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

Zbigniew Wróbel

Institute of Organic Chemistry, Polish Academy of Sciences, ul. Kasprzaka 44/52, PL-01-224 Warsaw, Poland

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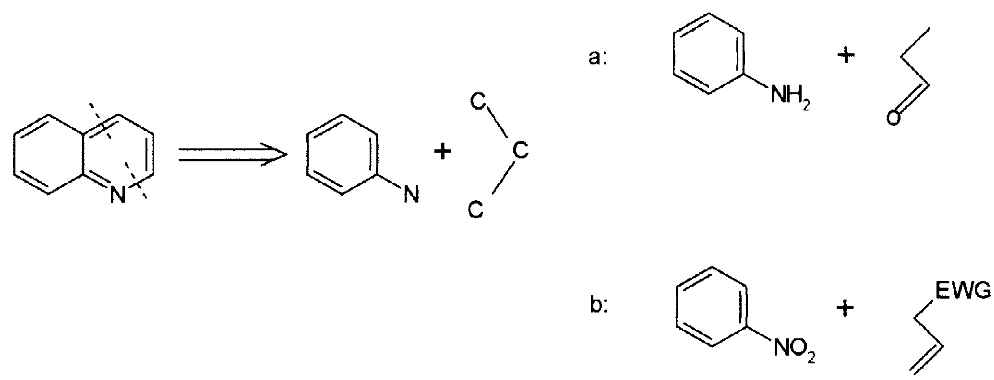
Abstract: DBU/silane mediated double condensation of nitroarenes with cinnamyl-type sulfones proceeds smoothly to yield 2-aryl-4-arylsulfonyl quinolines and their hetero analogs. Arylsulfonyl group can be easily replaced by different nucleophiles.

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[1] (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[2] (Scheme 1, path b).

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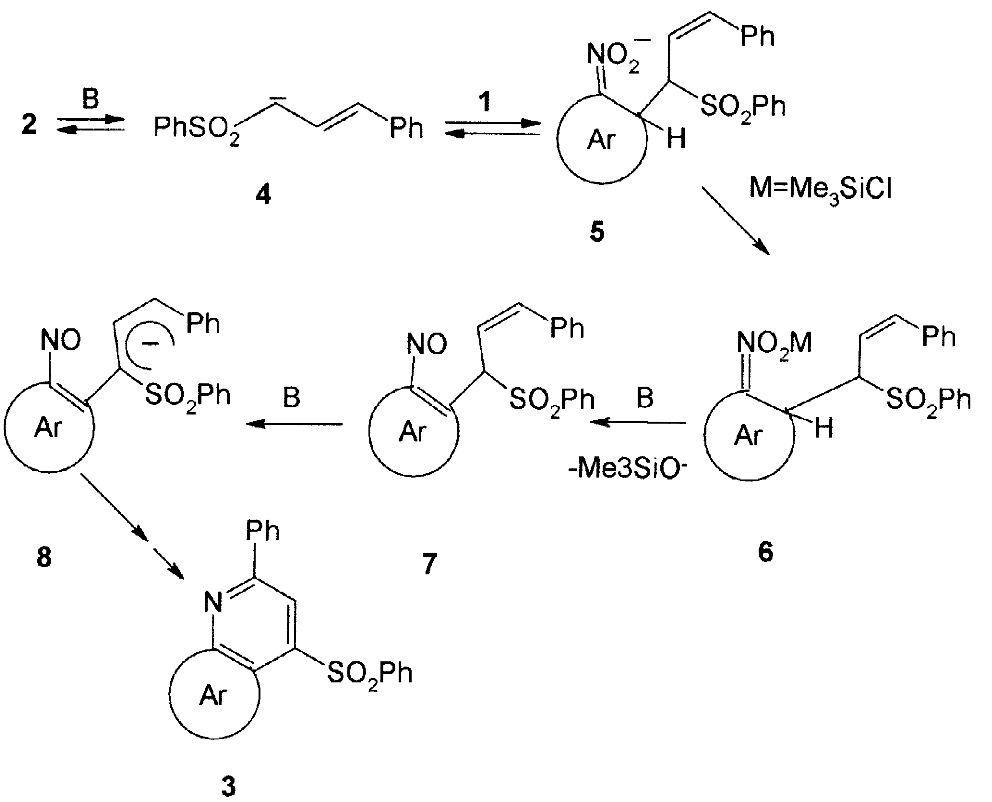
Thus, when the equimolar DMF solution of 1-nitronaphthalene **1a** and cinnamyl phenyl sulfone **2a** was treated with 5eq. of DBU in the presence of 5eq. of Me_3SiCl, 2-phenyl-4-phenylsulfonylbenzo[h]quinoline **3aa** was formed in 44% yield during 24h.

