Dibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepines: Facile Construction of a Rare Heterocyclic System via Tandem Aromatic Nucleophilic Substitution–Smiles Rearrangement–Denitrocyclization

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Abstract: Condensation of 2-(1*H*-pyrazol-5-yl)phenols with 1-chloro-2-nitrobenzenes under basic conditions in *N*,*N*-dimethylformamide results in a tandem, atom-economical, aromatic nucleophilic substitution–Smiles rearrangement–denitrocyclization process to provide pyrazolo-fused dibenzo[*b*,*f*][1,4]oxazepines as a single regioisomer.

Key words: tetracyclic scaffolds, privileged structures, atom-economical syntheses, dibenzo[*b*,*f*][1,4]oxazepines, Smiles rearrangement, nucleophilic aromatic substitution, denitrocyclization, regiospecific reaction

The range of biological activity displayed by compounds containing the dibenzo[*b*,*f*][1,4]oxazepine scaffold is strikingly vast. From early applications of such compounds as psychotropic drugs [e.g., Loxapine (**1**)[1]] and, even more prominently, as prostaglandin receptors antagonists [e.g., Searle's SC-19220 (**2**)[2]], the utility of dibenzo[*b*,*f*][1,4]oxazepines has recently extended to the design of potent progesterone receptor antagonists **3**,[3] p38 MAP kinase inhibitors **4**,[4] TRPA1 ion channel modulators **5**,[5] and histone deacetylase inhibitors **6**[6] (Figure 1). This provides ample evidence for the privileged character of this scaffold (as defined by Evans[7]) and makes the development of novel synthetic methodologies toward this and related heterocyclic systems particularly worthwhile.

Of special value are tandem synthetic strategies, these are atom-economical,[8] generally more efficient, and less time-consuming than linear multistep strategies. Earlier, we reported a practically simple and streamlined entry to dibenzo[*b*,*f*][1,4]oxazepin-11(10*H*)-ones **7** and their 9-aza analogues **8** via condensation of 1-chloro-2-nitro derivatives of benzene **9** and pyridine **10**, respectively, with secondary salicylamides **11** under basic conditions.[9] The reaction proceeded, as anticipated, via a denitrocyclization step,[10] but was accompanied by an unexpected (though not unprecedented[11]) Smiles rearrangement of the initial diaryl ether adduct **12**. Encouraged by this finding, we became curious to see if NH-acidic azoles, such as pyrazole, could be effective participants in a similar tandem process in lieu of the secondary amide functionality. This would lead to the formation of a rare pyrazole-including framework **13** (Scheme 1). Such tetracyclic scaffolds are

