HETEROCYCLES, Vol. 61, 2003, pp. 197 - 223
Received, 26th May, 2003, Accepted, 28th July, 2003, Published online, 4th August, 2003

TRANSFORMATIONS OF ALKYL (5-OXO-1-PHENYL-4,5-DIHYDRO-1*H*-PYRAZOL-3-YL)ACETATES INTO 5-HETEROARYL-3-OXO-2-PHENYL-3,5-DIHYDRO-2*H*-PYRAZOLO[4,3–*c*]PYRIDINE-7-CARBOXYLATES

David Bevk, Renata Jakše, Jurij Svete,* Amalija Golobič, Ljubo Golič, and Branko Stanovnik*

Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, 1000 Ljubljana, Slovenia

On the occasion of the 30th Anniversary of *HETEROCYCLES*.

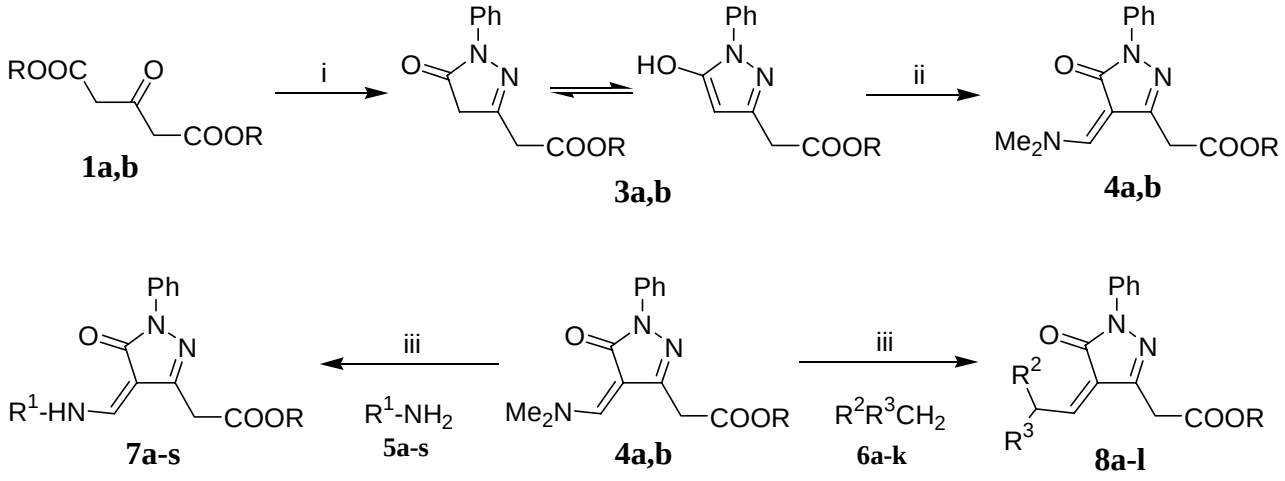
Abstract – Alkyl [(*Z*)-4-dimethylaminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (**4**) was transformed with *N*- and *C*-nucleophiles into alkyl [4-(substituted amino)methylidene-4,5-dihydro-1*H*-pyrazol-3-yl]acetates (**7**) and alkyl (4-heteroarylmethylidene-4,5-dihydro-1*H*-pyrazol-3-yl)acetates (**8**), respectively. Compounds (**7**) cyclize by heating with DMFDMA in DMF into 2*H*-pyrazolo[4,3–*c*]pyridine-7-carboxylates (**9**).

Pyrazolo[4,3–*c*]pyridines and their [3,4–*c*] analogues are structurally related to some biologically active compounds, like the nucleotide antibiotics formycin[1,2] and allopurinol.[3] Some of pyrazolo[4,3–*c*]pyridine derivatives exhibit a broad spectrum of antitumor activity.[4] There are only few methods starting from substituted pyrazoles described in the literature.[5] Other methods for the preparation of pyrazolo-[4,3–*c*]-pyridines involve an aza Wittig-type reaction starting from 5-formyl-1-phenylpyrazole,[6] intramolecular cycloaddition of azomethine imines,[7] ring opening of pyrido[4,3–*d*]pyrimidine derivatives with sodium methoxide followed by rearrangement and cyclization,[8] photochemical irradiation of 4-hydrazino-isoxazolo[5,4–*b*]pyridines,[9] cyclization of diazonium salts, generated from 5-alkyl-4-amino-2-trifluoro-methylpyridines,[10] nitrosation of *N*-acylated 4-amino-3-methylpyridines,[11] treatment of piperidones with hydrazines which afforded 1,4,5,6-tetrahydropyrazolo[4,3–*c*]pyridines,[12] treatment of (*E*)-1-methyl-3,5-

bis(4-methylbenzylidene)-4-piperidone and analogues with hyrazines,[4] from 4-amino-5-methylnicotic acid,[13] and from *N*-substituted 4-pyridone benzoylhydrazones.[14] 5-Alkoxy-3-(*N*-substituted carbamoyl)-1-phenylpyrazoles were prepared and tested for antiinflamatory and hypnotic activity.[15]

In continuation of our research, we describe in this paper the synthesis of 5-heteroaryl-3-oxo-2-phenyl-3,5-dihydro-2*H*-pyrazolo[4,3–*c*]pyridine-7-carboxylates (**9**) from alkyl (5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)acetates (**3**). Ethyl (5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)acetate[16a,b] (**3a**) and its corresponding methyl ester[16c] (**3b**) have been prepared according to the methods described in the literature.

Compounds (**3a,b**) were transformed with *N*,*N*-dimethylformamide dimethylacetal (DMFDMA) in toluene at room temperature into ethyl [(*Z*)-4-(dimethylamino)methylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (**4a**) and the corresponding methyl ester (**4b**). They reacted with *N*- and *C*-nucleophiles in ethanol in the presence of small amounts of hydrochloric acid at room temperature to give the corresponding dimethylamine substitution products (**7**) and (**8**). In the *N*-nucleophile series, aromatic and heterocyclic amines (**5a–s**) were used. The corresponding methyl and ethyl (*Z*)-[5-oxo-1-phenyl-4-(hetero)arylaminomethylidene-4,5-dihydro-1*H*-pyrazol-3-yl]acetates (**7a–s**) were produced. In IR spectra of **7q** and **7r**, obtained from **3a,b** and aminoacetonitrile (**5q**), we did not observe any absorption in the region between 2100cm^{-1} and 2200cm^{-1}, characteristic for the C≡N group. We thought at first that cyclization occured to give alkyl (7-imino-1-phenyl-6,7-dihydro-1*H*-pyrazolo[4,3–*f*][1,4]oxazepin-3-yl)acetates. However, the X-Ray analysis shows, that compounds (**7q**) and (**7r**) in fact exist in the cyano form. Reactions with *C*-nucleophiles proceeded under the same conditions to form **8a–l** in 57–98% yield (Scheme 1).



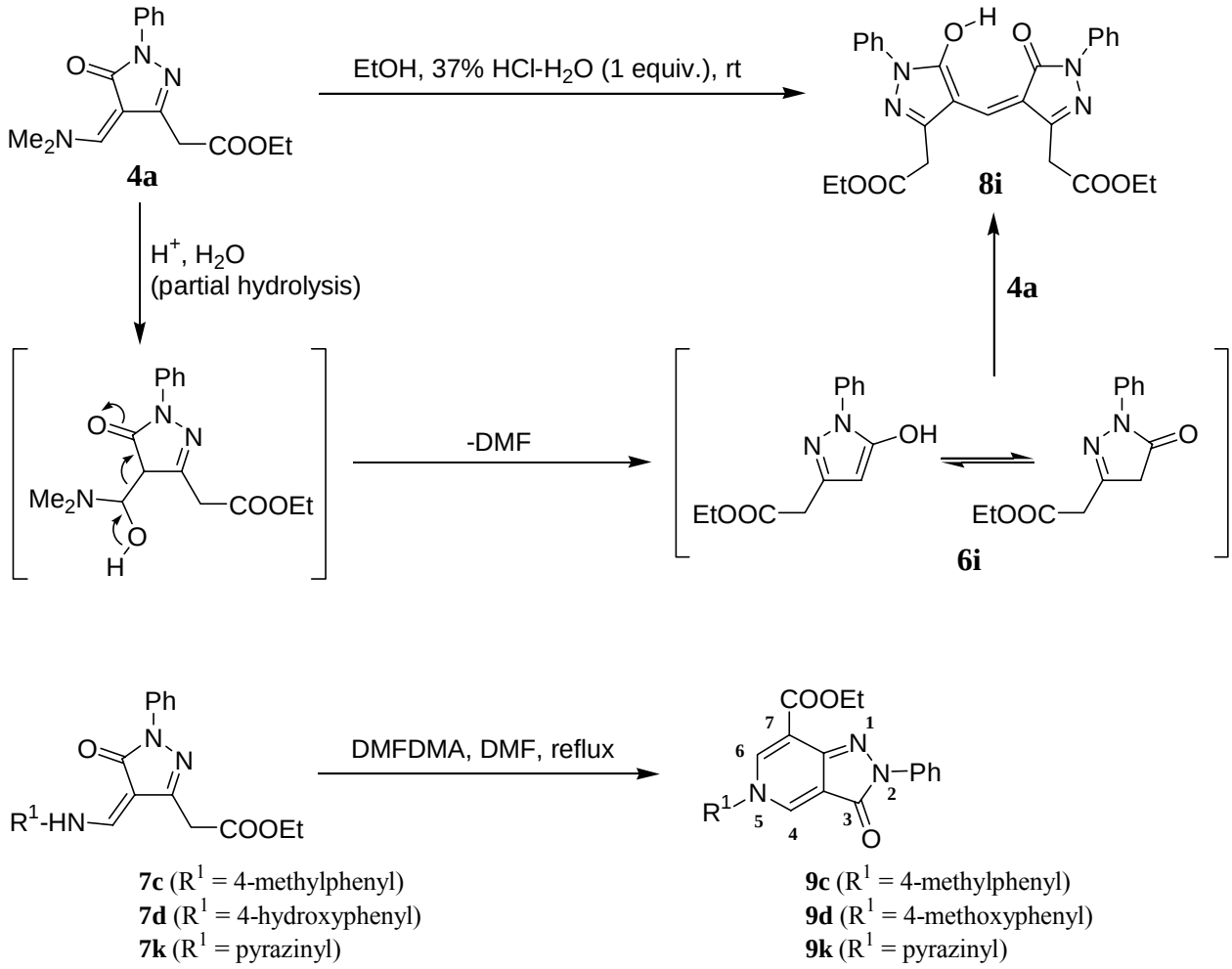
Scheme 1. (i) Ph–NHNH$_2$ (**2**), rt–70 °C; (ii) DMFDMA, toluene, rt; (iii) R^1–NH$_2$ (**5a–s**, **5**→**7**) or R^{2}R^{3}CH$_2$ (**6a–k**, **6**→**8**), EtOH, 37% HCl–H$_2$O (1 equiv.), rt

Reaction	R	R^1	Reaction	R	R^1
5a→7a	Et	phenyl	**5q→7q**	Et	cyanomethyl
5a→7b	Me	phenyl	**5q→7r**	Me	cyanomethyl
5c→7c	Et	4-methylphenyl	**5s→7s**	Et	phenylamino
5d→7d	Et	4-hydroxyphenyl	**Reaction**	**R**	**R^2R^3CH**
5e→7e	Me	4-methoxyphenyl	**6a→8a**	Et	6-hydroxy-2,2-dimethyl-4-oxo-4*H*-[1,3]-dioxin-5-yl
5f→7f	Et	pyridin-2-yl	**6b→8b**	Et	6-hydroxy-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl
5f→7g	Me	pyridin-2-yl	**6b→8c**	Me	6-hydroxy-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl
5h→7h	Et	quinolin-3-yl	**6d→8d**	Et	6-hydroxy-4-oxo-2-thioxo-1,2,3,4-tetra-hydropyrimidin-5-yl
5i→7i	Et	2,4-dihydroxypyri-midin-5-yl	**6e→8e**	Et	6-hydroxy-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl
5i→7j	Me	2,4-dihydroxypyri-midin-5-yl	**6e→8f**	Me	6-hydroxy-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl
5k→7k	Et	pyrazinyl	**6g→8g**	Et	3-hydroxy-1-oxo-1*H*-inden-2-yl
5k→7l	Me	pyrazinyl	**6g→8h**	Me	3-hydroxy-1-oxo-1*H*-inden-2-yl
5m→7m	Et	1*H*-pyrazol-3-yl	**6i→8i**	Et	3-ethoxycarbonylmethyl-5-oxo-1-phenyl-1,5-dihydro-1*H*-pyrazol-4-yl
5n→7n	Me	1*H*-indazol-3-yl	**6i→8j**	Me	3-ethoxycarbonylmethyl-5-oxo-1-phenyl-1,5-dihydro-1*H*-pyrazol-4-yl
5o→7o	Et	benzothiazol-3-yl	**6k→8k**	Et	5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl
5p→7p	Et	hydroxy	**6l→8l**	Et	5-hydroxy-1,3-diphenyl-1*H*-pyrazol-4-yl

Scheme 1 (Continued).

When compound (**4a**) was heated in ethanol under reflux in the presence of hydrochloric acid (*Z*)-[4-(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-ylmethylidene)-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]-acetate (**8i**) was obtained in 75%. This compound was identical with the compound (**8i**) prepared from **4a** and **6i** in 90% yield. Apparently, partial hydrolysis of enamine (**4a**) took place to furnish *in situ* the

pyrazole derivative (**6i**) as the *C*-nucleophile, which reacted with the non-hydrolysed enaminone (**4a**) to afford **8i**. Preparation of analogous compound from 3-ethoxycarbonyl-5-oxo-1-phenyl-1*H*-pyrazole and 1,3,5-triazine has been reported previously.[17] Compounds (**7c,d,k**) were heated with 2 equivalents of DMFDMA in DMF at reflux temperature to give pyrazolo[4,3–*c*]pyridines (**9c,d,k**) in moderate yields. Cyclisation proceeds by incorporation of DMFDMA as C_1 synthon between the nucleophilic NH and CH_2 groups. In the reaction of **7d** with DMFDMA, also methylation of the phenolic hydroxy group took place to give the 5-(4-methoxyphenyl)pyrazolo[4,3–*c*]pyridine derivative (**9d**) (Scheme 2).

