarenes with cinnamyl-type sulfones proceeds smoothly to yield 2-aryl-4-arylsulfonyl quinolines and their hetero analogs. Arylsulfonyl group can be easily replaced by different nucleophiles. © 1998 Published by Elsevier Science Ltd. All rights reserved.

Quinoline derivatives play a very important part in the chemistry of biologically active and natural products so many methods of synthesis have been developed. Particularly interesting seems the approach employing aromatic amine as the nucleophilic nitrogen donating component and electrophilic three-carbon unit, usually carbonyl compound, referring to Skraup, Doebner- von Miller, Combes, Conrad-Limpach and Knorr syntheses<sup>1</sup> (Scheme 1, path a).

This approach usually demands harsh reaction conditions such as elevated temperatures and the presence of strong acids as catalysts.



Scheme1

Recently we have shown that the same disconnection scheme can be realized employing synthetic equivalents with the opposite polarity, namely nitroarene as the electrophilic nitrogen donating aromatic system and the allylic compound bearing an electronwithdrawing substituent which, in mild basic conditions, can be transformed into the nucleophilic three-carbon unit<sup>2</sup> (Scheme 1, path b).

Thus, when the equimolar DMF solution of 1-nitronaphthalene 1a and cinnamyl phenyl sulfone 2a was treated with 5eq. of DBU in the presence of 5eq. of Me<sub>3</sub>SiCl, 2-phenyl-4-phenylsulfonylbenzo[h]quinoline 3aa was formed in 44% yield during 24h.

The proposed mechanism of the reaction consists in reversible deprotonation of sulfone 2, reversible addition of carbanion 4 to nitroarene 1 to form  $\sigma^{H}$  adduct 5 followed by its silane-mediated conversion to a nitroso intermediate 7 (probably *via* 6) and intramolecular condensation with aromatization to yield quinoline 3 (Scheme 2).



Scheme 2

Since the reaction does not proceed without the silvlating agent, some other additives were also examined in order to determine their influence on the formation of **3aa** (Table 1).

The most effective additives were silvlating agents like Me<sub>3</sub>SiCl, *t*-BuSiMe<sub>2</sub>Cl, bis-(trimethylsilyl)acetamide (BTMSA) or some Lewis acids like Ti(OEt)<sub>4</sub> and MgCl<sub>2</sub>. Less effective were LiCl, Bu<sub>3</sub>SnCl or trityl cation. It seems that the role of additive is in fact not limited to the binding of water produced in the reaction since the common dehydrating agents such as MgSO<sub>4</sub>, CaCl<sub>2</sub> or powdered molecular sieves had no influence at all. At this point it is important to mention that although the reaction mixtures were examined only by tlc, quinoline **3aa** (and most of other quinolines **3**) showed a characteristic blue spot when irradiated with a 254 nm mercury lamp with such a strong absorption that even traces (<5%, entry 18) can be identified. Among the solvents examined acetonitrile turned out to be the best. As a dipolar aprotic solvent it probably assured higher concentration and activity of the carbanion than THF or CH<sub>2</sub>Cl<sub>2</sub>. On the other hand it did not



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entry	additive	solvent	time <sup>a</sup>	3aa yield <sup>b</sup> [%]	1a/2a yield <sup>b</sup> [%]
1	none	DMF	1d	0	c
2	Me <sub>3</sub> SiCl <sup>d</sup>	DMF	1 <b>d</b>	44	e
3	t-BuSiMe <sub>2</sub>	MeCN	$1d^{f}$	69	26/16
4	t-BuSiMe <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub>	6d	44.5	44/47
5	t-BuSiMe <sub>2</sub>	PhH	6d	49	31/32
6	t-BuSiMe <sub>2</sub>	THF	6d	45	34/33
7	t-BuSiMe <sub>2</sub>	DMF	6d	22	71/0 <sup>8</sup>
8	BTMSA	MeCN <sup>h</sup>	1d	82	12/0
9	Ti(Oet) <sub>4</sub>	MeCN	2d	87	11/0
10	Ti(Oet)₄	THF	6d	24	44/38
11	Ti(Oet)₄	$CH_2Cl_2$	6d	22	53/47
12	TiCl₄	MeCN	1 <b>d</b>	tr	tars
13	BF3 Et2O	MeCN	4d	0	c
14	LiCl	MeCN	6d	28	46/13
15	MgCl <sub>2</sub>	MeCN	6d	70	26/12
16	MgCl <sub>2</sub>	DMF	1d	57	e
17	MgSO <sub>4</sub>	MeCN	6d	0	c
18	CdCl <sub>2</sub>	MeCN	6d	5	90/87
19	ZnCl <sub>2</sub>	MeCN	6d	0	c
20	CaCl <sub>2</sub>	MeCN	6d	0	c
21	4A sieves	MeCN	6d	0	e
22	Bu <sub>3</sub> SnCl	MeCN	6d	46.5	50/34
23	MeOH	MeCN	6d	0	c
24	Ph <sub>3</sub> CCl	MeCN	4d	ca.25	i

a. progress of the reaction roughly estimated by tlc; b. isolated *via* column chromatography; c. not estimated, absence of **3aa** ascertained by tlc; d. 5eq.; e. not estimated; f. no changes after 6d; g. product 9 isolated (see text) in 24% yield; h. 2 mL; i. complicated mixture of different products and unreacted substrates.

interact with Lewis acids or silylating agents to the same extent as DMF. In the extreme case DMF reacted



5 to form a side product 9 (entry 7). The main problem with the reaction was that in most cases it stopped after a low or moderate conversion despite of the presence of both substrates (balance of the reaction

was usually 70-90%) and reagents taken in an excess. Prolongation of the reaction time did not improve the yield.

