New Heterocycles from 8-Hydroxyquinoline *via* Dipolar 1,3-Cycloadditions: Synthesis & Biological Evaluation

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Diarylnitrilimine and arylnitriloxide dipoles react with two 8-hydroxyquinoline substrates to give respectively pyrazolinic and isoxazolinic derivatives. The structure of these new heterocycles was established on the basis of their spectroscopic data and by chemical methods. The inhibition activity of one of these heterocycles was evaluated *in vitro* against 8 pathogenic µ-organisms.

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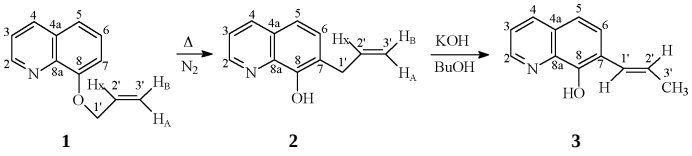
Introduction.

Although 8-hydroxyquinoline derivatives are endowed with some interesting biological properties [1], they are more often known as selective metal extractants [2]. In the course of the research completed in our respective laboratories for the development of heterocyclic compounds of both synthetic and biological interest [3], we report here about new polycyclic derivatives synthesized by 1,3-dipolar cycloadditions of diarylnitrilimines (DANI) and arylnitriloxides (ANO) with 7-(2'-propenyl)-8-hydroxyquinoline **2** and 7-(1'-propenyl)-8-hydroxyquinoline **3**.

Results and Discussion.

Allyl derivative **2** has been briefly claimed in two German patents [4] and was obtained by a Williamson synthesis from 8-hydroxyquinoline [5] and allyl bromide *via* allyloxyquinoline **1** which underwent a Claisen rearrangement to yield **2** [6]. Dipolarophile **3** was obtained by isomerization of **2** in a strong basic medium [7] as depicted in Scheme 1.

Scheme 1



1 **2** **3**

The *E* configuration of **3** was ascertained by the high coupling constant (*ie.* 16 Hz) connecting H-1' and H-2'. The *Z* isomer would imply a coupling constant of only *ca.* 8 Hz by comparison to related described structures [8]. The reaction of **2** and **3** with nitrilimine 1,3-dipoles **4** [9] in refluxing benzene for 48 hours led respectively to cycloadducts **5a-d** and **6a-c** in 60-80% yields of pure isolated products.

The chemical structure of 7-[5'-(3'-aryl-4',5'-dihydro-1'-phenyl-pyrazolo)-methyl]-8-hydroxyquinolines **5a-d** was established on the basis of their ^{1}H- and ^{13}C-NMR data (see Table 1). This common structure is in favor of a highly regioselective reaction.

Scheme 2

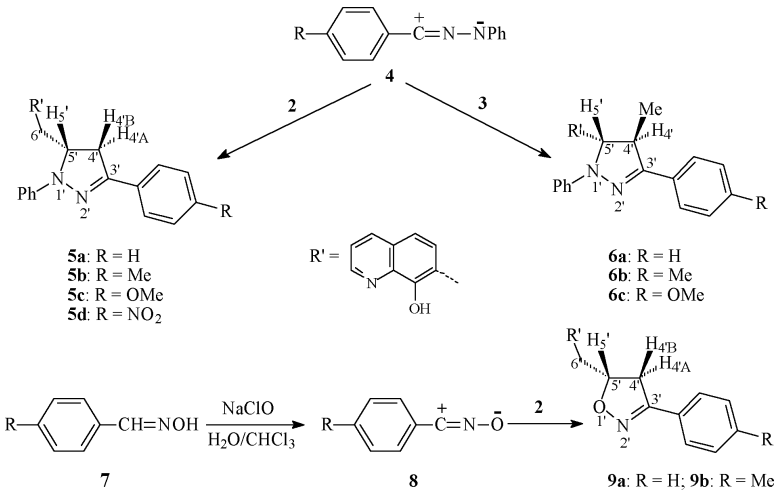


Table 1
^{1}H- and ^{13}C-NMR Data of Adducts **5a-d** in $CDCl_3$, δ (ppm/TMS), *J* (Hz)

