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An Efficient Synthesis of 7-(Arylmethyl)-3-*tert*-butyl-1-phenyl-6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazines

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Keywords: 5-Aminopyrazoles / Etherification / Pyrazolo-oxazines / Heterocycles / Cyclization / Fused-ring systems

An efficient and three-step procedure for the synthesis of novel 6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazine derivatives in good to excellent yields by treatment of pyrazolamines with aqueous formaldehyde in the presence of acetic acid is provided. The reactions proceeded through an intramolecular etherification process by dehydration of a 1,5-diol intermediate formed in the course of the reaction and promoted by acid media.

Introduction

Compounds containing oxazine moieties in their structures have been intensively studied owing to the activities against different diseases displayed by many of their analogues (Figure 1).[1]

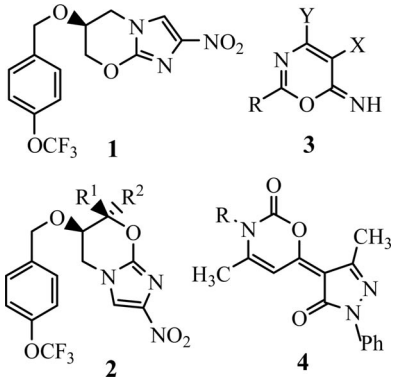

Figure 1. Some oxazine derivatives of biological interest.

PA-824 (**1**) is a promising imidazolo-oxazine derivative with a novel mechanism of action against *Mycobacterium tuberculosis* and *Helicobacter pylori*, comparable with that of isoniazid,[2a–2e] whereas compounds **2** were synthesized as PA-824 analogues, also showing significant activities against *Mycobacterium tuberculosis*.[2f] The polysubstituted 6-imino-1,3-oxazines **3** showed significant hepatoprotective activities,[2g] whereas the pyrazolo-oxazin-2-ones **4** were obtained and evaluated in silico as potential pharmacotherapeutic agents.[2h]

Considerable attention has in particular been focused on the benzo-oxazines and analogues since the discovery of the trifluoromethyl-1,3-oxazin-2-one **5** (Figure 2), known as Efavirenz, a non-nucleoside reverse-transcriptase inhibitor and selective anti-HIV drug.[3a] In this context, the benzo-oxazines **6** and pyrazolo-oxazines **7** were obtained through a new approach based on the Friedländer reaction,[3b] whereas the benzo-oxazines **8** were obtained in satisfactory yields by a four-step sequence.[3c]

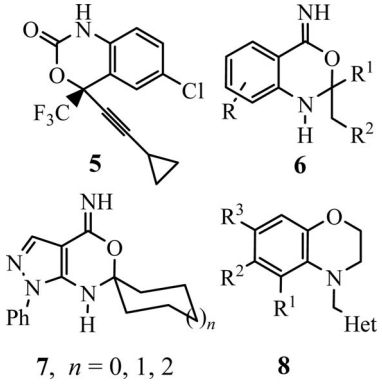

Figure 2. Efavirenz (**5**) and some fused oxazine derivatives of chemical interest.

Results and Discussion

In continuation of our current studies on the synthetic utility of 5-aminopyrazole derivatives,[4] we intended to synthesize a series of pyrazoloazepine derivatives **15** (Scheme 2, below) based on intramolecular cyclizations of hydroxy derivatives[5] similar to that depicted in Scheme 1.[5a] Contrary to our expectations, however, a series of new pyrazolo-oxazines **16** was obtained from the last step of our approach [step 4 (ii), Scheme 2], instead of the expected compounds **15**.

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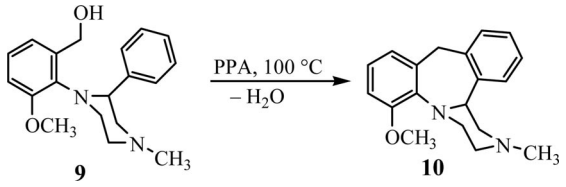
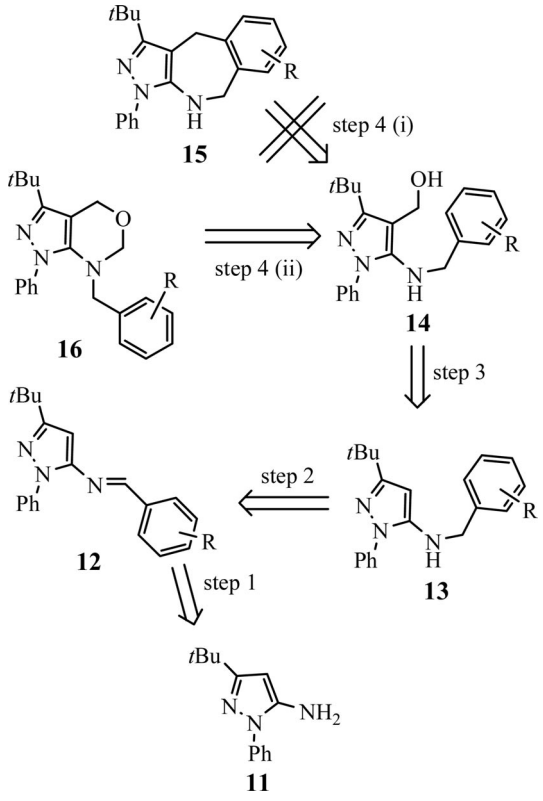


Scheme 1. Synthesis of the pyrazinoazepine **10** by the intramolecular cyclization of the hydroxy derivative **9**.

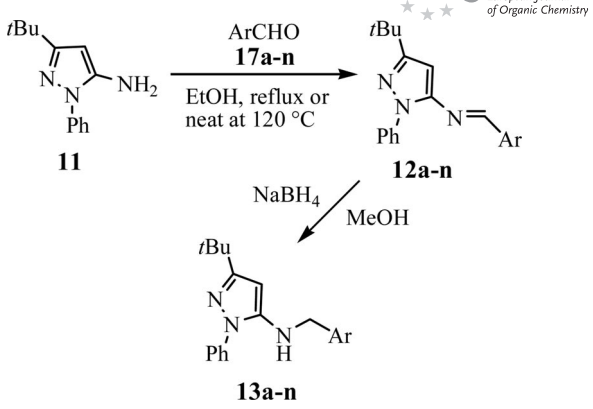


Scheme 2. Retrosynthetic pathway for the synthesis of compounds **15** and **16**.

Before the beginning of the experiments, the synthesis of the initially planned target compounds **15** according to the retrosynthetic pathway depicted in Scheme 2 was envisaged. As the last step an intramolecular cyclization process was involved, in the same way as shown in Scheme 1. A four-step sequence including the synthesis and isolation of the pyrazolimine and pyrazolamine intermediates **12** and **13**, respectively, was proposed.

A series of pyrazolimines **12** for this purpose was readily obtained from reactions between equimolar amounts of the aminopyrazole **11** and the arenealdehydes **17a**–**n** either at reflux in EtOH or under solvent-free reaction conditions (Scheme 3).

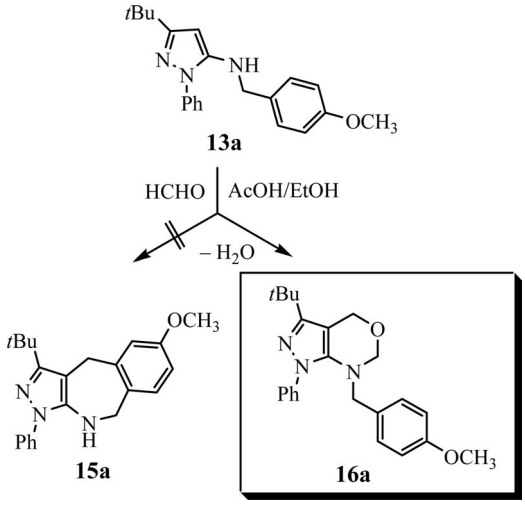
The structures of the imines **12** were assigned through their IR, NMR, and mass spectra (see Experimental Section) and in the cases of compounds **12b**–**k**, **12m**, and **12n** were confirmed by single-crystal X-ray diffraction.[6a] Reduction of the imines **12** by treatment with methanolic $NaBH_4$ afforded the corresponding pyrazolamines **13** in



Scheme 3. Synthesis of the pyrazolimines **12** and the pyrazolamines **13** from the 5-aminopyrazole **11**.

quantitative yields (Scheme 3). The appearance in each case of a IR absorption band attributable to the NH functionality in the 3307–3422 cm^{-1} range confirmed the reduction of **12**. The complete characterization of compounds **13** is reported in the Experimental Section. Again, confirmation of structures **13** was achieved without ambiguity by single-crystal X-ray diffraction with compounds **13a**–**d** and **13h**–**j**.[6b]

Finally, in an attempt to complete the synthesis of a compound **15**, the amine **13a** (1 mmol) was treated with an excess of aqueous formaldehyde (3 mmol) in an EtOH/AcOH mixture (1:1, v/v) and heated to 60 °C (Scheme 4). After complete consumption of the starting amine **13a** (TLC monitoring), the white solid formed was filtered off and recrystallized from EtOH.



Scheme 4. Structure of the product **16a** isolated from the reaction between the pyrazolamine **13a** and formaldehyde.