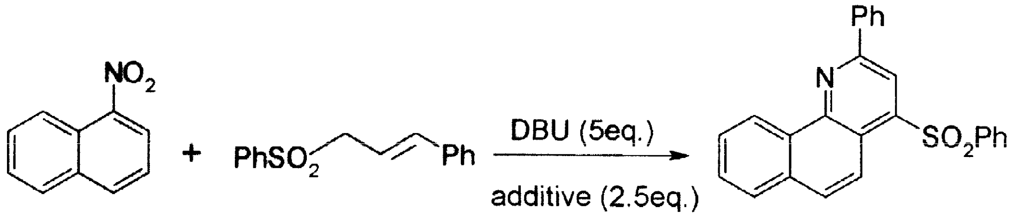
The proposed mechanism of the reaction consists in reversible deprotonation of sulfone **2**, reversible addition of carbanion **4** to nitroarene **1** to form σ^H adduct **5** followed by its silane-mediated conversion to a nitroso intermediate **7** (probably *via* **6**) and intramolecular condensation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



Scheme 2

Since the reaction does not proceed without the silylating 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 silylating agents like Me_3SiCl, *t*-$BuSiMe_2Cl$, bis-(trimethylsilyl)acetamide (BTMSA) or some Lewis acids like $Ti(OEt)_4$ and $MgCl_2$. Less effective were LiCl, Bu_3SnCl 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 $MgSO_4$, $CaCl_2$ 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_2Cl_2. On the other hand it did not



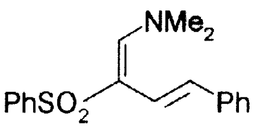
1a (1eq.) **2a** (1eq.) **3aa** (1)

Table 1

entry	additive	solvent	time[a]	**3aa** yield[b] [%]	**1a/2a** yield[b][%]
1	none	DMF	1d	0	[c]
2	Me_3SiCl[d]	DMF	1d	44	[e]
3	*t*-$BuSiMe_2$	MeCN	1d[f]	69	26/16
4	*t*-$BuSiMe_2$	CH_2Cl_2	6d	44.5	44/47
5	*t*-$BuSiMe_2$	PhH	6d	49	31/32
6	*t*-$BuSiMe_2$	THF	6d	45	34/33
7	*t*-$BuSiMe_2$	DMF	6d	22	71/0 [g]
8	BTMSA	MeCN[h]	1d	82	12/0
9	$Ti(Oet)_4$	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	$TiCl_4$	MeCN	1d	tr	tars
13	$BF_3 \cdot Et_2O$	MeCN	4d	0	[c]
14	LiCl	MeCN	6d	28	46/13
15	$MgCl_2$	MeCN	6d	70	26/12
16	$MgCl_2$	DMF	1d	57	[e]
17	$MgSO_4$	MeCN	6d	0	[c]
18	$CdCl_2$	MeCN	6d	5	90/87
19	$ZnCl_2$	MeCN	6d	0	[c]
20	$CaCl_2$	MeCN	6d	0	[c]
21	4A sieves	MeCN	6d	0	[c]
22	Bu_3SnCl	MeCN	6d	46.5	50/34
23	MeOH	MeCN	6d	0	[c]
24	Ph_3CCl	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 with t-BuSiMe$_2$Cl yielding Vilsmeyer-type reagent which subsequently **added to anion 5 to form a side product 9** (entry 7).