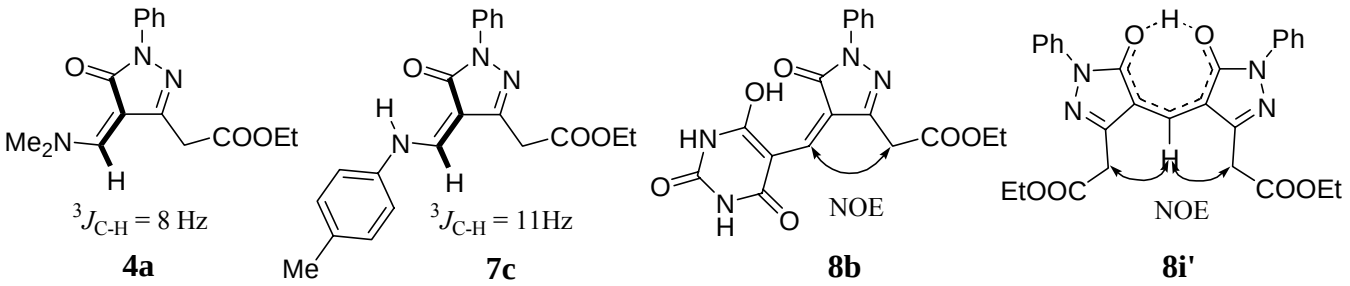


Scheme 2

Structure determination

The structures of all compounds were established on the basis of elemental analysis for C H N, IR, MS and NMR spectra. The orientation around the exocyclic double bond in compounds (**4a**) and (**7c**) was

established on the basis of 2D-HMBC NMR technique. Namely, the magnitude of the coupling constants, $^3J_{1H\text{-}13C,}$ for nuclei with (*Z*)-orientation around the C=C double bond are smaller (2–6 Hz) than those for the (*E*)-oriented ones (8-12 Hz).[18] The HMBC correlation technique has been found the most suitable for the determination of the orientation around the C=C double bond in analogous compounds.[19] Accordingly, for compound (**4a**) the heteronuclear coupling constant, $^3J_{1H–13C}$ = 8 Hz, indicates the (*Z*)-orientation and similarly for compound (**7c**), $^3J_{1H–13C}$ = 11 Hz, clearly indicates the (*Z*)-orientation, while for compounds (**8b**) and (**8i**) the (*Z*)-orientation was established on the basis of the NOE effect between methylidene proton and CH_2 group of the ethoxycarbonylmethyl group. Compound (**8i**) exhibits only one singlet for both CH_2 groups of ethoxymethyl groups at δ = 3.803 ppm and only one singlet for the methylidene proton at δ = 7.657 ppm. This means that fast tautomerisation between two identical structures is taking place. Since the NOE effect was observed between the methylidene proton and both CH_2 groups the compound is best represented by structure (**8i'**) (Scheme 3).



Scheme 3

The ^{1}H NMR spectra of compounds (**9**) exhibit beside the signals characteristic for ethoxy groups and groups attached to nitrogen atoms at 2- and 5-positions, a doublet in the range at δ = 8.15–8.76 ppm for 4–H and at δ = 8.32–8.97 ppm for 6-H with a coupling constant $J_{4H–6H}$= 1.5 Hz.

The structures for compounds (**4a**), (**7f**), (**7r**) and (**8g**) in the solid state were confirmed by the X-Ray analysis.

X-Ray structure analysis

Diffraction data for compounds (**4a**), (**7f**), (**7r**) and (**8g**) were collected on a Nonius Kappa CCD diffractometer with graphite monochromated Mo*Kα* radiation. The data were processed using DENZO[20] program. Structures were solved by direct methods using SIR97.[21] We employed full-matrix least-squares

refinements on F magnitudes with anisotropic displacement factors for all non-hydrogen atoms using Xtal3.6.[22] The positions of hydrogen atoms were obtained from the difference Fourier maps, only the positions of some of H atoms of ethyl group in **8g** were calculated according to expected geometry. For **4a** H-atoms parameters were not refined, for **7f** and **8g** only positional parameters of H atoms were refined (the exception were H atoms of ethyl group in **8g**, which were not refined) and for **7s** the positional parameters of H atoms together with their isotropic displacement factors were refined (the exception were H atoms bonded to C8a and C8b, which were not refined). In the final cycle of the refinement we used 2945, 2931, 5825 and 3068 reflections and 199, 290, 485 and 311 parameters for **4a**, **7f**, **7r** and **8g**, respectively. The resulting crystal data and details concerning data collection and refinement for all four compounds are quoted in Table 1. Final atomic coordinates and equivalent isotropic displacement parameters with their e.s.d.'s are reported in Tables 2, 3, 4 and 5. Bond lengths and bond angles for nonhydrogen atoms are listed in Tables 6, 7, 8 and 9 for **4a**, **7f**, **7r** and **8g**, respectively. ORTEP[23] drawings of the content of asymmetric units of all four compounds showing the atom-labeling scheme are presented in Figures 1, 2, 3 and 4.

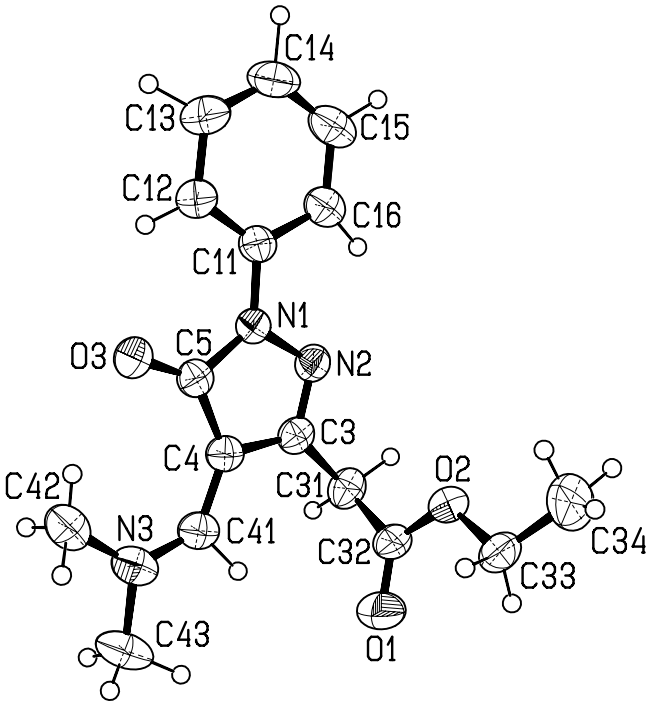


Figure 1. ORTEP view of the asymmetric unit of compound (4a) with labeling of nonhydrogen atoms. (Ellipsoids are drawn at 50% probability level.)

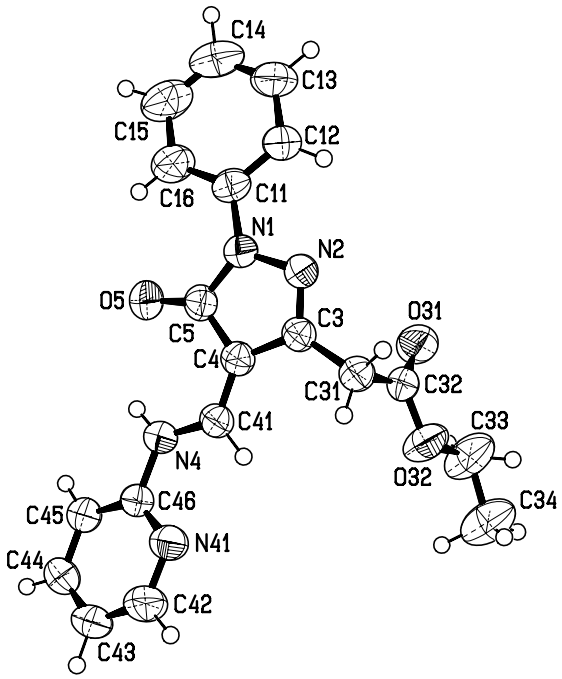


Figure 2. ORTEP view of the asymmetric unit of compound (**7f**) with labeling of nonhydrogen atoms. (Ellipsoids are drawn at 50% probability level.)

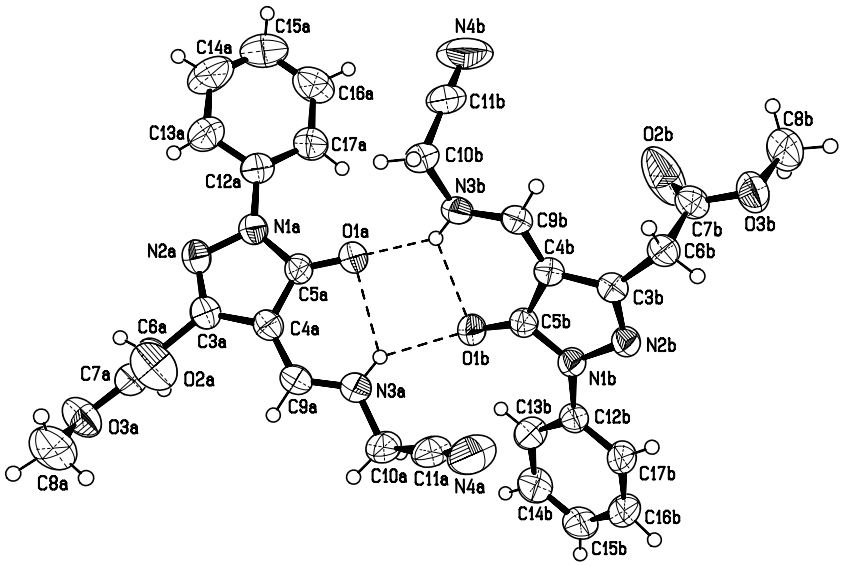


Figure 3. ORTEP view of the asymmetric unit of compound (**7r**) with labeling of nonhydrogen atoms. (Ellipsoids are drawn at 50% probability level.)

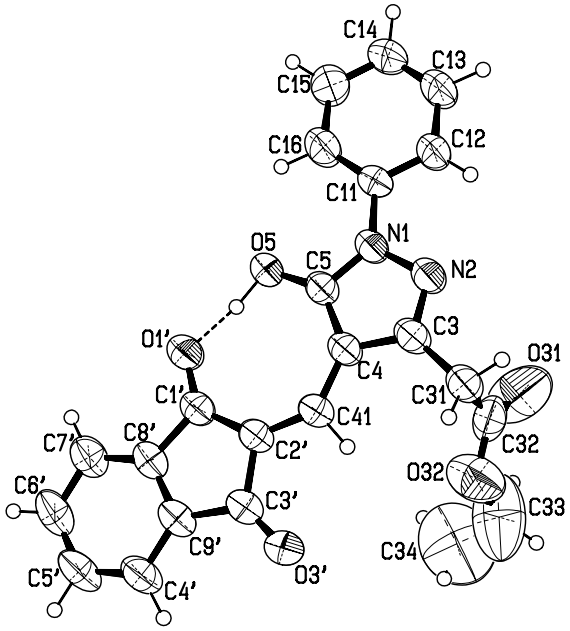


Figure 4. ORTEP view of the asymmetric unit of compound (**8g**) with labeling of nonhydrogen atoms. (Ellipsoids are drawn at 50% probability level.)

Table 1. Crystal data, data collection and structure refinement for compounds (**4a**), (**7f**), (**7r**), and (**8g**).

	compound (**4a**)	compound (**7f**)	compound (**7r**)	compound (**8g**)
Formula	$C_{16}H_{19}N_3O_3$	$C_{19}H_{18}N_4O_3$	$C_{15}H_{14}N_4O_3$	$C_{23}H_{18}N_2O_5$
Rel. formula weight	301.35	350.38	298.30	402.41
Crystal System	triclinic	triclinic	triclinic	triclinic
Space group	P-1, No. 2	P-1, No. 2	P-1, No. 2	P-1, No. 2
a (Å)	7.0295(2)	7.5228(2)	11.2154(2)	8.3447(2)
b (Å)	10.7698(3)	10.6141(2)	11.4495(2)	10.6533(2)
c (Å)	11.6596(3)	11.2966(2)	13.0384(2)	12.5502(3)
α (˚)	102.445(1)	87.576(1)	69.463(1)	103.267(1)
β (˚)	105.817(1)	78.894(1)	71.304(1)	109.266(1)
γ (˚)	105.791(1)	76.511(1)	78.807(1)	103.557(1)
V (Å^3)	776.20(4)	860.70(3)	1478.82(4)	964.94(4)
Z	2	2	4	2
ρ (Mg m^{-3})	1.289	1.352	1.340	1.385
μ (mm^{-1})	0.091	0.094	0.097	0.099
Color of crystal	colorless	yellow	yellow	orange-red
Shape of crystal	prism	prism	prism	prism
Dimensions (mm)	0.40×0.20×0.20	0.30×0.20×0.10	0.40×0.40×0.20	0.35×0.30×0.20
Temperature (K)	293	293	293	293
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073

θ_{max} (°)	27.5	27.5	27.5	27.5
No. of integr. refl.	13480	19287	24317	16592
No. of indep. refl.	3536	3918	6714	4343
R_{int}	0.052	0.042	0.036	0.038
No. of observed refl.	2093	2931	4572	3068
Threshold criterion	$F^2 > 2.0\sigma(F^2)$	$F^2 > 2.5\sigma(F^2)$	$F^2 > 2.0\sigma(F^2)$	$F^2 > 3.0\sigma(F^2)$
Final R and R_w	0.067, 0.048	0.058, 0.060	0.057, 0.044	0.072, 0.075
$(\Delta/\sigma)_{max}$	0.0003	0.136	0.0004	0.203
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.32, -0.38	0.38, -0.24	0.42, -0.38	0.34, -0.24