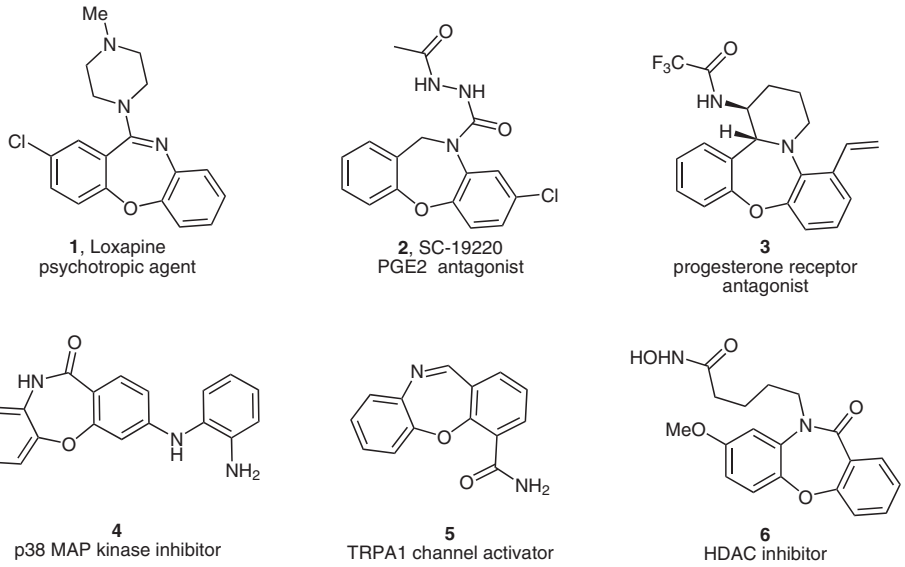

Figure 1 Examples of pharmacologically active dibenzo[*b*,*f*][1,4]oxazepines

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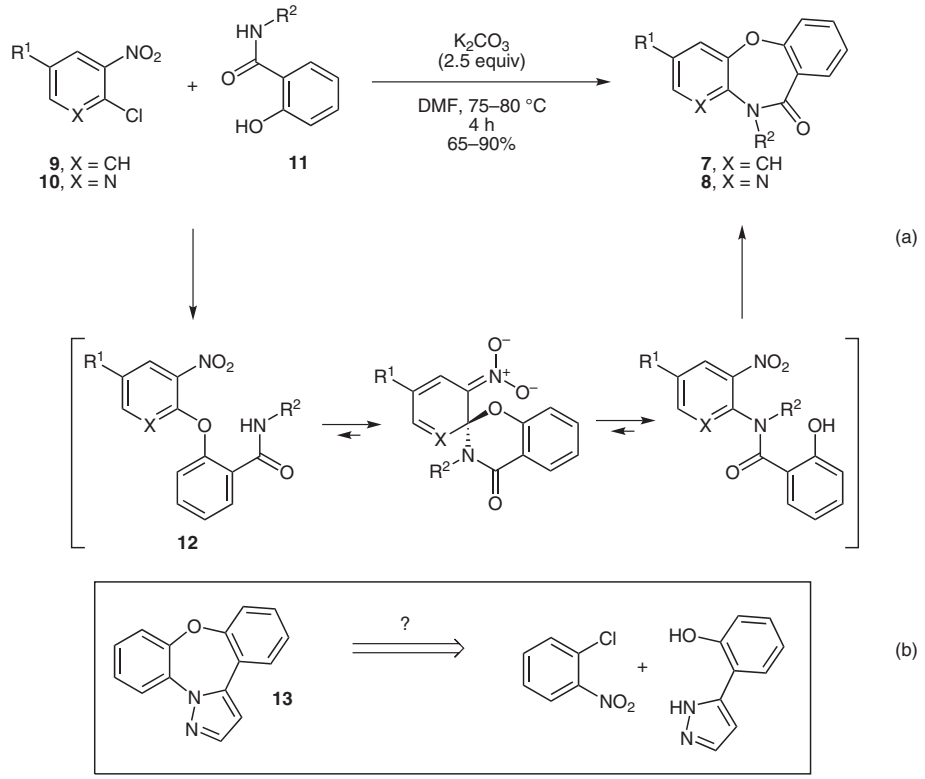


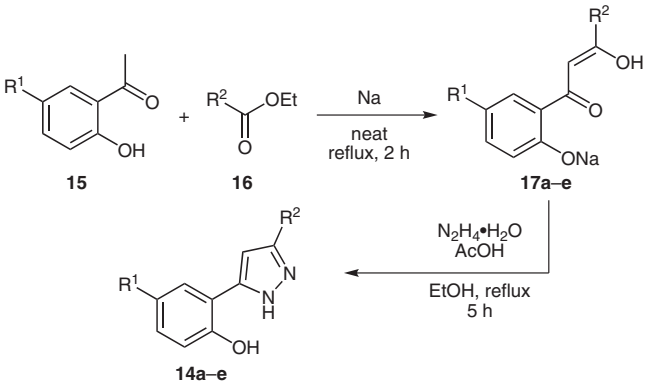
Scheme 1 Strategies for construction of the dibenzo[*b*,*f*][1,4]oxazepine scaffold: (a) described earlier[9] and (b) investigated in this work

of much interest considering that fusion of five-membered cycles onto a dibenzo[*b*,*f*][1,4]oxazepine core has been shown to attenuate the pharmacological properties of the resulting compounds.[12] Moreover, dibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepines **13** have recently found application in the design of organic light-emitting devices (OLEDs).[13] Herein, we would like to report on a successful realization of a new synthetic strategy toward **13**.