In order to extend the scope of the reaction several nitroarenes were subjected to the reaction with the selected allylic type sulfones under the conditions exemplified in entry 8 of Table 1. The data were collected in Table 2.



ArNO <sub>2</sub>	1	ArNO <sub>2</sub>	1	Ar <sup>1</sup>	Ar <sup>2</sup>	R	2
1-nitronaphthalene	a	4-fluoronitrobenzene	j	Ph	Ph	Н	a
6-nitroquinoline	b	4-methylsulfonyl-nitrobenzene	k	Tol	p-ClC <sub>6</sub> H₄	Η	b
5-nitroquinoline	c	4-trifluoromethyl-nitrobenzene	1	Tol	Ph	Н	с
8-methoxy-5-nitroquinoline	d	3-trifluoromethyl-nitrobenzene	m	Tol	Н	Me	d
8-nitroquinoline	e	nitrobenzene	n				
4-chloronitrobenzene	f	4-methoxynitrobenzene	0				
3-chloronitrobenzene	g	2-methoxy-5-nitropyridine	р				
2-chloronitrobenzene h		4-ethoxy-3-nitropyridine	r				
4-bromonitrobenzene	i	2-nitrothiophene	S				

The best results were obtained with bicyclic nitroarenes such as nitronaphthalene and nitroquinolines, known as the strong electrophiles. In the monocyclic series more electrophilic nitroarenes like 1f, 1i, 1k, 1l or 1m gave better yields than less activated such as 1j or 1n. For chloronitrobenzenes, para substituted turned out to be the most reactive, whereas, meta substituted hardly reacted and in the case of the ortho isomer no product was indicated (entries 10-12).

In the case of 8-nitroquinoline le as nitroarene an anthranil (2,1-benzisoxazole) derivative 10 was isolated as a byproduct (entry 7). It was probably formed from intermediate 8ea (Scheme 3). Besides intramolecular addition of the side chain positioned carbanion to nitroso group, 8ea can undergo



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entry	substrates	time*	·····			product			Yield
			No	R <sup>1</sup>	R <sup>2</sup>	Ar <sup>1</sup>	Ar <sup>2</sup>	Z	[%]
1	1a+2a	5d	3aa	CH=CI	H-CH=CH	Ph	Ph	Н	82
2	1 <b>a+2b</b>	1 d	3ab	CH=CH	H-CH=CH	Tol	pClC <sub>6</sub> H <sub>4</sub>	Н	63
3	1a+2c	8d	3ad	c					3
4	1b+2a	1d	3ba	c					73
5	1c+2a	2h	3ca	CH=CH	H-CH=N	Ph	Ph	Н	87
6	1d+2a	2h	3da	CH=CH	H-CH=N	Ph	Ph	Me	56
7	1e+2a	3d	3ea	N=CH-	-CH=CH	Ph	Ph	Н	53 <sup>d</sup>
8	1f+2a	ld	3fa	Н	Н	Ph	Ph	Cl	62
9	1f+2b	1 d	3fb	Н	Н	Tol	pClC <sub>6</sub> H <sub>4</sub>	Cl	54
10	1f+2c	1 d	3fc	Н	H	Tol	Ph	Cl	64
11	1g+2a	5d	3ga	Н	Cl	Ph	Ph	Н	8
12	1h+2a	6d		e					
13	1i+2 <b>a</b>	3d	3ia	Н	Н	Ph	Ph	Br	62
14	1j+2a	3d	3ja	Н	Н	Ph	Ph	F	42
15	1k+2a	4d	3ka	Н	Н	Ph	Ph	SO <sub>2</sub> Me	53
16	1 <b>l+2a</b>	1d	3la	Н	Н	Ph	Ph	CF <sub>3</sub>	41
17	1m+2a	1d	3ma	Н	CF <sub>3</sub>	Ph	Ph	Н	57
18	1n+2a	3d	3na	Н	Н	Ph	Ph	Н	17
19	1o+2a	6d	30a	Н	Н	Ph	Ph	OMe	7
20	1p+2a	3d	Зра	c					54
21	1r+2a	3d	3ra	c					14
22	1s+2a	1 <b>d</b>	3sa	c					23

a.roughly estimated on the basis of tlc; b. Isolated via column chromatography; c. see above; d. product 10 (18%) also isolated, see text; e. not observed

intramolecular displacement to form a 5-membered ring similar to those described by Davis for the cyano group.<sup>3</sup> Such displacement had already been observed for the arylsulfonyl group.<sup>4</sup>





It is necessary to mention that in the 4-halogen substituted nitrobenzene series no  $S_NAr$  displacement took place even in the case of fluorine (entry 14). Moreover, without the silylating agent (or Lewis acid) no fluorine displacement was observed either, even after 3 days stirring at room temperature. On the other hand when NaH/DMF was applied as the base/solvent system, substitution of fluorine by carbanion 4 was completed in less than 5 min.(eq. 1). This means that the concentration of carbanion 4 in the reaction system (DBU/MeCN) is very small and that the presence of silylating agent or Lewis acid facilitate *ortho*  $\sigma^H$  adduct formation.