Adducts	H-4'A	H-4'B	H-5'	H-6'	R = C*H*$_3$ or OC*H*$_3$	C-4'	C-5'	C-6' or OCH$_3$	R = H, C*H*$_3$
5a	3.56	2.72 (dd)	4.94 (m)	3.15 (d)	-	37.4	59.2	2.5	-
		J_{AB} = 13.4		$J_{5'-6'}$ = 7.5					
		$J_{4'A-5'}$ = 3.3							
		$J_{4'B-5'}$ = 10.3							
5b	3.63	2.75 (dd)	4.90 (m)	3.13 (d)	2.35 (s)	37.5	59.1	32.5	21.1
		J_{AB} = 13.3		$J_{5'-6'}$ = 6.9					
		$J_{4'A-5'}$ = 3.3							
		$J_{4'B-5'}$ = 10.3							
5c	3.62	2.72 (dd)	4.90 (m)	3.15 (d)	3.80 (s)	38.0	59.0	31.7	55.0
		J_{AB} = 13.1		$J_{5'-6'}$ = 6.3					
		$J_{4'A-5'}$ = 3.2							
		$J_{4'B-5'}$ = 10.3							
5d	3.62	2.75 (dd)	5.10 (m)	3.20 (d)	-	36.6	60.0	32.0	-
		J_{AB} = 13.4		$J_{5'-6'}$ = 7.6					
		$J_{4'A-5'}$ = 3.1							
		$J_{4'B-5'}$ = 10.1							

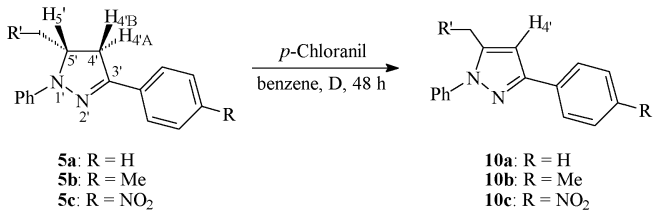
The ^{1}H-NMR spectrum of **5c** in $CDCl_3$ (see Table 1) displays a peculiar doublet at 3.15 ppm which was assigned to the two isochronous protons H-6' coupled with H-5'. The two protons H-4' and H-5' form an ABM system, the two split doublets at 3.62 and 2.72 ppm being respectively assigned to H-4'A and H-4'B, and the multiplet downfield shifted at 4.90 ppm by an adjacent heteroatom assigned to H-5' [10]. This resonance has been already observed on products resulting from the addition of nitrile imine derivatives on allyl dipolarophiles [11].

Substituting $CDCl_3$ for DMSO-d_6 made the two protons H-6' anisochronous and thus led protons H-4', -5', and -6' to form an ABMXY system in **5c** [12]. It is well known that the nature of solvent, concentration and temperature affect the resonance of certain nuclei in a given structure [13]. In DMSO-d_6, H-5' appears in the form of a 16 transitions resonance at 4.89 ppm, H-6'A and H-6'B as two split doublets centered respectively at 3.15 and 3.28 ppm. The coupling constants between these three protons were: $J_{6'A-6'B}$ = 17 Hz, $J_{6'A-5'}$ = 5 Hz, and $J_{6'B-5'}$ = 10.5 Hz, these two last values suggesting H-6'B and H-6'A are respectively *cis* and *trans* in respect to H-5'.

To ascertain this regiochemistry adducts **5a-c** were subjected to a reaction of heteroaromatization (see Scheme 3).

p-Chloranil mild dehydrogenation of **5a-c** yielded only 7-[5'-(1'-phenyl-3'-arylpyrazolo)methyl]-8-hydroxyquinolines **10a-c**. All ^{1}H-NMR spectra in $CDCl_3$ displayed a singlet around 6.4 ppm assigned to H-4 ' in good agreement with literature values [9b,14].