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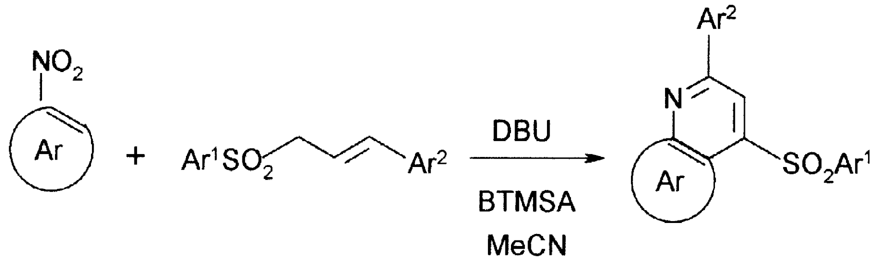
The main problem with the reaction was that in most cases it stopped after a low or moderate conversion despite of the presence of both substrates (balance of the reaction was usually 70-90%) and reagents taken in an excess. Prolongation of the reaction time did not improve the yield.

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 .



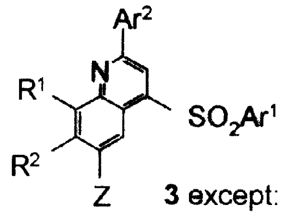
1 **2** **3**

ArNO$_2$	1	ArNO$_2$	1
1-nitronaphthalene	**a**	4-fluoronitrobenzene	**j**
6-nitroquinoline	**b**	4-methylsulfonyl-nitrobenzene	**k**
5-nitroquinoline	**c**	4-trifluoromethyl-nitrobenzene	**l**
8-methoxy-5-nitroquinoline	**d**	3-trifluoromethyl-nitrobenzene	**m**
8-nitroquinoline	**e**	nitrobenzene	**n**
4-chloronitrobenzene	**f**	4-methoxynitrobenzene	**o**
3-chloronitrobenzene	**g**	2-methoxy-5-nitropyridine	**p**
2-chloronitrobenzene	**h**	4-ethoxy-3-nitropyridine	**r**
4-bromonitrobenzene	**i**	2-nitrothiophene	**s**

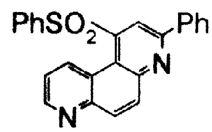
Ar^1	Ar^2	R	2
Ph	Ph	H	**a**
Tol	p-ClC$_6$H$_4$	H	**b**
Tol	Ph	H	**c**
Tol	H	Me	**d**

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).

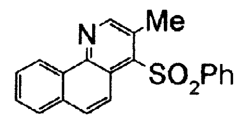
In the case of 8-nitroquinoline **1e** as nitroarene an anthranil (2,1-benzisoxazole) derivative **10** was isolated as a byproduct (entry 7). It was probably formed from intermediate **8ea** (Scheme 3). Besides intramolecular addition of the side chain positioned carbanion to nitroso group, **8ea**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



3 except: **3ad**, **ba**,**pa**, **ra**, **sa**



3ba



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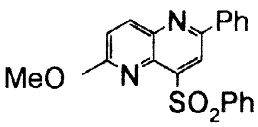

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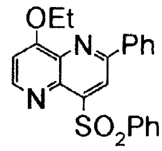
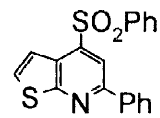


