

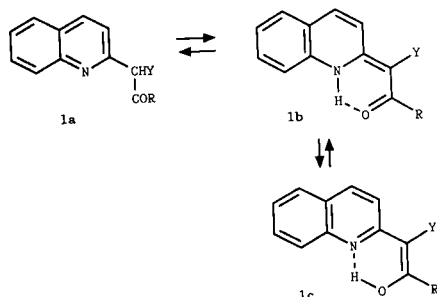
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A series of quinaldyl sulfones was synthesized and their tautomeric composition was determined by ^1H nmr.

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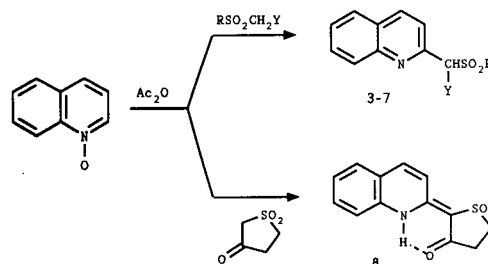
Tautomerism in 2-substituted quinolines, and in quinaldyl ketones **1** in particular, has been studied in some detail over the past two decades. The position of the equilibrium between the azomethine form **1a** and the intramolecularly hydrogen-bonded enamine form **1b** is sensitive to the structure of Y and R. When Y is a strong electron-withdrawing group (e.g., $-\text{COR}$, $-\text{COOR}$, $-\text{CN}$), the resulting compounds exist exclusively (based upon ^1H nmr) as form **1b** [1-5]. When Y is hydrogen, a mixture of both tautomers is observed [4,6-10]. The only exceptions to the



latter appear to be those reported by Greenhill and co-workers [10] where $\text{R} = -\text{COOEt}$ and $-\text{CN}$. There is an abundance of evidence supporting the enamine tautomer **1b** as opposed to the corresponding enol tautomer **1c**: (a) ^1H - ^1H coupling [6]; (b) ^1H - ^{15}N coupling [9]; (c) UV-visible

absorption [6,8]; and (d) infrared absorption [10].

As an extension of our earlier work on the synthesis of 2-substituted quinolines by the reaction of quinoline 1-oxide with active methylenes in the presence of acetic



anhydride [4,11], we sought to study the behavior of sulfones of the type, $\text{RSO}_2\text{CH}_2\text{Y}$, in the reaction. See Table 1 for characterization of quinaldyl sulfones **3-8** and Table 2 for their ^1H nmr data and tautomeric compositions.

All of the starting sulfones behaved as expected, with the exception of methylsulfonylacetone ($\text{R} = -\text{CH}_3$, $\text{Y} = -\text{COCH}_3$), which underwent spontaneous decylation during the course of the reaction to give the known compound quinaldyl methyl ketone (**2**) [12]. This result was not totally unexpected in view of our earlier finding that 2,4-pentanedione behaves in the same manner to afford 2-quinolyllactone [4].

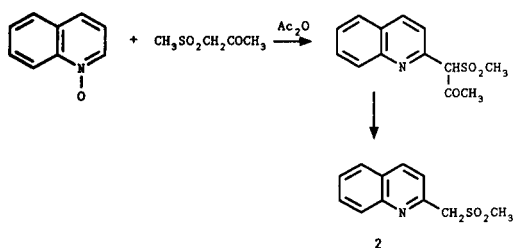
Table 1
Synthesis and Characterization of Quinaldyl Sulfones (3-8)