Moreover, no products of transformation of *para*  $\sigma^{H}$  adducts were observed (in the cases when it was possible) in spite of rather a bulky carbanion 4. Investigations of the mechanistic aspects of the reaction are in progress.

Quinolines are known to undergo  $S_NAr$  displacement at position 2- and 4- in heterocyclic ring.<sup>5</sup> In accordance with this fact the arylsulfonyl group (which is a potential leaving group) in some compound **3**'s was substituted by a few common nitrogen, oxygen, sulfur and carbon nucleophiles (Table 3).



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Table 3

entry	subs.	nucleophile	conditions		product	yield
	3		solv./temp./time	12	Nu	[%]
1	fa	MeOH/K <sub>2</sub> CO <sub>3</sub>	MeOH/RT/1d	a	OMe	92
2	fa	NaN <sub>3</sub>	DMF/50°C/1d	b	N <sub>3</sub>	94
3	fc	NCCH <sub>2</sub> CO <sub>2</sub> Me/K <sub>2</sub> CO <sub>3</sub>	DMF/RT/1d	с	NCCHCO₂Me	61
4	fc	NaBH₄	DMF/RT/1d	d	Н	94
5	fc	t-BuSH/K <sub>2</sub> CO <sub>3</sub>	DMF/RT/2d	e	SBu-t	90
6	fc	Et <sub>4</sub> NCN	CH <sub>2</sub> Cl <sub>2</sub> /RT/5d	f	CN	42
7	fc	NaOH	DMSO-H <sub>2</sub> O/50°C/2d	g	ОН	82

Thus it was shown that the presented reaction between the nitroarenes and cinnamyl-type sulfones can serve as a general method of synthesis of quinolines (and other arenopyridines) with aryl substituent at position 2- and wide range of substituents at position 4-.

#### **EXPERIMENTAL**

Melting points are uncorrected. <sup>1</sup>H NMR spectra were recorded on Varian Gemini (200 MHz) in DMSOd<sub>6</sub> solutions. Chemical shifts are expressed in ppm with reference to TMS as an internal standard. Coupling constants are given in hertz (Hz). The mass spectra were obtained on ADM-604 (ADM Intectra GmbH Germany). Column chromatographies were performed on silica gel 240-400 mesh (Merck), using ethyl acetatehexane mixtures or toluene as eluants. Sulfones  $2a^6$ ,  $2c^7$  and  $2d^8$  were known compounds. All nitroarenes were commercially available. Reagents were used in commercially available form without additional purification. Solvents were purified according to common procedures and stored over 4A molecular sieves. 3-(4-Chlorophenyl)propen-2-yl 4-methylphenyl sulfone 2b was prepared from 4-chlorocinnamyl alcohol as follows: Alcohol (1.69g, 10 mmols) was dissolved in dry methylene chloride (20 mL), pyridine (1 mL) was added, the resulting solution cooled to -20°C and treated with MsCl (1.81g, 12.5 mmol). The cooling bath was removed and the mixture stirred at room temperature for 24h. After completion of the reaction the mixture was washed with 10% aq. HCl, brine, dried (MgSO<sub>4</sub>) and evaporated. The residue was dissolved in DMSO (10 mL), sodium 4-toluenesulfinate (2.23g, 12.5 mmol) was added and the mixture stirred at 50-60°C for 2h. After pouring onto cold water (100 mL), extraction with ethyl acetate ( $3\times30$  mL), and evaporation of the solvent, the residue was recrystallized from ethyl acetate-hexane to give 2b, yield 30%; mp 140-2°C; NMR: 2.40 (s, 3H), 4.21 (dd, J=7.5, 0.9, 1H), 6.12 (dt, J=15.8, 7.5, 1H), 6.50 (d, J=15.8, 1H), 7.34-7.47 (m, 6H), 7.70-7.77 (m, 2H); MS (m/z, %): 308 (0.7), 306 (1.2), 227 (1.8), 153 (33.1), 151 (100), 116 (29.6), 115 (35.5).

## Reaction between the nitroarene 1 and sulfone 2, general procedure:

Nitroarene (1 mmol) and sulfone (1 mmol) were dissolved in 2-10 mL of appropriate solvent and than 2.5-5.0 mmols of silylating agent or Lewis acid were added. The resulted mixture was stirred at room temperature until dissolution then treated with DBU (776 $\mu$ L, 5 mmols) added in one portion, the reaction vial was stoppered and the mixture stirred at room temperature. Progress of the reaction was examined by tlc. After completion of the reaction the mixture was poured onto cold saturated aqueous ammonium chloride solution, extracted with methylene chloride (3×20 mL), the extract washed with brine (20 mL), dried (MgSO<sub>4</sub>) and evaporated. The residue was treated with CHCl<sub>3</sub> (3 mL). Usually at this point some quinoline derivative precipitated out, which was filtered off. The filtrate was separated using hexane-ethyl acetate mixtures or toluene as eluants on a chromatography column.

