Preparation of *NH*-Pyrazoleacetic Acid Anilides from Trilithiated Acetoacetanilide, Select Aromatic Esters, and Hydrazine

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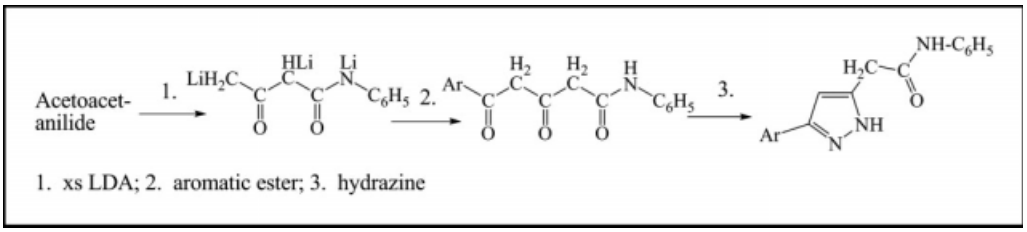

Acetoacetanilide was trilithiated with excess lithium diisopropylamide to form a reactive trianion-type intermediate. This was followed by a regioselective Claisen-type condensation of the trilithiated intermediate with a variety of aromatic esters to afford new *C*-acylated intermediates, 3,5-diketopentane-carboxanilides, that were not isolated but immediately condensed-cyclized with hydrazine to afford the *NH*-pyrazoleacetanilides, 5-aryl-1*H*-pyrazole-3-acetanilides, before these *C*-acylated intermediates had an opportunity to rearrange to anilino-pyranones, 4-anilino-6-aryl-2*H*-pyran-2-ones.

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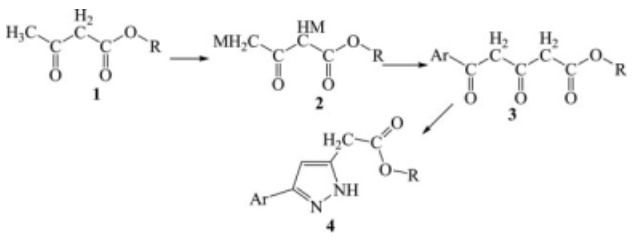
INTRODUCTION

Pyrazoles of all substitution types continue to be prepared and studied, either as stand alone molecular systems, or as part of a fused-ring group of compounds, such as, indazoles and dihydrobenzindazoles [1]. *NH*-Pyrazole-3-acetic acids and their derivatives have received limited investigation [2], with a single recent citation dealing with the preparation of *NH*-pyrazole-3-acetanilides [3], and a single report for *NH*-pyrazole-3-acetic acid hydrazides [4]. Of the possible pyrazole substitution types, the *NH*-pyrazoles continue to receive increasing interest, especially in ligand investigations [5] (Scheme 1).

Claisen type strong base studies with β-ketoesters dianions **2** resulting from deprotonation of **1** with alkali metal amides (M = Li, Na, or K), lithium diisopropylamide (LDA), and other strong bases [6] was followed by condensation with carboxy electrophiles, usually an ester, and sometimes *N*-acylaziridines [7]. This afforded *C*-acylated products **3**, diketoesters, that could be isolated and transformed by condensation-cyclization with hydrazine into additional products, *NH*-pyrazoles **4**.

Scheme 1. Syntheses with dimetalated β-ketoesters.

