Synthesis of New Benzylpyridines as Potential Photochromic Compounds

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Photoinduced proton transfer systems such as 2-(2',4'-dinitrobenzyl)pyridine derivatives have been developed in an attempt to apply the compounds to variable optical transmission materials. However their fatigue resistance property is a limitation for these applications. New benzylpyridines have been synthesized and tested. 2-(2',4'-Diphenylsulfonybenzyl)pyridine was found to be photochromic in the crystalline state and in ethanolic solution (λ_{max}= 485 nm) upon UV flash photolysis.

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Introduction.

In recent years, the photoinduced proton transfer (PIPT) reaction occurring in 2-(2',4'-dinitrobenzyl)pyridine (α-DNBP) and in some of its derivatives has drawn much attention due to the potential applications of these compounds as optically bistable systems for optical data storage, in holography, and as optical switching devices[1].

For these applications, a lot of effort has been focused on the optimization of the efficiency of the photoreaction, the increase of the lifetime of the metastable form and a best understanding of the PIPT mechanism. The pathways leading to the phototautomers of α-DNBP and the structure of the different tautomers [1c] are presented in Figure 1.

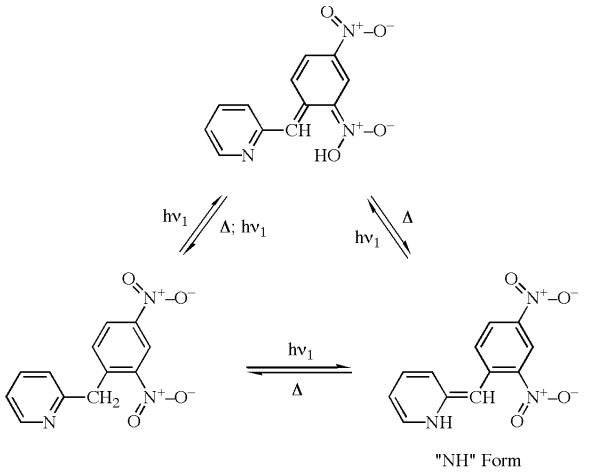
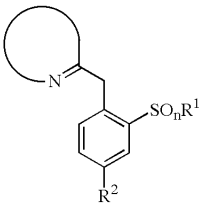


Figure 1

Photochromism takes place in solution [2], in polymer matrix [1a], and in the pure crystal [3].

Obviously, the ortho-nitro group, which acidifies the hydrogen atom of the methylene group, plays an important role in the photochemical reaction. Regarding literature data, this structural requirement appears to be a *sine qua non* condition to observe PIPT.

The major inconvenient property of these PIPT systems is the degradation [4] of the material after several cycles of coloration-fading. As part of our effort to bypass the fatigue resistance of such compounds, we decided to investigate the PIPT of new benzylpyridines substituted by electron withdrawing groups other than the *o*-nitro group. We first tried to establish if either a sulfoxide or a sulfone group could be used for that aim. Prompted by the literature, we attempted to design and synthesize compounds with the pyridine or pyridine-1-oxide ring (Figure 2).



Nitrogenated cycle = Pyridine, Pyridine-*N*-oxide
n = 1 or 2
R^1 = Et, Ph
R^2 = H, NO_2SO_2Ph

Figure 2

Synthesis.

Only one versatile synthetic route was employed for the preparation of the compounds used in this study and the experimental conditions were not optimized. 2-Lithio pyridine, derived from the reaction of 2-bromopyridine [5] with *n*-butyllithium, was coupled with substituted benzaldehydes **1**-**4** to give expected 2-(α-hydroxybenzyl)-pyridines **5**-**8** in moderate to good yield. In the next step, treatment of alcohols **5**-**8** with thionyl chloride provided chloromethylene derivatives as determined by their ^{1}H-NMR spectrum. Then, reduction of these intermediates with Zn powder in acetic acid afforded 2-benzylpyridines **9**-**12** [6] (Scheme I, Table I).

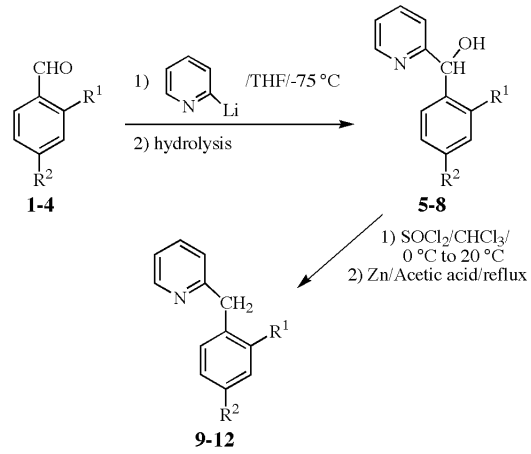
Finally, sulfoxide **13** was prepared from the corresponding thioether **9** by selective oxidation with *m*-chloroperoxybenzoic acid (*m*-CPBA) in chloroform and the sulfones **14**-**17** were provided using either the same methodology or by treating the thioether with an excess of hydrogen peroxide in acetic acid (Scheme II, Table II).