2-Phenyl-4-phenylsulfonylbenzo[h]quinoline, **3aa**: mp 227-8°C; NMR lit<sup>2</sup>; MS (m/z, %): 395 (100), 346 (5.3), 330 (35.3), 254 (25.9), 243 (21.2); Anal. calcd. for  $C_{25}H_{17}NO_2S$ : C, 75.92; H, 4.22; N, 3.54%; found: C, 75.69; H, 4.06; N, 3.33%.

2-(4-Chlorophenyl)-4-(4-methylphenyl )sulfonylbenzo[h]quinoline, **3ab**: mp 226-8°C (1,2-dichloroethane); NMR: 2,35 (s, 1H), 7.41-7.46 (m, 2H), 7.69-7.76 (m, 2H), 7.81-7.90 (m, 2H), 8.06-8.13 (m, 4H), 8.44 (d, J=9.3, 1H), 8.51-8.57 (m, 2H), 8.88 (s, 1H), 9.33-9.40 (m, 1H); MS (m/z, %): 446 (11.8), 445 (42.0), 444 (29.6), 443 (100), 394 (2.4), 381 (5.9), 380 (11.2), 379 (16.6), 378 (21.9), 366 (7.1), 364 (18.9), 288 (7.1), 253 (23.7); HRMS: 443.0752; calcd for  $C_{26}H_{18}NO_2SCI$ : 443.0747; Anal. calcd: C, 70.34; H, 4.09; N, 3.16%; found: C, 69.98; H, 4.02; N, 3.21%.

*3-Methyl-4-phenylsulfonylbenzo[h]quinoline*, **3ad**: mp 153-4°C; NMR: 2.34 (s, 3H), 2.95 (s,3H), 7.39-7.45 (m,2H), 7.75-7.83 (m,2H), 7.87-7.93 (m,2H), 7.98-8.16 (m, 2H), 8.74 (d, J=9.5, 1H), 9.13 (s,1H), 9.15-9.22 (m,1H); MS (m/z, %): 348 (18.9), 347 (89.9), 330 (1.2), 312 (3.0), 283 (65.7), 282 (89.9), 269 (18.9), 268 (100), 191 (54.4); HRMS: 347.0977; calcd for C<sub>21</sub>H<sub>17</sub>NO<sub>2</sub>S: 347.0980.

2-Phenyl-4-phenylsulfonylpyrido[3,2-f]quinoline, **3ba**: mp 172-6°C; NMR lit<sup>2</sup>.; MS (m/z, %): 395 (100), 331 (58.5), 305 (2.9), 255 (58.5), 243 (2.9); Anal. calcd. for  $C_{25}H_{16}N_2O_2S$ : C, 72.70; H, 4.07; N, 7.07%; found: C, 72.50, H, 3,82; N, 6.82%.

2-Phenyl-4-phenylsulfonylpyrido[2,3-h]quinoline, **3ca**: mp 267-9°C (1,2-dichloroethane); NMR lit<sup>2</sup>; MS (m/z, %): 396 (100), 347 (7.1), 331 (49.1), 255 (26.0), 243 (11.2); Anal. calcd. for C<sub>25</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>S: C, 72.70; H, 4.07, N, 7.07%; found: C,72.81; H, 3.89; N, 6.97%.

6-Methoxy-2phenyl-4-phenylsulfonylpyrido[2,3-h]quinoline, 3da: mp 258-62°C; NMR: 4.07 (s, 3H), 7.58-7.76 (m, 6H), 7.83 (s, 1H), 7.90 (dd, J=8.4, 4.3, 1H), 8.20-8.26 (m, 2H), 8.44-8.50 (m, 2H), 8.87 (s, 1H), 9.11 (dd, J=4.3, 1.7, 1H), 9.65 (dd, J=8.4, 1.7, 1H); MS (m/z, %): 428 (7.1), 427 (30.8), 426 (100), 425 (52.1), 409 (4.7), 398 (13.0), 397 (53.3), 396 (8.9), 361 (20.1), 344 (4.1), 331 (8.9), 284 (44.4); HRMS: 426.1041; calcd. for  $C_{23}H_{18}N_2O_3S$ :426.1038.

2-Phenyl-4-phenylsulfonylpyrido[3,2-h]quinoline, **3ea**: mp 246-8°C; NMR: 7.58 (m, 6H), 7.86 (dd, J=8.1, 4.3, 1H), 8.14 (d, J=9.3, 1H), 8.20-8.26 (m, 2H), 8.47-8.55 (m, 3H), 8.56 (d, J=9.3, 1H), 8.95 (s, 1H), 9.22 (dd, J=4.3, 1.7, 1H); MS (m/z, %): 397 (18.9), 396 (66.2), 395 (55.6), 379 (1.8), 347 (25.4), 332 (29.0), 331 (100), 319 (2.4), 255 (17.8); HRMS: 396.0936; calcd for  $C_{24}H_{16}N_2O_2S$ : 396.0933.

6-Chloro-2-phenyl-4-phenylsulfonylquinoline, **3fa**: mp 218-9°C; NMR: 7.58-7.81 (m, 6H), 7.92 (dd, J=9.0, 2.3, 1H), 8.16-8.21 (m, 2H), 8.25 (d, J=9.0, 1H), 8.31-8.37 (m, 2H), 8.47 (d, J=2.3, 1H), 8.79 (s, 1H); MS (m/z, %): 379 (100), 330 (5.3), 314 (30.7), 280 (27.8), 238 (10.6), 203 (29.0); HRMS: 379.0432; calcd for C<sub>21</sub>H<sub>14</sub>NO<sub>2</sub>SCI: 379.0434.

