HETEROCYCLES FROM YLIDES. PART XI. SYNTHESIS OF 2-SUBSTITUTED QUINOLINE DERIVATIVES

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Abstract – The reaction of 2-N-phenylsulfonylaminobenzaldehyde (1) with stabilized alkylidene phosphoranes (2) gives, through a Wittig condensation followed by reduction of intermediate alkenes and cyclization with PPA, quinoline derivatives (5).

INTRODUCTION
A part of our researches deals with the synthesis of heterocyclic systems from ylides. Some our recent papers describe the preparation of 1-phenylsulfonyl-2,3-disubstituted-2,3-dihydroindoles and 1-phenylsulfonyl-3-hydroxy-2,3-dihydroindoles starting from sulfonium ylides. Taking into account the easy availability of 2-N-phenylsulfonylaminobenzaldehyde (1), in our opinion stable synthetic equivalent of 2-aminobenzaldehyde, we report a new method of preparation of quinoline derivatives according to a Friedländer-type synthesis.

RESULTS AND DISCUSSION
The treatment of 1 with preformed stabilized phosphonium ylides (2), in acetonitrile solution, leads to the corresponding (E) alkenes (3) according to a typical Wittig reaction. The selective catalytic reduction of C-C double bond gives 4 which, treated with PPA at 120 °C for 2-4 h in presence of air, cyclize to quinoline system. The loss of phenylsulfonyl group and the final oxidation allow to gain aromaticity. (Scheme 1).
Analytical and spectroscopic data of all the new compounds isolated are consistent with the assigned structure.

**EXPERIMENTAL**

Melting points were determined on a Büchi B-540 apparatus and are uncorrected. Elemental analyses were performed by the Microanalytical Laboratory of the Department. $^1$H NMR spectra were recorded in CDCl$_3$ solution using a Bruker AMX 300 MHz spectrometer, and chemical shifts are given in ppm relative to TMS. IR spectroscopy was performed using a Jasco FT-IR 4100 spectrometer.

2-N-phenylsulfonylaminobenzaldehyde (1) was prepared according to the reported procedure.$^3$ Ylides 2a, 2b, 2c, 2d are commercially available.

**Preparation of alkenes (3a-d): general procedure.**

To a solution of ylide 2a-d (6.0 mmol) in MeCN (20 mL), a solution of (1) (3.0 mmol) in the same solvent was added dropwise. The mixture was stirred 16 h at rt and then heated at 50 °C for 4 h. The solvent was evaporated off and the residue taken up with AcOEt (20 mL) and HCl 5% solution (10 mL) to pH 6. The organic layer was separated, dried (Na$_2$SO$_4$), filtered and the solvent was evaporated off. The residue was purified by column chromatography (SiO$_2$ – toluene/AcOEt : 80/20). In this way were prepared.

N-[2-(3-Oxo-but-1-enyl)phenyl]benzenesulfonamide (3a): Solid, mp 182-184 °C (toluene). Yield 85%.

$^1$H NMR δ : 2.35 (s, 3H, CH$_3$); 6.45 (d, 1H, $J$ = 15.2 Hz, H-2); 6.55 (d, 1H, $J$ = 15.2 Hz, H-1); 7.00 (s, 1H,
NH); 7.25-7.80 (m, 9H, Ar). IR (nujol, cm⁻¹): 3280 (NH). Anal. Calcd for C₁₆H₁₅NO₃S: C, 63.77; H, 5.02; N, 4.65. Found: C, 63.65; H, 4.95; N, 4.75.

N-[2-(3-Oxo-3-phenylprop-1-enyl)phenyl]benzenesulfonamide (3b): Solid, mp 127-129 °C (toluene). Yield 75%. ¹H NMR δ: 7.00 (s, 1H, NH); 7.15-7.95 (m, 16H, Ar, H-1, H-2). IR (nujol, cm⁻¹): 3270 (NH). Anal. Calcd for C₂₁H₁₇NO₃S: C, 69.40; H, 4.71; N, 3.85. Found: C, 69.62; H, 4.80; N, 3.78.

Ethyl 3-(2-benzenesulfonylamino phenyl)acrylate (3c): Solid, mp 125-127 °C (toluene). Yield 50%. ¹H NMR δ: 1.30 (t, 3H, J = 7.5 Hz, CH₃); 4.22 (q, 2H, J = 7.5 Hz, CH₂); 6.25 (d, 1H, J = 15.8 Hz, H-2); 6.90 (s, 1H, NH); 7.20-7.90 (m, 10H, Ar, H-3). IR (nujol, cm⁻¹): 3295 (NH). Anal. Calcd for C₁₇H₁₇NO₄S: C, 61.61; H, 5.17; N, 4.23. Found: C, 61.70; H, 5.10; N, 4.12.