Table 2. Fractional Coordinates and Equivalent Temperature Factors (Å2) for compound (**4a**). U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U_{eq}
N(1)	0.0987(3)	0.8120(2)	0.4318(2)	0.041(1)
N(2)	0.1103(2)	0.8060(2)	0.5516(1)	0.044(1)
N(3)	0.4577(3)	1.2703(2)	0.5997(2)	0.054(1)
O(1)	0.5926(3)	1.1037(2)	0.9127(2)	0.071(1)
O(2)	0.5342(2)	0.8841(1)	0.8253(1)	0.049(1)
O(3)	0.1995(2)	0.9733(1)	0.3353(1)	0.055(1)
C(3)	0.2122(3)	0.9292(2)	0.6268(2)	0.042(1)
C(4)	0.2739(3)	1.0249(2)	0.5631(2)	0.041(1)
C(5)	0.1944(3)	0.9440(2)	0.4313(2)	0.041(1)
C(11)	0.0001(3)	0.6904(2)	0.3310(2)	0.043(1)
C(12)	-0.0316(4)	0.6875(2)	0.2077(2)	0.060(2)
C(13)	-0.1293(5)	0.5628(3)	0.1129(2)	0.075(2)
C(14)	-0.1919(4)	0.4423(2)	0.1384(2)	0.070(2)
C(15)	-0.1598(4)	0.4463(2)	0.2609(3)	0.064(2)
C(16)	-0.0658(3)	0.5680(2)	0.3569(2)	0.052(1)
C(31)	0.2484(3)	0.9575(2)	0.7639(2)	0.051(1)
C(32)	0.4770(3)	0.9920(2)	0.8422(2)	0.046(1)
C(33)	0.7518(3)	0.9057(2)	0.8945(2)	0.053(1)
C(34)	0.7745(5)	0.7716(3)	0.8811(4)	0.091(2)
C(41)	0.3846(3)	1.1620(2)	0.6309(2)	0.046(1)
C(42)	0.4349(4)	1.2732(2)	0.4740(3)	0.066(2)
C(43)	0.5641(4)	1.4026(2)	0.6969(3)	0.069(2)

Table 3. Fractional Coordinates and Equivalent Temperature Factors (Å2) for compound (**7f**). U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U_{eq}
O(31)	0.6850(3)	0.21256(17)	0.71094(16)	0.0686(7)
O(32)	0.6359(3)	0.34658(18)	0.86560(14)	0.0655(7)
O(5)	0.67952(25)	0.57897(16)	0.31008(14)	0.0610(6)
N(1)	0.86953(24)	0.38792(16)	0.37000(15)	0.0442(6)
N(2)	0.91557(24)	0.33352(16)	0.47880(15)	0.0446(6)
N(4)	0.50546(25)	0.73704(16)	0.52501(17)	0.0450(6)
N(41)	0.4560(3)	0.86994(19)	0.69128(17)	0.0575(7)
C(11)	0.9399(3)	0.31370(21)	0.26292(19)	0.0466(7)
C(12)	1.0402(4)	0.18757(23)	0.26887(23)	0.0615(9)
C(13)	1.1021(5)	0.1118(3)	0.16536(25)	0.0768(12)
C(14)	1.0656(5)	0.1613(3)	0.0563(3)	0.0797(12)

C(15)	0.9708(5)	0.2878(4)	0.04979(25)	0.0830(13)
C(16)	0.9067(4)	0.3656(3)	0.15231(22)	0.0675(10)
C(3)	0.82396(25)	0.41604(18)	0.56323(18)	0.0411(6)
C(31)	0.8390(3)	0.38927(22)	0.69257(19)	0.0468(7)
C(32)	0.7118(3)	0.30586(20)	0.75467(18)	0.0463(7)
C(33)	0.5120(6)	0.2717(4)	0.9358(3)	0.0875(15)
C(34)	0.4412(6)	0.3324(5)	1.0538(3)	0.0920(16)
C(4)	0.71268(25)	0.52868(19)	0.51661(18)	0.0415(6)
C(41)	0.6071(3)	0.63828(19)	0.57660(19)	0.0425(7)
C(42)	0.3753(4)	0.98296(25)	0.74813(24)	0.0681(10)
C(43)	0.2535(4)	1.08057(24)	0.70255(23)	0.0647(9)
C(44)	0.2083(4)	1.06181(22)	0.59347(22)	0.0568(8)
C(45)	0.2885(3)	0.94688(21)	0.53263(20)	0.0489(7)
C(46)	0.4124(3)	0.85467(19)	0.58563(18)	0.0431(6)
C(5)	0.7443(3)	0.50755(20)	0.38796(18)	0.0445(7)

Table 4. Fractional Coordinates and Equivalent Temperature Factors ($Å^2$) for compound (**7r**). U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U_{eq}
O(1a)	0.7716(1)	-0.0565(1)	0.6351(1)	0.0577(8)
O(1b)	0.7002(1)	0.1584(1)	0.74241(9)	0.0530(7)
O(2a)	1.1582(2)	-0.3855(2)	0.7437(1)	0.087(1)
O(2b)	0.1885(2)	0.2388(4)	0.8800(2)	0.132(2)
O(3a)	1.3566(1)	-0.3839(2)	0.6360(2)	0.078(1)
O(3b)	0.0835(1)	0.2655(2)	1.0459(1)	0.080(1)
N(1a)	0.8842(1)	-0.1950(1)	0.5340(1)	0.0488(8)
N(1b)	0.5927(1)	0.2825(1)	0.8599(1)	0.0451(8)
N(2a)	1.0075(1)	-0.2535(1)	0.5101(1)	0.0518(8)
N(2b)	0.4769(1)	0.2847(1)	0.9433(1)	0.0458(8)
N(3a)	0.9470(1)	0.0139(1)	0.7233(1)	0.0505(9)
N(3b)	0.5358(1)	-0.0368(1)	0.7881(1)	0.0466(9)
N(4a)	0.8371(2)	0.0793(3)	0.9752(2)	0.093(2)
N(4b)	0.3054(3)	-0.1353(3)	0.7268(4)	0.130(3)
C(3a)	1.0692(2)	-0.2155(1)	0.5601(1)	0.0483(9)
C(3b)	0.4173(1)	0.1953(1)	0.9475(1)	0.0440(9)
C(4a)	0.9913(1)	-0.1317(1)	0.6193(1)	0.0469(9)
C(4b)	0.4895(1)	0.1284(1)	0.8711(1)	0.0428(9)
C(5a)	0.8692(1)	-0.1195(1)	0.6008(1)	0.0450(9)
C(5b)	0.6065(1)	0.1866(1)	0.8144(1)	0.0424(9)
C(6a)	1.2061(2)	-0.2571(2)	0.5480(2)	0.058(1)
C(6b)	0.2891(2)	0.1727(2)	1.0300(1)	0.048(1)
C(7a)	1.2346(2)	-0.3480(2)	0.6539(2)	0.054(1)
C(7b)	0.1839(2)	0.2304(2)	0.9744(1)	0.052(1)
C(8a)	1.3987(3)	-0.4692(3)	0.7314(3)	0.102(2)
C(8b)	-0.0243(2)	0.3269(3)	1.0026(3)	0.095(2)
C(9a)	1.0234(1)	-0.0691(2)	0.6782(1)	0.048(1)
C(9b)	0.4606(1)	0.0241(1)	0.8575(1)	0.0450(9)
C(10a)	0.9886(2)	0.0864(2)	0.7748(2)	0.062(1)
C(10b)	0.5086(2)	-0.1544(2)	0.7860(2)	0.055(1)
C(11a)	0.9051(2)	0.0810(2)	0.8875(2)	0.064(1)
C(11b)	0.3949(2)	-0.1435(2)	0.7531(2)	0.068(1)
C(12a)	0.7931(2)	-0.2217(2)	0.4933(1)	0.051(1)
C(12b)	0.6774(1)	0.3704(1)	0.8385(1)	0.0443(9)
C(13a)	0.8185(3)	-0.3225(2)	0.4524(2)	0.075(2)
C(13b)	0.7793(2)	0.3942(2)	0.7411(2)	0.057(1)
C(14a)	0.7292(4)	-0.3464(3)	0.4104(3)	0.102(3)
C(14b)	0.8592(2)	0.4819(2)	0.7236(2)	0.065(1)

C(15a)	0.6161(3)	-0.2751(3)	0.4120(2)	0.093(2)
C(15b)	0.8402(2)	0.5462(2)	0.7989(2)	0.063(1)
C(16a)	0.5928(2)	-0.1746(3)	0.4507(2)	0.084(2)
C(16b)	0.7395(2)	0.5224(2)	0.8959(2)	0.065(1)
C(17a)	0.6816(2)	-0.1457(2)	0.4898(2)	0.066(1)
C(17b)	0.6582(2)	0.4351(2)	0.9156(2)	0.056(1)

Table 5. Fractional Coordinates and Equivalent Temperature Factors ($Å^2$) for compound (**8g**). U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U_{eq}
O(31)	0.779(1)	0.1666(4)	0.8225(3)	0.205(4)
O(32)	0.7211(5)	0.0521(4)	0.6412(3)	0.132(2)
O(5)	0.7291(3)	0.6353(2)	0.6436(2)	0.070(1)
O(1')	0.8061(3)	0.6020(2)	0.4692(2)	0.075(1)
O(3')	0.6904(4)	0.1256(2)	0.3151(2)	0.087(1)
N(1)	0.6320(3)	0.5324(2)	0.7637(2)	0.060(1)
N(2)	0.5729(4)	0.4029(2)	0.7725(2)	0.069(1)
C(11)	0.6461(4)	0.6484(3)	0.8552(2)	0.058(1)
C(12)	0.6087(5)	0.6256(3)	0.9484(3)	0.080(2)
C(13)	0.6127(6)	0.7331(4)	1.0366(3)	0.094(2)
C(14)	0.6576(6)	0.8626(3)	1.0343(3)	0.085(2)
C(15)	0.6929(7)	0.8851(4)	0.9402(4)	0.103(2)
C(16)	0.6861(7)	0.7781(3)	0.8494(3)	0.095(2)
C(3)	0.5772(4)	0.3179(3)	0.6812(2)	0.064(1)
C(31)	0.5262(5)	0.1688(3)	0.6659(3)	0.078(2)
C(32)	0.6911(7)	0.1313(3)	0.7200(3)	0.095(2)
C(33)	0.877(1)	0.001(1)	0.682(1)	0.216(8)
C(34)	0.973(2)	0.024(2)	0.631(2)	0.27(1)
C(4)	0.6403(3)	0.3856(3)	0.6088(2)	0.057(1)
C(41)	0.6637(4)	0.3171(3)	0.5077(2)	0.057(1)
C(5)	0.6727(3)	0.5253(3)	0.6674(2)	0.055(1)
C(1')	0.7873(4)	0.4844(3)	0.4096(2)	0.058(1)
C(2')	0.7237(4)	0.3550(3)	0.4262(2)	0.057(1)
C(3')	0.7322(4)	0.2477(3)	0.3301(2)	0.064(1)
C(4')	0.8305(5)	0.2680(4)	0.1559(3)	0.079(2)
C(5')	0.8918(5)	0.3587(4)	0.1037(3)	0.086(2)
C(6')	0.9224(5)	0.4959(4)	0.1507(3)	0.087(2)
C(7')	0.8935(5)	0.5487(4)	0.2520(3)	0.076(1)
C(8')	0.8312(4)	0.4575(3)	0.3034(2)	0.061(1)
C(9')	0.7997(4)	0.3191(3)	0.2565(2)	0.065(1)

Table 6. Bond Distances (Å) and Bond Angles (°) with e.s.d.'s in parentheses for compound (**4a**).

N(1)-N(2)	1.394(3)	C(3)-C(31)	1.497(3)
N(1)-C(5)	1.399(3)	C(4)-C(5)	1.457(3)
N(1)-C(11)	1.406(2)	C(4)-C(41)	1.396(2)
N(2)-C(3)	1.297(2)	C(11)-C(12)	1.385(3)
N(3)-C(41)	1.309(3)	C(11)-C(16)	1.401(3)
N(3)-C(42)	1.439(4)	C(12)-C(13)	1.393(3)
N(3)-C(43)	1.461(3)	C(13)-C(14)	1.376(4)
O(1)-C(32)	1.208(2)	C(14)-C(15)	1.373(4)
O(2)-C(32)	1.322(3)	C(15)-C(16)	1.379(3)
O(2)-C(33)	1.448(2)	C(31)-C(32)	1.511(3)
O(3)-C(5)	1.233(3)	C(33)-C(34)	1.475(5)
C(3)-C(4)	1.437(3)		

N(2)-N(1)-C(5)	112.6(1)	N(1)-C(5)-C(4)	103.6(2)
N(2)-N(1)-C(11)	118.3(2)	O(3)-C(5)-C(4)	132.8(2)
C(5)-N(1)-C(11)	129.1(2)	N(1)-C(11)-C(12)	122.4(2)
N(1)-N(2)-C(3)	106.1(2)	N(1)-C(11)-C(16)	118.5(2)
C(41)-N(3)-C(42)	125.5(2)	C(12)-C(11)-C(16)	119.1(2)
C(41)-N(3)-C(43)	119.4(2)	C(11)-C(12)-C(13)	119.1(2)
C(42)-N(3)-C(43)	115.1(2)	C(12)-C(13)-C(14)	121.9(2)
C(32)-O(2)-C(33)	116.3(1)	C(13)-C(14)-C(15)	118.6(2)
N(2)-C(3)-C(4)	113.0(2)	C(14)-C(15)-C(16)	121.0(2)
N(2)-C(3)-C(31)	119.3(2)	C(11)-C(16)-C(15)	120.3(2)
C(4)-C(3)-C(31)	127.7(2)	C(3)-C(31)-C(32)	112.6(2)
C(3)-C(4)-C(5)	104.7(2)	O(1)-C(32)-O(2)	124.1(2)
C(3)-C(4)-C(41)	120.1(2)	O(1)-C(32)-C(31)	124.4(2)
C(5)-C(4)-C(41)	135.2(2)	O(2)-C(32)-C(31)	111.5(1)
N(1)-C(5)-O(3)	123.6(2)	O(2)-C(33)-C(34)	108.1(2)

Table 7. Bond Distances (Å) and Bond Angles (°) with e.s.d.'s in parentheses for compound (**7f**).