No.	R	Y	Yield	mp ($^{\circ}\text{C}$) (Recrystallization solvent)	Molecular Formula	Analyses				IR, ν (cm^{-1})
						C	H	N	S	
3	Me	SO_2Me	37	170-171 (ethanol)	$\text{C}_{12}\text{H}_{13}\text{NO}_4\text{S}_2$	48.15	4.38	4.68	21.42	1307, 1124 (SO_2)
						47.91	4.45	4.45	21.13	
4	Ph	SO_2Ph	74	201-202 (methanol)	$\text{C}_{22}\text{H}_{17}\text{NO}_4\text{S}_2$	62.40	4.02	3.31	15.13	1328, 1152 (SO_2)
						62.09	4.13	3.32	15.00	
5	Me	CO_2Et	61	101-102 (ethanol)	$\text{C}_{14}\text{H}_{15}\text{NO}_4\text{S}$	57.32	5.15	4.78	10.93	1743 (CO), 1314, 1124 (SO_2)
						57.12	4.89	4.49	10.99	
6	Ph	CO_2Me	83	130-132 (ethanol)	$\text{C}_{18}\text{H}_{15}\text{NO}_4\text{S}$	63.34	4.40	4.10	9.38	1746 (CO), 1321, 1148 (SO_2)
						62.91	4.59	4.02	9.71	
7	Me	CN	60	249-252 (toluene)	$\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_2\text{S}$	58.52	4.09	11.37	13.02	2179 (CN), 1286, 1117 (SO_2)
						58.85	4.34	11.12	13.13	
8			68	232-235	$\text{C}_{13}\text{H}_{11}\text{NO}_3\text{S}$	59.61	4.60	5.11	12.29	1644 (CO), 1384, 1134 (SO_2)
						59.75	4.24	5.36	12.27	

Table 2
¹H NMR Spectra and Tautomeric Composition of Quinaldyl Sulfones 2-8

Compound	Solvent [a]	δ (ppm)		Composition, %		Other Resonances (δ)
		C-H [b]	N-H...O	Form a	Form b	
2	A	4.61 [c]	-	100	0	2.95 (s, 3H), 7.4-8.4 (m, 6H)
3	B	5.64	-	100	0	3.54 (s, 6H), 7.3-8.2 (m, 6H)
4	B	5.66	-	100	0	7.3-8.3 (m, 16H)
5	A	5.38	-	100	0	1.28 (t, 3H, J = 7.8 Hz), 3.12 (s, 3H), 4.76 (q, 2H, J = 7.8 Hz), 7.4-8.3 (m, 6H)
6	A	5.62	14.70	65	35	3.65 (s, 1.3H), 3.82 (s, 0.7H), 7.4-8.3 (m, 11H)
7	A	-	11.80	0	100	3.22 (s, 3H), 7.3-8.0 (m, 6H)
8	A	-	15.25	0	100	3.02 (t, 2H, J = 7.2 Hz), 3.50 (t, J = 7.2 Hz), 7.4-8.3 (m, 6H)

[a] A, deuteriochloroform; B, dimethyl sulfoxide-d₆. [b] All methine resonances are singlets. [c] Singlet due to methylene group.



The tautomeric composition of these quinaldyl sulfones is very sensitive to the nature of R and Y as shown in Table 2. Several observations can be made: (1) the parent quinaldyl sulfone **2** shows no enamine content and furthermore, the addition of a second sulfonyl group as in **3** and **4** (and regardless of R) does not cause a detectable shift in the direction of the enamine; (2) if Y is an excellent electron-withdrawing group as in compounds **7** and **8** (-CN and -CO-, respectively), only the enamine tautomer is observed; and (3) when Y is an ester function as in **5** and **6** (R = methyl and phenyl, respectively), the enamine tautomer is favored, although the extent to which it is favored is very sensitive to the structure of Y. The last mentioned effect is presumably steric in nature, although no clear-cut pattern emerges when compared to similar effects observed by Greenhill and co-workers [10].

EXPERIMENTAL

Melting points (uncorrected) were determined using a Mel-Temp apparatus. Infrared spectra were recorded as potassium bromide pellets using a Nicolet 20 DXB FT spectrophotometer. The ¹H nmr spectra were obtained using a Varian XL-200 spectrometer and are reported as δ values (ppm) relative to tetramethylsilane as internal standard.

Starting Materials.

Methylsulfonylacetone, ethyl methylsulfonylacetate, and methylsulfonylacetone nitrile were obtained from Parrish Chemical Company, and methyl phenylsulfonylacetate was obtained from

Aldrich Chemical Company. Bis(methylsulfonyl)methane and bis(phenylsulfonyl)methane were prepared following the method reported by Ang and Lee [13]. A sample of 3-oxotetrahydrothiophene 1,1-dioxide was kindly provided by Professor John Belletire, University of Cincinnati [14].