In principle, the absence of an absorption band around 3200–3300 cm^{-1} in the IR spectrum of this solid suggested a structure different from that of the expected pyrazoloazepine **15a**. The presence of three aliphatic methylene groups as determined by ^1H NMR and DEPT experiments confirmed our suspicions, and a complete analysis based on IR, ^1H and ^{13}C NMR, and MS data and on elemental

analyses surprisingly agreed with the pyrazolo-oxazinic structure **16a** for the isolated solid (Scheme 4). Growing of single crystals of this solid from a solution in EtOH and investigation by X-ray diffraction unambiguously confirmed the assigned structure for compound **16a** (Figure 3).[6c]

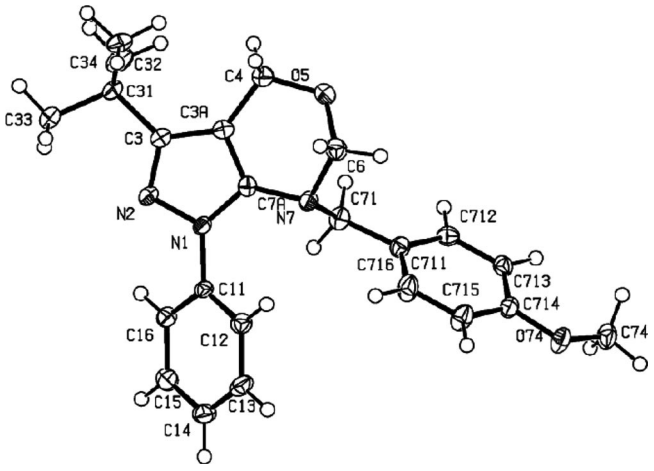
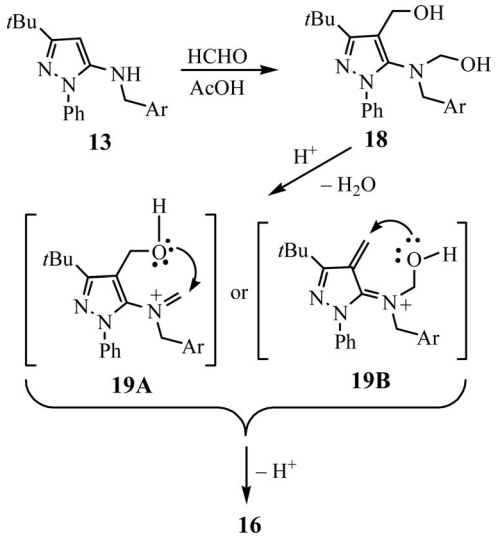


Figure 3. ORTEP drawing of the structure **16a** with 50% probability ellipsoids.

To evaluate the generality of this approach the remaining amines **13b**–**n** were treated with formaldehyde under the same reaction conditions, which afforded the corresponding pyrazolo-oxazines **16b**–**n** in 79–93% yields. Their structures were also confirmed by complete spectroscopic analysis (see the Experimental Section) and by single-crystal X-ray diffraction of compounds **16b**, **16d**, **16e**, **16h**, **16i**, **16k**, **16l**, and **16n**.[6c] Table 1 summarizes the obtained results for all compounds **12**, **13**, and **16**.

According to these results, it can be suggested that the formation of the oxazine ring starts with a double *C*- and *N*-hydroxymethylation of the amine **13** with formaldehyde, promoted by the acetic acid, to afford the dihydroxy intermediate **18** (Scheme 5). A dehydration process of any N–CH_2OH or C–CH_2OH functionality in **18** should then generate the stabilized carbocationic species **19A** or **19B**, respectively. Finally, intramolecular attack of the remaining hydroxy group on the stabilized primary carbocations in **19A/19B** should lead to the formation of the isolated pyrazolo-oxazine derivatives **16**. Although the formation of a species such as **19B** has previously been suggested, despite the loss of aromaticity in its pyrazole moiety,[4d] we believe that in this case the species **19A** is the more stable one, owing to direct assistance of the free electron pair of the nitrogen atom in stabilizing the primary carbocation formed after the dehydration process.



Scheme 5. Proposed S_N1-like sequence for the formation of the six-membered oxazine moiety in products **16**.

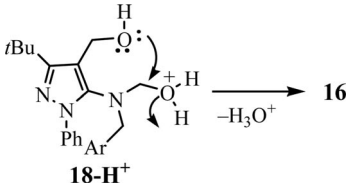
Alternatively, a simultaneous sequence resembling an S_N2 process might also be considered for the formation of products **16** directly from the protonated dyhydroxy intermediate **18-H$^+$**. In this case the acid medium should increase the leaving character of any hydroxy group by protonation, while the other one helps to remove it (in form of a water molecule), through an anchimeric-type assistance owing to their proximities (Scheme 5). It is worth emphasizing that no matter what alternative sequence type (S_N1 or

Table 1. Analytical data for intermediates **12a**–**n** and **13a**–**n** and for products **16a**–**n**.

Entry	Ar	Compounds **12**		Compounds **13**		Products **16**	
		Yield [%][a]	M.p. [°C]	Yield [%][a]	M.p. [°C]	Yield [%][a]	M.p. [°C]
a	*p*-$CH_3OC_6H_4$	92	131–2	93	97–8	85	163–4
b	C_6H_5	89	89–0	91	78–9	81	132–3
c	*p*-BrC_6H_4	72	122–3	83	92–3	82	135–6
d	*p*-$CH_3C_6H_4$	76	115–6	85	99–0	86	130–1
e	2,3-$(CH_3O)_2C_6H_3$	70	121–2	81	94–5	83	112–3
f	*p*-FC_6H_4	72	98–9	98	97–8	81	131–2
g	pyridin-3-yl	79	96–7	80	115–6	86	105–7
h	*p*-$CF_3C_6H_4$	69	103–4	82	97–8	82	152–3
i	*p*-$O_2NC_6H_4$	82	193–4	84	104–5	80	135–7
j	*p*-ClC_6H_4	80	118–9	89	113–4	82	110–2
k	3,4,5-$(CH_3O)_3C_6H_2$	84	147–8	83	119–0	83	166–8
l	1,3-benzodioxol-5-yl	70	160–1	94	96–7	81	163–5
m	pyridin-4-yl	78	113–4	81	115–6	79	129–0
n	3,4,5-$(CH_3O)_3C_6H_2$[b]	94	153–4	84	124–5	93	138–0

[a] Isolated yield. [b] Ph = *p*-$O_2NC_6H_4$ in the starting aminopyrazole **11**.

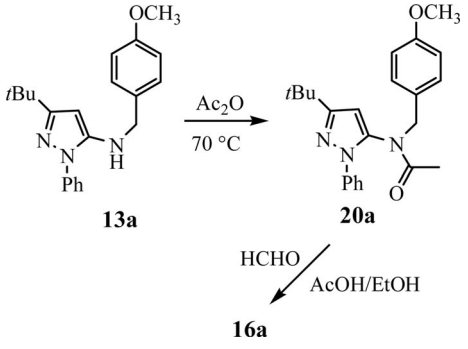
S_N2; Scheme 5 or Scheme 6, respectively), is followed during the cyclization process of **18**, the same products **16** will be obtained in any case.



Scheme 6. Proposed S_N2-like sequence for the formation of the six-membered oxazine moiety in products **16**.

Although an intramolecular cyclization process involving the *ortho*-carbon atom of the Ar substituent in the intermediate species **19B** should afford the expected pyrazoloazepine framework **15**, this product was not observed. This might indicate that nucleophilic attack of the remaining hydroxy group in **19B** prevailed over electrophilic attack of the stabilized carbocation in **19B** on the Ar substituent. It is likely that steric and conformational factors are involved. Moreover, if the process preferably involved a carbocation species such as **19A**, formation of structures **15** also should not be favored.

Finally, returning to the original attempt to obtain the expected pyrazoloazepine systems **15**, we decided to block the NH functionality in **13** to avoid the formation of the intermediate **18** through a double hydroxymethylation reaction. To this end, treatment of the amine **13a** with acetic anhydride afforded the *N*-acetyl derivative **20a** in quantitative yield (Scheme 7). The absence of an NH absorption band at 3321 cm^{-1} in the IR spectrum and the presence of a new absorption band corresponding to the C=O group at 1676 cm^{-1} confirmed the formation of this product (see the Experimental Section). The structure of compound **20a** was unambiguously assigned by single-crystal X-ray diffraction.[7]



Scheme 7. Synthesis of the oxazine **16a** from an alternative attempt to obtain the compounds of type **15** via the *N*-acetyl derivative **20a**.

Treatment of compound **20a** with formaldehyde under the established reaction conditions described in Scheme 4, contrary to our expectations, afforded the same compound **16a** as a unique product, although very slowly (Scheme 7). This result indicated that hydrolysis of the *N*-acetyl moiety occurred before the expected cyclization process affording product **15a** could take place, with subsequent regeneration of the free amine **13a**. The reaction then proceeded as previously (Scheme 4), again leading to the formation of the oxazine derivative **16a**.

Although the serendipitous formation of the oxazine moiety in products **16** was in principle surprising, some examples of the formation of similar structures have previously been reported from reactions between aminoacridine[8a] or aminopyrazole[8b] derivatives and formaldehyde in acidic media. These facts agree with and support our findings reported here.

Conclusions

As a consequence of an unplanned reaction we have developed an efficient and selective procedure for the synthesis of the novel pyrazolo-oxazines **16** in high yields through a short three-step sequence promoted by acetic acid. This approach involved intramolecular etherification of the 1,5-diol intermediates **18** formed from the reactions between the pyrazolamines **13** and formaldehyde in the presence of acetic acid. Growing of crystals and their analysis by single-crystal X-ray diffraction unambiguously confirmed the proposed structures for the intermediates pyrazolimines **12** and pyrazolamines **13**, as well as the final pyrazolo-oxazine products **16**.