O(31)-C(32)	1.199(3)	C(12)-C(13)	1.388(4)
O(32)-C(32)	1.3183(24)	C(13)-C(14)	1.371(5)
O(32)-C(33)	1.462(5)	C(14)-C(15)	1.371(5)
O(5)-C(5)	1.2339(2)	C(15)-C(16)	1.391(4)
N(1)-C(5)	1.3898(2)	C(3)-C(4)	1.4344(25)
N(1)-N(2)	1.4053(2)	C(3)-C(31)	1.497(3)
N(1)-C(11)	1.4155(2)	C(31)-C(32)	1.509(3)
N(2)-C(3)	1.2991(2)	C(33)-C(34)	1.455(5)
N(4)-C(41)	1.3301(2)	C(4)-C(41)	1.3681(25)
N(4)-C(46)	1.4134(2)	C(4)-C(5)	1.445(3)
N(41)-C(46)	1.323(3)	C(42)-C(43)	1.368(4)
N(41)-C(42)	1.340(3)	C(43)-C(44)	1.374(4)
C(11)-C(12)	1.381(3)	C(44)-C(45)	1.376(3)
C(11)-C(16)	1.387(3)	C(45)-C(46)	1.387(3)

C(32)-O(32)-C(33)	116.29(23)	C(3)-C(31)-C(32)	113.23(21)
C(5)-N(1)-N(2)	111.92(15)	O(31)-C(32)-O(32)	123.68(22)
C(5)-N(1)-C(11)	129.31(18)	O(31)-C(32)-C(31)	125.03(19)
N(2)-N(1)-C(11)	118.54(15)	O(32)-C(32)-C(31)	111.27(20)
C(3)-N(2)-N(1)	106.36(15)	C(34)-C(33)-O(32)	108.0(4)
C(41)-N(4)-C(46)	123.16(19)	C(41)-C(4)-C(3)	128.81(19)
C(46)-N(41)-C(42)	116.72(21)	C(41)-C(4)-C(5)	125.68(18)
C(12)-C(11)-C(16)	119.63(22)	C(3)-C(4)-C(5)	105.39(15)
C(12)-C(11)-N(1)	119.62(20)	N(4)-C(41)-C(4)	124.12(20)
C(16)-C(11)-N(1)	120.74(20)	N(41)-C(42)-C(43)	123.59(25)
C(11)-C(12)-C(13)	120.15(25)	C(42)-C(43)-C(44)	118.66(23)
C(14)-C(13)-C(12)	120.52(25)	C(43)-C(44)-C(45)	119.30(22)
C(13)-C(14)-C(15)	119.3(3)	C(44)-C(45)-C(46)	117.64(22)
C(14)-C(15)-C(16)	121.3(3)	N(41)-C(46)-C(45)	124.08(18)
C(11)-C(16)-C(15)	119.08(25)	N(41)-C(46)-N(4)	115.65(18)
N(2)-C(3)-C(4)	112.18(18)	C(45)-C(46)-N(4)	120.24(20)
N(2)-C(3)-C(31)	121.11(17)	O(5)-C(5)-N(1)	127.00(19)
C(4)-C(3)-C(31)	126.71(16)	O(5)-C(5)-C(4)	128.84(18)
N(1)-C(5)-C(4)	104.15(17)		

Table 8. Bond Distances (Å) and Bond Angles (°) with e.s.d.'s in parentheses for compound (**7r**).

O(1a)-C(5a)	1.235(2)	O(1b)-C(5b)	1.240(2)
O(2a)-C(7a)	1.198(2)	O(2b)-C(7b)	1.186(3)
O(3a)-C(7a)	1.319(2)	O(3b)-C(7b)	1.309(2)
O(3a)-C(8a)	1.438(4)	O(3b)-C(8b)	1.450(3)

N(1a)-N(2a)	1.403(2)	N(1b)-N(2b)	1.403(1)
N(1a)-C(5a)	1.384(2)	N(1b)-C(5b)	1.383(2)
N(1a)-C(12a)	1.414(3)	N(1b)-C(12b)	1.414(2)
N(2a)-C(3a)	1.304(3)	N(2b)-C(3b)	1.304(2)
N(3a)-C(9a)	1.317(2)	N(3b)-C(9b)	1.319(2)
N(3a)-C(10a)	1.450(3)	N(3b)-C(10b)	1.449(3)
N(4a)-C(11a)	1.149(3)	N(4b)-C(11b)	1.138(5)
C(3a)-C(4a)	1.428(2)	C(3b)-C(4b)	1.419(2)
C(3a)-C(6a)	1.491(2)	C(3b)-C(6b)	1.499(2)
C(4a)-C(5a)	1.437(2)	C(4b)-C(5b)	1.444(2)
C(4a)-C(9a)	1.378(3)	C(4b)-C(9b)	1.379(3)
C(6a)-C(7a)	1.495(2)	C(6b)-C(7b)	1.505(2)
C(10a)-C(11a)	1.455(3)	C(10b)-C(11b)	1.441(4)
C(12a)-C(13a)	1.380(3)	C(12b)-C(13b)	1.393(2)
C(12a)-C(17a)	1.382(3)	C(12b)-C(17b)	1.389(3)
C(13a)-C(14a)	1.394(6)	C(13b)-C(14b)	1.385(3)
C(14a)-C(15a)	1.367(5)	C(14b)-C(15b)	1.366(3)
C(15a)-C(16a)	1.362(5)	C(15b)-C(16b)	1.382(3)
C(7a)-O(3a)-C(8a)	117.3(2)	C(7b)-O(3b)-C(8b)	117.1(2)
N(2a)-N(1a)-C(5a)	111.9(1)	N(2b)-N(1b)-C(5b)	111.8(1)
N(2a)-N(1a)-C(12a)	119.2(1)	N(2b)-N(1b)-C(12b)	118.0(1)
C(5a)-N(1a)-C(12a)	128.9(1)	C(5b)-N(1b)-C(12b)	130.1(1)
N(1a)-N(2a)-C(3a)	106.2(1)	N(1b)-N(2b)-C(3b)	106.2(1)
C(9a)-N(3a)-C(10a)	122.6(2)	C(9b)-N(3b)-C(10b)	123.0(1)
N(2a)-C(3a)-C(4a)	112.0(1)	N(2b)-C(3b)-C(4b)	112.1(1)
N(2a)-C(3a)-C(6a)	120.0(2)	N(2b)-C(3b)-C(6b)	119.4(2)
C(4a)-C(3a)-C(6a)	128.0(2)	C(4b)-C(3b)-C(6b)	128.5(2)
C(3a)-C(4a)-C(5a)	105.6(2)	C(3b)-C(4b)-C(5b)	105.7(1)
C(3a)-C(4a)-C(9a)	128.9(2)	C(3b)-C(4b)-C(9b)	128.3(1)
C(5a)-C(4a)-C(9a)	125.4(1)	C(5b)-C(4b)-C(9b)	125.9(1)
O(1a)-C(5a)-N(1a)	126.4(2)	O(1b)-C(5b)-N(1b)	126.6(1)
O(1a)-C(5a)-C(4a)	129.2(2)	O(1b)-C(5b)-C(4b)	129.2(2)
N(1a)-C(5a)-C(4a)	104.4(1)	N(1b)-C(5b)-C(4b)	104.2(1)
C(3a)-C(6a)-C(7a)	114.3(1)	C(3b)-C(6b)-C(7b)	112.5(1)
O(2a)-C(7a)-O(3a)	123.4(2)	O(2b)-C(7b)-O(3b)	123.9(2)
O(2a)-C(7a)-C(6a)	125.5(2)	O(2b)-C(7b)-C(6b)	125.0(2)
O(3a)-C(7a)-C(6a)	111.0(1)	O(3b)-C(7b)-C(6b)	111.0(2)
N(3a)-C(9a)-C(4a)	124.6(2)	N(3b)-C(9b)-C(4b)	124.7(1)
N(3a)-C(10a)-C(11a)	111.5(2)	N(3b)-C(10b)-C(11b)	112.9(2)
N(4a)-C(11a)-C(10a)	178.2(2)	N(4b)-C(11b)-C(10b)	179.7(3)
N(1a)-C(12a)-C(13a)	119.2(2)	N(1b)-C(12b)-C(13b)	121.3(2)
N(1a)-C(12a)-C(17a)	121.1(2)	N(1b)-C(12b)-C(17b)	119.4(1)
C(13a)-C(12a)-C(17a)	119.6(2)	C(13b)-C(12b)-C(17b)	119.3(2)
C(12a)-C(13a)-C(14a)	118.7(3)	C(12b)-C(13b)-C(14b)	119.1(2)
C(13a)-C(14a)-C(15a)	121.8(4)	C(13b)-C(14b)-C(15b)	121.7(2)
C(14a)-C(15a)-C(16a)	119.0(4)	C(14b)-C(15b)-C(16b)	119.3(2)
C(15a)-C(16a)-C(17a)	120.7(3)	C(15b)-C(16b)-C(17b)	120.2(2)
C(12a)-C(17a)-C(16a)	120.1(2)	C(12b)-C(17b)-C(16b)	120.4(1)

Table 9. Bond Distances (Å) and Bond Angles (°) with e.s.d.'s in parentheses for compound (**8g**).

O(31)-C(32)	1.167(5)	C(3)-C(31)	1.494(4)
O(32)-C(32)	1.278(6)	C(31)-C(32)	1.510(6)
O(32)-C(33)	1.51(1)	C(33)-C(34)	1.19(3)
O(5)-C(5)	1.296(4)	C(4)-C(41)	1.408(4)
O(1')-C(1')	1.245(3)	C(4)-C(5)	1.416(4)
O(3')-C(3')	1.217(4)	C(41)-C(2')	1.376(4)
N(1)-C(5)	1.350(4)	C(1')-C(2')	1.445(4)
N(1)-N(2)	1.395(3)	C(1')-C(8')	1.480(4)
N(1)-C(11)	1.433(4)	C(2')-C(3')	1.492(4)

N(2)-C(3)	1.304(4)	C(3')-C(9')	1.489(5)
C(11)-C(12)	1.364(5)	C(4')-C(5')	1.380(6)
C(11)-C(16)	1.368(5)	C(4')-C(9')	1.385(5)
C(12)-C(13)	1.383(6)	C(5')-C(6')	1.371(6)
C(13)-C(14)	1.352(5)	C(6')-C(7')	1.389(6)
C(14)-C(15)	1.367(7)	C(7')-C(8')	1.379(5)
C(15)-C(16)	1.390(6)	C(8')-C(9')	1.381(4)
C(3)-C(4)	1.436(5)		

C(32)-O(32)-C(33)	118.6(6)	C(2')-C(41)-C(4)	135.8(3)
C(5)-N(1)-N(2)	111.4(2)	O(5)-C(5)-N(1)	120.6(2)
C(5)-N(1)-C(11)	130.5(2)	O(5)-C(5)-C(4)	132.0(3)
N(2)-N(1)-C(11)	118.1(3)	N(1)-C(5)-C(4)	107.4(2)
C(3)-N(2)-N(1)	105.4(3)	O(1')-C(1')-C(2')	129.8(3)
C(12)-C(11)-C(16)	119.4(3)	O(1')-C(1')-C(8')	122.3(3)
C(12)-C(11)-N(1)	117.7(3)	C(2')-C(1')-C(8')	108.0(2)
C(16)-C(11)-N(1)	122.8(3)	C(41)-C(2')-C(1')	133.9(3)
C(11)-C(12)-C(13)	120.1(3)	C(41)-C(2')-C(3')	119.2(3)
C(14)-C(13)-C(12)	121.3(4)	C(1')-C(2')-C(3')	106.9(3)
C(13)-C(14)-C(15)	118.5(4)	O(3')-C(3')-C(9')	127.1(3)
C(14)-C(15)-C(16)	121.1(4)	O(3')-C(3')-C(2')	126.3(3)
C(11)-C(16)-C(15)	119.5(4)	C(9')-C(3')-C(2')	106.7(3)
N(2)-C(3)-C(4)	112.7(3)	C(5')-C(4')-C(9')	118.3(4)
N(2)-C(3)-C(31)	119.2(3)	C(6')-C(5')-C(4')	120.8(4)
C(4)-C(3)-C(31)	128.0(3)	C(5')-C(6')-C(7')	121.6(4)
C(3)-C(31)-C(32)	110.9(3)	C(8')-C(7')-C(6')	117.4(4)
O(31)-C(32)-O(32)	123.3(6)	C(7')-C(8')-C(9')	121.4(3)
O(31)-C(32)-C(31)	124.1(6)	C(7')-C(8')-C(1')	129.0(3)
O(32)-C(32)-C(31)	112.6(3)	C(9')-C(8')-C(1')	109.6(3)
C(34)-C(33)-O(32)	111(2)	C(8')-C(9')-C(4')	120.6(3)
C(41)-C(4)-C(5)	133.2(3)	C(8')-C(9')-C(3')	108.8(3)
C(41)-C(4)-C(3)	123.7(3)	C(4')-C(9')-C(3')	130.5(3)
C(5)-C(4)-C(3)	103.0(2)		

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H NMR, ^{13}C NMR and 2D NMR HMBC, NOESY spectra were obtained on a Bruker Avance DPX 300 (300 MHz) spectrometer with DMSO-d_6 or $CDCl_3$ as solvent and TMS as internal standard (δ in ppm, *J* in Hz). IR spectra were recorded with Perkin–Elmer Spectrum BX FTIR spectrophotometer (KBr discs, ν in cm^{-1}). MS spectra were obtained on an Autospeck Q spectrometer. The microanalyses for C, H, and N were obtained on a Perkin Elmer CHN *Analyser* 2400.