6-Chloro-2-(4-chlorophenyl)-4-(4-methylphenyl)sulfonylquinoline, **3fb**: mp 261-3°C (1,2-dichloroethane-hexane); NMR: 2.37 (s,3H), 7.44-7.49 (m, 2H), 7.66-7.72 (m,2H), 7.93 (dd, J=9.1, 2.3, 1H), 8.02-8.08 (m, 2H), 8.24 (d, J=9.1, 1H), 8.34-8.43 (m, 2H), 8.47 (d, J=2.3, 1H), 8.80 (s, 1H); MS (m/z, %): 431 (12.4), 430 (15.3), 429 (59.2), 428 (22.5), 427 (81.1), 378 (4.1), 364 (13.0), 362 (17.2), 348 (5.9), 330 (36.7), 329 (24.9), 328 (100), 272 (4.7), 237 (36.7); Anal. calcd for  $C_{21}H_{15}NO_2SCl_2$ : C, 61.69; H, 3.53; N, 3.27%; found: C, 61.52; H, 3.50; N, 3.33%.

6-Chloro-4-(4-methylphenyl)sulfonyl-2-phenylquinoline, **3fc**: mp 215-8°C (1.2-dichloroethane); NMR: 2,37 (s, 3H), 7.44-7.51 (m, 2H), 7.58-7.67 (m, 3H), 7.93 (dd, J=9.1, 2.3, 1H), 8.03-8.09 (m, 2H), 8.25 (d, J=9.1, 1H), 8.32-8.38 (m, 3H), 8.48 (d, J=2.3, 1H); MS (m/z, %): 295 (23.7), 294 (100), 293 (7.1), 278 (1.8), 238 (9.5), 216 (3.6), 203 (32.0), 176 (4.1); Anal. calcd for  $C_{22}H_{16}NO_2SCl$ : C, 67.08; H, 4.10; N, 3.56%; found: C, 66.98; H, 4.03; N, 3.49%.

7-Chloro-2-phenyl-4-phenylsulfonylquinoline, **3ga**: mp 218-20°C (ethyl acetate); NMR: 7.60-7.82 (m,6H), 7.94 (dd, J=9.1, 2.2, 1H), 8.16-8.22 (m, 2H), 8.26 (d, J=9.1, 1H), 8.32-8.38 (m, 2H), 8.47 (d, J=2.2, 1H), 8.80 (s, 1H); MS (m/z, %): 381 (36), 379 (100), 350 (11.2), 348 (32.5), 333 (8.9), 316 (12.4), 314 (33.2), 280 (33.7), 274 (5.9), 272 (15.4), 240 (7.7), 238 (16.6), 223 (8.3), 203 (30.1); HRMS: 379.0425; calcd for  $C_{21}H_{14}NO_2SCI$ : 379.0434.

6-Bromo-2-phenyl-4-phenylsulfonylquinoline, **3ia**: mp 224-7°C (ethyl acetate); NMR: 7.58-7.80 (m, 6H), 8.03 (dd, J=9.0, 2.0, 1H), 8.14-8.20 (m, 3H), 8.31-8.37 (m, 2H), 8.62 (d, J=2.0, 1H), 8.78 (s, 1H); MS (m/z, %), 426 (24.0), 425 (100), 424 (38.5), 423 (94.0), 376 (10.7), 374 (10.7), 360 (34.9), 358 (34.9), 280 (67.4); HRMS: 422.9930; calcd for  $C_{21}H_{14}NO_2SBr^{79}$ : 422.9929; Anal. calcd: C, 59.44; H, 3.33; N, 3.30%; found: C, 59.43; H, 3.08: N, 3.30%.

6-Fluoro-2-phenyl-4-phenylsulfonylquinoline, **3ja**: mp 226-9°C (1,2-dichloroethane-hexane); NMR: 7.58-7.90 (m, 7H), 8.17 (dd, J=10.2, 2.7, 1H), 8.20-8.37 (m, 5H), 8.81 (s, 1H); MS (m/z, %): 364 (24.3), 363 (100), 362 (21.3), 346 (1.8), 314 (11.8), 299 (21.3), 298 (58.6); HRMS: 363.0724; calcd for  $C_{21}H_{14}NO_2SF$ : 363.0729.

6-Methylsulfonyl-2-phenyl-4-phenylsulfonylquinoline, 3ka: mp 235-6°C (1,2-dichloroethane-hexane); NMR: 3.90 (s, 3H), 7.63-7.81 (m, 6H), 8.17-8.21 (m, 2H), 8.34 (dd, J=8.9, 2.0, 1H), 8.38-8.44 (m, 2H), 8.46 (d, J=8.9, 1H), 8.89 (s, 1H), 9.11 (d, J=2.0, 1H); MS (m/z, %): 424 (26.6), 423 (100), 422 (18.9), 374 (3.6), 358 (23.6), 343 (3.0), 316 (6.5); HRMS: 423.0601; calcd for  $C_{22}H_{17}NO_4S_2$ : 423.0599.