Experimental Section

General: Melting points were determined with a Büchi melting point apparatus and are uncorrected. IR spectra were recorded with a Shimadzu FTIR 8400 spectrophotometer (KBr disks). ^1H and ^{13}C NMR spectra were recorded with a Bruker Avance 400 spectrophotometer operating at 400 MHz and 100 MHz, respectively, in $CDCl_3$ and $[D_6]$DMSO as solvents and with tetramethylsilane as internal standard. Mass spectra were recorded with a SHIMADZU-GC–MS 2010-DI-2010 spectrometer (with a direct inlet probe) operating at 70 eV. Microanalyses were performed with an Agilent elemental analyzer, and the values found are within ± 0.4% of the calcd. values. Silica gel aluminium plates (Merck 60 F_{254}) were used for analytical TLC. The starting aldehydes **17a**–**n** were purchased from Aldrich, Fluka, and Acros (analytical reagent grades) and were used without further purification. The starting aminopyrazole **11** was synthesized in 88% yield according to a literature procedure.[9]

General Procedure for the Synthesis of the Pyrazolimines 12

Approach 1: A mixture of 3-*tert*-butyl-1-phenyl-1*H*-pyrazol-5-amine (**11**, 0.5 g, 2.3 mmol) and the corresponding aldehyde **17** (2.3 mmol) in ethanol (3–5 mL) was heated under reflux with stirring for 2–3 h. After complete disappearance of the starting materials, as monitored by thin-layer chromatography, the mixture was allowed to cool to ambient temperature. The precipitate formed was collected by filtration and washed with ethanol (2× 0.5 mL) to give compounds **12**.

Approach 2: A mixture of 3-*tert*-butyl-1-phenyl-1*H*-pyrazol-5-amine (**11**, 0.5 g, 2.3 mmol) and the corresponding aldehyde **17** (2.3 mmol) was heated in an oil bath at 120 °C for 30–60 min. After complete disappearance of the starting materials, as monitored by thin-layer chromatography, the mixture was allowed to cool to ambient temperature and treated with ethanol (3 mL), and the precipitate, corresponding to compound **12**, was filtered and dried in air.

(*E*)-3-*tert*-Butyl-*N*-(4-methoxybenzylidene)-1-phenyl-1*H*-pyrazol-5-amine (12a): Yield: 0.713 g. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 9 H, *t*Bu), 3.85 (s, 3 H, OCH_3), 6.20 (s, 1 H, 4-H), 6.95 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.26 (t, *J* = 7.5 Hz, 1 H, Ar-H), 7.42 (t, *J* = 7.5 Hz, 2 H, Ar-H), 7.76–7.82 (m, 4 H, Ar-H), 8.58 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 55.4 (OCH_3), 89.7 (C-4), 114.3, 124.1, 126.1, 128.4, 129.0 (Cq), 130.8, 139.9 (Cq), 150.4 (Cq), 159.2 (C-7), 162.1 (Cq), 162.7 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3091, 2959, 2856, 1600 (C=N), 1257 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 333 (95) [M]$^+$, 318 (73) [M – 15], 291 (44) [M – 42], 91 (31), 77 (100) [Ph].

(*E*)-*N*-Benzylidene-3-*tert*-butyl-1-phenyl-1*H*-pyrazol-5-amine (12b): Yield: 0.628 g. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, *t*Bu), 6.27 (s, 1 H, 4-H), 7.30 (t, *J* = 7.5 Hz, 1 H, Ar-H), 7.43–7.50 (m, 5 H, Ar-H), 7.81 (d, *J* = 7.9 Hz, 2 H, Ar-H), 7.87 (d, *J* = 7.7 Hz, 2 H, Ar-H), 8.67 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 90.0 (C-4), 124.2, 126.2, 128.5, 128.8, 129.0, 131.7, 136.0 (Cq), 139.8 (Cq), 149.9 (Cq), 159.6 (C-7), 162.2 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3063, 2956, 2864, 1608 (C=N) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 303 (58) [M]$^+$, 288 (100) [M – 15], 261 (30) [M – 42], 77 (5) [Ph].

(*E*)-*N*-(4-Bromobenzylidene)-3-*tert*-butyl-1-phenyl-1*H*-pyrazol-5-amine (12c): Yield: 0.634 g. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, *t*Bu), 6.28 (s, 1 H, 4-H), 7.31 (t, *J* = 7.5 Hz, 1 H, Ar-H), 7.45 (t, *J* = 7.5 Hz, 2 H, Ar-H), 7.59 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.72 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.75 (d, *J* = 8.2 Hz, 2 H, Ar-H), 8.61 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 90.1 (C-4), 124.2, 126.3 (Cq), 126.4, 128.5, 130.2, 132.2, 134.9 (Cq), 139.6 (Cq), 149.6 (Cq), 158.2 (C-7), 162.2 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3055, 2963, 2863, 1614 (C=N) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 383/381 (40/42) [M]$^+$, 368/366 (81/81) [M – 15], 341/339 (41/46) [M – 42], 226 (12), 143 (21), 89 (42), 77 (100) [Ph].

(*E*)-3-*tert*-Butyl-*N*-(4-methylbenzylidene)-1-phenyl-1*H*-pyrazol-5-amine (12d): Yield: 0.560 g. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, *t*Bu), 2.43 (s, 3 H, CH_3), 6.25 (s, 1 H, 4-H), 7.27 (d, *J* = 8.2 Hz, 2 H, Ar-H), 7.29 (t, *J* = 7.3 Hz, 1 H, Ar-H), 7.45 (t, *J* = 7.3 Hz, 2 H, Ar-H), 7.76 (d, *J* = 8.2 Hz, 2 H, Ar-H), 7.81 (d, *J* = 7.9 Hz, 2 H, Ar-H), 8.64 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7 (CH_3), 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 89.9 (C-4), 124.1, 126.2, 128.5, 129.0, 129.6, 133.5 (Cq), 139.8 (Cq), 142.4 (Cq), 150.2 (Cq), 159.8 (C-7), 162.1 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3113, 2959, 2862, 1600 (C=N) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 317 (74) [M]$^+$, 302 (100) [M – 15], 275 (53) [M – 42], 226 (8), 143 (8), 91 (11), 77 (39) [Ph].

(*E*)-3-*tert*-Butyl-*N*-(2,3-dimethoxybenzylidene)-1-phenyl-1*H*-pyrazol-5-amine (12e): Yield: 0.593 g. White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, *t*Bu), 3.91 (s, 3 H, OCH_3), 3.97 (s, 3 H, OCH_3), 6.29 (s, 1 H, 4-H), 7.03 (d, *J* = 7.6 Hz, 1 H, Ar-H), 7.11 (t, *J* = 8.0 Hz, 1 H, Ar-H), 7.29 (t, *J* = 7.6 Hz, 1 H, Ar-H), 7.44 (t, *J* = 7.2 Hz, 2 H, Ar-H), 7.66 (d, *J* = 7.6 Hz, 1 H, Ar-H), 7.80 (d, *J* = 7.6 Hz, 2 H, Ar-H), 9.04 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 55.9 (OCH_3), 62.1 (OCH_3), 90.2 (C-4), 115.4, 119.1, 124.2 (2 C), 126.2, 128.5, 129.7 (Cq), 139.8 (Cq), 150.4 (×2Cq), 152.8 (Cq), 155.7 (C-7), 162.2 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3102, 2960, 2855, 1607 (C=N), 1272 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 363 (100) [M]$^+$, 348 (47) [M – 15], 332 (11) [M – 31], 321 (10) [M – 42], 226 (46), 200 (58), 173 (88), 149 (80), 77 (62) [Ph].

(*E*)-3-*tert*-Butyl-*N*-(4-fluorobenzylidene)-1-phenyl-1*H*-pyrazol-5-amine (12f): Yield: 0.534 g. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, *t*Bu), 6.26 (s, 1 H, 4-H), 7.15 (t, *J* = 8.8 Hz, 2 H, Ar-H), 7.30 (t, *J* = 7.3 Hz, 1 H, Ar-H), 7.46 (t, *J* = 7.7 Hz, 2 H, Ar-H), 7.79 (d, *J* = 7.3 Hz, 2 H, Ar-H), 7.86 (dd, *J* = 5.6, *J* = 8.7 Hz, 2 H, Ar-H), 8.63 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 89.9 (C-4), 116.0 (d, *J* = 21.8 Hz), 124.2, 126.3, 128.5, 130.9 (d, *J* = 9.0 Hz), 132.3 (Cq), 139.7 (Cq), 149.7 (Cq), 158.2 (C-7), 162.2 (Cq), 164.9 (d, *J* = 258.5 Hz, Cq-F) ppm. FTIR (KBr): $\tilde{\nu}$ = 3070, 2960, 2862, 1609 (C=N), 1600 (C=C) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 321 (62) [M]$^+$, 306 (100) [M – 15], 279 (47) [M – 42], 77 (42) [Ph].

(*E*)-3-*tert*-Butyl-1-phenyl-*N*-(pyridin-3-ylmethylene)-1*H*-pyrazol-5-amine (12g): Yield: 0.558 g. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, *t*Bu), 6.32 (s, 1 H, 4-H), 7.31 (t, *J* = 7.6 Hz, 1 H, Ar-H), 7.39 (dd, *J* = 8.0, *J* = 3.5 Hz, 1 H, Py-H), 7.45 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.76 (d, *J* = 8.1 Hz, 2 H, Ar-H), 8.19 (d, *J* = 8.1 Hz, 1 H, Py-H), 8.69 (br. s, 2 H, Py-H and 7-H), 9.00 (s, 1 H, Py-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 90.2 (C-4), 123.9, 124.3, 126.5, 128.5, 131.7 (Cq), 135.0, 139.6 (Cq), 149.3 (Cq), 150.9, 152.2, 156.3 (C-7), 162.3 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3065, 2959, 2863, 1604 (C=N), 1593 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 304 (49) [M]$^+$, 289 (100) [M – 15], 262 (36) [M – 42], 77 (14) [Ph].