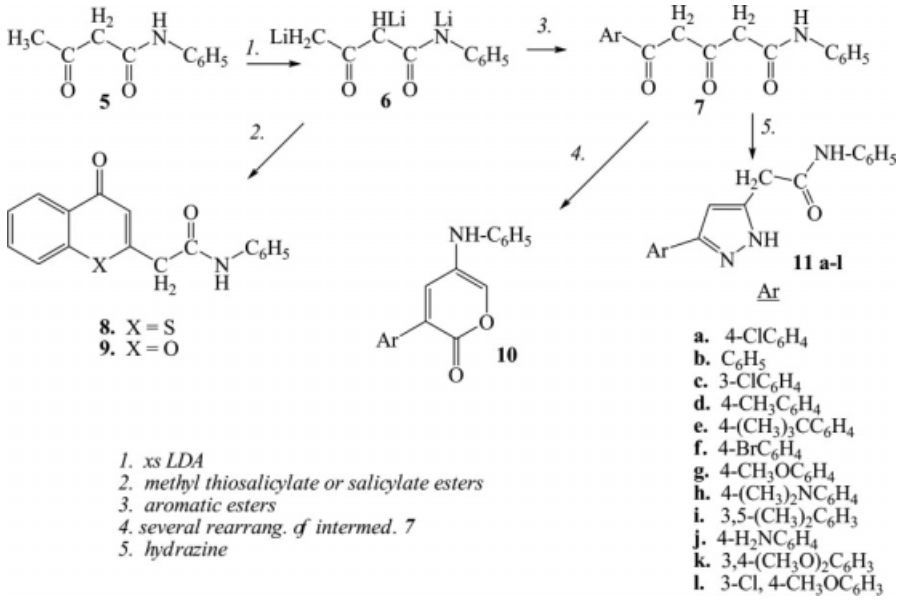


Some of the dianion-type β-ketoester systems **2** have been expanded to trianion-type β-ketoamide intermediates **6** that could be used in additional syntheses (Scheme 2). Recently, acetoacetanilide **5** has been trilithiated with excess LDA, and these intermediates **6** were regioselectively condensed at the terminal carbon atom with lithiated methyl thiosalicylate or a variety of lithiated methyl salicylates to afford *C*-acylation products **7** that were acid cyclized to 4*H*-1-benzothiopyran-4-ones (thiochromone-acetanilides) **8** [8] or 4*H*-1-benzopyran-4-ones (chromone-acetanilides) **9** [9], respectively. When the trilithiated intermediates **6** were condensed with other substituted benzoate esters, such as, methyl 4-methoxybenzoate, rearrangement products usually resulted and were identified as substituted 2-pyranones, 4-anilino-6-aryl-2*H*-pyran-2-ones **10** [10].

RESULTS AND DISCUSSION

During this investigation, 2-[3-(phenyl or substituted phenyl)-1*H*-pyrazol-5-yl]-*N*-phenylacetamides, *NH*-pyrazole

Scheme 2. Syntheses with trilithiated acetoacetanilide including 5-aryl-1*H*-pyrazole-3-acetanilides **11a–l.**



acetanilides, **11a–l** were prepared by the immediate condensation-cyclization of 5-(phenyl or substituted phenyl)-3,5-dioxo-*N*-phenylpentamides, diketopentanilides **7**, (from **5** and **6**) intermediate compounds with hydrazine. Intermediate diketopentanilides **7** were prepared by modification and extension of some strong-base multiple anion procedures where trianion **6** resulted from treatment of acetoacetanilide **5** with excess LDA to **6**, and then condensed with a variety of substituted benzoate esters, that did not contain an ortho-substituted nucleophilic functional group (e.g., thiophenol).

The purification of these diketopentanilide intermediates **7** presented a good possibility of rearrangements to anilino-pyranones **10**; consequently, they were treated with excess hydrazine which resulted in the preferential condensation of a hydrazine nitrogen with one of the two carbonyl carbons of diketopentanilide intermediates **7** followed by cyclodehydration to the targeted pyrazoleacetic acid anilides **11a–l**. Anilino-pyranones **10** were not found.

The pyrazole acetanilides **11a–l** can be represented as a molecular system with numerous tautomeric forms (**I–VI**), including the keto-enol and annular tautomers with the pyrazole *N*—*H* hydrogen bonded to either of the adjacent nitrogen atoms (annular tautomers). IR carbonyl absorptions from crystalline products were noted at 1651–1676 cm^{-1}. Proton magnetic spectra indicated predominantly or exclusively keto tautomer, with the methylene absorptions appearing as a singlet at δ 3.44–3.78 ppm. The C_4—H absorptions of the pyrazole ring were noted at δ 6.31−6.69 ppm. Carbon-13 NMR spectra were indicative of structure but they were inconclusive. Even after extensive scans, the projected number of carbon absorptions were usually not obtained [3]. The C4 (CH carbon) resonance absorptions of the pyrazole ring in all cases were noted δ 101–107 ppm, which is in accord with estimates and recent experimental data reported by others [3,4]. DEPT taken after 5000 C-13 NMR scans on **11b** followed by HMQC indicated the presence of the methylene carbon absorptions at δ 35.8 ppm, which was matched with H-1 NMR methylene protons absorption at δ 3.72 ppm; the C-13 NMR absorption at δ 102.5 ppm was matched with H-1 NMR C_4—H of the pyrazole ring absorption at δ 6.61 ppm. Other C-13 NMR absorptions were noted for the methylene carbons from δ 32.9 to 40.2 ppm. LC-MS for all compounds, $(M+H)^+$, were also satisfactory and combustion analysis for the compounds were supportive. The single crystal X-ray analysis obtained for product **11c** indicated that a single tautomer in the keto form (**I**, Fig. 1) with a hydrogen bonded to the nitrogen adjacent to the pyrazole carbon also bonded to the methylene (C3 in the ORTEP diagram illustrated in Fig. 2) and that the pyrazole ring is nearly planar [12].