Scheme 3



5a: R = H
5b: R = Me
5c: R = NO_2

10a: R = H
10b: R = Me
10c: R = NO_2

Altogether ^{1}H- and ^{13}C-NMR data of isolated adducts **6a-c** (see Table 2) indicate that this 1,3-dipolar cycloaddition reaction led to a single regioisomer (see Scheme 2). Usually, similar reactions yield both regioisomers with a prevalence of those resulting from weaker steric effects [9a,11a,15]. Of particular significance were a multiplet around 3.5 ppm and a doublet around 5.6 ppm. These resonances were assigned respectively to vicinal protons H-4' and H-5' which are obviously *trans* in all these adducts judging from their low coupling constant (< 4 Hz).

In order to enlighten the regiospecificity of the cycloaddition products of *N*-phenyl-*C*-arylnitrilimines, dipolarophile **2** was reacted with two arylaldoximes (**7a**: R = H; **7b**: R = Me) in a two-phase medium (*ie*. aqueous NaClO and $CHCl_3$ [16]) at -10 °C for 1 hour (see Scheme 2). Comparison of ^{1}H- and ^{13}C-NMR chemical shifts at 4'- and 5'-positions in both kinds of adducts are in favor of the postulated structure taking into account that replacement of the nitrogen by an oxygen in **9a-b** led to an important shielding of *ca.* 21 ppm. From all these data, it appears that the regiochemistry of the reaction of DANI and ANO with dipolarophiles **2** and **3** does not depend on the nature of the 1,3-dipoles used but on steric hindrance effects [11a,15].

In vitro antimicrobial activity of compound **9a** was evaluated against seven pathogenic strains and one yeast (*C. albicans*) by the disc-diffusion method [17]. As indicated in Table 3, compound **9a** displays a measurable antibacterial activity against all the microorganisms tested, the lowest activity being observed against Gram-negative bacteria and especially *Salmonella enterica* which developed recently multidrug-resistance [18]. The largest diameters of inhibition (m/m) were measured against *Enterococcus feacalis* and *Mycobacterium smegmatis*, which is an acid-

Table 2

^{1}H- and ^{13}C-NMR Data of Adducts **6a-c** in $CDCl_3$, δ (ppm/TMS), *J* (Hz)

Adducts	H-4'	H-5'	CH_3 on C-4'	R = C*H*$_3$ or OC*H*$_3$	C-4'	C-5'	CH_3 on C-4'	R = H, C*H*$_3$ or OC*H*$_3$
6a	3.55 (m) ^3J = 7.1	5.60 (d) $J_{4'-5'}$ = 3.5	1.55 (d) ^3J = 7.1	-	49.6	65.3	19.1	-
6b	3.57 (m) ^3J = 7.1	5.60 (d) $J_{4'-5'}$ = 3.6	1.55 (d) ^3J = 7.2	2.36 (s)	49.6	65.4	19.2	21.3
6c	3.54 (m) ^3J = 7.1	5.57 (d) $J_{4'-5'}$ = 3.6	1.55 (d) ^3J = 7.1	3.83 (s)	49.7	65.4	19.1	55.2

fast staining rod [19]. The higher *in vitro* activity of **9a** against Gram-positive bacteria was not surprising since Gram-negative rods are endowed with an outer membrane that decreases the transfer of drugs through the cytoplasmic membrane. It has been suggested that hydroxyquinoline and its derivatives could exert their biological activities as membrane-active agents *via* metal ion chelation [20,21]. Our preliminary results are in good agreement with those reported by Shen *et al*. [20] and Lentz *et al*. [22]. A signicative fungistatic activity was also observed against *Candida albicans*, the sole yeast of our test.

Further investigations of compound **9a** on other bacteria, fungi, and protozoa are in progress to throw light on its antimicrobial spectrum.

Conclusion.

1,3-Dipolar cycloaddition reactions of DANI and ANO with two isomers, namely the 7-(2'-propenyl)-8-hydroxyquinoline **2** and the 7-(1'-propenyl)-8-hydroxyquinoline **3**, were used to synthesize new chelating molecules from 8-hydroxyquinoline. The regiochemistry of this reaction relies on already discussed steric effects. Some of these new heteroadducts behave like selective extractants of metal ions in liquid-liquid extraction [23] and compound **9a** is endowed with interesting *in vitro* antimicrobial activity against both Gram-positive and Gram-negative bacteria.