(*E*)-3-*tert*-Butyl-1-phenyl-*N*-[4-(trifluoromethyl)benzylidene]-1*H*-pyrazol-5-amine (12h): Yield: 0.595 g. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (s, 9 H, *t*Bu), 6.33 (s, 1 H, 4-H), 7.33 (t, *J* = 7.5 Hz, 1 H, Ar-H), 7.47 (t, *J* = 7.8 Hz, 2 H, Ar-H), 7.72 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.76 (d, *J* = 7.8 Hz, 2 H, Ar-H), 7.96 (d, *J* = 8.1 Hz, 2 H, Ar-H), 8.71 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.6 (Cq, *t*Bu), 90.3 (C-4), 123.8 (q, *J* = 269.9 Hz, CF_3), 124.3, 125.8 (q, *J* = 3.7 Hz), 126.6, 128.6, 129.0, 132.9 (q, *J* = 32 Hz, Cq), 139.0 (Cq), 139.5 (Cq), 149.2 (Cq), 157.6 (C-7), 162.3 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3075, 2959, 2885, 1619 (C=N) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 371 (50) [M]$^+$, 356 (100) [M – 15], 329 (45) [M – 42], 143 (10), 77 (61) [Ph].

(*E*)-3-*tert*-Butyl-*N*-(4-nitrobenzylidene)-1-phenyl-1*H*-pyrazol-5-amine (12i): Yield: 0.665 g. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, *t*Bu), 6.37 (s, 1 H, 4-H), 7.35 (t, *J* = 7.5 Hz, 1 H, Ar-H), 7.48 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.74 (d, *J* = 7.6 Hz, 2 H, Ar-H), 8.00 (d, *J* = 8.6 Hz, 2 H, Ar-H), 8.31 (d, *J* = 8.6 Hz, 2 H, Ar-H), 8.73 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.6 (Cq, *t*Bu), 90.5 (C-4), 124.1, 124.4, 126.8, 128.6, 129.4, 139.4 (Cq), 141.4 (Cq), 148.8 (Cq), 149.4 (Cq), 156.3 (C-7), 162.5 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3051, 2962, 2865, 1596 (C=N), 1524 (NO_2), 1340 (NO_2) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 348 (47) [M]$^+$, 333 (100) [M – 15], 306 (39) [M – 42], 287 (27), 77 (24) [Ph].

(*E*)-3-*tert*-Butyl-*N*-(4-chlorobenzylidene)-1-phenyl-1*H*-pyrazol-5-amine (12j): Yield: 0.625 g. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, *t*Bu), 6.27 (s, 1 H, 4-H), 7.31 (t, *J* = 7.3 Hz, 1 H, Ar-H), 7.43–7.47 (m, 4 H, Ar-H), 7.76–7.80 (m, 4 H, Ar-H), 8.63 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 90.1 (C-4), 124.2, 126.4, 128.5, 129.2, 130.1, 134.5 (Cq), 137.8 (Cq), 139.7 (Cq), 149.6 (Cq), 158.1 (C-7), 162.2 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3067, 2962, 2866, 1616 (C=N) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 339/337 (24/66) [M]$^+$, 324/322 (35/100) [M – 15], 297/295 (16/47) [M – 42], 89 (19), 77 (49) [Ph].

(*E*)-3-*tert*-Butyl-1-phenyl-*N*-(3,4,5-trimethoxybenzylidene)-1*H*-pyrazol-5-amine (12k): Yield: 0.768 g. White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, *t*Bu), 3.91 (s, 6 H, OCH_3), 3.93 (s, 3 H, OCH_3), 6.25 (s, 1 H, 4-H), 7.13 (s, 2 H, Ar-H), 7.28 (t, *J* = 8.0 Hz, 1 H, Ar-H), 7.43 (t, *J* = 8.0 Hz, 2 H, Ar-H), 7.80 (d, *J* = 8.2 Hz, 2 H, Ar-H), 8.57 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 56.2 (2 OCH_3),

61.0 (OCH_3), 89.9 (C-4), 106.0, 124.2, 126.2, 128.3, 131.5 (Cq), 139.7 (Cq), 141.4 (Cq), 149.7 (Cq), 153.5 (Cq), 158.9 (C-7), 162.2 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3117, 2959, 2885, 1615 (C=N), 1125 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 393 (100) $[M]^+$, 378 (81) [M – 15], 351 (42) [M – 42], 317 (7), 226 (17), 210 (8), 189 (14), 77 (27) [Ph].

(*E*)-*N*-[(1,3-Benzodioxol-5-yl)methylene]-3-*tert*-butyl-1-phenyl-1*H*-pyrazol-5-amine (12l): Yield: 0.565 g. Yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, *t*Bu), 6.04 (s, 2 H, CH_2), 6.22 (s, 1 H, 4-H), 6.88 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.25–7.31 (m, 2 H, Ar-H), 7.43–7.47 (m, 3 H, Ar-H), 7.79 (d, *J* = 8.0 Hz, 2 H, Ar-H), 8.54 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 89.8 (C-4), 101.7 (OCH_2O), 106.8, 108.3, 124.1, 126.2, 126.3, 128.5, 131.0 (Cq), 139.8 (Cq), 148.5 (Cq), 150.1 (Cq), 150.9 (Cq), 158.9 (C-7), 162.1 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3095, 2957, 2861, 1617 (C=N), 1254 (C–O), 1039 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 347 (90) $[M]^+$, 332 (100) [M – 15], 305 (61) [M – 42], 226 (8), 166 (11), 77 (35) [Ph].

(*E*)-3-*tert*-Butyl-1-phenyl-*N*-(pyridin-4-ylmethylene)-1*H*-pyrazol-5-amine (12m): Yield: 0.550 g. Yellow solid. ^1H NMR (400 MHz. $CDCl_3$): δ = 1.41 (s, 9 H, *t*Bu), 6.35 (s, 1 H, 4-H), 7.33 (t, *J* = 7.6 Hz, 1 H, Ar-H), 7.47 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.68 (d, *J* = 4.6 Hz, 2 H, Py-H), 7.75 (d, *J* = 8.1 Hz, 2 H, Ar-H), 8.63 (s, 1 H, 7-H), 8.73 (d, *J* = 5.0 Hz, 2 H, Py-H) ppm. ^{13}C NMR (100 MHz. $CDCl_3$): δ = 30.4 (*t*Bu), 32.5 (Cq, *t*Bu), 90.6 (C-4), 122.1, 124.4, 126.7, 128.6, 139.5 (Cq), 142.6 (Cq), 148.8 (Cq), 150.6, 156.8 (C-7), 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3082, 2958, 2862, 1606 (C=N) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 304 (48) $[M]^+$, 289 (100) [M – 15], 262 (29) [M – 42], 117 (6), 77 (19) [Ph].

(*E*)-3-*tert*-Butyl-1-(4-nitrophenyl)-*N*-(3,4,5-trimethoxybenzylidene)-1*H*-pyrazol-5-amine (12n): This imine was obtained by starting from 3-*tert*-butyl-1-(4-nitrophenyl)-1*H*-pyrazol-5-amine (0.5 g, 1.9 mmol). Yield: 0.793 g. Brown solid. ^1H NMR (400 MHz, [D_6] DMSO): δ = 1.35 (s, 9 H, *t*Bu), 3.77 (s, 3 H, OCH_3), 3.88 (s, 6 H, OCH_3), 6.65 (s, 1 H, 4-H), 7.30 (s, 2 H, Ar-H), 8.17 (d, *J* = 9.1 Hz, 2 H, Ar-H), 8.39 (d, *J* = 8.9 Hz, 2 H, Ar-H), 8.87 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 29.9 (*t*Bu), 32.3 (Cq, *t*Bu), 55.9 (2 OCH_3), 60.2 (OCH_3), 92.6 (C-4), 106.4, 122.6, 124.5, 130.8 (Cq), 141.3 (Cq), 144.3 (Cq), 144.5 (Cq), 151.1 (Cq), 153.2 (Cq), 162.3 (C-7), 163.0 (Cq) ppm. IR (KBr): $\tilde{\nu}$ = 3082, 2962, 2851, 1618 (C=N), 1509 (NO_2), 1334 (NO_2), 1131 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 438 (100) $[M]^+$, 423 (65) [M – 15], 396 (34), 211 (25), 181 (168).

General Procedure for the Synthesis of the Pyrazolamines 13: Solid $NaBH_4$ (2.5 mmol) was added portionwise with stirring, over a period of 5 min, to a solution of an imine **12** (1 mmol) in methanol (3–4 mL). The stirring was continued at ambient temperature for 1 h. After the reaction was complete (monitored by TLC), the volume of the reaction mixture was reduced to 1 mL under reduced pressure, and water (5 mL) was added. The aqueous solution was extracted with ethyl acetate (2 × 5 mL), and the combined organic extracts were dried with anhydrous Na_2SO_4; after removal of the solvent, the resulting products were crystallized from ethanol. All reactions started with 0.5 g of an imine **12**.

3-*tert*-Butyl-*N*-(4-methoxybenzyl)-1-phenyl-1*H*-pyrazol-5-amine (13a): Yield: 0.468 g. White solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 9 H, *t*Bu), 3.90 (s, 3 H, OCH_3), 3.96 (t, *J* = 5.4 Hz, 1 H, NH), 4.22 (d, *J* = 5.4 Hz, 2 H, CH_2), 5.50 (s, 1 H, 4-H), 6.88 (d, *J* = 8.3 Hz, 2 H, Ar-H), 7.26 (d, *J* = 8.3 Hz, 2 H, Ar-H), 7.30 (t, *J* = 7.7 Hz, 1 H, Ar-H), 7.44 (t, *J* = 7.3 Hz, 2 H, Ar-H), 7.54 (d, *J* = 8.0 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.1 (*t*Bu), 32.3 (Cq, *t*Bu), 46.1 (CH_2), 55.2 (OCH_3), 85.2 (C-4), 114.1, 124.6, 127.7, 128.8, 129.6, 130.0 (Cq), 137.4 (Cq), 148.4 (Cq), 159.2 (Cq), 162.1 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3321 (NH), 2957, 2862, 1255 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 335 (16) $[M]^+$, 121 (100) $[C_8H_9O]$, 77 (8) [Ph].