Ethyl 4-(2-benzenesulfonylamino phenyl)-2-oxo-3-butenoate (3d): Solid, mp 168-170 °C (toluene). Yield 65%. ¹H NMR δ: 1.41 (t, 3H, J = 7.5 Hz, CH₃); 4.44 (q, 2H, J = 7.5 Hz, CH₂); 6.82 (s, 1H, NH); 7.10 (d, 1H, J = 15.6 Hz, H-3) 7.40-7.80 (m, 10H, Ar, H-4). IR (nujol, cm⁻¹): 3310 (NH). Anal. Calcd for C₁₈H₁₇NO₅S: C, 60.15; H, 4.77; N, 3.90. Found: C, 60.25; H, 4.68; N, 3.82.

Preparation of compounds (4a-d): general procedure.
A mixture of 3 (1.5 mmol) in AcOEt (20 mL) was treated with catalytic amount of 5% Pd/C and hydrogenated at rt and 1 atm until the requested amount of hydrogen was consumed. The catalyst was filtered on a celite pad and the solvent evaporated off. The residue was purified by crystallization.

N-[2-(3-Oxo-butyl)phenyl]benzenesulfonamide (4a): Solid, mp 85-86 °C (toluene). Yield 95%. ¹H NMR δ: 2.05 (s, 3H, CH₃); 2.25 (t, 2H, J = 6.3 Hz, CH₂-2); 2.72 (t, 2H, J = 6.3 Hz, CH₂-1); 7.10-7.80 (m, 9H, Ar); 8.50 (s, 1H, NH). IR (nujol, cm⁻¹): 3305 (NH). Anal. Calcd for C₁₆H₁₇NO₃S: C, 63.34; H, 5.65; N, 4.62. Found: C, 63.28; H, 5.62; N, 4.58.

N-[2-(3-Oxo-3-phenylpropyl)phenyl]benzenesulfonamide (4b): Solid, mp 131-132 °C (toluene). Yield 96%. ¹H NMR δ: 2.55 (t, 2H, J = 6.5 Hz, CH₂-2); 3.25 (t, 2H, J = 6.5 Hz, CH₂-1); 7.05-7.95 (m, 14H, Ar); 8.71 (s, 1H, NH). IR (nujol, cm⁻¹): 3295 (NH). Anal. Calcd for C₂₁H₁₉NO₃S: C, 63.34; H, 5.65; N, 4.62. Found: C, 63.28; H, 5.62; N, 4.58.

Ethyl 3-(2-benzenesulfonylamino phenyl)propionate (4c): Solid, mp 78-80 °C (toluene). Yield 94%. ¹H NMR δ: 1.25 (t, 3H, J = 7.5 Hz, CH₃); 2.50 (m, 4H, H-2, H-3); 4.15 (q, 2H, J = 7.5 Hz, CH₂); 7.00-7.95 (m, 9H, Ar); 8.20 (s, 1H, NH). IR (nujol, cm⁻¹): 3295 (NH). Anal. Calcd for C₁₇H₁₉NO₄S: C, 63.42; H, 5.74; N, 3.83. Found: C, 68.95; H, 5.25; N, 3.78.

Ethyl 4-(2-benzenesulfonylamino phenyl)-2-oxobutyrate (4d): Solid, mp 154-156 °C (toluene). Yield 90%. ¹H NMR δ: 1.39 (t, 3H, J = 7.5 Hz, CH₃); 2.61 (t, 2H, J = 6.7 Hz, H-3); 3.09 (t, 2H, J = 6.7 Hz, H-4); 4.42 (q, 2H, J = 7.5 Hz, CH₂); 7.25-7.85 (m, 9H, Ar); 8.02 (s, 1H, NH). IR (nujol, cm⁻¹): 3295 (NH). Anal. Calcd for C₁₈H₁₉NO₅S: C, 59.82; H, 5.30; N, 3.88. Found: C, 59.76; H, 5.21; N, 3.82.
Preparation of quinolines (5a-d): general procedure.
A mixture of 4 (0.5 g) and PPA (2.5 g) was heated at 120 °C for 3 h in air current. The reaction mixture was cooled to rt, diluted with water (10 mL), and extracted with AcOEt. The organic phase was dried (Na₂SO₄), filtered and the solvent evaporated off. The residue was purified by distillation or crystallization. All the products are known compounds and the physical constants are in satisfactory agreement with literature data.

2-Methylquinoline (5a): Oil, bp 120-125 °C / 20 mmHg. Yield 80%. Lit.,4 bp 105-107 °C / 10 mmHg.

2-Phenylquinoline (5b): Solid, mp 82-84 °C (hexane). Yield 85%. Lit.,5 84-86 °C.

2-Hydroxyquinoline (5c): Solid, mp 198-200 °C (H₂O). Yield 82%. Lit.,6 195-200 °C.

Ethyl 2-quinolinecarboxylate (5d): Oil, bp 120-125 °C / 0.5 mmHg. Yield 70%. Lit.,7 180 °C/ 14 mmHg.

REFERENCES