Table I

Synthesis of 2-benzylpyridines

R^1	R^2	Product	Yield (%)	Product	Yield (%)
SPh	H	**5**	95	**9**	92
SO_2Ph	H	**6**	40	**10**	90
SEt	H	**7**	88	**11**	85
SPh	SPh	**8**	96	**12**	60

Scheme I



Scheme II

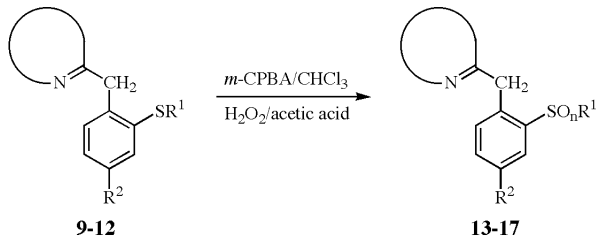


Table II

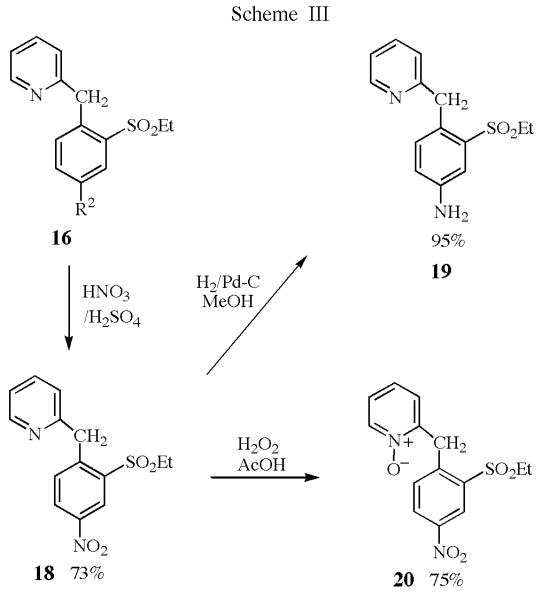
Oxidation of thioethers into sulfoxides or sulfones groups

Product	Heterocycle	n	R^1	R^2	Yield (%)
13	Pyridine	1	Ph	H	90
14	Pyridine-1-oxide	2	Ph	H	57
15	Pyridine-1-oxide [a]	2	Ph	SO_2Ph	31
16	Pyridine	2	Et	H	80
17	Pyridine	2	Ph	SO_2Ph	46

[a] Products **15** and **17** were isolated from the same reactions.

In view of tracking the impact of a nitro substituent in such structure, the nitration of compound **16**, at the 4' position has been accomplished [7]. Derivatives **19** and **20** were obtained from **18**, by hydrogenation on Pd/C and by oxidation with hydrogen peroxide in acetic acid, respectively (Scheme III).

Scheme III



Photochromic Properties.

We observed that only crystals of 2-(2',4'-diphenylsulfonybenzyl)pyridine **17**, grown by slow evaporation of an ethanolic solution in the dark, were photochromic. A purple color is developed under sunlight irradiation and fading occured after several hours in the dark.

According to earlier reports, the PIPT process has been found to be strongly dependent on the crystal packing [8]. Thus, we tried to obtain different polymorphs of the new molecules under different crystallisation conditions, but the resulting crystals were still photoinert.

The UV absorption spectrum of the unexposed 2-(2',4'-diphenylsulfonybenzyl)pyridine **17** is quite similar to those of (α-DNBP). UV flash photolysis of its ethanolic solution ($2.5\ 10^{-5}$ *M*) gives rise to photoinduced absorption in the visible region (λ_{max}= 485 nm, colorability A_0= 0.035) [9]. The rate constant for the reverse decoloration of the metastable form is about 0.27 s^{-1} (Figure 3).

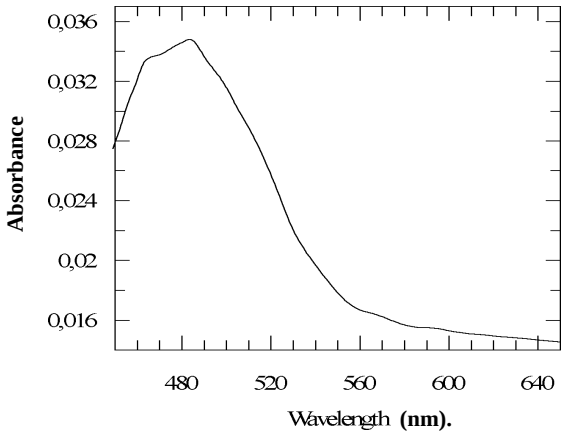


Figure 3

We have assigned this photogenerated metastable form to the enamine "NH" form . The main support for this assignment came from the similarity of its visible absorption with the spectrum of the molecule **21** (λ_{max}= 485 nm in ethanolic solution) usually called "*N*-methyl enamine" in the literature [1c,2c], which has an isoelectronic structure to the "NH" quinoid form (Figure 4). The presence of another short-lived species has not been excluded but has not been demonstrated yet.

