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HETEROCYCLES FROM YLIDES. PART XI.[1] SYNTHESIS OF 2-SUBSTITUTED QUINOLINE DERIVATIVES [§]

Giuseppe Cremonesi,[a] Piero Dalla Croce,[b,*] Francesco Fontana,[b] and Concetta La Rosa[a]

[a] Institute of Organic Chemistry "Alessandro Marchesini", Faculty of Pharmacy, Via Venezian 21, I-20133 Milano, Italy

[b] Department of Organic and Industrial Chemistry, C.N.R. - I.S.T.M., Via Venezian 21, I-20133 Milano, Italy

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[2] and 1-phenylsulfonyl-3-hydroxy-2,3-dihydroindoles[1] 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.

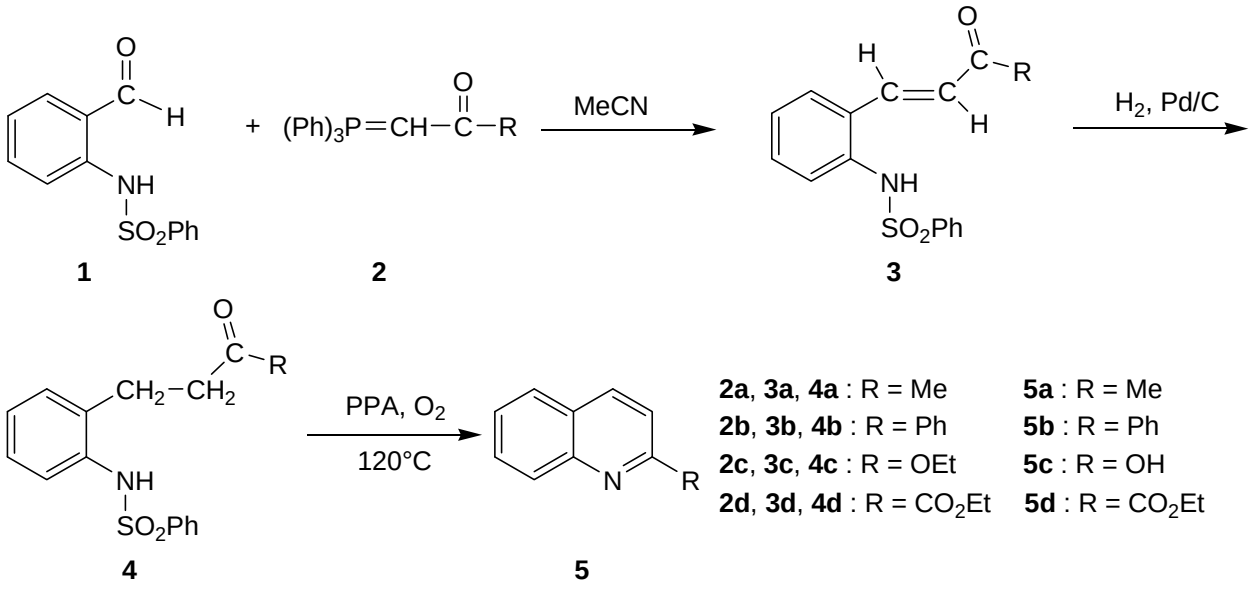
RESULTS AND DISCUSSION

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**).

[§] This paper is dedicated to Prof. Ekkehard Winterfeldt in the occasion of his 75th birthday.

[*] Corresponding author: piero.dallacroce@unimi.it

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_2SO_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 $C_{16}H_{15}NO_3S$: 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%. ^{1}H 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 $C_{21}H_{17}NO_3S$: C, 69.40; H, 4.71; N, 3.85. Found: C, 69.62; H, 4.80; N, 3.78.

Ethyl 3-(2-benzenesulfonylaminophenyl)acrylate (3c): Solid, mp 125-127 °C (toluene). Yield 50%. ^{1}H NMR δ: 1.30 (t, 3H, J = 7.5 Hz, CH_3); 4.22 (q, 2H, J = 7.5 Hz, CH_2); 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 $C_{17}H_{17}NO_4S$: C, 61.61; H, 5.17; N, 4.23. Found: C, 61.70; H, 5.10; N, 4.12.

Ethyl 4-(2-benzenesulfonylaminophenyl)-2-oxo-3-butenoate (3d): Solid, mp 168-170 °C (toluene). Yield 65%. ^{1}H NMR δ: 1.41 (t, 3H, J = 7.5 Hz, CH_3); 4.44 (q, 2H, J = 7.5 Hz, CH_2); 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 $C_{18}H_{17}NO_5S$: 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%. ^{1}H NMR δ: 2.05 (s, 3H, CH_3); 2.25 (t, 2H, J = 6.3 Hz, CH_2-2); 2.72 (t, 2H, J = 6.3 Hz, CH_2-1); 7.10-7.80 (m, 9H, Ar); 8.50 (s, 1H, NH). IR (*Nujol*, cm^{-1}): 3305 (NH). *Anal.* Calcd for $C_{16}H_{17}NO_3S$: 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%. ^{1}H NMR δ: 2.55 (t, 2H, J = 6.5 Hz, CH_2-2); 3.25 (t, 2H, J = 6.5 Hz, CH_2-1); 7.05-7.95 (m, 14H, Ar); 8.71 (s, 1H, NH). IR (*Nujol*, cm^{-1}): 3295 (NH). *Anal.* Calcd for $C_{21}H_{19}NO_3S$: C, 69.02; H, 5.24; N, 3.83. Found: C, 68.95; H, 5.25; N, 3.78.

Ethyl 3-(2-benzenesulfonylaminophenyl)propionate (4c): Solid, mp 78-80 °C (toluene). Yield 94%. ^{1}H NMR δ: 1.25 (t, 3H, J = 7.5 Hz, CH_3); 2.50 (m, 4H, H-2, H-3); 4.15 (q, 2H, J = 7.5 Hz, CH_2); 7.00-7.95 (m, 9H, Ar); 8.20 (s, 1H, NH). IR (*Nujol*, cm^{-1}): 3315 (NH). *Anal.* Calcd for $C_{17}H_{19}NO_4S$: C, 61.24; H, 5.74; N, 4.20. Found: C, 61.18; H, 5.65; N, 4.25.

Ethyl 4-(2-benzenesulfonylaminophenyl)-2-oxobutyrate (4d): Solid, mp 154-156 °C (toluene). Yield 90%. ^{1}H NMR δ: 1.39 (t, 3H, J = 7.5 Hz, CH_3); 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, CH_2); 7.25-7.85 (m, 9H, Ar); 8.02 (s, 1H, NH). IR (*Nujol*, cm^{-1}): 3295 (NH). *Anal.* Calcd for $C_{18}H_{19}NO_5S$: 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 (Na_2SO_4), 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 (H_2O). 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.

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