***N*-Benzyl-3-*tert*-butyl-1-phenyl-1*H*-pyrazol-5-amine (13b):** Yield: 0.458 g. White solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.34 (s, 9 H, *t*Bu), 3.97 (br. s, 1 H, NH), 4.28 (br. s, 2 H, CH_2), 5.49 (s, 1 H, 4-H), 7.26–7.46 (m, 8 H, Ar-H), 7.56 (br. s, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.3 (Cq, *t*Bu), 50.3 (CH_2), 85.0 (C-4), 124.1, 126.7, 127.6, 127.7, 128.7, 129.4, 138.5 (Cq), 139.2 (Cq), 148.0 (Cq), 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3334 (NH), 2961, 2860, 1594 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 305 (100) $[M]^+$, 290 (59) [M – 15], 263 (69) [M – 42], 91 (34), 77 (13) [Ph].

***N*-(4-Bromobenzyl)-3-*tert*-butyl-1-phenyl-1*H*-pyrazol-5-amine (13c):** Yield: 0.417 g. Yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 9 H, *t*Bu), 3.99 (t, *J* = 5.8 Hz, 1 H, NH), 4.24 (d, *J* = 5.8 Hz, 2 H, CH_2), 5.44 (s, 1 H, 4-H), 7.24 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.29 (t, *J* = 7.2 Hz, 1 H, Ar-H), 7.43–7.49 (m, 4 H, Ar-H), 7.56 (d, *J* = 8.0 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3 (*t*Bu), 32.3 (Cq, *t*Bu), 49.6 (CH_2), 85.0 (C-4), 121.3 (Cq), 124.1, 126.9, 129.2, 129.5, 131.8, 137.5 (Cq), 139.0 (Cq), 147.6 (Cq), 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3331 (NH), 2959, 2865, 1595 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 385/383 (96/100) $[M]^+$, 370/368 (45/44) [M – 15], 343/341 (70/73) [M – 42], 214 (70), 171/169 (72/67) $[C_7H_6Br]$.

3-*tert*-Butyl-*N*-(4-methylbenzyl)-1-phenyl-1*H*-pyrazol-5-amine (13d): Yield: 0.428 g. White solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 9 H, *t*Bu), 2.36 (s, 3 H, CH_3), 3.94 (t, *J* = 5.8 Hz, 1 H, NH), 4.24 (d, *J* = 5.8 Hz, 2 H, CH_2), 5.51 (s, 1 H, 4-H), 7.17 (d, *J* = 7.9 Hz, 2 H, Ar-H), 7.25–7.31 (m, 3 H, Ar-H), 7.43 (t, *J* = 7.4 Hz, 2 H, Ar-H), 7.57 (d, *J* = 8.5 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 (CH_3), 30.4 (*t*Bu), 32.3 (Cq, *t*Bu), 50.1 (CH_2), 84.8 (C-4), 124.0, 126.7, 127.7, 129.3, 129.4, 135.4 (Cq), 137.3 (Cq), 139.1 (Cq), 148.0 (Cq), 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3325 (NH), 2962, 2857, 1595 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 319 (76) $[M]^+$, 304 (18) [M – 15], 277 (30) [M – 42], 105 (100) $[C_8H_9]$, 77 (8) [Ph].

3-*tert*-Butyl-*N*-(2,3-dimethoxybenzyl)-1-phenyl-1*H*-pyrazol-5-amine (13e): Yield: 0.407 g. Yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 9 H, *t*Bu), 3.82 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 4.13 (t, *J* = 5.7 Hz, 1 H, NH), 4.28 (d, *J* = 5.7 Hz, 2 H, CH_2), 5.54 (s, 1 H, 4-H), 6.88 (d, *J* = 8.0 Hz, 1 H, Ar-H), 6.93 (d, *J* = 7.3 Hz, 1 H, Ar-H), 7.04 (t, *J* = 7.3 Hz, 1 H, Ar-H), 7.27 (t, *J* = 6.8 Hz, 1 H, Ar-H), 7.42 (t, *J* = 7.9 Hz, 2 H, Ar-H), 7.55 (d, *J* = 7.9 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (*t*Bu), 32.3 (Cq, *t*Bu), 45.6 (CH_2), 55.7 (OCH_3), 60.8 (OCH_3), 85.0 (C-4), 111.9, 121.2, 124.0, 124.1, 126.7, 129.4, 132.1 (Cq), 139.1 (Cq), 147.2 (Cq), 148.1 (Cq), 152.7 (Cq), 162.3 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3382 (NH), 2960, 2861, 1595, 1274 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 365 (48) $[M]^+$, 334 (6) [M – 31], 151 (77) $[C_9H_{11}O_2]$, 136 (100) $[C_8H_{10}O_2]$, 91 (27).

3-*tert*-Butyl-*N*-(4-fluorobenzyl)-1-phenyl-1*H*-pyrazol-5-amine (13f): Yield: 0.493 g. Yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 9 H, *t*Bu), 3.95 (t, *J* = 5.4 Hz, 1 H, NH), 4.24 (d, *J* = 5.4 Hz, 2 H, CH_2), 5.45 (s, 1 H, 4-H), 7.03 (t, *J* = 8.6 Hz, 2 H, Ar-H), 7.28 (t, *J* = 7.2 Hz, 1 H, Ar-H), 7.33 (t, *J* = 8.6 Hz, 2 H, Ar-H), 7.43 (t, *J* = 7.5 Hz, 2 H, Ar-H), 7.56 (d, *J* = 7.8 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3 (*t*Bu), 32.3 (Cq, *t*Bu), 49.6 (CH_2), 85.1 (C-4), 115.4 (d, *J* = 22.1 Hz), 124.1, 126.8, 129.2 (d, *J* = 8.8 Hz), 129.4, 134.2 (Cq), 139.1 (Cq), 147.7 (Cq), 162.2 (d, *J* = 244.9 Hz, Cq-F), 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3332 (NH),

2965, 2867, 1601 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 323 (100) $[M]^+$, 308 (50) [M – 15], 281 (65) [M – 42], 214 (28), 109 (67) $[C_7H_6F]$, 77 (10).

3-*tert*-Butyl-1-phenyl-*N*-(pyridin-3-ylmethyl)-1*H*-pyrazol-5-amine (13g): Yield: 0.403 g. White solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 9 H, *t*Bu), 4.03 (t, *J* = 5.8 Hz, 1 H, NH), 4.30 (d, *J* = 5.8 Hz, 2 H, CH_2), 5.46 (s, 1 H, 4-H), 7.27–7.33 (m, 2 H, Ar-H and Py-H), 7.44 (t, *J* = 7.4 Hz, 2 H, Ar-H), 7.55 (d, *J* = 7.5 Hz, 2 H, Ar-H), 7.70 (d, *J* = 7.7 Hz, 1 H, Py-H), 8.54 (d, *J* = 7.8 Hz, 1 H, Py-H), 8.61 (s, 1 H, Py-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3 (*t*Bu), 32.3 (Cq, *t*Bu), 47.7 (CH_2), 85.2 (C-4), 123.6, 124.1, 127.0, 129.5, 134.0 (Cq), 135.3, 138.9 (Cq), 147.4 (Cq), 149.0, 149.2, 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3382 (NH), 2960, 2861, 1603 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 306 (100) $[M]^+$, 291 (61), 264 (71), 214 (8), 158 (10), 92 (35), 77 (20) [Ph].

3-*tert*-Butyl-1-phenyl-*N*-[4-(trifluoromethyl)benzyl]-1*H*-pyrazol-5-amine (13h): Yield: 0.412 g. White solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 9 H, *t*Bu), 4.06 (t, *J* = 6.0 Hz, 1 H, NH), 4.35 (d, *J* = 6.0 Hz, 2 H, CH_2), 5.43 (s, 1 H, 4-H), 7.31 (t, *J* = 7.5 Hz, 1 H, Ar-H), 7.46 (t, *J* = 7.9 Hz, 2 H, Ar-H), 7.49 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.58 (d, *J* = 7.9 Hz, 2 H, Ar-H), 7.62 (d, *J* = 8.3 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3 (*t*Bu), 32.3 (Cq, *t*Bu), 49.8 (CH_2), 85.2 (C-4), 121.4 (q, *J* = 271.4 Hz, CF_3), 124.1, 125.6 (q, *J* = 3.4 Hz), 126.9, 127.7, 129.5, 129.8 (q, *J* = 32.0 Hz, Cq), 139.0 (Cq), 142.7 (Cq), 147.5 (Cq), 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3326 (NH), 2964, 2868, 1594 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 373 (100) $[M]^+$, 358 (84) [M – 15], 331 (98) [M – 42], 214 (19), 159 (38) $[C_8H_6F_3]$, 77 (10).

3-*tert*-Butyl-*N*-(4-nitrobenzyl)-1-phenyl-1*H*-pyrazol-5-amine (13i): Yield: 0.422 g. Yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 9 H, *t*Bu), 4.18 (t, *J* = 5.8 Hz, 1 H, NH), 4.41 (d, *J* = 5.8 Hz, 2 H, CH_2), 5.36 (s, 1 H, 4-H), 7.32 (t, *J* = 6.5 Hz, 1 H, Ar-H), 7.47 (t, *J* = 7.0 Hz, 2 H, Ar-H), 7.53–7.59 (m, 4 H, Ar-H), 8.22 (d, *J* = 8.3 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3 (*t*Bu), 32.3 (Cq, *t*Bu), 49.5 (CH_2), 85.2 (C-4), 123.9, 124.1, 127.0, 127.9, 129.5, 138.8 (Cq), 146.1 (Cq), 147.2 (Cq), 147.3 (Cq), 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3364 (NH), 2962, 2868, 1597, 1527 (NO_2), 1341 (NO_2) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 350 (95) $[M]^+$, 335 (85) [M – 15], 308 (100) [M – 42], 214 (15), 158 (15).