Ethyl (5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)acetate (3a).[16a,b]

Phenylhydrazine (**2**) (9.9 mL, 100 mmol) was added at a rapid dropwise rate to diethyl acetone-1,3-dicarboxylate (**1**) (18.1 mL, 100 mmol), stirred vigorously. Temperature rose to 70 °C, mixture was then heated on steam bath for 1.5 h. The glassy product obtained on cooling was dissolved in a boiling mixture of methanol (50 mL) and water (50 mL), filtered hot, and the filtrate was cooled to –20 °C. The

precipitate was collected by filtration, to give **3a**. White solid. Yield: 56% (14.6 g) mp 75–76 °C (methanol/water) (lit.,[16a] 85 °C). IR (cm^{-1}): 1740, 1600, 1560, 1400, 1340, 1190, 760. ^1H NMR ($CDCl_3$): δ 1.31 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.59 (s, 2H, CH_2); 3.64 (s, 2H, CH_2); 4.23 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.17–7.22 (m, 1H, Ph); 7.37–7.42 (m, 2H, Ph); 7.83–7.84 (m, 2H, Ph). (DMSO-d_6): δ 1.20 (t, 3H, *J* = 7.0, OCH_2CH_3); 3.54 (s, 2H, CH_2); 4.10 (q, 2H, *J* = 7.2, OCH_2CH_3); 5.50 (s, 1H, 4–H); 7.21–7.27 (m, 1H, Ph); 7.40–7.46 (m, 2H, Ph); 7.68–7.72 (m, 2H, Ph); 11.58 (br s, 1H, OH).

Methyl (5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)acetate (3b).[16c]
Phenylhydrazine (**2**) (9.9 mL, 100 mmol) was added at a rapid dropwise rate to dimethyl acetone-1,3-dicarboxylate (**1**) (17.4 mL, 100 mmol), stirred vigorously. Temperature rose to 70 °C, mixture was then heated on steam bath for 1.5 h. The glassy product obtained on cooling was crystallized from a mixture of methanol (100 mL) and water (100 mL). The precipitate was collected by filtration to give **3b**. White solid. Yield: 62% (14.4 g), mp 89–92 °C (methanol/water) (lit.,[16c] 86–89 °C). IR (cm^{-1}): 1740, 1590, 1550, 1530, 1410, 1330, 1200, 1150, 760, 690. ^1H NMR ($CDCl_3$): δ 3.60 (s, 2H, CH_2); 3.63 (s, 2H, CH_2); 3.78 (s, 3H, OCH_3); 7.16–7.22 (m, 1H, Ph); 7.36–7.43 (m, 2H, Ph); 7.83–7.86 (m, 2H, Ph).

General Procedure for the Preparation of Alkyl [(*Z*)-4-Dimethylaminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetates (4a,b). DMFDMA (3 mL, 20 mmol) was added to a solution of **3a,b** (10 mmol) in toluene (30 mL) and the mixture was left at rt overnight (~12 h). The precipitate was collected by filtration, and recrystallized from mixture of ethanol and toluene to give **4a,b**.
The following compounds were prepared in this manner:

Ethyl [(*Z*)-4-dimethylaminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (4a). This compound was prepared from **3a** (2.46 g, 10 mmol) and DMFDMA. White crystals. Yield: 78% (2.36 g), mp 106–110 °C (ethanol/toluene). *Anal.* Calcd for $C_{16}H_{19}N_3O_3$: C 63.77; H 6.36; N 13.94. Found, C 64.03; H 6.52; N 13.80. MS: *m/z* (M^+, 301; MH^+, 302). IR (cm^{-1}): 1730, 1680, 1620, 1560, 1490, 1430, 1290, 770. ^1H NMR ($CDCl_3$): δ 1.21 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.35 (s, 3H, NMe); 3.67 (s, 2H, CH_2); 3.79 (s, 3H, NMe); 4.11 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.05–7.10 (m, 1H, Ph); 7.31–7.37 (m, 2H, Ph); 7.91–7.95 (m, 2H, Ph); 7.59 (s, 1H, =CH). ^{13}C NMR ($CDCl_3$): δ 14.5; 35.7; 43.9; 48.6; 61.8; 99.0; 120.0; 124.6; 128.9; 139.8; 147.2; 153.8; 162.5; 170.3.

Methyl [(*Z*)-4-dimethylaminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (4b). This compound was prepared from **3b** (2.32 g, 10 mmol) and DMFDMA. White crystals. Yield: 53%

(1.87 g), mp 138–140 °C (ethanol/toluene). *Anal*. Calcd for $C_{15}H_{17}N_3O_3$: C 62.71; H 5.96; N 14.63. Found, C 62.52; H 5.88; N 14.60. IR (cm^{-1}): 1740, 1670, 1610, 1550, 1490, 1430, 1400, 1260, 770. ^1H NMR ($CDCl_3$): δ 3.32 (s, 3H, NMe); 3.62 (s, 2H, CH_2); 3.73 (s, 3H, OCH_3); 3.88 (s, 3H, NMe); 7.09–7.14 (m, 1H, Ph); 7.28 (s, 1H, =CH); 7.33–7.38 (m, 2H, Ph); 7.42–7.59 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$): δ 35.3; 43.9; 48.6; 52.8; 99.0; 120.0; 124.6; 128.9; 139.8; 147.0; 153.7; 162.4; 170.8.

General Procedures for the Preparation of Alkyl {5-oxo-1-phenyl-4-[(*Z*)-(substituted methylidene)]-4,5-dihydro-1*H*-pyrazol-3-yl}acetates (7a–s) and (8a–l).

Procedure A. Hydrochloric acid (37%, 2 drops, ~0.6 mmol) was added to a mixture of **4a,b** (0.5 mmol) and nucleophile (**5**) or (**6**) (0.5 mmol) in anhydrous ethanol (5 mL), and the mixture was left at rt overnight (~12 h). The precipitate was collected by filtration, washed with anhydrous ethanol, crystallized from anhydrous ethanol, to give **7** and **8**.

Procedure B. A mixture of **4a,b** (0.5 mmol) and amine hydrochloride (**5)** (0.5 mmol) in anhydrous ethanol (5 mL) was left at rt overnight (~12 h). The precipitate was collected by filtration, washed with anhydrous ethanol, crystallized from anhydrous ethanol, to give **7** and **8**.

Procedure C. A mixture of **4a** (80 mg, 0.265 mmol), ethanol (3 mL), and hydrochloric acid (37%, 1 drop, ~0.3 mmol), was heated at reflux temperature for 4 h. After cooling, the precipitate was collected by filtration to give **8i**.

The following compounds were prepared in this manner:

Ethyl [(*Z*)-5-oxo-1-phenyl-4-phenylaminomethylidene-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7a). This compound was prepared from **4a** (151 mg, 0.5 mmol) and aniline hydrochloride (**5a**) (65 mg, 0.5 mmol), Procedure B. Yellow solid. Yield: 83% (145 mg), mp 138–140 °C (ethanol). *Anal*. Calcd for $C_{20}H_{19}N_3O_3$: C 68.75; H 5.48; N 12.03. Found, C 68.79; H 5.61; N 12.32. MS: *m/z* (M^+, 349; MH^+, 350). IR (cm^{-1}): 1730, 1680, 1630, 1590, 1500, 1320, 1200, 750, 690. ^1H NMR ($CDCl_3$): δ 1.30 (t, 3H, J = 7.2, OCH_2CH_3); 3.74 (s, 2H, CH_2); 4.22 (q, 2H, J = 7.2, OCH_2CH_3); 7.15–7.72 (m, 4H, Ph); 7.39–7.46 (m, 4H, Ph); 7.98–8.02 (m, 2H, Ph); 8.29 (s, 1H, =CH); 11.68 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 14.6; 35.6; 62.0; 102.3; 117.8; 119.1; 125.1; 126.4; 129.4; 130.4; 138.8; 139.2; 144.8; 145.3 164.7; 170.1.

Methyl [(*Z*)-5-oxo-1-phenyl-4-phenylaminomethylidene-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7b). This compound was prepared from **4b** (144 mg, 0.5 mmol) and aniline hydrochloride (**5a**) (65 mg, 0.5 mmol), Procedure B. Yellow solid. Yield: 50% (84 mg), mp 142–143 °C (ethanol). *Anal*. Calcd for $C_{19}H_{17}N_3O_3$: C 68.05; H 5.11; N 12.53. Found, C 68.16; H 5.38; N 12.75. IR (cm^{-1}): 1730, 1670, 1630,

1590, 1500, 1320, 1210, 750. ^{1}H NMR ($CDCl_3$): δ 3.76 (s, 2H, CH_2); 3.77 (s, 3H, OMe); 7.15–7.24 (m, 4H, Ph); 7.38–7.46 (m, 4H, Ph); 7.99–8.01 (m, 2H, Ph); 8.27 (br s, 1H, =CH);11.71 (br s, 1H, NH).

Ethyl [(*Z*)-5-oxo-1-phenyl-4-(4-methylphenyl)aminomethylidene-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7c). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 4-methylaniline hydrochloride (**5c**) (72 mg, 0.5 mmol), Procedure B. Yellow solid. Yield: 96% (175 mg), mp 128–140 °C (ethanol). *Anal*. Calcd for $C_{21}H_{21}N_3O_3$: C 69.41; H 5.82; N 11.56. Found, 69.74; H 5.92; N 11.64. MS: *m/z* (M^+, 363). IR (cm^{-1}): 1730, 1670, 1630, 1400. ^{1}H NMR ($CDCl_3$): δ 1.32 (t, 3H, *J* = 7.2, OCH_2CH_3); 2.39 (s, 3H, Ph-Me); 3.76 (s, 2H, CH_2); 4.24 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.14–7.23 (m, 5H, Ph); 7.40–7.46 (m, 2H, Ph); 8.01–8.04 (m, 2H, Ph); 8.26 (s, 1H, =CH); 11.70 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 14.6; 21.3; 35.6; 62.0; 101.9; 117.8; 119.5; 125.1; 129.2; 130.9; 136.4; 139.2; 144.7; 145.4; 160.7; 166.1; 170.1.

Ethyl [(*Z*)-4-(4-hydroxyphenyl)aminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]-acetate (7d). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 4-hydroxyaniline (**5d**) (55 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 67% (122 mg), mp 220–224 °C (ethanol). *Anal*. Calcd for $C_{20}H_{19}N_3O_4$: C 65.74; H 5.24; N 11.50. Found, C 65.70; H 5.48; N 11.53. MS: *m/z* (M^+, 365; MH^+, 366). IR (cm^{-1}): 3310, 1730, 1670, 1600, 1520, 1490, 1340, 1270, 1200, 830, 750. ^{1}H NMR (DMSO-d_6): δ 1.21 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.82 (s, 2H, CH_2); 4.14 (q, 2H, *J* = 7.0, OCH_2CH_3); 6.83–6.86 (m, 2H, Ph); 7.12–7.18 (m, 1H, Ph); 7.36–7.44 (m, 4H, Ph); 7.98–8.01 (m, 2H, Ph); 8.54 (s, 1H, =CH); 9.64 (s, 1H, NH); 11.41 (br s, 1H, OH). ^{13}C NMR (DMSO-d_6): δ 14.9; 34.2; 61.5; 101.0; 117.0; 118.6; 120.5; 124.8; 129.6; 131.4; 139.9; 146.7; 147.6; 156.6; 165.6; 170.3.

Methyl [(*Z*)-4-(4-methoxyphenyl)aminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]-acetate (7e). This compound was prepared from **4b** (144 mg, 0.5 mmol) and 4-methoxyaniline (**5e**) (62 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 76% (138 mg), mp 131–133 °C (ethanol). *Anal*. Calcd for $C_{20}H_{19}N_3O_4$: C 65.74; H 5.24; N 11.50. Found, C 65.83; H 5.43; N 11.60. IR (cm^{-1}): 1730, 1670, 1230, 1500, 1390, 1250, 830, 750. ^{1}H NMR ($CDCl_3$): δ 3.75 (s, 2H, CH_2); 3.76 (s, 3H, OCH_3); 3.83 (s, 3H, $PhOCH_3$); 6.93–6.97 (m, 2H, Ph); 7.17–7.20 (m, 3H, Ph); 7.38–7.43 (m, 2H, Ph); 7.98–8.02 (m, 2H, Ph); 8.16 (br s, 1H, =CH); 11.72 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 33.9; 52.9; 56.3; 101.4; 115.7; 118.6; 120.4; 124.8; 129.6; 132.8; 139.9; 146.6; 147.6; 158.2; 165.5; 170.8.

Ethyl [(*Z*)-5-oxo-1-phenyl-4-(pyridin-2-yl)aminomethylidene-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7f). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 2-aminopyridine (**5f**) (47 mg, 0.5

mmol), Procedure A. Yellow crystals. Yield: 58% (102 mg), mp 126–127 °C (ethanol). *Anal*. Calcd for $C_{19}H_{18}N_4O_3$: C 65.15; H 5.18; N 15.99. Found, C 65.34; H 5.24; N 16.09. MS: *m/z* (M^+, 350). IR (cm^{-1}): 3270, 1730, 1670, 1630, 1600, 1570, 1500, 1480, 1320, 1280, 1030, 760, 680. ^{1}H NMR ($CDCl_3$): δ 1.30 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.72 (s, 2H, CH_2); 4.23 (q, 2H, *J* = 7.2, OCH_2CH_3); 6.99 (ddd, 1H, *J* = 8.3, 1.8, 0.9, 3'–H); 7.12 (ddd, 1H, *J* = 7.5, 4.9, 1.0, 5'–H); 7.16–7.21 (m, 1H, Ph); 7.39–7.45 (m, 2H, Ph); 7.72 (ddd, 1H, *J* = 8.2, 7.4, 1.9, 4'–H); 7.98–8.02 (m, 2H, Ph); 8.40 (ddd, 1H, *J* = 4.9, 1.9, 0.9, 6'–H); 8.94 (bd, 1H, *J* = 8.5, =CH); 11.76 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 14.5; 35.2; 61.9; 103.9; 113.7; 113.1; 119.4; 121.0; 125.2; 129.2; 139.1; 139.3; 143.4; 145.6; 149.3; 150.3; 166.2; 169.7.