3ra

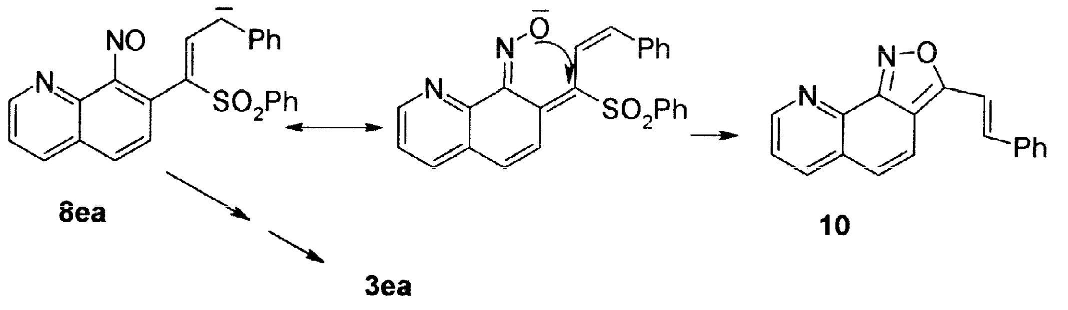


3sa

Table 2

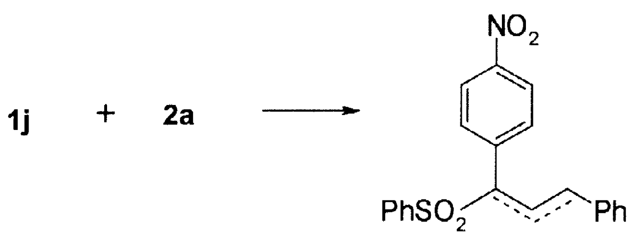
entry	substrates	time[a]	product No	R^1	R^2	Ar^1	Ar^2	Z	Yield [%]
1	**1a+2a**	5d	**3aa**	CH=CH-CH=CH		Ph	Ph	H	82
2	**1a+2b**	1d	**3ab**	CH=CH-CH=CH		Tol	p.-ClC_6H_4	H	63
3	**1a+2c**	8d	**3ad**	[c]					3
4	**1b+2a**	1d	**3ba**	[c]					73
5	**1c+2a**	2h	**3ca**	CH=CH-CH=N		Ph	Ph	H	87
6	**1d+2a**	2h	**3da**	CH=CH-CH=N		Ph	Ph	Me	56
7	**1e+2a**	3d	**3ea**	N=CH-CH=CH		Ph	Ph	H	53[d]
8	**1f+2a**	1d	**3fa**	H	H	Ph	Ph	Cl	62
9	**1f+2b**	1d	**3fb**	H	H	Tol	p.-ClC_6H_4	Cl	54
10	**1f+2c**	1d	**3fc**	H	H	Tol	Ph	Cl	64
11	**1g+2a**	5d	**3ga**	H	Cl	Ph	Ph	H	8
12	**1h+2a**	6d		[e]					
13	**1i+2a**	3d	**3ia**	H	H	Ph	Ph	Br	62
14	**1j+2a**	3d	**3ja**	H	H	Ph	Ph	F	42
15	**1k+2a**	4d	**3ka**	H	H	Ph	Ph	SO_2Me	53
16	**1l+2a**	1d	**3la**	H	H	Ph	Ph	CF_3	41
17	**1m+2a**	1d	**3ma**	H	CF_3	Ph	Ph	H	57
18	**1n+2a**	3d	**3na**	H	H	Ph	Ph	H	17
19	**1o+2a**	6d	**3oa**	H	H	Ph	Ph	OMe	7
20	**1p+2a**	3d	**3pa**	[c]					54
21	**1r+2a**	3d	**3ra**	[c]					14
22	**1s+2a**	1d	**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.[3] Such displacement had already been observed for the arylsulfonyl group.[4]



Scheme 3

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* σ^H adduct formation.



(eq. 1)

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conditions:	DBU/MeCN/3d/RT	no product
	NaH/DMF/5min/RT	70%

Moreover, no products of transformation of *para* σ^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.[5] 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).