EXPERIMENTAL

Chemistry.

Melting points were measured with a Buchi 510 apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ using a Bruker AC200 spectrometer operating at 200 MHz for ^{1}H and 50 MHz for ^{13}C with TMS as internal standard. Assignments of the various protons were supported by successive irradiations. IR spectra were recorded with a Perkin Elmer 577 spectrometer, solid products being palletized in KBr. DANI precursors were prepared according to Huisgen [9a,15]. Elemental analyses were carried out by the 'Service Central de Microanalysis' of the CNRS in Vernaison, France.

Microbiology.

Strains were purchased from the American Type Culture Collection (ATCC), Manassas, VA 20108, USA and from the

Table 3

In Vitro Activities of 7-[5'-(3'-Phenyl-isoxazolino)-methyl]-8-hydroxyquinoline **9a** *vs* Penicillin G or Amphothericine B

Strains *Inhibition-zone diameter (m/m)*	**9a**	**Penicillin G**	**Amphotericine B**
Escherichia coli (ATCC 10536)	12	25	-
Escherichia coli (ATCC 8739)	11	25	-
Pseudomonas aeruginosa (CIP 105526)	11	25	-
Pseudomonas aeruginosa (ATCC 9027)	11	25	-
Salmonella enterica (CIP 80.39)	10	25	-
Staphylococcus aureus (ATCC 9144)	15	26	-
Staphylococcus aureus (ATCC 6538)	15	25	-
Enterococcus feacalis (ATCC 10541)	18	26	-
Bacillus subtilis (ATCC 6633)	11	25	-
Mycobacterium smegmatis (CIP 73.26)	18	25	-
Candida albicans (ATCC 10231)	13	-	22

Institut Pasteur de Paris (IPP), 25-28 rue du Docteur Roux, 75724 Paris, France. Sterile paper discs of 6 m/m diameter (Wattmann N°3) were impregnated with a 3 mg/mL CH_2Cl_2 solution of the compound to be tested and dried at 37 °C before use. The rest of the procedure was identical to the method reported in **§ 2.8.** of ref. [17].

7-(2-Propenyl)-8-hydroxyquinoline (**2**).

A suspension of 0.2 mole of 8-hydroxyquinoline and 0.3 mole of K_2CO_3 in 300 mL of anhydrous acetone was refluxed for 15 minutes in a 0.5 L reactor equipped with a drying funnel ($CaCl_2$). Allyl bromide (18 mL, ~ 1 eq.) was then dropped and the mixture stirred and refluxed for 24 additional hours. After cooling, the suspension was filtered under a fume board and the resulting solids washed with acetone (3 x 100 mL). The solvent was evaporated under reduced pressure to an oily residue which was dissolved in ether (200 mL), washed successively with 5% aq. KOH and water until neutral, dried with Na_2SO_4, and finally concentrated under *vacuo* to yield the crude allyl ether **1** (~ 37 g, 100%) as a brown oil. ^{1}H-NMR: 4.86 (d, 2H, $J_{1'\text{-}X}$ 5.4 Hz, H-1'), 5.34 (dd, 1H, $J_{A\text{-}X}$ 17.3 Hz, $J_{A\text{-}B}$ 1.2 Hz, H-A), 5.4 (dd, 1H, $J_{B\text{-}X}$ 10.4 Hz, H-B), 6.2 (m, 1H, H-X), 7.0-8.8 (m, 6H, Ar.). The Claisen rearrangement of ether **1** was initiated by heating at approximately 160 °C on a sand bath under a nitrogen atmosphere. An exothermic reaction took place and the temperature raised up to 200 °C in a few minutes [6]. After cooling, the residue was distilled under reduced pressure (bp 165-170 °C/0.5) to give **2** (29.63 g, 80%) as a yellowish oil which crystallized on standing: mp 42 °C (*n*-heptane), Litt. [6] mp 41.5-42 °C (pentane); ^{1}H-NMR: 3.68 (d, 2H, $J_{1'\text{-}X}$ 6.5 Hz, H-1'), 5.1 (dd, 1H, $J_{A\text{-}B}$ 1.8 Hz, $J_{A\text{-}X}$ 16.6 Hz , H-A), 5.18 (dd, 1H, $J_{B\text{-}X}$ 10.0 Hz, H-B), 6.1 (m, 1H, H-X), 8.58 (bs, 1H, OH), 7.3-8.9 (m, 5H, Ar.); ^{13}C-NMR: 149.1 (C-8), 147.6 (C-2), 137.8 (C-8a), 136.4 (C-2'), 136.1 (C-4), 129.5 (C-6), 127.1 (C-4a), 122.0 (C-7), 120.9 (C-3), 117.3 (C-5), 115.7 (C-3'), 34.0 (C-1').