Methyl [(*Z*)-5-oxo-1-phenyl-4-(pyridin-2-yl)aminomethylidene-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7g). This compound was prepared from **4b** (144 mg, 0.5 mmol) and 2-aminopyridine (**5f**) (47 mg, 0.5 mmol)**,** Procedure A. Yellow solid. Yield: 48% (80 mg), mp 132–134 °C (ethanol). *Anal*. Calcd for $C_{18}H_{16}N_4O_3$: C 64.28; H 4.79; N 16.66. Found, C 64.38; H 4.84; N 16.76. IR (cm^{-1}): 3280, 1730, 1670, 1630, 1480, 1280, 1150, 760. ^{1}H NMR ($CDCl_3$): δ 3.77 (s, 3H, OCH_3); 3.78 (s, 2H, CH_2); 6.99 (d, 1H, *J* = 7.9, 3'–H); 7.12 (ddd, 1H, *J* = 7.2, 4.9, 0.8, 5'–H); 7.16–7.21 (m, 1H, Ph); 7.39–7.44 (m, 2H, Ph); 7.72 (ddd, 1H, *J* = 7.9, 7.5, 1.9, 4'–H); 7.98–8.01 (m, 2H, Ph); 8.40 (dd, 1H, *J* = 4.9, 0.8, 6'–H); 8.94 (bd, 1H, *J* = 7.2, =CH); 11.76 (br s, 1H, NH).

Ethyl (*Z*)-[5-oxo-1-phenyl-4-(quinolin-3-yl)aminomethylidene-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7h). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 3-aminoquinoline (**5h**) (72 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 92% (185 mg), mp 203–206 °C (ethanol). *Anal*. Calcd for $C_{23}H_{20}N_4O_3$: C 68.99; H 5.03; N 13.99. Found, C 68.77; H 5.15; N 13.96. MS: *m/z* (M^+, 400; MH^+, 401). IR (cm^{-1}): 1720, 1670, 1630, 1600, 1550, 1500, 1400, 1340, 1300, 1200, 750. ^{1}H NMR ($CDCl_3$): δ 1.33 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.80 (s, 2H, CH_2); 4.25 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.18–7.24 (m, 1H, Ph); 7.40–7.46 (m, 2H, Ph); 7.59–7.65 (m, 1H, 1H of quinoline); 7.69–7.74 (m, 1H, 1H of quinoline); 7.85 (dd, 1H, *J* = 8.3, 1.5, 1H of quinoline); 7.95 (d, 1H, *J* = 2.6, 4–H of quinoline); 8.00–8.03 (m, 2H, Ph); 8.13 (d, 1H, *J* = 8.7, 1H of quinoline); 8.43 (s, 1H, =CH); 8.92 (d, 1H, *J* = 2.6, 2–H of quinoline). ^{13}C NMR ($CDCl_3$): δ 14.6; 35.6; 62.0; 102.3; 117.8; 119.1; 125.1; 126.4; 129.4; 130.4; 138.8; 139.2; 144.8; 145.3 164.7; 170.1.

Ethyl [(*Z*)-4-(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)aminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7i). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 4-aminouracil (**5i**) (64 mg, 0.5 mmol), Procedure A. Pale orange solid. Yield: 84% (160 mg), mp 244–246

°C (ethanol). *Anal*. Calcd for $C_{18}H_{17}N_5O_5$: C 56.39; H 4.47; N 18.27. Found, C 56.11; H 4.70; N 18.21. MS: *m/z* (M^+, 383; MH^+, 384). IR (cm^{-1}): 3390, 3340, 3200, 1750, 1730, 1640, 1590, 1500, 1420, 1350, 1250, 760. ^{1}H NMR (DMSO-d_6): δ 1.20 (t, 3H, *J* = 7.0, OCH_2CH_3); 3.77 (s, 2H, CH_2); 4.13 (q, 2H, *J* = 7.2, OCH_2CH_3); 6.15 (br s, 1H, NH); 7.18–7.23 (m, 1H, Ph); 7.41–7.46 (m, 2H, Ph); 7.89–7.91 (m, 2H, Ph); 7.99 (s, 1H, =CH); 10.03 (br s, 1H, NH); 11.12 (br s, 1H, NH); 11.22 (s, 1H, 6'–H). ^{13}C NMR (DMSO-d_6): δ 14.8; 34.8; 61.7; 94.0; 110.8; 119.9; 125.8; 129.6; 139.2; 142.2; 149.3; 150.7; 158.2; 164.0; 164.4; 169.9.

Methyl [(*Z*)-4-(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)aminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7j). This compound was prepared from **4b** (144 mg, 0.5 mmol) and 4-aminouracil (**5i**) (64 mg, 0.5 mmol), Procedure A. Pale orange solid. Yield: 70% (129 mg), mp 265–266 °C (ethanol). *Anal*. Calcd for $C_{17}H_{15}N_5O_5$: C 55.28; H 4.09; N 18.96. Found, C 55.14; H 4.32; N 18.84. IR (cm^{-1}): 3360, 1740, 1660, 1590, 1440, 1390, 1260, 940, 760. ^{1}H NMR (DMSO-d_6): δ 3.66 (s, 3H, OCH_3); 3.79 (s, 2H, CH_2); 7.19–7.23 (m, 1H, Ph); 7.41–7.46 (m, 2H, Ph); 7.89–7.91 (m, 2H, Ph); 7.97 (s, 1H, =CH); 11.08 (br s, 1H, NH); 11.23 (s, 1H, 6'–H).

Ethyl [(*Z*)-5-oxo-1-phenyl-4-pyrazinylaminomethylidene-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7k). This compound was prepared from **4a** (151 mg, 0.5 mmol) and aminopyrazine (**5k**) (48 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 84% (148 mg), mp 164–166 °C (ethanol). *Anal*. Calcd for $C_{18}H_{17}N_5O_3$: C 61.53; H 4.88; N 19.93. Found, C 61.78; H 5.09; N 19.89. MS: *m/z* (M^+, 351). IR (cm^{-1}): 1720, 1670, 1630, 1500, 1400, 1340, 1280, 1210, 750. ^{1}H NMR ($CDCl_3$): δ 1.31 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.77 (s, 2H, CH_2); 4.23 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.17–7.23 (m, 1H, Ph); 7.40–7.45 (m, 2H, Ph); 7.96–8.00 (m, 2H, Ph); 8.34 (dd, 1H, *J* = 2.6, 1.5, 5'–H); 8.39 (d, 1H, *J* = 2.6, 6'–H); 8.44 (d, 1H, *J* = 1.5, 3'–H); 8.85 (s, 1H, =CH); 11.89 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 14.5; 35.2; 62.0; 105.5; 119.2; 125.4; 129.2; 135.8; 138.8; 141.3; 142.5; 143.0; 145.4; 147.2; 166.1; 169.5.

Methyl (*Z*)-[5-oxo-1-phenyl-4-(pyrazin-2-ylaminomethylidene)-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7l). This compound was prepared from **4b** (144 mg, 0.5 mmol) and aminopyrazine (**5k**) (48 mg, 0.5 mmol), Procedure A. Yellow crystals. Yield: 81% (136 mg), mp 192–195 °C (ethanol). *Anal*. Calcd for $C_{17}H_{15}N_5O_3$: C 60.53; H 4.48; N 20.76. Found, C 60.48; H 4.64; N 20.72. IR (cm^{-1}): 1740, 1680, 1630, 1500, 1390, 1270, 1050, 770. ^{1}H NMR ($CDCl_3$): δ 3.77 (s, 3H, OCH_3); 3.78 (s, 2H, CH_2); 7.18–7.23 (m, 1H, Ph); 7.40–7.45 (m, 2H, Ph); 7.97–8.00 (m, 2H, Ph); 8.35 (dd, 1H, *J* = 2.6, 1.5, 5'–H); 8.39 (d, 1H, *J* = 2.6, 6'–H); 8.44 (d, 1H, *J* = 1.1, 3'H); 8.82 (s, 1H, =CH); 11.89 (br s, 1H, NH).

Ethyl [(*Z*)-5-oxo-1-phenyl-4-(1*H*-pyrazol-3-yl)aminomethylidene-4,5-dihydro-1*H*-pyrazol-3-yl]-acetate (7m). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 3-aminopyrazole (**5m**) (42 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 91% (155 mg), mp 172–175 °C (ethanol). *Anal*. Calcd for $C_{17}H_{17}N_5O_3$: C 60.17; H 5.05; N 20.64. Found, C 60.38; H 5.28; N 20.75. MS: *m/z* (M^+, 339; MH^+, 340). IR (cm^{-1}): 3420, 1720, 1670, 1630, 1540, 1320, 1260, 1030, 750. ^{1}H NMR (DMSO-d_6): δ 1.22 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.83 (s, 2H, CH_2); 4.14 (q, 2H, *J* = 7.2, OCH_2CH_3); 6.46 (br s, 1H, 4'–H); 7.13–7.19 (m, 1H, Ph); 7.40–7.45 (m, 2H, Ph); 7.78 (br s, 1H, 1H, 5'–H); 7.96–8.00 (m, 2H, Ph); 8.57 (s, 1H, =CH); 11.48 (br s, 1H, NH); 12.79 (br s, 1H, 1'–NH). ^{13}C NMR ($CDCl_3$): δ 14.6; 35.5; 62.0; 94.6; 102.2; 119.8; 125.3; 129.2; 130.6; 139.1; 145.5; 146.0; 149.4; 165.5; 170.1.

Ethyl [(*Z*)-4-(1*H*-indazol-3-yl)aminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]-acetate (7n). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 3-aminoindazole (**5n**) (67 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 90% (175 mg), mp 187–189 °C (ethanol). *Anal*. Calcd for $C_{21}H_{19}N_5O_3$: C 64.77; H 4.92; N 17.98. Found, C 64.33; H 5.13; N 18.06. MS: *m/z* (M^+, 389; MH^+, 390). IR (cm^{-1}): 3460, 1730, 1680, 1620, 1540, 1500, 1350, 1280, 750. ^{1}H NMR (DMSO-d_6): δ 1.23 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.90 (s, 2H, CH_2); 4.16 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.16–7.26 (m, 2H, Ph); 7.42–7.49 (m, 3H, Ph); 7.55–7.58 (m, 1H, Ph); 7.91–7.94 (m, 1H, Ph); 7.99–8.02 (m, 2H, Ph); 8.75 (s, 1H, =CH); 11.78 (br s, 1H, NH); 13.07 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 14.5; 35.2; 62.1; 103.1; 110.8; 114.2; 118.8; 119.7; 122.0; 125.3; 128.3; 129.3; 139.0; 141.7; 142.1; 145.2; 166.2; 170.1.

Ethyl [(*Z*)-4-(benzothiazol-2-yl)aminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]-acetate (7o). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 2-aminobenzothiazole (**5o**) (75 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 70% (142 mg), mp 150–153 °C (ethanol). *Anal*. Calcd for $C_{21}H_{18}N_4O_3S$: C 62.05; H 4.46; N 13.78. Found, C 62.12; H 4.64; N 13.86. MS: *m/z* (M^+, 406; MH^+, 407). IR (cm^{-1}): 1720, 1670, 1630, 1520, 1500, 1350, 1260, 750. ^{1}H NMR ($CDCl_3$): δ 1.33 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.78 (s, 2H, CH_2); 4.26 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.18–7.24 (m, 1H, Ph); 7.35–7.51 (m, 4H, Ph); 7.78 (dd, 1H, J = 7.9, 0.8, Ph'); 7.84 (dd, 1H, *J* = 8.3, 0.8, Ph'); 7.97–8.00 (m, 2H, Ph); 8.67 (s, 1H, =CH). ^{13}C NMR ($CDCl_3$): δ 14.6; 19.3; 35.2; 62.1; 106.0; 119.3; 121.9; 122.2; 125.2; 125.5; 127.3; 129.3; 138.7; 142.7; 145.7; 151.3; 159.2; 165.8; 169.4.

Ethyl [(*Z*)-4-hydroxyaminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7p). This compound was prepared from **4a** (151 mg, 0.5 mmol) and hydroxylamine hydrochloride (**5p**) (35 mg, 0.5 mmol), Procedure B. Light yellow crystals. Yield: 45% (65 mg), mp 140–143 °C (ethanol). *Anal*.

Calcd for $C_{14}H_{15}N_3O_4$: C 58.13; H 5.23. N 14.53. Found, C 58.08; H 5.21; N 14.56. MS: *m/z* (M^+, 289). IR (cm^{-1}): 1780, 1630, 1410, 1210, 1030, 760. ^1H NMR (DMSO-d_6): δ 1.20 (t, 3H, *J* = 7.0, OCH_2CH_3); 3.71 (s, 2H, CH_2); 4.11 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.18–7.23 (m, 1H, Ph); 7.39–7.44 (m, 2H, Ph); 7.80–7.87 (m, 2H, Ph); 8.08 (s, 1H, =CH); 10.62 (br s, 1H, NH); 12.82 (br s, 1H, OH).