The starting 2-(1*H*-pyrazol-5-yl)phenols **14a**–**e** were prepared via Claisen condensation of *o*-hydroxyacetophenones **15** with aliphatic esters **16** followed by treatment of the isolated sodium phenolates **17a**–**e** with hydrazine hydrate (Scheme 2). Both steps involved only filtration as the means of solid product isolation and provided good to excellent yields of the desired material (Table 1).

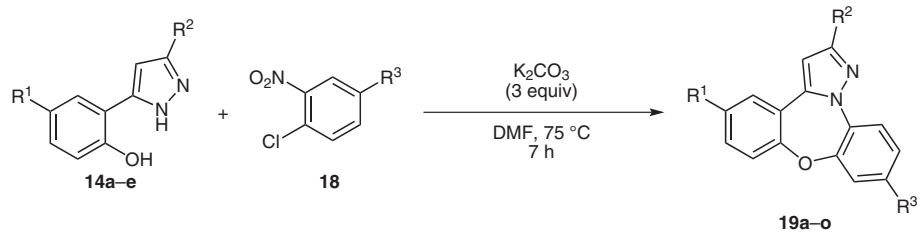
Table 1 2-(1*H*-Pyrazol-5-yl)phenols **14a**–**e** and Their Precursors **17a**–**e** Synthesized

Compd	R^1	R^2	Yield of **17** (%)	Yield of **14** (%)
14a, **17a**	H	H	75	84
14b, **17b**	H	Me	60	76
14c, **17c**	H	Et	58	65
14d, **17d**	Cl	Me	67	74
14e, **17e**	Me	Me	72	63



Scheme 2 Preparation of 2-(1*H*-pyrazol-5-yl)phenols **14a**–**c**

To our delight, compounds **14a**–**e** underwent facile condensation with a number of 1-chloro-2-nitrobenzenes **18**, on heating with three equivalents of anhydrous potassium carbonate in *N*,*N*-dimethylformamide. Moreover, ^{1}H NMR analyses of the crude reaction mixtures confirmed the disappearance of the characteristic broad singlets corresponding to both the pyrazole moiety (NH, δ = 13.55–12.70) and the phenol functionality (OH, δ = 11.40–10.03), clearly indicating that the former participated in the reaction. Additionally, the ^{1}H NMR signals corresponding to the aromatic portions of **14** and **18** exhibited pronounced (~0.3 ppm) downfield and upfield shifts, respectively. This, according to our previous denitrocyclization experience,[9] strongly attested to the formation of



Scheme 3 Preparation of dibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepines **19a–o**