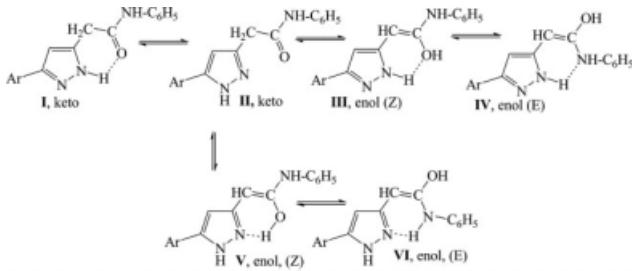


Figure 1. 5-Aryl-1*H*-pyrazole-3-acetanilide tautomers **I–VI**.

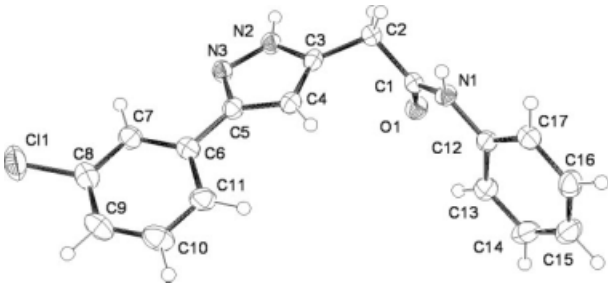


Figure 2. ORTEP diagram (50% ellipsoids for nonhydrogen atoms), $C_{17}H_{14}ClN_3O$ **11c** [11].

The molecular structure of **11c** is shown in Figure 2 and selected bond distances and angles are listed in Table 1. The bond lengths agree with the assignment of the double bond shown between C1 and O1 for the keto form (see ORTEP diagram for numbering of atoms).

The least squares best planes representing the rings containing C6 and C5 are nearly coplanar with an angle of 18.3° between them. There is likely some extended pi bonding between these rings. Each molecule is hydrogen bonded to four molecules: N3 to the H atom on N1, H on N2 to O1, O1 to the H atom on N2, and H on N1 to N3.

The overall yields for the two-step synthesis may not be optimal for an individual product, with the strong base reactions usually having the greatest variance. A practical side to the synthesis is the availability of starting materials, the use of less toxic acylating reagents (aromatic esters vs. acyl aziridines), a procedure that is reproducible by someone not necessarily familiar with strong base synthesis methods, and that the procedure is conducive to making targeted products which can be prepared in gram quantities after recrystallization from common solvents. Although not investigated extensively, tetramethylethylenediamine (TMEDA) did not markedly increase the overall yield, on occasion ~5% [6g]. In addition to all products targeted and prepared being new, they have the potential for use in agriculture and medicine, applications in other syntheses, and for spectral and theoretical studies.

EXPERIMENTAL

Melting points were obtained with a Mel-Temp II melting point apparatus in open capillary tubes and are uncorrected. Fourier transform infrared spectra were obtained with a Mattson Genesis II FTIR with Specac Golden Gate Accessory. Proton and C-13 nuclear magnetic resonance spectra were obtained with a Varian Associates Mercury Oxford (300 MHz for H-1 and 75 MHz for C-13) nuclear magnetic resonance spectrometer, and chemical shifts are recorded in δ ppm downfield from an internal tetramethylsilane (TMS) standard. Combustion analyses were performed by Quantitative Technologies, Inc., P.O. Box 470, Whitehouse, NJ 08888. LCMS analyses were measured on a Thermo-Finnigan LCQ Advantage system with the Surveyor autosampler, Surveyor pump, and LCQ Advantage Max mass spectral detector using electrospray ionization; 2 mg samples were prepared in 2 mL min^{-1} of acetonitrile; 10 μL injections were pumped at 1.00 mL min^{-1} isocratically with 70% acetonitrile and 30% water, each buffered with 0.1% formic acid by volume; 15 min runs were reproduced in positive MS modes. Data were collected at full scan from 100 to 650 amu.