Ethyl [(*Z*)-4-cyanomethylaminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7q). This compound was prepared from **4a** (151 mg, 0.5 mmol) and aminoacetonitrile hydrochloride (**5q**) (46 mg, 0.5 mmol), Procedure B. Pale yellow solid. Yield: 74% (115 mg), mp 131–134 °C (ethanol). *Anal*. Calcd for $C_{16}H_{16}N_4O_3$: C 61.53; H 5.16; N 17.94. Found, C 61.56; H 5.22; N 18.03. MS: *m/z* (M^+, 312). IR (cm^{-1}): 3250, 2980, 1720, 1670, 1620, 1600, 1340, 1210, 750. ^1H NMR (DMSO-d_6): δ 1.22 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.69 (s, 2H, CH_2); 4.13 (q, 2H, *J* = 7.2, OCH_2CH_3); 4.59 (s, 2H, 6–H); 7.11–7.16 (m, 1H, Ph); 7.37–7.42 (m, 2H, Ph); 7.93–7.97 (m, 2H, Ph); 8.07 (br s, 1H, =CH); 9.80 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 14.5; 35.4; 36.9; 62.1; 102.6; 114.7; 120.0; 125.5; 129.3; 138.9; 144.7; 152.1; 166.0; 170.0.

Methyl [(*Z*)-cyanomethylaminomethylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (7r). This compound was prepared from **4b** (144 mg, 0.5 mmol) and aminoacetonitrile hydrochloride (**5q**) (46 mg, 0.5 mmol), Procedure B. Pale yellow solid. Yield: 78% (116 mg), mp 143–146 °C (ethanol). *Anal*. Calcd for $C_{15}H_{14}N_4O_3$: C 60.40; H 4.73; N 18.78. Found, C 60.68; H 4.79; N 19.00. IR (cm^{-1}): 3260, 1730, 1670, 1620, 1600, 1340, 1220, 750. ^1H NMR (DMSO-d_6): δ 3.67 (s, 3H, OCH_3); 3.71 (s, 2H, CH_2); 4.59 (s, 2H, 6–H); 7.11–7.16 (m, 1H, Ph); 7.37–7.42 (m, 2H, Ph); 7.93–7.96 (m, 2H, Ph); 8.06 (s, 1H, =CH); 9.79 (br s, 1H, NH).

Ethyl [5-hydroxy-1-phenyl-4-phenylhydrazonomethylidene-1*H*-pyrazol-3-yl]acetate (7s). This compound was prepared from **4a** (151 mg, 0.5 mmol) and phenylhyrazine hydrochloride (**5s**) (72 mg, 0.5 mmol), Procedure B. White crystals. Yield: 82% (150 mg), mp 135–136 °C (ethanol). *Anal*. Calcd for $C_{20}H_{20}N_4O_3$: C 65.92; H 5.53; N 15.38. Found, C 66.10; H 5.72; N 15.38. MS: *m/z* (M^+, 364; MH^+, 365). IR (cm^{-1}): 3200, 3180, 1730, 1670, 1620, 1560, 1540, 1500, 1310, 1260, 1030, 690. ^1H NMR (DMSO-d_6): δ 1.19 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.78 (s, 2H, CH_2); 4.09 (q, 2H, *J* = 7.0, OCH_2CH_3); 6.81–6.86 (m, 3H, Ph); 7.14–7.27 (m, 3H, Ph); 7.39–7.44 (m, 2H, Ph); 7.91–7.93 (m, 2H, Ph); 8.09 (s, 1H, =CH); 8.99 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 14.9; 34.7; 61.4; 113.6; 119.3; 119.7; 120.9; 125.1; 129.5; 129.7; 129.9; 139.8; 146.0; 148.4; 162.4; 170.3.

Ethyl [(*Z*)-4-(6-hydroxy-2,2-dimethyl-4-oxo-4*H*-[1,3]dioxin-5-yl)methylidene-5-oxo-1-phenyl-4,5-

dihydro-1*H*-pyrazol-3-yl]acetate (8a). This compound was prepared from **4a** (151 mg, 0.5 mmol) and Meldrum's acid (**6a**) (72 mg, 0.5 mmol), Procedure A. Yellow crystals. Yield: 67% (135 mg), mp 79–81 °C (ethanol). *Anal*. Calcd for $C_{20}H_{20}N_2O_7$: C 60.00; H 5.03; N 7.00. Found, C 59.68; H 5.20; N 6.61. MS: *m/z* (M^+, 400; MH^+, 401). IR (cm^{-1}): 1730, 1650, 1580, 1290, 760. ^{1}H NMR ($CDCl_3$): δ 1.32 (t, 3H, *J* = 7.2, OCH_2CH_3); 1.82 (s, 6H, $2CH_3$); 3.87 (s, 2H, CH_2); 4.25 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.36–7.41 (m, 1H, Ph); 7.47–7.53 (m, 2H, Ph); 7.80–7.83 (m, 2H, Ph); 8.43 (s, 1H, =CH); 14.51 (s, 1H, OH). ^{13}C NMR ($CDCl_3$): δ 14.5; 27.5; 34.1; 62.1; 100.2; 103.7; 105.3; 122.8; 128.3; 129.5; 137.2; 148.7; 151.9; 157.4; 163.6; 168.2; 169.3.

Ethyl [(*Z*)-4-(6-hydroxy-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (8b). This compound was prepared from **4a** (151 mg, 0.5 mmol) and barbituric acid (**6b**) (64 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 60% (116 mg), mp 213–215 °C (ethanol). *Anal*. Calcd for $C_{18}H_{16}N_4O_6$: C 56.25; H 4.20; N 14.58. Found, C 56.38; H 4.31; N 14.61. MS: *m/z* (M^+, 384; MH^+, 385). IR (cm^{-1}): 3480, 3190, 1740, 1690, 1630, 1580, 1490, 1380, 1250, 760. ^{1}H NMR ($CDCl_3$): δ 1.29 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.87 (s, 2H, CH_2); 4.23 (q, 2H, *J* = 7.0, OCH_2CH_3); 7.34–7.39 (m, 1H, Ph); 7.45–7.51 (m, 2H, Ph); 7.80–7.83 (m, 2H, Ph); 8.05 (br s, 1H, NH); 8.14 (br s, 1H, NH); 8.42 (s, 1H, =CH); 15.70 (s, 1H, OH). ^{13}C NMR (DMSO-d_6): δ 14.8; 34.6; 61.7; 104.1; 106.1; 121.9; 122.4; 128.1; 130.1; 137.8; 145.6; 150.3; 151.8; 158.5; 170.0.

Methyl [(*Z*)-4-(6-hydroxy-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (8c). This compound was prepared from **4b** (144 mg, 0.5 mmol) and barbituric acid (**6b**) (64 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 85% (158 mg), mp 269–272 °C (ethanol). *Anal*. Calcd for $C_{17}H_{14}N_4O_6$: C 55.14; H 3.81; N 15.13. Found, C 54.86; H 4.04; N 14.97. IR (cm^{-1}): 3180, 3050, 1730, 1690, 1570, 1380, 760. ^{1}H NMR (DMSO-d_6): δ 3.63 (s, 3H, OMe); 3.91 (s, 2H, CH_2); 7.31–7.36 (m, 1H, Ph); 7.48–7.53 (m, 2H, Ph); 7.80–7.83 (m, 2H, Ph); 8.13 (s, 1H, =CH);11.41 (br s, 2H, 2 × NH).

Ethyl [(*Z*)-4-(6-hydroxy-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (8d). This compound was prepared from **4a** (151 mg, 0.5 mmol) and thiobarbituric acid (**6d**) (72 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 97% (195 mg), mp 224–230 °C (ethanol). *Anal*. Calcd for $C_{18}H_{16}N_4O_5S$: C 53.99; H 4.03; N 13.99. Found, C 53.91; H 4.12; N 13.99. MS: *m/z* (M^+, 400). IR (cm^{-1}): 3120, 1740, 1680, 1620, 1570, 1540, 1450, 1360, 1300, 1150, 760, 680, 540. ^{1}H NMR ($CDCl_3$): δ 1.32 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.88 (s, 2H, CH_2); 4.25 (q, 2H,

J = 7.2, OC*H*$_2$CH$_3$); 7.37–7.42 (m, 1H, Ph); 7.48–7.53 (m, 2H, Ph); 7.83–7.85 (m, 2H, Ph); 8.41 (s, 1H, =CH); 9.08 (br s, 2H, 2 × NH); 14.51 (s, 1H, OH). ^{13}C NMR (DMSO-d$_6$): δ 14.8; 35.3; 61.6; 105.2; 107.0; 121.6; 122.0; 129.9; 130.0; 138.2; 145.4; 151.2; 161.8; 163.9; 170.0; 177.6.

Ethyl [(*Z*)-4-(6-hydroxy-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (8e). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 1,3-dimethylbarbituric acid (**6e**) (78 mg, 0.5 mmol), Procedure A. Yellow needles. Yield: 98% (203 mg), mp 153–155 °C (ethanol). *Anal*. Calcd for $C_{20}H_{20}N_4O_6$: C 58.25; H 4.89; N 13.59. Found, C 58.40; H 5.11; N 13.71. MS: *m/z* (M^+, 412; MH^+, 413). IR (cm^{-1}): 1740, 1670, 1580, 1370, 790, 770. ^{1}H NMR ($CDCl_3$): δ 1.29 (t, 3H, *J* = 7.2, OCH$_2$C*H*$_3$); 3.42 (s, 3H, NMe); 3.45 (s, 3H, NMe); 3.86 (s, 2H, CH$_2$); 4.22 (q, 2H, *J* = 7.2, OC*H*$_2$CH$_3$); 7.35–7.40 (m, 1H, Ph); 7.47–7.52 (m, 2H, Ph); 7.84–7.87 (m, 2H, Ph); 8.50 (s, 1H, =CH); 15.59 (s, 1H, OH). ^{13}C NMR ($CDCl_3$): δ 14.5; 29.5; 29.5; 34.2; 62.1; 104.8; 104.9; 116.4; 122.5; 128.0; 129.4; 137.5; 148.3; 152.0; 158.1; 163.0; 166.6; 169.4.

Methyl [(*Z*)-4-(6-hydroxy-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (8f). This compound was prepared from **4b** (144 mg, 0.5 mmol) and 1,3-dimethylbarbituric acid (**6e**) (78 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 75% (149 mg), mp 176–179 °C (ethanol). *Anal*. Calcd for $C_{19}H_{18}N_4O_6$: C 57.28; H 4.55; N 14.06. Found, C 57.36; H 4.65; N 14.10. IR (cm^{-1}): 1750, 1670, 1580, 1370, 790. ^{1}H NMR (DMSO-d$_6$): δ 3.58 (s, 3H, OCH$_3$); 3.87 (s, 2H, CH$_2$); 4.53 (br s, 6H, 2 × NMe); 7.24–7.29 (m, 1H, Ph); 7.44–7.49 (m, 2H, Ph); 7.86–7.89 (m, 2H, Ph); 8.15 (s, 1H, =CH).

Ethyl [(*Z*)-4-(3-hydroxy-1-oxo-1*H*-inden-2-yl)methylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (8g). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 1,3-indandione (**6g**) (73 mg, 0.5 mmol), Procedure A. Dark red needles. Yield: 59% (119 mg), mp 155–157 °C (ethanol). *Anal*. Calcd for $C_{23}H_{18}N_2O_5$: C 68.65; H 4.51. N 6.96. Found, C 68.66; H 4.81; N 7.01. MS: *m/z* (M^+, 402; MH^+, 403). IR (cm^{-1}): 1740, 1710, 1640, 1610, 1580, 1490, 1370, 1220, 740. ^{1}H NMR ($CDCl_3$): δ 1.31 (t, 3H, *J* = 7.2, OCH$_2$C*H*$_3$); 3.87 (s, 2H, CH$_2$); 4.23 (q, 2H, *J* = 7.2, OC*H*$_2$CH$_3$); 7.32–7.38 (m, 1H, Ph); 7.46–7.51 (m, 2H, Ph); 7.71 (s, 1H, =CH); 7.76–7.81 (m, 2H, Ph); 7.85–7.88 (m, 2H, Ph); 7.92–7.96 (m, 2H, Ph); 16.40 (s, 1H, OH). ^{13}C NMR ($CDCl_3$): δ 14.5; 34.2; 62.0; 105.0; 117.5; 122.5; 123.3; 123.8; 127.8; 129.4; 134.9; 136.2; 136.6; 137.7; 139.7; 141.1; 151.1; 157.7; 169.5; 190.0; 195.2.

Methyl [(*Z*)-4-(3-hydroxy-1-oxo-1*H*-inden-2-yl)methylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-

3-yl]acetate (8h). This compound was prepared from **4b** (144 mg, 0.5 mmol) and 1,3-indandione (**6g**) (73 mg, 0.5 mmol), Procedure A. Dark red needles. Yield: 57% (111 mg), mp 185–188 °C (ethanol). *Anal*. Calcd for $C_{22}H_{16}N_2O_5$: C 68.04; H 4.15; N 7.21. Found, C 67.94; H 4.30; N 7.34. IR (cm^{-1}): 1740, 1590, 1360, 740. ^{1}H NMR (DMSO-d_6): δ 3.59 (s, 3H, OMe); 4.09 (s, 2H, CH_2); 7.26–7.31 (m, 1H, Ph); 7.46–7.51 (m, 2H, Ph); 7.61 (s, 1H, =CH); 7.82 (br s, 4H, Ph); 7.87–7.90 (m, 2H, Ph).

Ethyl [(*Z*)-4-(3-ethoxycarbonylmethyl-5-oxo-1-phenyl-1,5-dihydro-pyrazol-4-ylidene)methyl-5-hydroxy-1-phenyl-1*H*-pyrazol-3-yl]acetate (8i). This compound was prepared in two ways: a) from **4a** (151 mg, 0.5 mmol) and ethyl (5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)carboxylate (**3a**) (123 mg, 0.5 mmol) (Procedure A) and b) from **4a** (151 mg, 0.5 mmol) (Procedure C). Yellow solid. Yield: 90% (226 mg, Procedure A), 75% (50 mg, Procedure C), mp 172–174 °C (ethanol). *Anal*. Calcd for $C_{27}H_{26}N_4O_6$: C 64.53; H 5.22; N 11.15. Found, C 64.90; H 5.28; N 11.47. MS: *m/z* (M^+, 502; MH^+, 503). IR (cm^{-1}): 1720, 1620, 1590, 1540, 1490, 1360, 1200, 1100, 1010, 760. ^{1}H NMR ($CDCl_3$): δ 1.32 (t, 6H, *J* = 7.2, OCH_2CH_3); 3.80 (s, 4H, CH_2); 4.25 (q, 4H, *J* = 7.2, OCH_2CH_3); 7.29–7.34 (m, 2H, Ph); 7.44–7.49 (m, 4H, Ph); 7.66 (s, 1H, =CH); 7.91–7.93 (m, 4H, Ph). ^{13}C NMR ($CDCl_3$): δ 14.6; 34.7; 62.1; 109.7; 121.7; 127.2; 129.3; 137.9; 140.7; 149.7; 161.8; 169.4.