2-Phenyl-4-phenylsulfonyl-6-trifluoromethylquinoline, **3la**: mp 208-9°C (ethyl acetate-hexane); NMR: 7.62-7.82 (m, 6H), 8.12-8.22 (m, 3H), 8.35-8.46 (m, 3H), 8.81 (s, 1H), 8.88 (s, 1H); MS (m/z, %): 414 (26.6), 413 (100), 412 (34.9), 394 (3.6), 364 (18.9), 348 (82.8); anal. calcd for  $C_{21}H_{14}NO_2SF_3$ : C, 63.91; H, 3.41; N, 3.39%; found: C, 63.73: H, 3.21; N, 3.46%.

2-Phenyl-4-phenylsulfonyl-7-trifluoromethylquinoline, **3ma**: mp 171-2°C (1,2-dichloroethane-hexane); NMR: 7.61-7.80 (m, 6H), 7.82 (dd, J=9.0, 2.0, 1H), 8.20-8.27 (m, 2H), 8.35-8.43 (m, 2H), 8.57 (d, J=9.0, 1H), 8.77 (d, J=9.0, 1H), 8.91 (s, 1H); MS (m/z, %): 413 (100), 394 (4.1), 364 (14.2), 348 (69.2), 280 (4.1), 272 (18.3); HRMS: 413.0707; calcd for  $C_{22}H_{14}NO_2SF_3$ : 413.0697; anal. calcd: C, 63.91; H, 3.41; N, 3.39%; found: C, 63.68, H, 3.35: N, 3.20%.

2-Phenyl-4-phenylsulfonylquinoline, **3na**: mp 195-8°C; NMR: 7.58-7.79 (m, 7H), 7.85-7.94 (m, 1H), 8.16-8.27 (m, 3H), 8.32-8.38 (m, 2H), 8.53 (dd, J=8.4, 0.8, 1H), 8.76 (s, 1H); MS (m/z, %): 346 (24.8), 345 (100), 344 (29.6), 333 (21.9), 331 (17.8), 296 (10.0), 281 (14.2), 280 (58.5), 223 (16.5), 204 (15.4); HRMS: 345.0827; calcd for  $C_{21}H_{13}NO_2S$ : 345.0823.

6-Methoxy-2phenyl-4-phenylsulfonylquinoline, **30a**: mp 178-81°C (ethyl acetate-hexane); NMR: 3.89 (s, 3H), 7.54 (dd, J=9.3, 2.7, 1H), 7.57-7.75 (m, 7H), 8.13 (d, J=9.3, 1H), 8.18-8.21 (m, 2H), 8.27-8.33 (m, 2H), 8.74 (s, 1H); MS (m/z, %): 375 (100), 326 (2.10), 310 (10.0), 296 (13.0), 280 (14.8); HRMS: 375.0920; calcd for C<sub>22</sub>H<sub>17</sub>NO<sub>3</sub>S: 375.0929.

6-Methoxy-2-phenyl-4-phenylsulfonylpyrido[3,2-b]pyridine, **3pa**: mp 245-6°C (1,2-dichloroethane); NMR lit<sup>2</sup>; MS (m/z, %): 376 (5.3), 311 (100), 296 (23.7), 281 (5.9), 268 (11.2); HRMS: 376.0870; calcd for  $C_{21}H_{16}N_2O_3S$ : 376.0882.

*8-Ethoxy-2-phenyl-4-phenylsulfonyl*[3,2-*b*]*pyridopyridine*, **3ra**: mp 243-5°C; NMR: 1.49 (t, J=7.0, 3H), 4.37 (q, J=7.0, 2H), 7.30 (d, J=5.3, 1H), 7.54-7.73 (m, 6H), 8.17-8.22 (m, 2H), 8.74 (d, J=5.3, 1H), 8.90 (s, 1H); MS (m/z, %): 391 (0.2), 389 (0.5), 375 (5.0), 324 (42.6), 325 (71.0), 297 (100); LSIMS HRMS: 391.1115(M.+H)<sup>+</sup>, calcd for  $C_{22}H_{19}N_2O_3S$ : 391.1116.

2-Phenyl-4-phenylsulfonylthieno[2,3-b]pyridine, **3sa**: mp 182-3°C (ethyl acetate-hexane); NMR: 7.53-7.79 (m, 6H), 7.87 (d, J=6.1, 1H), 8.19-8.27 (m, 5H), 8.53 (s, 1H); MS (m/z, %): 351 (100), 302 (4.7), 286 (23.1), 210 (14.2), 198 (16.0); anal. calcd for  $C_{19}H_{13}NO_2S_2$ : C, 64.93; H, 3.73; N, 3.99%; found: C, 64.81; H, 3.66; N, 3.74%.

*Phenyl 1-(N,N-dimethylamino)-4-phenylbutadien-1,3-yl-2 sulfone*, **9**: mp 188-90°C (ethyl acetate); NMR: 3.10 (s, 6H), 6.51 (d, J=16.2, 1H), 6.88 (d, J=16.2, 1H), 7.12-7.38 (m, 5H), 7.45 (s, 1H), 7.46-7.55 (m, 3H), 7.74-7.80 (m, 2H); MS (m/z, %): 313 (29.6), 249 (5.9), 172 (100), 157 (30.2); HRMS: 313.1139; calcd for  $C_{18}H_{19}NO_2S$ : 313.1137.