General procedure for the preparation of 5-aryl-1*H*-pyrazole-3-acetic acid anilides (11a–l). Ratio of reagents—Acetoacetanilide:LDA:ester, 1:4:1 for 11a–g, and 1:5:1 for 11h and 11j. In a typical reaction sequence, LDA was prepared in a round bottomed flask by the addition of 39–40 mL (50 mL for **11h** and **11j**) of 1.60*M* *n*-butyllithium (0.0630 mol/0.0788 mol for **11h** and **11j**) in hexanes (e.g., 500 mL), equipped with a nitrogen inlet tube, and a side-arm addition funnel (recommended). The flask was cooled in an ice water bath, and 6.41 g (0.0630 mol) or 8.01 g (0.0788 mol for **11h** and **11j**) of diisopropylamine (99.5%, Aldrich Chemical Co.), dissolved in 25–35 mL of dry THF was added from the addition funnel at a fast drop wise rate during a 5 min period. The solution was stirred for an additional 15–20 min, and then treated during 5 min with acetoacetanilide **6** (99.5%, Aldrich Chemical Co.),

Table 1

Selected bond distances (Å) and angles (°), $C_{17}H_{14}ClN_3O$ **11c.**

C1—O1	1.235(4)	C1—N1—C12	128.5(3)
C1—N1	1.341(4)	O1—C1—N1	124.4(3)
N1—C12	1.420(4)	O1—C1—C2	120.9(3)
C1—C2	1.519(4)	N1—C1—C2	114.7(3)
C2—C3	1.500(4)	C3—C2—C1	108.7(3)
N2—C3	1.345(4)	C4—C3—C2	131.5(3)
N3—N2	1.353(4)	C3—C4—C5	105.8(3)
N3—C5	1.347(4)	N3—C5—C4	110.4(3)
C4—C5	1.403(4)	C5—N3—N2	104.7(2)
C3—C4	1.375(5)	C3—N2—N3	112.8(3)
C6—C5	1.473(5)	N2—C3—C2	122.1(3)
		N2—C3—C4	106.4(3)
C11—C6—C5—C4	−18.3(5)	C4—C3—C2—C1	50.5(5)
N1—C1—C2—C3	−103.2(3)	C12—N1—C1—C2	174.5(3)
C1—N1—C12—C17	162.8(3)		

Table 2

Crystallographic data, $C_{17}H_{14}ClN_3O$ **11c**.

CCDC deposit number [14]	738,969
Color/shape	Yellow/chip
Crystal dimensions (mm)	0.34 × 0.14 × 0.12
Formula	$C_{17}H_{14}ClN_3O$
Formula mass	311.76
T (K)	163
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	12.451(2)
b (Å)	9.642(2)
c (Å)	12.581(3)
β(°)	104.884(7)
V (Å^3)	1459.8(5)
Z	4
d_{calc} (g cm^{-3})	1.419
λ (Å)	0.71073
μ (mm^{-1})	0.267
F(000)	648
θ range (°)	2.70–25.15
Reflections collected	9944
Miller indices	$-14 \leq h \leq 13$, $-10 \leq k \leq 11$, $-15 \leq l \leq 15$
Unique reflections	2605
Unique reflections $I > 2\sigma(I)$	1915
Max and min transmission	1.000, 0.932
Data, restraints, parameters	2605, 0, 199
Final R indices $I > 2\sigma(I)$	$R_1 = 0.0613$, $wR_2 = 0.1425$
R indices all data	$R_1 = 0.0883$, $wR_2 = 0.1687$
Goodness of fit on F^2	1.052
Largest diff peak and hole (e Å^{-3})	0.322, −0.403

2.65 g (0.015 mol) dissolved in 40–60 mL of THF. After 3 h, a solution of 0.0158 mol (5% molar excess) of substituted benzoate ester dissolved in 25–35 mL of THF, was added, during 5 min, to the trilithiated intermediate **7**, and the solution was stirred overnight (N_2) at room temperature. Finally, 100 mL of 3*M* hydrochloric acid was added all at once, followed by an additional 100 mL of reagent grade ether, and the two-phase mixture was separated, followed by extraction of the aqueous layer with ether (2 × 50 mL). The combined organic fractions were extracted with 25 mL of 5% sodium bicarbonate solution, then 25 mL water. The resulting solution was dried ($MgSO_4$), decanted, and evaporated (if rotoevap. used, temperature of water bath ~40°C). An oil usually resulted, which was taken up in 50–75 mL of methanol followed by 6 mL of hydrazine hydrate, 1 mL of acetic acid, and the solution heated under reflux for 2–4 h. The resulting solution was allowed to evaporate, and the resulting solid was recrystallized, usually from common solvents to afford products **11a–l**.