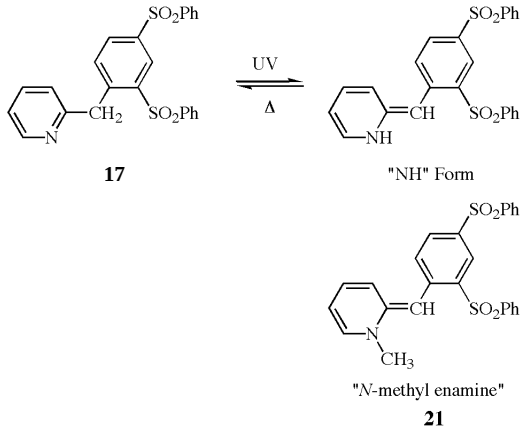


Figure 4

These preliminary results demonstrate that, contrarily to the opinion expressed previously, the presence of a nitro group in the *ortho* position of the benzyl group is not a necessary requirement to observe PIPT.

Conclusion.

New benzylpyridines, substituted either by a sulfoxide or sulfone group in *ortho* position to the benzyl hydrogen, have been synthesized starting from 2-lithiopyridine. It has been observed that 2-(2',4'-diphenylsulfonyl)pyridine **17** underwent a reversible photoinduced proton transfer reaction in the crystalline phase as well as in ethanolic solution at ambient temperature. The metastable coloured form was attribued to a "NH" quinoid tautomer.

It has also been concluded that contrarily to what was generally assumed, the presence of a nitro group at the *ortho* position of the benzyl group is not a necessary condition to provide proton transfer upon UV irradiation.

EXPERIMENTAL

Melting points were determined on a Buchi 510 apparatus in capillary tubes and are uncorrected. The ^{1}H nmr and ^{13}C nmr spectra were recorded in deuteriochloroform on a Brüker AM 250 spectrometer (250 and 62.5 MHz, respectively) using tetramethylsilane as the internal standard. Column liquid chromatography were carried out on silica gel Merck 60 (70-230 mesh). The infrared spectral data (ir) were recorded on a Avatar 320 spectrometer and were performed in potassium bromide pellets. The electron impact mass spectra (ms) were obtained on a Shimadzu QP-5000 spectrometer. Microanalyses were performed by the Microanalytical Centre of the University of Aix-Marseille III.

Photoirradiation was carried out by using a xenon lamp (150 W) or a mercury lamp (500 W). UV flash photolysis was performed with a xenon lamp (60 J) by the Institute of Topology and Dynamics of Systems (ITODYS, Paris-Jussieu)

Solvents (SDS Company, France) were used without further purification and were dried over sieves if necessary. Tetrahydrofuran was distilled under nitrogen from sodium benzophenone ketyl and used immediately. Metalation were performed under an argon atmosphere and reagents were handled with syringes through septa.

The substituted benzaldehydes **1**-**4** were prepared according to modified literature procedures [10-13].

2-(Phenylthio)benzaldehyde (**1**).

To a stirred solution of benzenethiol (29.4 g, 0.27 mole) and anhydride sodium carbonate (37.3 g) in dry DMF (80 ml), at 80-90°, was added slowly 2-chlorobenzaldehyde (30 g, 0.213 mole) during 10 minutes. The resulting mixture was stirred at the same temperature for 3 hours. After cooling, the reaction mixture was poured into 200 ml of water and extracted with ether. The extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated to afford an oil that crystallized by adding hexane. Recrystallisation from hexane gave colorless prisms (34.2 g, 75%), mp 50° (lit. mp 47°-48°); ^{1}H nmr (deuteriochloroform): δ 7.03 (dd, 1H, J = 1.0, 7.8 Hz), 7.18-7.45 (m, 7H), 7.82 (dd, 1H, J = 1.8, 7.4 Hz), 10.32 (s, 1H, CHO).

Anal. Calcd.. for $C_{13}H_{10}OS$: C, 72.87; H, 4.70. Found: C, 72.83; H, 4.62.

2-(Phenylsulfonyl)benzaldehyde (**2**).

To a solution of 2-(phenylthio)benzaldehyde **1** (2.67 g, 12.4 mmoles) in acetic anhydride (25 ml) was added, slowly, concentrated sulphuric acid (0.1 ml). After being stirred for 4 hours, the mixture was poured into 100 ml of cold water, neutralized by adding solid sodium carbonate and extracted with ethyl acetate. The extracts were dried over magnesium sulfate and concentrated *in vacuo* to afford 2-(phenylthio)benzylidene diacetate (3 g) as a oil.

To a solution of this crude product (3 g, 9.5 mmoles) in glacial acetic acid (100 ml) was added, slowly at 0° with stirring, a solution of hydrogen peroxide (36%, 15 ml). After 24 hours at room temperature, the reaction mixture was poured into cold water (100 ml). The resulting precipitate was collected by filtration and heated during 30 minutes under reflux with diluted sulfuric acid (6 *N*, 50 ml) and acetic acid (40 ml). The mixture was poured into water (100 ml) and cooled by a ice bath. The precipitate was collected by filtration and dried. The product obtained was recrystallized from toluene-pentane to afford 2-(phenylsulfonyl)benzaldehyde **2** (1,75 g, 75%), mp 91°; ^{1}H nmr (deuteriochloroform): δ 7.42-7.64 (m, 3H), 7.65-7.99 (m, 2H), 7.84 (dd, 2H, J = 1.4, 8.3 Hz), 7.97 (dd, 1H, J = 1.8, 7.1 Hz), 8.36 (dd, 1H, J = 1.9, 8.9 Hz), 10.79 (s, 1H, CHO).