3-(2-Phenylethenyl)-quinolo[8,7-c]-1,2-isoxazole, 10: mp172-5°C (ethyl acetate-hexane); NMR: 7.40-7.44 (m,1H), 7.46-7.48 (m, 2H), 7.49 (d, J=9.1, 1H), 7.73 (d, J=16.5, 1H), 7.76 (dd, J=8.1, 4.5, 1H), 7.85 (m, 2H), 7.87 (d, J=16.5, 1H), 7.95 (d, J=9.1, 1H), 8.36 (dd, J=8.1, 1.6, 1H), 9.1 (dd, J=4.5, 1.6, 1H); MS (m/z, %): 273 (20.7), 272 (100), 271 (27.8), 245 (12.4), 244 (66.3), 243 (84.0), 242 (17,2), 216 (13.0), 197 (4.1); HRMS: 272.0959; calcd for  $C_{18}H_{12}N_2O$ : 272.0949.

Nitroarylation of the sulfone 2a: a). Reaction in the presence of DBU as a base was performed according to the general procedure. No product 11 was observed. b). Reaction in the presence of NaH as a

base. A solution of the sulfone 2a (258mg, 1mmol), and 4-fluoronitrobenzene (155mg, 1.1mmol) in dry DMF (2.5mL) was added with stirring to a suspension of NaH (150mg, 5mmol, 80% suspension in paraffin oil) in DMF (2.5mL) at room temperature. After stirring for 5min the reaction was quenched with aq. NH<sub>4</sub>Cl, extracted with ethyl acetate and chromatographed yielding 265mg (70%) of 11 as a 1:1 mixture of isomers which were further separated *via* additional chromatography.

3-Phenyl-1-phenylsulfonyl-1-(4-nitrophenyl)propene, 11A ( $\alpha$ , $\beta$ -unsaturated isomer); oil; NMR: 4.06 (d, J=7.9, 2H), 6.11+6.26 (two t, ratio 1:3 two isomers), 6.98-7.80 (m, 12H), 8.15-8.20 (m, 2H); MS (m/z, %): 379 (0.2), 279 (0.5), 252 (1.0), 238 (85.8), 221 (7.8), 192 (100); HRMS: 379.0874; calcd for C<sub>21</sub>H<sub>17</sub>NO<sub>4</sub>S: 379.0878.

*I-Phenyl-3-phenylsulfonyl-3-(4-nitrophenyl)propene*, **11B** ( $\beta$ , $\gamma$ -unsaturated, *trans* isomer); mp 180-2°C; NMR: 5.78 (d, J=9.4, 1H), 6.52 (d, J=15.6, 1H), 6.74 (dd, J=15.6, 9.4, 1H), 7.30-7.80 (m, 12H), 8.20-8.26 (m, 2H); MS (m/z, %): 379 (2.9), 254 (1.5), 238 (100), 221 (8.3), 192 (93.5); HRMS: 379.0874; calcd for C<sub>21</sub>H<sub>17</sub>NO<sub>4</sub>S: 379.0878.

## Reaction of sulfones 3 with nucleophiles.

6-Chloro-4-methoxy-2-phenylquinoline, 12a: Sulfone **3fa** (190mg, 0.5mmol) was dissolved in MeCN (5 mL) and MeOH (5 mL),  $K_2CO_3$  (690mg, 5 mmol) was added and the mixture stirred at room temperature for 24h. After pouring onto satd aq. NH<sub>4</sub>Cl solution, extraction with CH<sub>2</sub>Cl<sub>2</sub> (3×20 mL) followed by column chromatography the product was isolated in 92% yield: mp 103-6°C; NMR: 4.20 (s, 3H), 7.53-7.62 (m, 1H), 7.80 (dd, J=(.0, 2.4, 1H), 8.07 (d, J=9.0, 1H), 8.11 (d, J=2.4, 1H), 8.24-8.31 (m, 2H); MS (m/z, %): 271 (33.7), 270 (37.2), 269 (100), 268 (69.2), 254 (2.9), 242 (13.6), 241 (16.0), 240 (42.6), 239 (31.4), 238 (14.8), 234 (4.7), 219 (3.5), 204 (26.0); HRMS: 269.0604; calcd for C<sub>16</sub>H<sub>12</sub>NOCI: 269.0607.

4-Azido-6-chloro-2-phenylquinoline, 12b: Sulfone **3fa** (190mg, 0.5mmol) was dissolved in dry DMF (5mL), NaN<sub>3</sub> (325mg, 5mmol) was added and the resulting mixture stirred at room temperature for 24h. After work-up and column chromatography as above the product was obtained in 94% yield. mp 120-4°C; NMR: 7.52-7.63 (m, 3H), 7.83 (dd, J=9.0, 2.5, 1H), 7.99 (d, J=2.5, 1H), 8.03 (s, 1H), 8.08 (d, J=9.0, 1H), 8.27-8.34 (m, 2H); MS (m/z, %): 282 (11.2), 281 (5.9), 280 (39.0), 253 (22.5), 252 (100), 217 (26.0), 190 (16.6); HRMS: 280.0521; calcd for  $C_{15}H_9N_4Cl$ : 280.0516.