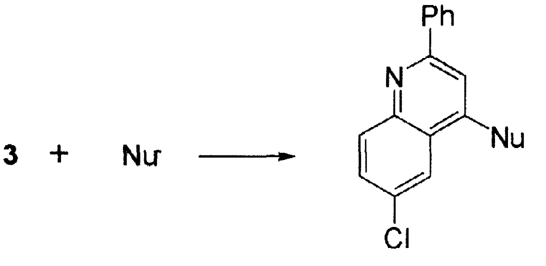

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Table 3

entry	subs. **3**	nucleophile	conditions solv./temp./time	product **12**	product Nu	yield [%]
1	**fa**	$MeOH/K_2CO_3$	MeOH/RT/1d	**a**	OMe	92
2	**fa**	NaN_3	DMF/50°C/1d	**b**	N_3	94
3	**fc**	$NCCH_2CO_2Me/K_2CO_3$	DMF/RT/1d	**c**	$NCCHCO_2Me$	61
4	**fc**	$NaBH_4$	DMF/RT/1d	**d**	H	94
5	**fc**	$t\text{-}BuSH/K_2CO_3$	DMF/RT/2d	**e**	SBu-t	90
6	**fc**	Et_4NCN	CH_2Cl_2/RT/5d	**f**	CN	42
7	**fc**	NaOH	DMSO-H_2O/50°C/2d	**g**	OH	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. ^1H NMR spectra were recorded on Varian Gemini (200 MHz) in DMSO-d_6 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 acetate-hexane mixtures or toluene as eluants. Sulfones **2a**[6], **2c**[7] and **2d**[8] were known compounds. All nitroarenes were commercialy 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 ($MgSO_4$) 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 (3×30 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 (776μL, 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 ($MgSO_4$) and evaporated. The residue was treated with $CHCl_3$ (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[2]; 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 $C_{26}H_{18}NO_2SCl$: 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 $C_{21}H_{17}NO_2S$: 347.0980.

2-Phenyl-4-phenylsulfonylpyrido[3,2-f]quinoline, **3ba**: mp 172-6°C; NMR lit[2].; 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[2]; MS (m/z, %): 396 (100), 347 (7.1), 331 (49.1), 255 (26.0), 243 (11.2); Anal. calcd. for $C_{25}H_{16}N_2O_2S$: 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 $C_{25}H_{18}N_2O_3S$: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 $C_{21}H_{14}NO_2SCl$: 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 $C_{21}H_{14}NO_2SCl$: 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 $C_{21}H_{15}NO_2S$: 345.0823.

6-Methoxy-2phenyl-4-phenylsulfonylquinoline, **3oa**: 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 $C_{22}H_{17}NO_3S$: 375.0929.

6-Methoxy-2-phenyl-4-phenylsulfonylpyrido[3,2-b]pyridine, **3pa**: mp 245-6°C (1,2-dichloroethane); NMR lit[2]; 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$(M.+H)^+$, 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_4Cl, 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** (α,β-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 $C_{21}H_{17}NO_4S$: 379.0878.

1-Phenyl-3-phenylsulfonyl-3-(4-nitrophenyl)propene, **11B** (β,γ-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 $C_{21}H_{17}NO_4S$: 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_4Cl solution, extraction with CH_2Cl_2 (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 $C_{16}H_{12}NOCl$: 269.0607.

4-Azido-6-chloro-2-phenylquinoline, **12b**: Sulfone **3fa** (190mg, 0.5mmol) was dissolved in dry DMF (5mL), NaN_3 (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 $C_{19}H_{13}N_2O_2Cl$: 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 $C_{15}H_{10}NCl$: 239.0502;

4-tert-Butyl-6-chloro-2-phenylquinoline, **12e**: Sulfone **3fc** (197mg, 0.5mmol), *tert*-butylthiol (218mg, 2.5mmol) and K_2CO_3 (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 $C_{19}H_{18}NSCl$: 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 $MgSO_4$ 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 $C_{16}H_9N_2Cl$: 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_4Cl (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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