2-[3-(4-Chlorophenyl)-1H-pyrazol-5-yl]-N-phenylacetamide (11a). Compound **11a** was obtained in 34% yield, mp 234–235°C (methanol), from the two-step procedure for the condensation-cyclization of **6** and methyl 4-chlorobenzoate. IR: 1651, 3217, and 3332 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.78 (s, 2H, CH_2), 6.63 (s, 1H, C_4—H, pyrazole), 7.05 (t, 1H, ArH, J = 7.5 Hz), 7.31 (t, 2H, ArH, J = 7.8 Hz), 7.45 (m, 2H, ArH), 7.63 (d, 2H, ArH, J = 7.8 Hz), 7.79 (m, 2H, ArH), 10.22 (s, 1H, NH), and 12.86 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 31.37, 102.78 (C4, pyrazole), 119.8, 124.0, 127.4, 129.4, 139.8, 147.3, 174.1, 178.5. LCMS, theor. exact mass, 311.08: exp. $(M+H)^+$ 312.0. Anal. Calcd for $C_{17}H_{14}ClN_3O \cdot 1/8\ H_2O$ [13]: C, 65.02; H, 4.57; N, 13.38. Found: C, 64.97; H, 4.28; N, 12.98.

2-[3-Phenyl-1H-pyrazol-5-yl]-N-phenylacetamide (11b). Compound **11b** was obtained in 31% yield, mp 222–224°C (methanol/benzene), from the two-step procedure for the condensation-cyclization of **6** and methyl benzoate. IR: 1668, 3195 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.72 (s, 2H, CH_2), 6.61 (s, 1H, C_4—H, pyrazole), 7.04 (t, 1H, ArH, J = 7.5 Hz), 7.31–7.43 (m, 5H, ArH), 7.64 (d, 2H, ArH, J = 7.5 Hz), 7.76 (d, 2H, ArH, J = 7.5 Hz), and 10.23 (NH). ^{13}C NMR (DMSO-d_6): 35.8, 102.6 (C4, pyrazole), 119.8, 124.0, 125.7, 128.2, 129.5, 132.6, 139.9, 168.4. LCMS, theor. exact mass, 277.12: exp. $(M+H)^+$, 278.04. Anal. Calcd for $C_{17}H_{15}N_3O$: C, 73.63; H, 5.45; N, 15.04. Found: C, 73.22; H, 5.47; N, 15.04.

2-[3-(3-Chlorophenyl)-1H-pyrazol-5-yl]-N-phenylacetamide (11c). Compound **11c** was obtained in 49% yield, mp 191–194°C (methanol), from the two-step procedure for the condensation-cyclization of **6** and methyl 3-chlorobenzoate. IR: 753, 1655, 3132, and 3194 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.78 (s, 2H, CH_2), 6.69 (s, 1H, C_4—H, pyrazole), 7.06 (t, 1H, ArH, J = 7.8 Hz), 7.29–7.44 (m, 4H, ArH), 7.63 (d, 2H, ArH, J = 7.5 Hz), 7.76 (d, 2H, ArH, J = 7.5 Hz), and 10.23 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 34.59, 103.5 (C4, pyrazole), 119.5, 124.7, 125.7, 127.8, 129.1, 131.7, 134.5, 139.9. LCMS, theor. exact mass, 311.08: exp. $(M+H)^+$, 312.01. Anal. Calcd for $C_{17}H_{14}\ ClN_3O \cdot 1/3\ H_2O$ [13]: C, 64.25; H, 4.65; N, 13.22. Found: C, 64.34; H, 4.84; N, 13.04.