*Methyl (6-chloro-2-phenylquinolin-2-yl) cyanoacetate*, **12c**: Sulfone **3fc** (197mg, 0.5mmol) was dissolved in dry DMF (5 mL), methyl cyanoacetate (99mg, 1mmol) was added followed by the addition of  $K_2CO_3$  (345mg, 2.5mmol) and the resulting mixture was stirred at room temperature for 72h. After pouring onto cold water the precipitate was filtered off, dried and boiled with 1,2-dichloroethane. Undissolved solid was filtered off to give **12c**, yield 61%. This compound exists exclusively as the enol form. mp 259-60°C; NMR: 3.69 (s, 3H), 7.68-7.70 (m, 3H), 7.82-7.97 (m, 4H), 8.70 (s, 1H), 9.17 (d, J=1.9, 1H), 13.05 (s, 1H); MS (m/z, 5): 338 (33.7), 337 (22.5), 336 (100), 321 (2.4), 305 (11.2), 294 (7.1), 293 (8.3), 292 (18.3), 291 (11.8), 280 (12.4), 279 (16.0), 278 (41.4), 277 (30.2), 276 (14.2), 257 (7.1), 242 (39.6); HRMS: 336. 0664; calcd for C<sub>19</sub>H<sub>13</sub>N<sub>2</sub>O<sub>2</sub>Cl: 336.0666; Anal. calcd: C, 67.76; H, 3.89; N, 8.31%; found: C, 67.30; H, 3.52; N, 8.19%.

6-Chloro-2-phenylquinoline, 12d: Sodium borohydride ( total 185mg, 5mmol) was added in 3 portions every 12h to the stirred solution of 3fc (197mg, 0.5mmol) in dry DMF (5mL) at room temperature. After work-up and column chromatography (as for 12a, b) the product was obtained in 94% yield. mp 104-8°C; NMR: 7.5-7.62 (m,3H), 7.79(dd, J=9.0, 2.4, 1H), 8/09 (d, J=9.0, 1H), 8.15 (d, J=2.4, 1H), 8.22 (d, J=8.7, 1H), 8.25-8.32 (m, 2H), 8.46 (d, J=8.7, 1H); MS (m/z, %): 241 (32.0), 240 (27.8), 239 (100), 238 (39.0), 205 (4.7), 204 (31.3), 203 (17.1), 176 (4.7), 151 (1.7); HRMS: 239.0498; calcd for C<sub>15</sub>H<sub>10</sub>NCl: 239.0502;

*4-tert-Butyl-6-chloro-2-phenylquinoline*, **12e**: Sulfone **3fc** (197mg, 0.5mmol), *tert*-butylthiol (218mg, 2.5mmol) and K<sub>2</sub>CO<sub>3</sub> (690mg, 5mmol) were stirred in DMF (5 mL) at room temperature for 24h. After work-up and column chromatography as above the product was isolated in 90% yield. mp 96-98°C (hexane); NMR: 1.39 (s, 3H), 7.54-7.64 (m, 3H), 7.86 (dd, J=9.0, 2.4, 1H), 8.15 (d, J=9.0, 1H), 8.25-8.32 (m, 2H), 8,30 (s, 1H), 8.51(d, J=2.4, 1H); MS (m/z, %): 329 (8.3), 327 (19.5), 273 (36.4), 271 (100), 235 (8.2); HRMS: 327.0847; calcd for  $C_{19}H_{18}NSCI: 327.0848$ .

6-Chloro-4-cyano-2-phenylquinoline, 12f:: Sulfone 3fc (197mg, 0.5mmol) and tetraethylammonium cyanide (468mg, 3mmol) were stirred in 5 mL of dry methylene dichloride at room temperature for 5 days. After washing with water, drying with MgSO<sub>4</sub> and evaporation of the solvent, the residue was chromatographed to give 12f in 42% yield: mp 182-3°C; NMR: 7.55 (m, 3H), 7.99 (dd, J=9.0, 2.3, 1H), 8.08 (d, J=2.3, 1H), 8.25 (d, J=9.0, 1H), 8.32-8.38 (m, 2H), 8.90 (s, 1H); MS (m/z, %): 267 (5.9), 266 (30.2), 265 (28.4), 264 (100), 263 (25.4), 239 (5.3), 238 (4.1), 230 (8.3), 229 (46.1), 228 (14.2), 228 (5.3), 201 (5.9); HRMS: 264.0455; calcd for  $C_{16}H_9N_2CI$ : 264.0454.

6-Chloro-4-hydroxy-2-phenylquinoline, 12g: sulfone, NaOH (100mg, 2.5mmol) were stirred in 1mL of water and 5mL of DMSO at 50° for 2 days. After completion of the reaction the mixture was poured onto saturated aqueous NH<sub>4</sub>Cl (30mL), the precipitate was filtered off and dried giving practically pure 12g in 82% yield: mp> 290°C; NMR: 6.38 (s, 1H), 7.58-7.63 (m, 3H), 7.72 (dd, J=8.9, 2.4, 1H), 7.79-7.88 (m, 3H), 8.04 (d, J=2.4, 1H); MS (m/z, %): 258 (5.9), 257 (33.1), 256 (22.5), 255 (100), 254 (17.8), 240 (3.6), 239 (1.8), 238 (10.7), 229 (8.3), 228 (4.7), 227 (24.9), 220 (4.7), 219 (5.3), 199 (3.0); HRMS: 255.0450; calcd for  $C_{15}H_{10}NOCl$ : 255.0451.

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