Anal. Calcd. for $C_{13}H_{10}O_3S$: C, 63.40; H, 4.09. Found: C, 63.38; H, 3.96.

2-(Ethylthio)benzaldehyde (**3**).

This was prepared in the same manner as described for the 2-(phenylthio)benzaldehyde **1**, starting from ethanethiol (16.7 g, 0.27 mole). The reaction was conducted at 100° for 24 hours. The crude material was purified by vacuum distillation to afford colourless liquid of 2-(ethylthio)benzaldehyde in 80% yield

(35.8 g, 0.216 mole), bp 150° (15 mmHg); ^{1}H nmr (deuteriochloroform): δ 1.41 (t, 3H, J = 7.4 Hz), 3.03 (q, 2H, J = 7.4), 7.31-7.60 (m, 3H), 7.88 (dd, 1H, J = 1.5, 7.6 Hz), 10.41 (s, 1H, CHO).

Anal. Calcd. for $C_9H_{10}OS$: C, 65.02; H, 6.06. Found: C, 65.14; H, 6.10.

2,4-Di(phenylthio)benzaldehyde (**4**).

A solution of commercial 2,4-dichlorobenzaldehyde (50 g, 0.285 mole), benzenethiol (78.7 g, 0.714 mole) and NaOH (28.6 g, 0.715 mole) in ethanol (200 ml) was refluxed for 16 hours with stirring. After evaporation of the solvent *in vacuo*, the residue was triturated with dichloromethane (200 ml) and H_2O (100 ml). The aqueous layer was extracted with dichloromethane (50 ml). The extract was dried over magnesium sulfate and removed on a rotary evaporation. The product obtained was recrystallized from ethanol-hexane to afford 2,4-di(phenylthio)benzaldehyde **4** (90.9 g, 99%) as a white solid, mp 91°; ^{1}H nmr (deuteriochloroform): δ 6.54 (d, 1H, J = 1.7 Hz), 6.94 (dd, 1H, J = 1.8, 8.1 Hz), 7.20-7.35 (m, 10H), 7.62 (d, 1H, J = 8.1 Hz), 10.15 (s, 1H, CHO).

Anal. Calcd. for $C_{19}H_{14}OS_2$: C, 70.77; H, 4.38. Found: C, 70.63 H, 4.31.

General Procedure for the Synthesis of Substituted 2-(α-Hydroxybenzyl)pyridines **5-8**.

To a solution of 2-lithiopyridine (12.6 mmoles) prepared by bromo-lithium exchange reaction [5], in THF (75 ml), at –78° under N_2 atmosphere, was slowly added a solution of substituted benzaldehydes (13.8 mmoles) in THF (50 ml), with the temperature of the reaction mixture being maintained at –78°. The stirring was continued for 1 hour at –78° and hydrolysis was then carried out using a mixture of 35% aqueous hydrochloric acid (4 ml), ethanol (4 ml) and THF (16 ml). The solution was gently warmed to room temperature, made slightly basic with saturated sodium hydrogenocarbonate solution and evaporated nearly to dryness under vacuum. The residue was extracted with dichloromethane (4 x 40 ml). The organic extract was dried over magnesium sulfate and evaporated to dryness.

2-[α-Hydroxy-2-(phenylthio)benzyl]pyridine (**5**).

This compound was prepared employing the general procedure described above, starting from 2-(phenylthio)benzaldehyde **1** (13.8 mmoles, 2.95 g). The crude product was purified by column chromatography (silica gel, eluted by pentane-ether 1:1) to provide 3.51 g (95% overall) of **5** as oil; ^{1}H nmr (deuteriochloroform): δ 5.68 (s, 1H, OH), 6.41 (s, 1H, CH), 7.15-7.25 (m, 9H), 7.28 (dd, 1H, J = 1.4, 7.6 Hz), 7.36-7.42 (m, 2H), 8.45 (d, 1H, J = 4.8 Hz).

Anal. Calcd. for $C_{18}H_{15}NOS$: C, 73.69; H, 5.15; N, 4.77. Found: C, 73.81; H, 5.10, N, 4.85.

2-[α-Hydroxy-2-(ph'enylsulfonyl)benzyl]pyridine (**6**).