7-(1-Propenyl)-8-hydroxyquinoline (**3**).

A solution of **2** (20.0 g) in 200 mL of *n*-butanol was refluxed for 4 h with KOH pellets (34.0 g). After cooling, the solvent was evaporated under reduced pressure, the residue carefully neutralized with 6 *N* HCl and extracted with ether (3 x 100 mL). The organic phases were combined, washed twice with water, and dried on Na_2SO_4. Evaporation of solvents and crystallization of the residue from hot ethanol gave compound **3** (14.4 g, 72%) as yellow needles: mp 86-88 °C, Litt. [7] 86-87 °C; ^{1}H-NMR: 2.0 (dd, 3H, $J_{1'\text{-}3'}$ 1.5 Hz, $J_{2'\text{-}3'}$ 6.6 Hz, Me), 6.4 (dq, 1H, $J_{1'\text{-}2'}$ 16.0 Hz, H-2'), 6.95 (m, 1H, H-1'), 8.6 (bs, 1H, OH), 7.2-7.8 (m, 5H, Ar.); ^{13}C-NMR: 148.0 (C-2, -8), 138.5 (C-8a), 135.5 (C-4), 127.2 (C-6), 127.0 (C-4a), 126.0 (C-1'), 125.0 (C-2'), 121.0 (C-3), 120.0 (C-7), 117.0 (C-5), 19.0 (C-3').

Addition of *N*-Phenyl-*C*-arylnitrilimines on Dipolarophiles **2** and **3**.

Onto a magnetically stirred solution of the dipolarophile (**2** or **3**, 10 mmoles) and 13 mmoles of the selected hydrazonoyl hydrochloride precursor of DANI [3c,9a,24] in 30 mL of anhydrous benzene in a 100 mL reactor equipped with a reflux condenser and a drying funnel ($CaCl_2$) were dropped 2 mL of triethylamine over 15 minutes as the mixture was heated to reflux. The reflux was kept for 48 hours. After complete cooling, 20 mL of anhydrous benzene was added and the hydrochloride eliminated by filtration through a sinter glass under an efficient fume board. The solvents were evaporated and the residue diluted in a small volume of an ether-ethanol mixture (1:1) in which the cycloadducts solidified on standing in the refrigerator.

Adducts from Dipolarophile **2**.

7-(2,5-Diphenyl-3,4-dihydro-2*H*-pyrazol-3-ylmethyl)-quinolin-8-ol (**5a**).

Compound **5a** was obtained in 82% yield; mp 218 °C; IR: 3300-3400, 1580 cm^{-1}; ^{1}H- and ^{13}C-NMR, see Table 1.

Anal. Calcd. for $C_{25}H_{21}N_3O$: C, 79.16; H, 5.54. Found: C, 78.94; H 5.40.

7-(2-Phenyl-5-*p*-tolyl-3,4-dihydro-2*H*-pyrazol-3-ylmethyl)-quinolin-8-ol (**5b**).

Compound **5b** was obtained in 80% yield; mp 205 °C; IR: 3300-3400, 1580 cm^{-1}; ^{1}H- and ^{13}C-NMR, see Table 1.