3-*tert*-Butyl-*N*-(4-chlorobenzyl)-1-phenyl-1*H*-pyrazol-5-amine (13j): Yield: 0.448 g. White solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 9 H, *t*Bu), 3.99 (t, *J* = 5.7 Hz, 1 H, NH), 4.25 (d, *J* = 5.7 Hz, 2 H, CH_2), 5.44 (s, 1 H, 4-H), 7.29–7.34 (m, 5 H, Ar-H), 7.45 (t, *J* = 7.7 Hz, 2 H, Ar-H), 7.56 (d, *J* = 7.7 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3 (*t*Bu), 32.3 (Cq, *t*Bu), 49.6 (CH_2), 85.0 (C-4), 124.1, 126.9, 128.8, 128.9, 129.5, 133.3 (Cq), 137.0 (Cq), 139.0 (Cq), 147.7 (Cq), 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3422 (NH), 2959, 2864, 1595 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 341/339 (28/84) $[M]^+$, 326/324 (13/35) [M – 15], 299/297 (20/58) [M – 42], 214 (37), 158 (38), 127/125 (29/100) $[C_7H_6Cl]$, 77 (63) [Ph].

3-*tert*-Butyl-1-phenyl-*N*-(3,4,5-trimethoxybenzyl)-1*H*-pyrazol-5-amine (13k): Yield: 0.417 g. White solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 9 H, *t*Bu), 3.85 (br. s, 9 H, OCH_3), 3.94 (t, *J* = 5.6 Hz, 1 H, NH), 4.21 (d, *J* = 5.6 Hz, 2 H, CH_2), 5.51 (s, 1 H, 4-H), 6.58 (s, 2 H, Ar-H), 7.29 (t, *J* = 7.7 Hz, 1 H, Ar-H), 7.44 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.56 (d, *J* = 7.9 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3 (*t*Bu), 32.3 (Cq, *t*Bu), 50.7 (CH_2), 56.2 (2 OCH_3), 60.8 (OCH_3), 85.2 (C-4), 104.8, 124.1, 126.8, 129.4, 134.2 (Cq), 139.1 (Cq), 146.6 (Cq), 147.9 (Cq), 153.4 (Cq), 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3307 (NH), 2962, 2867, 1594, 1127 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 395 (8) $[M]^+$, 181 (100) $[C_{10}H_{13}O_3]$.

***N*-[(1,3-Benzodioxol-5-yl)methyl]-3-*tert*-butyl-1-phenyl-1*H*-pyrazol-5-amine (13l):** Yield: 0.473 g. White solid. ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 1.20 (s, 9 H, *t*Bu), 4.08 (d, *J* = 5.8 Hz, 2 H, CH_2), 5.43 (s, 1 H, 4-H), 5.82 (t, *J* = 5.8 Hz, 1 H, NH), 5.97 (s, 2 H, OCH_2O), 6.83–6.86 (m, 2 H, Ar-H), 6.97 (s, 1 H, Ar-H), 7.28 (t, *J* = 7.2 Hz, 1 H, Ar-H), 7.46 (t, *J* = 7.4 Hz, 2 H, Ar-H), 7.58 (d, *J* = 7.4 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 30.1 (*t*Bu), 31.9 (Cq, *t*Bu), 48.6 (CH_2), 85.1 (C-4), 100.7 (OCH_2O), 107.8, 107.9, 120.6, 122.9, 125.8, 129.0, 133.6 (Cq), 139.5 (Cq), 146.0 (Cq), 147.2 (Cq), 148.4 (Cq), 160.7 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3331 (NH), 2959, 2863, 1598, 1243 (C–O), 1034 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 349 (16) $[M]^+$, 135 (100) $[C_8H_7O_2]$.

3-*tert*-Butyl-1-phenyl-*N*-(pyridin-4-ylmethyl)-1*H*-pyrazol-5-amine (13m): Yield: 0.408 g. White solid; m.p. 115–116 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 9 H, *t*Bu), 4.15 (t, *J* = 5.8 Hz, 1 H, NH), 4.33 (d, *J* = 5.9 Hz, 2 H, CH_2), 5.37 (s, 1 H, 4-H), 7.29–7.35 (m, 3 H, Ar-H), 7.48 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.60 (dd, *J* = 8.4, *J* = 1.4 Hz, 2 H, Py-H), 8.59 (dd, *J* = 8.0, *J* = 1.6 Hz, 2 H, Py-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3 (*t*Bu), 32.3 (Cq, *t*Bu), 49.0 (CH_2), 85.1 (C-4), 122.1, 124.2, 127.1, 129.6, 138.9 (Cq), 147.3 (Cq), 147.7 (Cq), 150.1, 162.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3224 (NH), 2960, 2865, 1599 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 306 (100) $[M]^+$, 291 (40), 264 (52), 214 (5), 158 (12), 92 (25), 77 (30) [Ph].

3-*tert*-Butyl-1-(4-nitrophenyl)-*N*-(3,4,5-trimethoxybenzyl)-1*H*-pyrazol-5-amine (13n): Yield: 0.422 g. Brown solid. ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 1.23 (s, 9 H, *t*Bu), 3.64 (s, 3 H, OCH_3), 3.77 (s, 6 H, OCH_3), 4.14 (d, *J* = 5.6 Hz, 2 H, CH_2), 5.66 (s, 1 H, 4-H), 6.26 (t, *J* = 5.6 Hz, 1 H, NH), 6.77 (s, 2 H, Ar-H), 7.97 (d, *J* = 9.1 Hz, 2 H, Ar-H), 8.34 (d, *J* = 8.9 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 29.8 (*t*Bu), 32.1 (Cq, *t*Bu), 49.4 (CH_2), 55.8 (2 OCH_3), 59.9 (OCH_3), 87.4 (C-4), 105.2, 121.7, 124.8, 134.8 (Cq), 136.4 (Cq), 143.8 (Cq), 145.0 (Cq), 149.8 (Cq), 152.7 (Cq), 162.9 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3309 (NH), 2961, 2866, 1599, 1509 (NO_2), 1333 (NO_2), 1126 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 440 (2) $[M]^+$, 181 (100), 148 (5).

General Procedure for the Synthesis of the Pyrazolo-oxazines 16: A mixture of an amine **13** (1 mmol), ethanol (0.5 mL), AcOH (0.5 mL), and aq. formaldehyde (3 mmol) was heated to 50–60 °C for 10–16 h. After the reaction was complete (monitored by TLC), the volume of the mixture was reduced to 0.5 mL under reduced pressure, and the solid formed was filtered and crystallized from ethanol. All reactions started with 0.3 g of the amine **13**.

3-*tert*-Butyl-7-(4-methoxybenzyl)-1-phenyl-1,4,6,7-tetrahydropyrazolo[3,4-*d*][1,3]oxazine (16a): Yield: 0.287 g. White solid. ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 1.26 (s, 9 H, *t*Bu), 3.73 (s, 3 H, OCH_3), 3.77 (s, 2 H, 8-H), 4.41 (s, 2 H, 6-H), 4.82 (s, 2 H, 4-H), 6.88 (d, *J* = 8.5 Hz, 2 H, Ar-H), 7.15 (d, *J* = 8.5 Hz, 2 H, Ar-H), 7.31 (t, *J* = 7.5 Hz, 1 H, Ar-H), 7.50 (t, *J* = 8.3 Hz, 2 H, Ar-H), 7.80 (d, *J* = 7.7 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 29.2 (*t*Bu), 32.8 (Cq, *t*Bu), 54.2 (C-8), 55.0 (OCH_3), 63.0 (C-4), 77.1 (C-6), 103.0 (Cq), 113.8, 121.8, 126.3, 128.3 (Cq), 129.1, 129.7, 139.1 (Cq), 143.7 (Cq), 155.2 (Cq), 158.6 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3045, 2960, 2854, 1612 (C=N), 1594 (C=C), 1509, 1243 (C–O), 1022 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 377 (10) $[M]^+$, 121 (100) $[C_8H_9O]$. $C_{23}H_{27}N_3O_2$ (377.21): calcd. C 73.18, H 7.21, N 11.13; found C 72.90, H 7.10, N 10.89.

7-Benzyl-3-*tert*-butyl-1-phenyl-1,4,6,7-tetrahydropyrazolo[3,4-*d*][1,3]oxazine (16b): Yield: 0.277 g. White solid. ^1H NMR (400 MHz,

$CDCl_3$): δ = 1.35 (s, 9 H, *t*Bu), 3.96 (s, 2 H, 8-H), 4.49 (s, 2 H, 6-H), 4.90 (s, 2 H, 4-H), 7.22–7.34 (m, 6 H, Ar-H), 7.44 (t, J = 7.7 Hz, 2 H, Ar-H), 7.89 (d, J = 7.7 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.5 (*t*Bu), 32.2 (Cq, *t*Bu), 55.3 (C-8), 64.2 (C-4), 77.9 (C-6), 103.2 (Cq), 122.3, 126.3, 127.5, 128.5, 128.8, 129.1, 136.9 (Cq), 139.5 (Cq), 144.1 (Cq), 156.1 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3060, 2964, 2859, 1596 (C=N), 1592 (C=C), 1502, 1023 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 347 (100) $[M]^+$, 316 (11), 302 (12), 256 (29), 228 (9), 91 (16), 77 (9) [Ph]. $C_{22}H_{25}N_3O$ (347.45): calcd. C 76.05, H 7.25, N 12.09; found C 75.91, H 7.51, N 12.30.