Methyl Quinaldyl Sulfone (2).

Methylsulfonylacetone (4.08 g, 30.0 mmoles) dissolved in 15 ml of dry glyme was added dropwise under nitrogen to a stirred solution of 4.35 g (30.0 mmoles) of freshly distilled quinoline 1-oxide dissolved in 6.12 g (60.0 mmoles) of acetic anhydride. The reaction was moderately exothermic and the temperature of the reaction mixture was maintained at 20-25° by means of an ice bath. The mixture turned dark red almost immediately after addition was begun. After addition of the solution was complete (ca. 20 minutes), the mixture was allowed to stand at room temperature overnight. Methanol (5 ml) was added and the resulting mixture was heated under reflux for one hour under reflux in order to remove unreacted acetic anhydride. Upon cooling, white crystals formed which were filtered off and recrystallized from ethanol to yield 4.1 g (62%) of methyl quinaldyl sulfone (**2**) as white flakes, mp 180-181°, lit [12] mp 179-181°.

Quinaldyl Sulfones 5-8.

In like manner, quinaldyl sulfones, **5-8** were prepared from ethyl methylsulfonylacetate, methyl phenylsulfonylacetate, methylsulfonylacetone nitrile, and 3-oxotetrahydrothiophene 1,1-dioxide, respectively. See Table 1 for recrystallization solvents, melting points, and analytical data.

Quinaldylidene Disulfones 3 and 4.

Compounds **3** and **4** were synthesized from bis(methylsulfonyl)methane and bis(phenylsulfonyl)methane, respectively. Following the method of Douglass and Hunt [11], a solution of 30.0 mmoles of bis(sulfonyl)methane and 60.0 mmoles of dry triethylamine dissolved in 20 ml of dry glyme was added over a period of 30 minutes to a stirred and heated (ca. 65°) solution of 30.0 mmoles of quinoline 1-oxide dissolved in 60.0 mmoles of acetic anhydride. The mixture was heated at 60-70° for 4 days under nitrogen, after which time the product which had precipitated was isolated and recrystallized.

REFERENCES AND NOTES

- [1] A. L. Borror and A. F. Haeberer, *J. Org. Chem.*, **30**, 243 (1965).
- [2] M. Yamazaki, K. Hoda and M. Hamana, *Chem. Pharm. Bull.*, **18**, 908 (1970).
- [3] J. Kacens and O. Neilands, *Lat. PSR Zinat. Akad. Vestis, Khim. Ser.*, 606 (1970); *Chem. Abstr.*, **74**, 53473 (1971).
- [4] J. E. Douglass and H. D. Fortner, *J. Heterocyclic Chem.*, **10**, 115 (1973).
- [5] M. M. Yousef, S. Saeki and M. Hamana, *Chem. Pharm. Bull.*, **30**, 1680 (1982).
- [6] R. Mondelli and L. Merlini, *Tetrahedron*, **22**, 3253 (1966).
- [7] G. Fukata, C. O'Brien and R. A. M. O'Ferrall, *J. Chem. Soc., Perkin Trans. II*, 792 (1979).
- [8] B. Roussel, M. O. de Guerrero, P. Spegt and J. C. Galin, *J. Heterocyclic Chem.*, **19**, 785 (1982).
- [9] N. Mueller and V. V. Lapachev, *Monatsh. Chem.*, **118**, 1201 (1987).
- [10] J. V. Greenhill, H. Loghmani-Khonzani and D. J. Maitland, *Tetrahedron*, **44**, 3319 (1988).
- [11] J. E. Douglass and D. A. Hunt, *J. Org. Chem.*, **42**, 3974 (1977).
- [12] H. Hirano and K. Masuda, Japan Patent 19111 (1967); *Chem. Abstr.*, **69**, 10381 (1968).
- [13] K. P. Ang and T. W. S. Lee, *Aust. J. Chem.*, **30**, 521 (1977).
- [14] J. L. Belletire and E. G. Spletzer, *Synth. Commun.*, **13**, 269 (1983).