This compound was prepared employing the general procedure described above, starting from 2-(phenylsulfonyl) benzaldehyde **2** (3.39 g). The crude product was purified by column chromatography (silica gel, eluted by dichloromethane-ethyl acetate, gradient 1:1) and recrystallized from benzene-pentane to provide 1.64 g (40% overall) of **6** as white solid, mp 171°; ^{1}H nmr (deuteriochloroform): δ 5.65 (s, 1H, OH), 6.61 (s, 1H, CH), 7.13 (t, 1H, J = 6.6 Hz), 7.21 (d, 1H, J = 7.2 Hz), 7.28 (dd, 1H, J = 1.4, 7.6 Hz), 7.35-7.56 (m, 6H, m), 7.87 (dd, 2H, J = 1.3, 7.0 Hz), 8.15 (dd, 1H, J = 1.5, 7.9 Hz), 8.45 (dd, 1H, J = 1.0, 5.0 Hz).

Anal. Calcd. for $C_{18}H_{15}NO_3S$: C, 64.44; H, 4.65; N, 4.30. Found: C, 64.32; H, 4.56; N, 4.20.

2-[α-Hydroxy-2-(ethylthio)benzyl]pyridine (**7**).

This compound was prepared employing the general procedure described above, and starting from 2-(ethylthio)benzaldehyde **3** (13.8 mmoles, 2.29 g). The crude product was purified by column chromatography (silica gel, eluted by dichloromethane-ethyl acetate 5:2, gradient) to provide 2.72 g (88 % overall) of **7** as yellow solid, mp 89°; ^{1}H nmr (deuteriochloroform): δ 1.15 (t, 3H, J = 7.4 Hz, CH_3), 2.89 (q, 2H, J = 7.4 Hz, CH_2), 5.39 (s, 1H, OH), 6.33 (s, 1H, CH), 7.05-7.23 (m, 5H), 7.33 (dd, 1H, J = 1.7, 7.7 Hz), 7.51 (dt, 1H, J = 1.7, 7.9 Hz), 8.47 (d, 1H, J = 4.7 Hz).

Anal. Calcd. for $C_{14}H_{15}NOS$: C, 68.54; H, 6.16; N, 5.71 Found: C, 68.55; H, 6.27; N, 5.59.

2-[α-Hydroxy-2,4-di(phenylthio)benzyl]pyridine (**8**).

This compound was prepared by a modification of the general procedure described above, starting from 2,4-di(phenylthio)benzaldehyde **4** (13.8 mmoles, 4.44 g). After complete addition of the aldehyde, the reaction mixture was allowed to warm to 0° for 1 hour before quenching. The crude product was purified by column chromatography (silica gel, eluted by dichloromethane-ether 6:1, gradient) to provide 4.86 g (96 % overall) of **8** as oil; ^{1}H nmr (deuteriochloroform): δ 5.39 (s, 1H, OH), 6.30 (s, 1H, CH), 7.05-7.27 (m, 15H), 7.52 (dt, 1H, J = 1.8, 7.8 Hz), 8.54 (d, 1H, J= 5.0 Hz).

Anal. Calcd. for $C_{24}H_{19}NOS_2$: C, 71.79; H, 4.77; N, 3.49. Found: C, 71.70; H, 4.77; N, 3.45.

General Procedure for Reduction of Alcohols to Substituted 2-(Benzyl)pyridines **9-12** [6].

To a stirred, cooled solution (5°) of substituted 2-(α-hydroxybenzyl)pyridine **5-8** (12 mmoles) in chloroform (30 ml) was added dropwise thionyl chloride (2.2 g, 18 mmoles) at such a rate that the temperature did not exceed 20°. The red mixture was then stirred for 3 hours at ambient temperature. After cooling at 5°, water (15 ml) was poured slowly into the reaction mixture and adjusted to pH 8 with aqueous sodium carbonate solution. The layers were separated and the aqueous layer extracted twice with dichloromethane (2 x 10 ml). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo* to give 2-(α-chlorobenzyl)pyridine.

This product was taken on without further purification, dissolved in glacial acetic acid (30 ml), and refluxed with stirring. Zinc dust (3.9 g, 60 mmoles) was added over the period of one hour. The heating was maintained 6 hours, then the insoluble material was filtered and the acetic acid removed *in vacuo*. The residue was treated with a mixture of dichloromethane (20 ml) and water (20 ml). The resulting solution was adjusted to pH 8 with potassium carbonate. The layers were separated and the aqueous layer extracted twice with dichloromethane (2 x 10 ml). The combined organic layers were washed with brine (10 ml), dried over magnesium sulfate, filtered, and concentrated *in vacuo* to give the reduced product **9-12**.

2-[2'-(Phenylthio)benzyl]pyridine (**9**).

The title product was analogously prepared from **5** (3.52 g). Purification by chromatography (silica gel, eluted by pentane-ether 1:1) afforded 3.06 g (11 mmoles, 92%) of **9** as an oil; ^{1}H nmr (deuteriochloroform): δ 4.35 (s, 2H, CH_2), 6.97-7.07 (m,

2H), 7.09-7.38 (m, 9H), 7.45 (dt, 1H, J = 1.8, 7.6 Hz), 8.52 (d, 1H, J = 4.8 Hz).

Anal. Calcd for $C_{18}H_{15}NS$: C, 77.94; H, 5.45; N, 5.05 Found: C, 77.87; H, 5.38; N, 4.97.

2-[2'-(Phenylsulfonyl)benzyl]pyridine (**10**).