Methyl [(*Z*)-4-(3-methoxycarbonylmethyl-5-oxo-1-phenyl-1,5-dihydro-1*H*-pyrazol-4-ylidene)methyl-5-hydroxy-1-phenyl-1*H*-pyrazol-3-yl]acetate (8j). This compound was prepared from **4b** (144 mg, 0.5 mmol) and methyl (5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)acetate (**3b**) (116 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 59% (140 mg), mp 179–180 °C (ethanol). *Anal*. Calcd for $C_{25}H_{22}N_4O_6$: C 63.29; H 4.67; N 11.81. Found, C 63.03; H 4.88; N 11.83. IR (cm^{-1}): 1730, 1610, 1590, 1360, 760. ^{1}H NMR (DMSO-d_6): δ 3.67 (s, 6H, OCH_3); 4.03 (s, 4H, CH_2); 7.31–7.36 (m, 2H, Ph); 7.48–7.54 (m, 4H, Ph); 7.66 (s, 1H, =CH); 7.84–7.87 (m, 4H, Ph). ^{13}C (DMSO-d_6): δ 19.3; 52.9; 109.6; 121.8; 127.7; 129.9; 137.9; 142.5; 151.3; 161.7; 170.2.

Ethyl [(*Z*)-4-(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (8k). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 3-methyl-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazole (**6k**) (87 mg, 0.5 mmol), Procedure A. Yellow solid. Yield: 58% (125 mg), mp 165–167 °C (ethanol). *Anal*. Calcd for $C_{24}H_{22}N_4O_4$: C 66.97; H 5.15; N 13.02. Found, C 66.89; H 5.19; N 13.16. MS: *m/z* (M^+, 430; MH^+, 431). IR (cm^{-1}): 1720, 1610, 1540, 1500, 1340, 1200, 1000, 820, 750, 690, 670. ^{1}H NMR ($CDCl_3$): δ 1.30 (t, 3H, *J* = 7.0, OCH_2CH_3); 2.37 (s, 3H, Me); 3.79 (s, 2H, CH_2); 4.23 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.25–7.32 (m, 2H, Ph); 7.42–7.48 (m, 4H, Ph); 7.50 (s, 1H,

=CH); 7.88–7.92 (m, 4H, Ph).

Ethyl [(*Z*)-4-(5-hydroxy-1,3-diphenyl-1*H*-pyrazol-4-yl)methylidene-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]acetate (8l). This compound was prepared from **4a** (151 mg, 0.5 mmol) and 1,3-diphenyl-5-oxo-4,5-dihydro-1*H*- pyrazole (**6l**) (118 mg, 0.5 mmol), Procedure A. Pale orange solid. Yield: 73% (180 mg), mp 168–169 °C (ethanol). *Anal*. Calcd for $C_{29}H_{24}N_4O_4$: C 70.72; H 4.91; N 11.38. Found, C 70.33; H 5.11; N 11.46. MS: *m/z* (M^+, 492; MH^+, 493). IR (cm^{-1}): 1720, 1610, 1590, 1520, 1490, 1350, 1240, 760. ^{1}H NMR ($CDCl_3$): δ 1.20 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.66 (s, 2H, CH_2); 4.14 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.27–7.35 (m, 2H, Ph); 7.43–7.55 (m, 7H, Ph); 7.60 (s, 1H, =CH); 7.65–7.68 (m, 2H, Ph); 7.91–7.94 (m, 2H, Ph); 7.99–8.03 (m, 2H, Ph). ^{13}C NMR (DMSO-d_6): δ 14.7; 34.2; 61.8; 108.6; 110.1; 121.8; 122.2; 127.8; 127.9; 129.8; 129.8; 129.9; 130.0; 130.7; 131.3; 137.8; 138.0; 143.3; 151.3; 155.6; 161.7; 161.8; 169.7.

General Procedure for the Preparation of Pyrazolo[4,3–*c*]pyridines (9c,d,k). A mixture of alkyl [(*Z*)-5-oxo-1-phenyl-4-(substituted amino)methylidene-4,5-dihydro-1*H*-pyrazol-3-yl)acetate (**7c,d,k**) (0.5 mmol) and DMFDMA (0.14 mL, 1 mmol) in DMF (3 mL) was heated under reflux for 2 h. Solvent was evaporated in *vacuo*, the oily residue was triturated with ethanol (2 mL), and the precipitate was collected by filtration to afford **9c,d,k**.

The following compounds were prepared in this manner:

Ethyl 3-oxo-2-phenyl-5-(4-methylphenyl)-3,5-dihydro-2*H*-pyrazolo[4,3–*c*]pyridine-7-carboxylate (9c). This compound was prepared from **7c** (182 mg, 0.5 mmol) and DMFDMA. Orange needles. Yield: 50% (100 mg), mp 233–235 °C (ethanol). *Anal*. Calcd for $C_{22}H_{19}N_3O_3$: C 70.76; H 5.13; N 11.25. Found, C 70.44; H 5.34; N 11.26. MS: *m/z* (M^+, 373). IR (cm^{-1}): 1730, 1670, 1650, 1590, 1490, 1310, 1150, 790, 760. ^{1}H NMR ($CDCl_3$): δ 1.48 (t, 3H, *J* = 7.2, OCH_2CH_3); 2.46 (s, 3H, Me); 4.49 (q, 2H, *J* = 7.2, OCH_2CH_3); 7.19–7.24 (m, 1H, Ph); 7.32–7.47 (m, 6H, Ph); 8.19 (d, 1H, *J* = 1.5, 4–H); 8.24–8.27 (m, 2H, Ph); 8.35 (d, 1H, *J* = 1.5, 6–H).

Ethyl 5-(4-methoxyphenyl)-3-oxo-2-phenyl-3,5-dihydro-2*H*-pyrazolo[4,3–*c*]pyridine-7-carboxylate (9d). This compound was prepared from **7d** (183 mg, 0.5 mmol) and DMFDMA. Orange solid. Yield: 60% (63 mg), mp 235–237 °C (ethanol). *Anal*. Calcd for $C_{22}H_{19}N_3O_4$: C 67.86; H 4.92; N 10.79. Found, C 67.62; H 5.19; N 10.80. MS: *m/z* (M^+, 389; MH^+, 390). IR (cm^{-1}): 1730, 1670, 1650, 1590, 1510, 1480, 1250, 1160, 840, 790, 760. ^{1}H NMR ($CDCl_3$): δ 1.48 (t, 3H, *J* = 7.2, OCH_2CH_3); 3.89 (s, 3H, OMe); 4.49

(q, 2H, J = 7.2, OCH_2CH$_3$); 7.05–7.08 (m, 2H, Ph); 7.18–7.24 (m, 1H, Ph); 7.35–7.46 (m, 4H, Ph); 8.15 (d, 1H, J = 1.5, 4–H); 8.32 (d, 1H, J = 1.5, 6–H); 8.24–8.27 (m, 2H, Ph).

Ethyl 3-oxo-2-phenyl-5-pyrazinyl-3,5-dihydro-2*H*-pyrazolo[4,3–*c*]pyridine-7-carboxylate (9k). This compound was prepared from **7k** (176 mg, 0.5 mmol) and DMFDMA. Red solid. Yield: 9% (16 mg), mp 215–218 °C (ethanol/DMF). *Anal*. Calcd for $C_{19}H_{15}N_5O_3$: C 63.15; H 4.18; N 19.38. Found, C 63.13; H 4.30; N 19.39. MS: *m/z* (M^+, 361; MH^+, 362). IR (cm^{-1}): 1730, 1720, 1670, 1640, 1320, 1140, 780, 760. ^{1}H NMR ($CDCl_3$): δ 1.50 (t, 3H, J = 7.2, OCH$_2$CH_3); 4.53 (q, 2H, J = 7.2, OCH_2CH$_3$); 7.20–7.25 (m, 1H, Ph); 7.42–7.47 (m, 2H, Ph); 8.21–8.24 (m, 2H, Ph); 8.60 (dd, 1H, J = 2.3, 1.5, 5'–H); 8.74 (d, 1H, J = 2.3, 6'–H); 8.76 (d, 1H, J = 1.5, 4–H); 8.97 (d, 1H, J = 1.5, 6–H); 9.01 (d, 1H, J = 1.1, 3'–H).

ACKNOWLEDGEMENTS

The financial support from the Ministry of Education, Science and Sport, Slovenia, through grant PS-502-0103, is gratefully acknowledged.

The crystallographic data were collected on the Nonius Kappa CCD diffractometer in the Laboratory of Inorganic Chemistry, Faculty of Chemistry and Chemical Technology, University of Ljubljana, Slovenia. We acknowledge with thanks the financial contribution of the Ministry of Education, Science and Sport, Republic of Slovenia through grants X-2000, PS-511-103 and Z1-3246.

REFERENCES

1. J.-C. Milhavet, A. Gueiffier, L. Bernal, and J.-C. Teulade, *Heterocycles*, 1999, **51**, 1661.
2. P. Marakos, N. Pouli, D. S. Wise, and L. B. Townsend, *Synlett*, 1997, 561.
3. A. Ellis, C. G. Li, and M. J. Rand, *Eur. J. Pharmacol.*, 1998, **356**, 41.
4. H. I. El-Subbagh, S. M. Abu-Zaid, M. A. Mahran, F. A. Badria, and A. M. Al-Obaid, *J. Med. Chem.*, 2000, **43**, 2915.
5. For a review see: J. V. Greenhill, Pyrazoles with Fused Six-membered Heterocyclic Rings. In *Comprehensive Heterocyclic Chemistry*; ed. by A. R. Katritzky, C. W. Rees, and K. T. Potts, Pergamon Press, Oxford 1984, Vol. 5, pp. 305–343.
6. P. Molina, E. Aller, and A. Lorenzo, *Tetrahedron*, 1991, **47**, 6737.
7. W. Oppolzer, *Tetrahedron Lett.*, 1970, 3091.
8. K.-Y. Tserng and L. Bauer, *J. Heterocycl. Chem.*, 1974, **11**, 163.

9. D. Donati, S. Fusi, F. Ponticelli, and P. Tedeschi, *Heterocycles*, 1988, **27**, 1899.
10. V. I. Tyvorskii, D. N. Bobrov, O. G. Kulinkovich, K. A. Tehrani, and N. De Kimpe, *Tetrahedron*, 2001, **57**, 2051.
11. W. J. Michaely, J. K. Curtis, and C. G. Knudsen, US Patent 5,300,478, 1994 (*Chem. Abstr.*, 1994, **121**, 57503n).
12. H. Fukui, K. Inoguchi, and J. Nakano, *Heterocycles*, 2002, **56**, 257.
13. K. Bodendorf and P. Niemeitz, *Arch. Pharm.* 1957, **290**, 494.
14. S. Hünig and G. Köbrich, *Liebigs Ann. Chem.*, 1958, **617**, 181.
15. S. Sugiura, S Ohno, O. Ohtani, K. Izumi, T. Kitamikado, H. Asai, K. Kato, M. Hori, and H. Fujimura, *J. Med. Chem.*, 1977, **20**, 80.
16. (a) H. V. Pechmann, *Liebigs Ann. Chem.*, 1891, **261**, 171; (b) Jpn. Kokai Tokkyo Koho JP 82 40,467 1982 (*Chem. Abstr.,* 1982, **97**, 92271t); (c) F. W. Short and E. J. Schoeb, *J. Heterocycl. Chem.*, 1969, **6**, 723.
17. A. Kreutzberger and K. Kolter, *Arch. Pharm.*, 1986, **319**, 18 (*Chem. Abstr.*, 1986, **105**, 42714c).
18. (a) S. Golič Grdadolnik and B. Stanovnik, *Magn. Res. Chem.*, 1997, **35**, 482; (b) P. Fischer, E. Schweizer, J. Langer, and U. Schmidt, *Magn. Res. Chem.*, 1994, **32**, 567.
19. (a) U. Bratušek, S. Rečnik, J. Svete, L. Golič, and B. Stanovnik, *Heterocycles*, 2002, **57**, 2045; (b) M. Škof, J. Svete, B. Stanovnik, L. Golič, S. Golič Grdadolnik, and L. Selič, *Helv. Chim. Acta*, 1998, **81**, 2332; (c) D. Bevk, M. Kmetič, S. Rečnik, J. Svete, L. Golič, A. Golobič, and B. Stanovnik, *Chemistry of Heterocyclic Compounds*, 2001, 1651; (d) J. Baš, S. Rečnik, J. Svete, S. Golič Grdadolnik, and B. Stanovnik, *Arkivoc*, 2001, **2**, 1189; (e) S. Pirc, S. Rečnik, M. Škof, J. Svete, L. Golič, A. Meden, and B. Stanovnik, *J. Heterocycl. Chem.*, 2002, **39**, 411; (f) U. Grošelj, S. Rečnik, J. Svete, A. Meden, and B. Stanovnik, *Tetrahedron Asymmetry*, 2002, **13**, 821.
20. Z. Otwinowski and W. Minor, *Methods Enzymol*., 1997, **276**, 307.
21. A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, A. Moliterni, G. Polidori, and R. Spagna, *J. Appl. Cryst.*, 1999**, 32**, 115.
22. S. R. Hall, D. J. du Boulay, and R. Olthof-Hazekamp, Xtal3.6 System . University of Western Australia, 1999.
23. C. K. Johnson, *ORTEPII*, Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA, 1976.