Single crystal X-ray structure determination. Yellow crystals of $C_{17}H_{14}ClN_3O$ **11c** were recrystallized from an ethanol-water solution in order to give satisfactory crystals for X-ray

determination. Crystal data for X-ray studies were collected at 20°C on a Mercury CCD area detector coupled with a Rigaku AFC8 diffractometer with graphite monochromated Mo-K radiation. Data were collected in 0.5° oscillations in ω with 40 s exposures. A sweep of data was done using ω oscillations from −40.0° to 90.0° at $\chi = 45°$ and $\phi = 0.0°$; a second sweep was performed using ω oscillations from −30.0° to 80.0° at $\chi = 45°$ and $\phi = 90.0°$. The crystal-to-detector distance was 27.7789 mm. Details of the data collection are reported in Table 2. Data were collected, processed, and corrected for Lorentz polarization and for absorption using CrystalClear (Rigaku) [15].

The nonhydrogen atoms were refined anistropically. Ideal hydrogen atom coordinates for the rings containing C6 and C12 (see numbering of atoms in ORTEP diagram, Fig. 2) were calculated and the hydrogen atoms were allowed to ride on their respective carbon atoms. The hydrogen atoms on N1, N2, C2, and C4 were located by difference and then ideal coordinates were calculated and these hydrogen atoms were allowed to ride on their respective atoms. The temperature factors of all hydrogen atoms were varied isotropically. Structure solution, refinement, and the calculation of derived results were performed using the SHELX-97 [16] package of computer programs. Neutral atom scattering factors were those of Cromer and Waber [16], and the real and imaginary anomalous dispersion corrections were those of Cromer [17].

2-[3-(4-Methylphenyl)-1H-pyrazol-5-yl]-N-phenylacetamide (11d). Compound **11d** was obtained in 40% yield, mp 196–198°C (methanol), from the two-step procedure for the condensation-cyclization of **6** and methyl 4-methylbenzoate. IR: 1338, 1660 cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.51 (s, 2H, CH_3), 3.72 (s, 2H, CH_2), 6.56 (s, 1H, C_4—H, pyrazole), 7.05 (t, 1H, ArH, $J = 7.5$ Hz), 7.20–7.34 (m, 4H, ArH), 7.62–7.66 (m, 4H, ArH), 10.22 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 25.79, 26.23, 39.51, 54.04, 106.98 (C4, pyrazole), 124.6, 128.7, 130.4, 134.2, 134.4, 134.8, 142.3, 144.6, 173.3. LCMS, theor. exact mass 291.14: exp. $(M+H)^+$, 292.08. Anal. Calcd for $C_{18}H_{17}N_3O \cdot 1/2\ H_2O$ [13]: C, 71.90; H, 6.04; N, 13.99. Found: C, 72.01; H, 6.26; N, 14.38.

2-[3-(4-(1,1-Dimethylethyl)phenyl)-1H-pyrazol-5-yl]-N-phenylacetamide (11e). Compound **11e** was obtained in 37% yield, mp 262–265°C (methanol), from the two-step procedure for the condensation-cyclization of **6** and methyl 4-(1,1-dimethylethyl)benzoate. IR: 1676, 3128 cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.26 (s, 9H, CH_3), 3.44 (s, 2H, CH_2), 6.55 (s, 1H, C_4—H, pyrazole), 7.03 (t, 1H, ArH, $J = 7.5$ Hz), 7.29 (t, 2H, ArH, $J = 8.1$ Hz), 7.40 (d, 2H, ArH, $J = 8.4$ Hz), 10.20 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 26.6, 31.8, 35.0, 102.3 (C4, pyrazole), 113.1, 119.9, 123.9, 125.5, 125.2, 126.2, 129.4, 139.9. LCMS, theor. exact mass 333.18: exp. $(M+H)^+$, 334.10. Anal. Calcd for $C_{20}H_{23}N_3O$: C, 75.65; H, 6.95; N, 12.60. Found: C, 75.28; H, 7.01; N, 12.54.