The title product was analogously prepared from **6** (3.90 g). Purification by chromatography (silica gel, eluted by ether) afforded 3.34 g (10.8 mmoles, 90%) of **10** as a white solid, mp 99°; ^{1}H nmr (deuteriochloroform): δ 4.40 (s, 2H, CH_2), 6.72 (d, 1H, J = 7.8 Hz), 6.98 (dd, 1H, J = 5.0, 6.7 Hz), 7.16 (dd, 1H, J = 1.0, 7.6 Hz), 7.28-7.48 (m, 6H), 7.74 (dd, 2H, J = 1.2, 7 Hz), 8.20 (dd, 1H, J = 1.7, 7.6 Hz), 8.37 (dd, 1H, J = 1.0, 5.0 Hz).

Anal. Calcd. for $C_{18}H_{15}NO_2S$: C, 69.88; H, 4.89 N, 4.53. Found: C, 69.75; H, 4.90; N, 4.49.

2-[2'-(Ethylthio)benzyl]pyridine (**11**).

The title product was analogously prepared from **7** (2.94 g). Purification by chromatography (silica gel, eluted by dichloromethane) afforded 2.34 g (10.2 mmoles, 85%) of **11** as a colorless oil; ^{1}H nmr (deuteriochloroform): δ 1.19 (t, 3H, J = 7.4 Hz, CH_3), 2.82 (q, 2H, J = 7.4 Hz, SCH_2), 4.26 (s, 2H, CH_2), 6.93-7.28 (m, 6H), 7.46 (dt, 1H, J = 1.7, 8.0 Hz), 8.49 (d, 1H, J = 5 Hz).

Anal. Calcd. for $C_{14}H_{15}NS$: C, 73.32; H, 6.59; N, 6.11. Found: C, 73.27; H, 6.48; N, 6.23.

2-[2',4'-Di(phenylthio)benzyl]pyridine (**12**).

The title product was analogously prepared from **8** (4.82 g). Purification by chromatography (silica gel, eluted by dichloromethane) afforded 2.77 g (7.2 mmoles, 60%) of **12** as a yellow oil; ^{1}H nmr (deuteriochloroform): δ 4.25 (s, 2H, CH_2), 6.90-7.26 (m, 15H), 7.48 (dt, 1H, J = 1.8, 7.8 Hz), 8.48 (dd, 1H, J = 1.0, 5.0 Hz).

Anal. Calcd. for $C_{24}H_{19}NS_2$: C, 74.77; H, 4.97; N, 3.63 Found: C, 74.70; H, 4.89, N, 3.52.

General Procedure to Oxidize Sulfides to Sulfoxides and Sulfones.

Method A.

To a stirred solution of sulfide (20 mmoles) in chloroform (100 ml) at 0° was added a solution of *m*-chloroperoxybenzoic acid (1.1, 2.1, or 4.1 equivalents) in chloroform (50 ml). The mixture was maintained at T° for t hours. At ambient temperature, the resulting solid was separated by filtration, and the filtrate poured into water (30 ml). The resulting solution was made slightly basic with sodium carbonate. The layers were separated and the aqueous layer extracted twice with dichloromethane (2 x 15 ml). The combined organic layers were dried over magnesium sulfate, filtered, and evaporated under reduce pressure to afford crude sulfoxide, or sulfone.

Method B.

To a solution of sulfide (20 mmoles) in acetic acid (100 ml) was added dropwise a solution of 35% hydrogen peroxide (100 ml). The mixture was warmed at T° for t hours. After cooling, the solution was reduced *in vacuo* and time to time diluted with water. The concentrated solution was adjusted to pH 8 with sodium hydrogenocarbonate, and extracted with dichloro methane. The combined organic extracts were dried over magnesium sulfate and concentratred *in vacuo* to provide crude sulfone.

2-[2'-(Phenylsulfinyl)benzyl]pyridine (**13**).

This compound was prepared by oxidation of **9** (5.55 g) according to the method A with *m*-CPBA (3.80 g, 1.1 eq.), T = 20°, and t = 24 hours. Purification by column chromatography (silica gel, eluted by ether) provided **13** (5.28 g, 18 mmoles, 90%) as a solid, mp 59°; ^{1}H nmr (deuteriochloroform): δ 4.26 (s, 2H, CH_2), 6.80 (d, 1H, J = 8 Hz), 7.00 (dd, 1H, J = 5.0, 6.7 Hz), 7.14 (dd, 1H, J = 2.2, 7.4 Hz), 7.20-7.50 (m, 8H), 7.86 (dd, 1H, J = 2.3, 7.0 Hz), 8.42 (dd, 1H, J = 1.0, 5.0 Hz).

Anal. Calcd. for $C_{18}H_{15}NOS$: C, 73.69; H, 5.15; N, 4.77. Found: C, 73.58; H, 5.26; N, 4.51.

2-[2'-(Phenylsulfonyl)benzyl]pyridine-1-oxide (**14**).