Anal. Calcd. for $C_{26}H_{23}N_3O$: C, 79.39; H, 5.85. Found: C, 79.18; H 5.71.

7-[5-(4-Methoxy-phenyl)-2-phenyl-3,4-dihydro-2*H*-pyrazol-3-ylmethyl]-quinolin-8-ol (**5c**).

Compound **5c** was obtained in 76% yield; mp 212 °C; IR: 3300-3400, 1595 cm^{-1}; ^{1}H- and ^{13}C-NMR, see Table 1.

Anal. Calcd. for $C_{26}H_{23}N_3O_2$: C, 76.28; H, 5.63. Found: C, 76.42; H 5.50.

7-(5-(4-Nitrophenyl)-2-phenyl-3,4-dihydro-2*H*-pyrazol-3-ylmethyl)-quinolin-8-ol (**5d**).

Compound **5d** was obtained in 70% yield; mp > 260 °C; IR: 3300-3400, 1590 cm^{-1}; ^{1}H- and ^{13}C-NMR, see Table 1.

Anal. Calcd. for $C_{25}H_{20}N_4O_3$: C, 70.75; H, 4.72. Found: C, 70.53; H 4.61.

Adducts from Dipolarophile **3**.

In the same manner, adducts **6a-c** were isolated after evaporation of benzene, purified by chromatography on silica gel column with chloroform as the mobile phase, and finally crystallized from 96% ethanol.

7-(4-Methyl-2,5-diphenyl-3,4-dihydro-2*H*-pyrazol-3-yl)-quinolin-8-ol (**6a**).

Compound **6a** was obtained in 54% yield; mp 192 °C; IR: 3300-3400, 1580 cm^{-1}; ^{1}H- and ^{13}C-NMR, see Table 2.

Anal. Calcd. for $C_{25}H_{21}N_3O$: C, 79.16; H, 5.54. Found: C, 79.37; 5.46.

7-(4-Methyl-2-phenyl-5-*p*-tolyl-3,4-dihydro-2*H*-pyrazol-3-yl)-quinolin-8-ol (**6b**).

Compound **6b** was obtained in 60% yield; mp 156 °C; IR: 3300-3400, 1590 cm^{-1}; ^{1}H- and ^{13}C-NMR, see Table 2.

Anal. Calcd. for $C_{26}H_{23}N_3O$: C, 79.39; H, 5.85. Found: C, 79.16; H, 5.61.

7-[5-(4-Methoxy-phenyl)-4-methyl-2-phenyl-3,4-dihydro-2*H*-pyrazol-3-yl]-quinolin-8-ol (**6c**).

Compound **6c** was obtained in 65% yield; IR: 3300-3400, 1580 cm^{-1}; mp 163 °C; ^{1}H- and ^{13}C-NMR, see Table 2.

Anal. Calcd. for $C_{26}H_{23}N_3O_2$: C, 76.28; H, 5.63. Found: C, 76.51; H, 5.46.

Cycloaddition of ANO **8** with Dipolarophile **2**.

Commercial bleach (40 mL, 24° ~ 23% NaClO w/w) was slowly dropped under magnetic stirring onto a solution of oxime **7** in 20 mL of $CHCl_3$ kept at -10 °C. The resulting two-phase system was vigorously stirred for one hour after complete addition at the same temperature. The organic phase was decanted, washed with water (3 x 10 mL), dried (Na_2SO_4), and finally concentrated to a gum which was chromatographied on silica gel with cyclohexane/ethyl acetate (9:1) as the eluent. Compounds **9a-b** were finally crystallized from a mixture ether/petroleum ether (2:3).

7-(3-Phenyl-4,5-dihydroisoxazol-5-ylmethyl)-quinolin-8-ol (**9a**).