2-[3-(4-Bromophenyl)-1H-pyrazol-5-yl]-N-phenylacetamide (11f). Compound **11f** was obtained in 19% yield, mp 246–249°C (methanol), from the two-step procedure for the condensation-cyclization of **6** and methyl 4-bromobenzoate. IR: 1651, 3209 cm^{-1}. ^1H NMR (DMSO-d_6): δ 3.44 (s, 2H, CH_2), 6.54 (s, 1H, C_4—H, pyrazole), 7.03 (d, 1H, ArH, $J = 8.3$ Hz), 7.31 (t, 2H, ArH, $J = 5.4$ Hz), and 7.57–7.62 (m, 4H, ArH) and 10.20 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 34.3, 102.6 (C4, pyrazole), 119.8, 124.0, 127.7, 129.4, 132.2, 139.0, 139.8, 142.2, 149.9, 172.2. LCMS, theor. exact mass 355.03: exp. $(M+H)^+$, 355.98. Anal. Calcd for $C_{17}H_{14}\ BrN_3O$: C, 57.32; H, 3.96; N, 11.85. Found: C, 56.94; H, 3.89; N, 11.83.

2-[3-(4-Methoxyphenyl)-1H-pyrazol-5-yl]-N-phenylacetamide (11g). Compound **11g** was obtained in 40% yield, mp 201–203°C (methanol), from the two-step procedure for the condensation-cyclization of **6** and methyl 4-methoxybenzoate. IR: 1660, 3283 cm^{-1}. ^1H NMR ($CDCl_3$): δ ^1H NMR (DMSO-d_6): δ 3.66 (s, 2H, CH_2), 3.75 (s, 3H, OCH_3), 6.47 (s, 1H, C_4—H, pyrazole), 6.94–7.05 (m, 3H, ArH), 7.24–7.31 (m, 2H, ArH), 7.58–7.67 (m, 4H, ArH) and 10.16 (s, NH). ^{13}C NMR (DMSO-d_6): 36.01, 54.86, 78.36, 100.94 (C4, pyrazole), 113.8, 119.2, 123.1, 126.3, 128.4, 129.4, 138.9, 158.8, 167.8. LCMS, theor. exact mass, 307.13: exp. $(M+H)^+$, 308.06. Anal. Calcd for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.11; H, 5.55; N, 13.51.

2-[3-[4-(Dimethylamino)phenyl]-1H-pyrazol-5-yl]-N-phenylacetamide (11h). Compound **11h** was obtained in a 19% yield, mp 272–275°C (DMF), from the two-step procedure for the condensation-cyclization of **6** and methyl 4-dimethylaminobenzoate. IR: 1610, 1670, 3184 cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.92 (s, 6H, CH_3), 3.67(s, 2H, CH_2), 6.38 (s, 1H, C_4—H, pyrazole), 6.72 (d, 2H, ArH, $J = 9.0$ Hz), 7.02 (t, 1H, ArH, $J = 7.2$ Hz), 7.27 (t, 2H, $J = 7.8$ Hz, ArH), 7.55 (d, 2H, ArH, $J = 8.7$ Hz), 7.62 (d, 2H, ArH, $J = 7.5$ Hz), 8.17 (d, 2H, ArH), 10.09 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 36.5, 44.0, 87.6, 101.0 (C4, pyrazole), 113.0, 119.8, 123.9, 126.6, 129.4, 139.2, 149.7, 139.9, 150.5. LCMS, theor. exact mass, 320.38: exp. $(M+H)^+$, 321.09. Anal. Calcd for $C_{19}H_{20}N_4O \cdot 1/4\ H_2O$ [13]: C, 70.24; H, 6.36; N, 17.34. Found: C, 70.30; H, 6.40; N, 17.49.

2-[3-(3,5-Dimethylphenyl)-1H-pyrazol-5-yl]-N-phenylacetamide (11i). Compound **11i** was obtained in a 40% yield, 222–224°C (ethanol/benzene), from the two-step procedure for the condensation-cyclization of **6** and methyl 3,5-dimethylbenzoate. IR: 1660, 3238 cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.29 (s, 6H, CH_3), 3.38 (s, 2H, CH_2), 6.55 (s, 1H, C_4—H, pyrazole), 6.92 (s, 1H, ArH), 7.05 (t, 1H, ArH, $J = 7.5$ Hz), 7.31 (t, 2H, ArH, $J = 7.5$ Hz), 7.37 (s, 1H, ArH), 7.61 (s, 2H, ArH), 7.64 (d, 2H, ArH, $J = 1.2$ Hz), 10.19 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 21.7, 37.6, 102.5 (C4, pyrazole), 107.0, 112.7, 119.8, 123.5, 123.9, 129.4, 130.0, 138.6, 139.9, 160.8. LCMS, theor. exact mass, 305.15: exp. $(M+H)^+$, 306.17. Anal. Calcd for $C_{19}H_{19}N_3O$: C, 74.73; H, 6.27; N, 13.76. Found: C, 74.34; H, 6.34; N, 13.66.