This compound was prepared by oxidation of **9** (6.19 g) according to the method B, T = 100°, and t = 0.75 hours. The crude product was recrystallised from benzene-hexane to provide **14** (3.71 g, 11 mmoles, 57%) as a solid, mp 161° ; ^{1}H nmr (deuteriochloroform): δ 4.48 (s, 2H, CH_2), 6.53 (dd, 1H, J = 2.0, 7.8 Hz), 7.01 (t, 1H, J = 7 Hz), 7.06 (dt, 1H, J = 2.0, 7.9 Hz), 7.20-7.54 (m, 6H), 7.79 (dd, 2H, J = 1.1, 7 Hz), 8.19 (d, 1H, J = 6.2 Hz), 8.27 (dd, 1H, J = 2.0, 7.6 Hz).

Anal. Calcd. for $C_{18}H_{15}NO_3S$: C, 66.44; H, 4.65; N, 4.30. Found: C, 66.33; H, 4.86; N, 4.09.

2-[2',4'-Di(phenylsulfonyl)benzyl]pyridine-1-oxide (**15**).

This compound was prepared by oxidation of **12** (7.71 g) according to the method B, T= 20°, and t= 72 h. Purification by chromatography (silica gel, eluted by ethyl acetate-ethanol, gradient) afforded 2.88 g (6.2 mmoles, 31%) of **15** as a solid, mp 208°; ^{1}H nmr (deuteriochloroform): δ 4.45 (s, 2H, CH_2), 6.52 (d, 1H, J = 7.8 Hz), 6.91 (t, 1H, J = 7.8 Hz), 7.02 (t, 1H, J = 7.4 Hz), 7.27-7.54 (m, 7H), 7.70 (dd, 2H, J = 1.5, 6.9 Hz), 7.85 (dd, 2H, J = 1.5, 6.9 Hz), 7.95 (dd, 1H, J = 2, 8 Hz), 8.09 (d, 1H, J = 6.3 Hz), 8.71 (d, 1H, J = 2 Hz).

Anal. Calcd. for $C_{24}H_{19}NO_5S_2$: C, 61.92; H, 4.11; N, 3.01. Found: C, 61.93; H, 4.23; N, 2.97.

2-[2'-(Ethylsulfonyl)benzyl]pyridine (**16**).

This was prepared by oxidation of **11** (4.59 g) according to the method B, T = 20°, and t = 12 hours. Purification by column chromatography (silica gel, eluted by dichloromethane-ether 5:2) provided **16** (4.18 g, 16 mmoles, 80%) as an oil; ^{1}H nmr (deuteriochloroform): δ 1.17 (t, 3H, J = 7.4 Hz, CH_3), 3.09 (q, 2H, J = 7.4 Hz, SO_2CH_2), 4.60 (s, 2H, CH_2), 7.08 (dd, 1H, J = 5.0, 6.6 Hz), 7.18 (d, 1H, J = 8.8 Hz), 7.29 (d, 1H, J = 8.5 Hz), 7.36 (d, 1H, J = 7.7 Hz), 7.48 (dt, 1H, J = 1.4, 7.5 Hz), 7.56 (dt, 1H, J = 1.8, 7.7 Hz), 7.99 (dd, 1H, J = 1.3, 7.9 Hz), 8.44 (d, 1H, J = 4.6 Hz).

Anal. Calcd. for $C_{14}H_{15}NO_2S$: C, 64.34; H, 5.79; N, 5.36. Found: C, 64.41; H, 5.82; N, 5.40.

2-[2',4'-Di(phenylsulfonyl)benzyl]pyridine (**17**).

The title product was isolated from the reaction leading to **15**. Purification by column chromatography (silica gel, eluted by ether-ethyl acetate, gradient) provided **17** (4.13 g, 9.2 mmoles, 46%) as a solid, mp 150°; ^{1}H nmr (deuteriochloroform): δ 4.39 (s, 2H, CH_2), 6.77 (d, 1H, J = 7.8 Hz), 7.00 (dd, 1H, J = 5.0, 6.6 Hz), 7.31-7.56 (m, 8H), 7.74 (dd, 2H, J = 1.5, 7.2 Hz), 7.88 (dd, 2H, J = 1.6, 6.9 Hz), 7.95 (dd, 1H, J = 2.0, 8.1 Hz), 8.32 (m, 1H), 8.74 (d, 1H, J = 2 Hz).

Anal. Calcd. for $C_{24}H_{19}NO_4S_2$: C, 64.12; H, 4.26; N, 3.12. Found: C, 64.15; H, 4.36; N, 3.07.

2-[2'-(Ethylsulfonyl)-4'-nitrobenzyl]pyridine (**18**).