Compound **9a** was obtained in 50% yield; mp 115 °C; IR: 3300-3400, 1580 cm^{-1}; ^{1}H-NMR: 3.19 (dd, 1H, J_{A-B} 16.7 Hz, $J_{4'A-5'}$ 7.8 Hz, H-4'A), 3.31 (dd, 1H, $J_{4'B-5'}$ 9.9 Hz, H-4'B), 5.25 (m, 1H, H-5'), 3.38 (d, 2H, H-6'), 7.1-8.8 (m, 11H, Ar. + OH);^{13}C-NMR (selected data): 117-158 (Ar.), 81.0 (C-5'), 39.0 (C-4'), 35.0 (C-6').

Anal. Calcd. for $C_{19}H_{16}N_2O_2$: C, 75.00; H, 5.26. Found: C, 75.24; H, 5.13.

7-(3-*p*-Tolyl-4,5-dihydro-isoxazol-5-ylmethyl)-quinolin-8-ol (**9b**).

Compound **9b** was isolated in 56% yield; mp 120 °C; IR: 3300-3400, 1590 cm^{-1}; ^{1}H-NMR: 2.35 (s, 3H, Me); 3.19 (dd, 1H, J_{A-B} 17.0 Hz, $J_{4'A-5'}$ 7.8 Hz, H-4'A), 3.3 (dd, 1H, $J_{4'B-5'}$ 10 Hz, H-4'B), 5.15 (m, 1H, H-5'), 3.27 (d, 2H, H-6'), 7.1-8.8 (m, 10H, Ar. + OH); ^{13}C-NMR (selected data): 117-158 (Ar.), 80.7 (C-5'), 39.5 (C-4'), 35.1 (C-6'), 21.4 (Me).

Anal. Calcd. for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.66. Found: C, 75.45; H, 5.81.

Heteroaromatization of Adducts **5a-c** into Pyrazoles **10a-c**.

An equimolar mixture of **5** (10 mmoles) and *p*-chloranil in 40 mL anhydrous benzene was refluxed for 48 hours. After complete cooling, the mixture was washed with 5% aq. KOH, the organic phase was separed, dried on Na_2SO_4, and the solvent evaporated under reduced pressure. Crude solid materials were recrystallized from 96% ethanol.

7-(2,5-Diphenyl-2*H*-pyrazol-3-ylmethyl)-quinolin-8-ol (**10a**).

Compound **10a** was obtained in 72% yield; mp 176 °C; IR: 3300-3400, 1610, 1590 cm^{-1}; ^{1}H-NMR: 4.26 (s, 2H, H-6'), 6.63 (s, 1H, H-4'), 7.4-8.6 (m, 16H, Ar. + OH); ^{13}C-NMR (selected datum): 105.04 (C-4').

Anal. Calcd. for $C_{25}H_{19}N_3O$: C, 79.57; H, 5.04. Found: C, 79.75; H, 5.13.

7-(2-Phenyl-5-*p*-tolyl-2*H*-pyrazol-3-ylmethyl)-quinolin-8-ol (**10b**).

Compound **10b** was obtained in 80% yield; mp 187 °C; IR: 3300-3400, 1610, 1595 cm^{-1}; ^{1}H-NMR: 2.41 (s, 3H, Me), 4.25 (s, 2H, H-6'), 6.38 (s, 1H, H-4'), 7.4-8.6 (m, 15H, Ar. + OH); ^{13}C-NMR (selected data): 105.0 (C-4'), 21.5 (Me).

Anal. Calcd. for $C_{26}H_{21}N_3O$: C, 79.79; H, 5.37. Found: C, 79.62; H, 5.28.

7-[5-(4-Methoxy-phenyl)-2-phenyl-2*H*-pyrazol-3-yl-methyl]quinolin-8-ol (**10c**).

Compound **10c** was obtained in 60% yield; mp 180 °C; ^{1}H-NMR: 4.4 (s, 2H, H-6'), 6.4 (s, 1H, H-4'), 7.4-8.6 (m, 15H, Ar. + OH); ^{13}C-NMR (selected datum): 105.1 (C-4').

Anal. Calcd. for $C_{25}H_{18}N_4O_3$: C, 71.09; H, 4.26. Found: C, 70.89; H, 4.19.

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