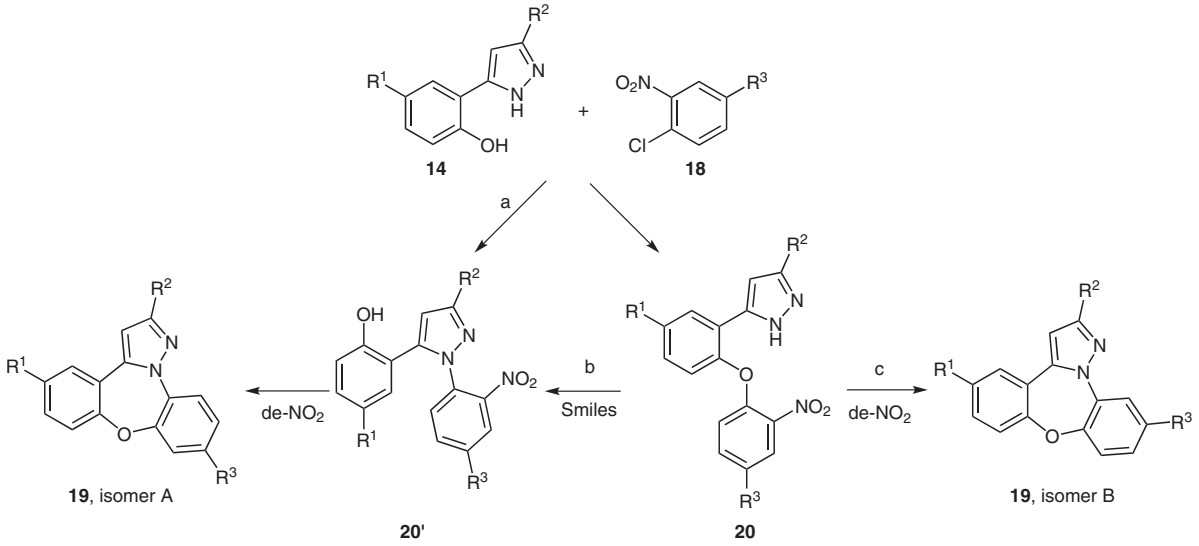
the previously undescribed tetracyclic compounds **19a–o** (Scheme 3).

The isolated yields of compounds **19a–o** were good to excellent (Table 2) and their analytical data (^{1}H and ^{13}C NMR and elemental analyses) were consistent with the anticipated dibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine structure. However, establishing the regiochemical identity of the products obtained presented a significant challenge, although it was evident from the NMR data that compounds **19a–o** belonged to the same isomeric series. Presumably, the regiochemistry of **19** would be determined (Scheme 4) by the ability of the pyrazole moiety to participate in the initial chlorine displacement event (path a) or in the subsequent Smiles rearrangement (path b) of the initially formed diphenyl ether adduct **20**.[9] In both cases regioisomer A would be formed in contrast to regioisomer B that might result from two sequential nucleophilic displacements (of the chlorine atom and the nitro group), not accompanied by the Smiles rearrangement (path c), a possibility that also should be considered.

Intermolecular displacement of the chlorine atom in **18** by the pyrazole moiety in **14** (path a) can be easily ruled out based on the results of a model experiment. Under the same reaction conditions, 3-methyl-5-phenyl-1*H*-pyrazole (**21**) failed to react with 4-chloro-3-nitrobenzonitrile (**22**), even on prolonged (3 days) heating at 110 °C (Scheme 5). Additionally, the absence in the reaction mix-

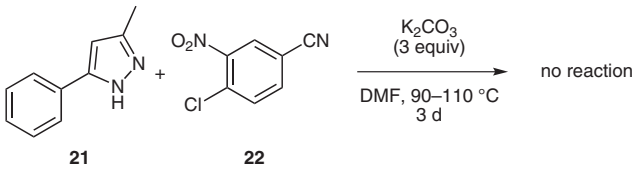
Table 2 Dibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepines **19a–o** Synthesized

Compd	R^1	R^2	R^3	Yield (%)
19a	H	H	CO_2Me	66
19b	H	H	CN	79
19c	H	H	NO_2	81
19d	H	Me	CO_2Me	77
19e	H	Me	CN	81
19f	H	Me	NO_2	68
19g	H	Et	CO_2Me	60
19h	H	Et	CN	73
19i	H	Et	NO_2	85
19j	Cl	Me	CO_2Me	74
19k	Cl	Me	CN	83
19l	Cl	Me	NO_2	85
19m	Me	Me	CO_2Me	76
19n	Me	Me	CN	69
19o	Me	Me	NO_2	80



Scheme 4 Possible reaction pathways determining the regiochemistry of dibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepines **19a–o**

ture of pyrazole N-arylation products regioisomeric to intermediate **20′** (which cannot be expected to participate in subsequent cyclization events due to steric reasons) also speak against the reaction proceeding via path a.