This product was prepared according to a modified procedure reported in the literature for the synthesis of 2,4-dinitrobenzylpyridine [7]. To a cooled (-5°) and well-stirred concentrated sulfuric acid (96%) (12 ml) was added gradually **16** (4.00 g, 15.3 mmoles). Then red fuming nitric acid (density = 1.5 g / ml, 0.7 ml, 16.8 mmoles) was added dropwise over a period of about 10 minutes. After complete addition, the mixture was stirred at 100° for 0.5 hours, and then poured onto about 100 g of ice. The resulting solution was basified (pH 10) by adding a saturated aqueous solution of sodium hydroxide, and extracted with ether (3 x 50 ml). The combined ethereal extracts were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by recrystallisation from benzene-cyclohexane or from ethanol to afford 3.51 g (11.4 mmoles, 75% overall) of **18** as white needless, mp 79°; ^{1}H nmr (deuteriochloroform): δ 1.18 (t, 3H, J = 7.4 Hz, CH_3), 3.21 (q, 2H, J = 7.4 Hz, SO_2CH_2), 4.67 (s, 2H, CH_2 benzylic), 7.10 (dd, 1H, J = 4.9, 7.4 Hz, H_5), 7.27 (d, 1H, J = 7.7 Hz, H_3), 7.53 (d, 1H, J = 8.5 Hz, $H_{6'}$), 7.60 (dt, 1H, J = 1.8, 7.9 Hz, H_4), 8.28 (dd, 1H, J = 2.5, 8.45 Hz, $H_{5'}$), 8.38 (d, 1H, J = 4.1 Hz, H_6), 8.81 (d, 1H, J = 2.5 Hz, $H_{3'}$). ^{13}C nmr (deuteriochloroform): 7.2; 40.5; 50.8; 122.2; 124.0; 126.1; 127.8; 134.6; 137.2; 138.8; 146.5; 147.2; 149.7;,158.2

Anal. Calcd. for $C_{14}H_{14}N_2O_4S$: C, 54.89; H, 4.61; N, 9.14 Found: C, 54.89; H, 4.64; N, 9.15.

The structure of **18** was confirmed by RX diffraction [14].

2-[4'-Amino-2'-(ethylsulfonyl)benzyl]pyridine (**19**).

A stirred solution of **18** (2.3 g, 7.5 mmoles) in absolute methanol (20 ml) was hydrogenated over 10% Pd-C (0.5 g) at room temperature under atmospheric pressure of H_2 for 2 hours. After removal of the catalyst by filtration on celite, the solution was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, eluted by dichloromethane-ether 1:1) to give **19** (1.97 g, 7.1 mmoles, 95%) as a white solid crystal, mp 107°; ^{1}H nmr (deuteriochloroform): δ 1.15 (t, 3H, J = 7.4 Hz, CH_3), 3.04 (q, 2H, J = 7.4 Hz, SO_2CH_2), 3.89 (s, 2H, NH_2), 4.42 (s, 2H, CH_2), 6.73 (dd, 1H, J = 2.5, 8.2 Hz), 7.03 (m, 2H), 7.11 (d, 1H, J = 7.8 Hz), 7.25 (d, 1H, J = 2.5 Hz), 7.50 (dt, 1H, J = 1.8, 7.7 Hz), 8.42 (d, 1H, J = 4.8 Hz).

Anal. Calcd. for $C_{14}H_{16}N_2O_2S$: C, 60.85; H, 5.84; N, 10.14. Found: C, 60.87; H, 5.84; N, 10.10.

2-[2'-(Ethylsulfonyl)-4'-nitrobenzyl]pyridine-1-oxide (**20**).

This compound was prepared by oxidation of 18 (6.12 g) according to the method B, T = 70°,and t = 8 hours. Recrystallisation from ethanol of the crude product give **20** (4.83 g, 15 mmoles, 75%) as a white solid, mp 188°; ^{1}H nmr (deuteriochloroform): δ 1.17 (t, 3H, J = 7.4 Hz, CH_3), 3.53 (q, 2H, J = 7.4 Hz, SO_2CH_2), 4.65 (s, 2H, CH_2), 7.15-7.35 (m, 3H), 7.41 (d, 1H, J = 1.0, 6.8 Hz), 8.17 (dd, 1H, J = 1, 5 Hz), 8.24 (dd, 1H, J = 2.4, 8.4 Hz), 8.86 (d, 1H, J = 2.4 Hz).

Anal. Calcd. for $C_{14}H_{14}N_2O_5S$: C, 52.17; H, 4.38; N, 8.69 Found: C, 52.16; H, 4.55; N, 8.52.

Synthesis of the "*N*-Methylenamine" (**21**).

This compound was prepared according to published procedure [2c] from the product **17** (100 mg, 0.7 mmole). After purification, the title product was obtained in 72% yield (222 mg, 0.48 mmole) as an orange-red solid, mp 206°; ^{1}H nmr (deuteriochloroform): δ 3.11 (s, 3H), 5.20 (s, 1H), 5.66 (t, 1H, J = 6.6 Hz), 6.53 (t, 1H, J = 8 Hz), 6.81 (d, 1H, J = 6.7 Hz), 6.92 (d, 1H, J = 9.4 Hz), 7.27-7.56 (m, 7H), 7.66 (dd, 1H, J = 2.0, 8.6 Hz), 7.72 (dd, 2H, J = 2.0, 8.5 Hz), 7.89 (dd, 2H, J = 2.0, 8.0 Hz), 8.62 (d, 1H, J = 2 Hz).

Anal. Calcd. for $C_{25}H_{21}NO_4S_2$: C, 64.77; H, 4.57; N, 3.02. Found: C, 64.61; H, 4.53; N, 3.00.

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