7-(4-Bromobenzyl)-3-*tert*-butyl-1-phenyl-1,4,6,7-tetrahydropyrazolo-[3,4-*d*][1,3]oxazine (16c): Yield: 0.273 g. White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 9 H, *t*Bu), 3.85 (s, 2 H, 8-H), 4.42 (s, 2 H, 6-H), 4.84 (s, 2 H, 4-H), 7.09 (d, J = 8.1 Hz, 2 H, Ar-H), 7.23 (t, J = 7.1 Hz, 1 H, Ar-H), 7.35–7.53 (m, 4 H, Ar-H), 7.79 (d, J = 7.3 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.4 (*t*Bu), 33.2 (Cq, *t*Bu), 54.7 (C-8), 64.1 (C-4), 78.1 (C-6), 103.2 (Cq), 121.5 (Cq), 122.4, 126.4, 129.1, 130.3, 131.6, 136.0 (Cq), 139.4 (Cq), 143.7 (Cq), 156.1 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3059, 2960, 2851, 1595 (C=N), 1573 (C=C), 1506, 1012 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 427/425 (53/54) $[M]^+$, 256 (100), 228 (50), 171/169 (30/32) $[C_7H_6Br]$. $C_{22}H_{24}BrN_3O$ (425.11): calcd. C 61.98, H 5.67, N 9.86; found C 70.01, H 5.72, N 9.75.

3-*tert*-Butyl-7-(4-methylbenzyl)-1-phenyl-1,4,6,7-tetrahydropyrazolo-[3,4-*d*][1,3]oxazine (16d): Yield: 0.292 g. White solid. ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 1.26 (s, 9 H, *t*Bu), 2.26 (s, 3 H, CH_3), 3.85 (s, 2 H, 8-H), 4.44 (s, 2 H, 6-H), 4.80 (s, 2 H, 4-H), 7.05–7.09 (m, 4 H, Ar-H), 7.26 (t, J = 7.4 Hz, 1 H, Ar-H), 7.43 (t, J = 7.4 Hz, 2 H, Ar-H), 7.76 (d, J = 8.1 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 19.9 (CH_3), 28.7 (*t*Bu), 32.2 (Cq, *t*Bu), 54.3 (C-8), 62.7 (C-4), 77.4 (C-6), 102.3 (Cq), 121.5, 125.6, 127.7, 128.4 (2 C), 133.1 (Cq), 136.0 (Cq), 138.9 (Cq), 143.4 (Cq), 154.9 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3048, 2962, 2857, 1594 (C=N), 1576 (C=C), 1506, 1023 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 361 (51) $[M]^+$, 256 (16), 105 (100) $[C_8H_9]$. $C_{23}H_{27}N_3O$ (361.22): calcd. C 76.42, H 7.53, N 11.62; found C 76.21, H 7.51, N 11.50.

3-*tert*-Butyl-7-(2,3-dimethoxybenzyl)-1-phenyl-1,4,6,7-tetrahydropyr-azolo[3,4-*d*][1,3]oxazine (16e): Yield: 0.278 g. White solid. ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 1.26 (s, 9 H, *t*Bu), 3.54 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.88 (s, 2 H, 8-H), 4.44 (s, 2 H, 6-H), 4.82 (s, 2 H, 4-H), 6.91 (d, J = 7.7 Hz, 1 H, Ar-H), 6.96 (d, J = 8.3 Hz, 1 H, Ar-H), 7.06 (t, J = 7.9 Hz, 1 H, Ar-H), 7.26 (t, J = 7.4 Hz, 1 H, Ar-H), 7.43 (t, J = 8.3 Hz, 2 H, Ar-H), 7.77 (d, J = 7.5 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 29.2 (*t*Bu), 32.8 (Cq, *t*Bu), 49.0 (C-8), 55.6 (OCH_3), 59.9 (OCH_3), 63.0 (C-4), 77.9 (C-6), 103.0 (Cq), 112.1, 120.7, 121.6, 123.9, 126.2, 129.0, 129.9 (Cq), 139.1 (Cq), 143.8 (Cq), 146.8 (Cq), 152.2 (Cq), 155.2 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3050, 2961, 2871, 1595 (C=N), 1576 (C=C), 1503, 1262 (C–O), 1040 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 407 (34) $[M]^+$, 151 (100) $[C_9H_{11}O_2]$, 136 (81), 91 (21), 77 (10) [Ph]. $C_{24}H_{29}N_3O_3$ (407.22): calcd. C 70.74, H 7.17, N 10.31; found C 70.52, H 7.30, N 10.20.

3-*tert*-Butyl-7-(4-fluorobenzyl)-1-phenyl-1,4,6,7-tetrahydropyrazolo-[3,4-*d*][1,3]oxazine (16f): Yield: 0.275 g. White solid. ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 1.26 (s, 9 H, *t*Bu), 3.84 (s, 2 H, 8-H), 4.44 (s, 2 H, 6-H), 4.82 (s, 2 H, 4-H), 7.11–7.30 (m, 5 H, Ar-H), 7.48 (t, J = 7.5 Hz, 2 H, Ar-H), 7.78 (d, J = 7.4 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 29.2 (*t*Bu), 32.7 (Cq, *t*Bu), 54.1 (C-8), 63.0 (C-4), 77.6 (C-6), 103.1 (Cq), 115.1 (d, J = 21.0 Hz), 121.8, 126.4, 129.1, 130.2 (d, J = 8.0 Hz), 132.7 (Cq), 139.0 (Cq), 143.5 (Cq), 155.2 (Cq), 161.4 (d, J = 242.0 Hz, Cq-F) ppm. FTIR (KBr): $\tilde{\nu}$ = 3056, 2965, 2865, 1598 (C=N), 1576 (C=C), 1509, 1024 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 365 (100) $[M]^+$, 256 (63), 228 (30), 109 (53) $[C_7H_6F]$. $C_{22}H_{24}FN_3O$ (365.19): calcd. C 72.31, H 6.62, N 11.50; found C 72.24, H 6.70, N 11.39.

3-*tert*-Butyl-1-phenyl-7-(pyridin-3-ylmethyl)-1,4,6,7-tetrahydropyr-azolo[3,4-*d*][1,3]oxazine (16g): Yield: 0.293 g. White solid. ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 1.25 (s, 9 H, *t*Bu), 3.90 (s, 2 H, 8-H), 4.49 (s, 2 H, 6-H), 4.80 (s, 2 H, 4-H), 7.29–7.34 (m, 2 H, Ar-H and Py-H), 7.48 (t, J = 7.7 Hz, 2 H, Ar-H), 7.58 (d, J = 7.9 Hz, 1 H, Py-H), 7.77 (d, J = 7.4 Hz, 2 H, Ar-H), 8.36 (d, J = 1.7 Hz, 1 H, Py-H), 8.47 (dd, J = 4.8, J = 1.7 Hz, 1 H, Py-H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 29.2 (*t*Bu), 32.7 (Cq, *t*Bu), 52.7 (C-8), 63.0 (C-4), 78.1 (C-6), 103.1 (Cq), 122.0, 123.4, 126.5, 129.2, 132.2 (Cq), 135.9, 139.0 (Cq), 143.2 (Cq), 148.7, 149.4, 155.3 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3060, 2965, 2882, 1595 (C=N), 1587 (C=C), 1506, 1022 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 348 (100) $[M]^+$, 303 (19), 228 (26), 170 (14), 92 (14) $[C_6H_6N]$. $C_{21}H_{24}N_4O$ (348.2): calcd. C 72.39, H 6.94, N 16.08; found C 72.45, H 7.00, N 16.00.

3-*tert*-Butyl-1-phenyl-7-[4-(trifluoromethyl)benzyl]-1,4,6,7-tetra-hydropyrazolo[3,4-*d*][1,3]oxazine (16h): Yield: 0.274 g. White solid. ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 1.26 (s, 9 H, *t*Bu), 3.97 (s, 2 H, 8-H), 4.48 (s, 2 H, 6-H), 4.83 (s, 2 H, 4-H), 7.27 (t, J = 7.5 Hz, 1 H, Ar-H), 7.45 (br. t, 4 H, Ar-H), 7.67 (d, J = 8.1 Hz, 2 H, Ar-H), 7.77 (d, J = 7.5 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 29.2 (*t*Bu), 32.7 (Cq, *t*Bu), 54.5 (C-8), 63.0 (C-4), 78.1 (C-6), 103.1 (Cq), 121.8, 124.1 (q, J = 271.0 Hz, CF_3), 125.1 (q, J = 4.0 Hz), 126.4, 128.2 (q, J = 31.0 Hz, Cq-F), 128.8, 129.2, 138.9 (Cq), 141.6 (Cq), 143.3 (Cq), 155.3 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3053, 2967, 2854, 1618 (C=N), 1600 (C=C), 1509, 1016 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 415 (100) $[M]^+$, 370 (24), 170 (31), 159 (24) $[C_8H_6F_3]$. $C_{23}H_{24}F_3N_3O$ (415.19): calcd. C 66.49, H 5.82, N 10.11; found C 66.60, H 5.93, N 9.93.

3-*tert*-Butyl-7-(4-nitrobenzyl)-1-phenyl-1,4,6,7-tetrahydropyrazolo-[3,4-*d*][1,3]oxazine (16i): Yield: 0.269 g. White solid. ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 1.26 (s, 9 H, *t*Bu), 4.02 (s, 2 H, 8-H), 4.50 (s, 2 H, 6-H), 4.83 (s, 2 H, 4-H), 7.26 (t, J = 7.4 Hz, 1 H, Ar-H), 7.44 (t, J = 8.3 Hz, 2 H, Ar-H), 7.51 (d, J = 8.9 Hz, 2 H, Ar-H), 7.75 (d, J = 7.4 Hz, 2 H, Ar-H), 8.17 (d, J = 8.9 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 29.2 (*t*Bu), 32.8 (Cq, *t*Bu), 54.5 (C-8), 63.0 (C-4), 78.4 (C-6), 103.1 (Cq), 121.9, 123.5, 126.4, 129.0, 129.1, 138.9 (Cq), 143.1 (Cq), 144.8 (Cq), 146.8 (Cq), 155.3 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3048, 2961, 2867, 1597 (C=N), 1581 (C=C), 1527 (NO_2), 1503, 1341 (NO_2), 1025 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 392 (100) $[M]^+$, 256 (41), 228 (24), 170 (25). $C_{22}H_{24}N_4O_3$ (392.18): calcd. C 67.33, H 6.16, N 14.28; found C 67.14, H 6.30, N 14.07.