2-[3-(4-Aminophenyl)-1H-pyrazol-5-yl]-N-phenylacetamide (11j). Compound **11j** was obtained in a 32% yield, 178–180°C (ethanol), from the two-step procedure for the condensation-cyclization of **6** and methyl 4-aminobenzoate. IR: 1662, 2777, 3322 cm^{-1}. ^1H NMR (DMSO-d_6): δ 3.62 (s, 2H, CH_2), 5.32 (s, 1H, NH), 6.32 (s, 1H, C_4—H, pyrazole), 6.53 (s, 2H, NH), 6.58 (d, 2H, ArH, $J = 7.2$ Hz), 7.02 (t, 1H, ArH, $J = 7.5$ Hz), 7.28 (t, 2H, ArH), 7.36 (d, 2H, ArH, $J = 8.7$ Hz), 7.61 (d, 2H, ArH, $J = 7.5$ Hz), 10.18 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 39.5, 100.8 (C4, pyrazole), 113.2, 115.1, 119.8, 120.8, 121.7, 123.9, 125.9, 126.7, 129.4, 130.1, 139.9, 168.9. LCMS, theor. exact mass, 292.34: exp. $(M+H)^+$ 293.04. Anal. Calcd for $C_{17}H_{16}N_4O \cdot 1/4\ H_2O$ [13]: C, 68.79; H, 5.60; N, 18.87. Found: C, 68.85; H, 5.49; N, 18.26.

2-[3-(3,4-Dimethoxyphenyl)-1H-pyrazol-5-yl]-N-phenylacetamide (11k). Compound **11k** was obtained in a 19% yield, 198–

200°C (methanol), from the two-step procedure for the condensation-cyclization of **6** and methyl 3,4-dimethoxybenzoate. IR: 1655, 2931, 3193 cm^{-1}. ^1H NMR (DMSO-d_6): δ 3.68 (s, 2H, CH_2), 3.78 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 5.28 (s, 1H, NH), 6.35 (s, 1H, C_4—H, pyrazole), 6.54–6.76 (m, 3H, ArH) 6.94–7.18 (m, 3H, ArH), 7.49–7.57 (m, 3H, ArH), and 9.22 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): 37.9, 56.2, 87.5, 102.1 (C4, pyrazole), 109.4, 112.6, 118.1, 119.8, 123.9, 129.4, 139.9, 147.9, 149.6, 168.0. LCMS, theor. exact mass, 337.37: exp. $(M+H)^+$ 338.08. Anal. Calcd for $C_{19}H_{19}N_3O_3 \cdot 1/4\ H_2O$ [13]: C, 66.75; H, 5.75; N, 12.29. Found: C, 67.11; H, 5.62; N, 12.23.

2-[3-(3-Chloro-4-methoxyphenyl)-1H-pyrazol-5-yl]-N-phenylacetamide (11l). Compound **11l** was obtained in a 30% yield, 215–218°C (ethanol) from the two-step procedure for the condensation-cyclization of **6** and methyl 3-chloro-4-methoxybenzoate. IR: 1502, 1600, 1667, 2839, 3263 cm^{-1}. ^1H NMR (DMSO-d_6): δ 3.77 (s, 2H, CH_2), 3.85 (s, 3H, CH_3O), 5.41 (s, 1H, NH) 6.56 (s, 1H, C_4—H, pyrazole), 7.03 (t, 1H, ArH, J = 7.2 Hz), 7.14 (d, 1H, ArH, J = 8.4 Hz), 7.31 (t, 2H, ArH, J = 7.5 Hz), 7.60 (d, 1H, ArH, J = 1.8 Hz), 7.69 (d, 2H, ArH, J = 1.8 Hz), 7.80 (s, 1H, ArH), 12.74 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 26.2, 40.2, 56.8, 103.3 (C4, pyrazole), 113.7, 119.8, 122.0, 124.0, 125.6, 126.9, 129.4, 139.8, 154.5, 167.9. LCMS, theor. exact mass, 341.09: exp. $(M+H)^+$, 342.01. Anal. Calcd for $C_{18}H_{16}ClN_3O_2$: C, 63.25; H, 4.72; N, 12.29. Found: C, 62.91; H, 4.79; N, 12.19.

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