3-*tert*-Butyl-7-(4-chlorobenzyl)-1-phenyl-1,4,6,7-tetrahydropyrazolo-[3,4-*d*][1,3]oxazine (16j): Yield: 0.276 g. White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (s, 9 H, *t*Bu), 3.92 (s, 2 H, 8-H), 4.47 (s, 2 H, 6-H), 4.89 (s, 2 H, 4-H), 7.19 (d, J = 8.3 Hz, 2 H, Ar-H), 7.25 (t, J = 7.7 Hz, 1 H, Ar-H), 7.28 (d, J = 8.3 Hz, 2 H, Ar-H), 7.43 (t, J = 7.7 Hz, 2 H, Ar-H), 7.84 (d, J = 8.0 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.4 (*t*Bu), 33.2 (Cq, *t*Bu), 54.6 (C-8), 64.1 (C-4), 78.1 (C-6), 103.2 (Cq), 122.4, 126.5, 128.6, 129.1, 130.0, 133.4 (Cq), 135.4 (Cq), 139.4 (Cq), 143.8 (Cq), 156.1 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3057, 2961, 2851, 1596 (C=N), 1573 (C=C), 1506, 1014 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 383/381 (24/70) $[M]^+$, 228 (50), 127/125 (24/68) $[C_7H_6Cl]$. $C_{22}H_{24}ClN_3O$ (381.16): calcd. C 69.19, H 6.33, N 11.00; found C 69.08, H 6.40, N 11.11.

3-*tert*-Butyl-7-(3,4,5-trimethoxybenzyl)-1-phenyl-1,4,6,7-tetrahydropyrazolo[3,4-*d*][1,3]oxazine (16k): Yield: 0.275 g. White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (s, 9 H, *t*Bu), 3.83 (s, 3 H, OCH_3), 3.84 (s, 6 H, OCH_3), 3.87 (s, 2 H, 8-H), 4.52 (s, 2 H, 6-H), 4.90 (s, 2 H, 4-H), 6.48 (s, 2 H, Ar-H), 7.26 (t, *J* = 7.5 Hz, 1 H, Ar-H), 7.43 (t, *J* = 7.5 Hz, 2 H, Ar-H), 7.86 (d, *J* = 8.1 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.4 (*t*Bu), 32.2 (Cq, *t*Bu), 55.8 (C-8), 56.1 (2 OCH_3), 60.8 (OCH_3), 64.2 (C-4), 78.2 (C-6), 103.2 (Cq), 106.0, 122.8, 126.5, 129.0, 132.5 (Cq), 137.5 (Cq), 139.5 (Cq), 143.9 (Cq), 153.2 (Cq), 156.1 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3062, 2963, 2849, 1592 (br, C=N, C=C), 1503, 1244 (C–O), 1129 (C–O), 1008 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 437 (5) $[M]^+$, 181 (100) $[C_{10}H_{13}O_3]$. $C_{25}H_{31}N_3O_4$ (437.23): calcd. C 68.63, H 7.14, N 9.60; found C 68.48, H 7.06, N 9.32.

7-[(1,3-Benzodioxol-5-yl)methyl]-3-*tert*-butyl-1-phenyl-1,4,6,7-tetrahydropyrazolo[3,4-*d*][1,3]oxazine (16l): Yield: 0.272 g. White solid. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.25 (s, 9 H, *t*Bu), 3.74 (s, 2 H, 8-H), 4.43 (s, 2 H, 6-H), 4.82 (s, 2 H, 4-H), 5.99 (s, 2 H, OCH_2O), 6.68 (dd, *J* = 7.9, *J* = 1.5 Hz, 1 H, Ar-H), 6.74 (d, *J* = 1.5 Hz, 1 H, Ar-H), 6.83 (d, *J* = 7.9 Hz, 1 H, Ar-H), 7.31 (t, *J* = 7.2 Hz, 1 H, Ar-H), 7.49 (t, *J* = 8.3 Hz, 2 H, Ar-H), 7.78 (d, *J* = 7.4 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 29.2 (*t*Bu), 32.8 (Cq, *t*Bu), 54.6 (C-8), 63.0 (C-4), 77.3 (C-6), 100.9 (OCH_2O), 103.0 (Cq), 108.0, 108.4, 121.8, 122.0, 126.5, 129.1, 130.2 (Cq), 139.0 (Cq), 143.6 (Cq), 146.6 (Cq), 147.4 (Cq), 155.2 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3028, 2960, 2862, 1595 (br., C=N), 1585 (C=C), 1499, 1261 (C–O), 1038 (br, C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 391 (11) $[M]^+$, 135 (100) $[C_8H_7O_2]$. $C_{23}H_{25}N_3O_3$ (391.19): calcd. C 70.57, H 6.44, N 10.73; found C 70.77, H 6.36, N 10.85.

3-*tert*-Butyl-1-phenyl-7-(pyridin-4-ylmethyl)-1,4,6,7-tetrahydropyrazolo[3,4-*d*][1,3]oxazine (16m): Yield: 0.270 g. White solid. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.26 (s, 9 H, *t*Bu), 3.91 (s, 2 H, 8-H), 4.49 (s, 2 H, 6-H), 4.83 (s, 2 H, 4-H), 7.21–7.29 (m, 3 H, Ar-H and Py-H), 7.42 (t, *J* = 7.5 Hz, 2 H, Ar-H), 7.75 (d, *J* = 7.4 Hz, 2 H, Ar-H), 8.50 (d, *J* = 6.0 Hz, 2 H, Py-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 29.2 (*t*Bu), 32.8 (Cq, *t*Bu), 53.9 (C-8), 63.0 (C-4), 78.4 (C-6), 103.1 (Cq), 121.8, 122.8, 126.4, 129.1, 138.9 (Cq), 143.2 (Cq), 145.8 (Cq), 149.6, 155.3 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3048, 2962, 2870, 1599 (C=N), 1584 (C=C), 1504, 1026 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 348 (100) $[M]^+$, 303 (33), 276 (20), 170 (26), 92 (10) $[C_6H_6N]$. $C_{21}H_{24}N_4O$ (348.2): calcd. C 72.39, H 6.94, N 16.08; found C 72.47, H 6.86, N 16.20.

3-*tert*-Butyl-1-(4-nitrophenyl)-7-(3,4,5-trimethoxybenzyl)-1,4,6,7-tetrahydropyrazolo[3,4-*d*][1,3]oxazine (16n): Yield: 0.306 g. White solid. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.26 (s, 9 H, *t*Bu), 3.62 (s, 3 H, OCH_3), 3.74 (s, 6 H, OCH_3), 3.92 (s, 2 H, 8-H), 4.59 (s, 2 H, 6-H), 4.86 (s, 2 H, 4-H), 6.47 (s, 2 H, Ar-H), 8.07 (d, *J* = 9.1 Hz, 2 H, Ar-H), 8.32 (d, *J* = 9.1 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 28.9 (*t*Bu), 32.9 (Cq, *t*Bu), 55.7 (2 OCH_3), 56.1 (C-8), 59.9 (OCH_3), 62.8 (C-4), 78.3 (C-6), 105.1 (Cq), 105.8, 121.1, 124.9, 131.5 (Cq), 136.8 (Cq), 144.0 (Cq), 144.4 (Cq), 144.5 (Cq), 152.7 (Cq), 157.4 (Cq) ppm. FTIR (KBr): $\tilde{\nu}$ = 3040, 2961, 2866, 1593 (br C=N, C=C), 1513, 1461 (NO_2), 1337 (NO_2), 1238 (C–O), 1125 (C–O), 1010 (C–O oxazine) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 482 (1) $[M]^+$, 181 (100) $[C_{10}H_{13}O_3]$. $C_{25}H_{30}N_4O_6$ (482.22): calcd. C 62.23, H 6.27, N 11.61; found C 62.30, H 6.16, N 11.72.

Synthesis of *N*-(3-*tert*-Butyl-1-phenyl-1*H*-pyrazol-5-yl)-*N*-(4-methoxybenzyl)acetamide (20a): A mixture of the aminopyrazole **13a** (0.5 g, 1.49 mmol) and acetic anhydride (0.26 g, 2.5 mmol) was heated to reflux for 5 min. After complete disappearance of the starting material **13a** (monitored by TLC), excess acetic anhydride was removed under reduced pressure to yield pure compound **20a**. Yield: 0.550 g (98% yield); m.p. 119–120 °C. White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 9 H, *t*Bu), 1.84 (s, 3 H, CH_3), 3.80 (s, 3 H, OCH_3), 3.95 (d, *J* = 12.1 Hz, 1 H, Bn-Ha), 5.25 (d, *J* = 12.1 Hz, 1 H, Bn-Hb), 5.78 (s, 1 H, 4-H), 6.80 (d, *J* = 8.8 Hz, 2 H, Ar-H), 7.10 (d, *J* = 8.8 Hz, 2 H, Ar-H), 7.32 (t, *J* = 7.1 Hz, 1 H, Ar-H), 7.36–7.45 (m, 4 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.2 (CH_3), 30.1 (*t*Bu), 32.4 (Cq, *t*Bu), 51.0 (CH_2), 55.2 (OCH_3), 102.5 (C-4), 113.7, 122.7, 127.3, 128.5, 129.4, 130.4, 138.7, 139.7, 159.1, 162.2, 170.8 (C=O) ppm. FTIR (KBr): $\tilde{\nu}$ = 2962, 2866, 1676 (C=O), 1252 (C–O) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 377 (7) $[M]^+$, 121 (100), 77 (6).

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