Scheme 5 Attempted reaction of a model pyrazole **21** with 3-chloro-4-nitrobenzonitrile (**22**)

Unfortunately, correlational NMR spectroscopy (NOESY, HSQC, HMBC) provided insufficient information for an unequivocal regiochemistry assignment of products **19a–o** and, thus, did not allow us to distinguish between reaction paths b and c. To our relief, we were able to obtain a single-crystal X-ray structure of a representative compound, **19h** (Figure 2).[14] It clearly showed that the compounds belonged to the isomeric series A and thus confirmed that the compounds **19** formed as a result of tandem aromatic nucleophilic substitution–Smiles rearrangement–denitrocyclization.

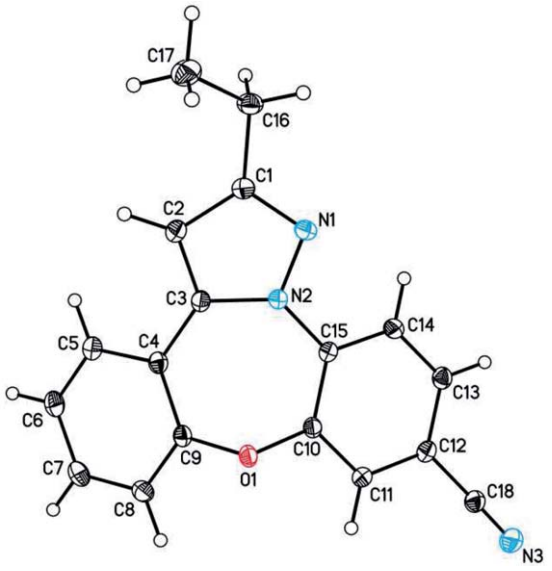


Figure 2 Single-crystal X-ray structure of compound **19h**

In summary, we have developed a streamlined synthetic methodology towards the previously undescribed dibenzo[*b*,*f*][1,4]oxazepines from readily available precursors. The compounds were obtained in high yields as a single regioisomer as a result of three chemical events occurring in tandem. This represents a remarkable example of atom economy and efficiency in constructing polycyclic heterocycles. Similar strategies involving other potentially nucleophilic azoles are under investigated in our laboratories and will be reported in due course.

All reactions were run in oven-dried glassware in an atmosphere of N_2. Melting points were measured with a Buchi B-520 melting point apparatus and were not corrected. Analytical TLC was carried out on Silufol UV-254 silica gel plates using appropriate EtOAc–hexane mixtures. Compounds were visualized with short-wavelength UV light. ^{1}H and ^{13}C NMR spectra were recorded on Bruker MSL-300 spectrometers in DMSO-d_6 using TMS as an internal standard. Elemental analyses were obtained at Research Institute for Chemical Crop Protection (Moscow, Russia) using Carlo Erba Strumentazione 1106 analyzer. The IR spectra were recorded using Specord M-80 spectrophotometer on compound samples prepared as KBr tablets. All and reagents were obtained from commercial sources and used without purification. DMF was dried according to the standard procedure[15] and K_2CO_3 was dried at 200 °C for 5 h prior to use.

4-Chloro-2-(3-methyl-1*H*-pyrazol-5-yl)phenol (14d); Typical Procedure for the Synthesis of Compounds 14a–e

Na metal (6.44 g, 0.280 mol) was carefully added to a soln of 5′-chloro-2′-hydroxyacetophenone (11.9 g, 0.070 mol) in ethyl acetate (100 mL) over 1 h. The resulting mixture was heated at reflux for 2 h, cooled to r.t., and poured over crushed ice–H_2O mixture (1 L total volume). The resulting precipitate was filtered off, washed with cold *i*-PrOH (50 mL), air dried, and further dried in vacuo (60 °C, overnight) to provide sodium 4-chloro-2-(3-hydroxybut-2-enoyl)phenolate (**17d**) (10.9 g, 67%) as a light-yellow solid.

^{1}H NMR (DMSO-d_6, 300 K): δ = 16.87–17.11 (br s, 1 H, OH), 7.44 (s, 1 H, H_{Ar}), 7.11 (d, J = 8.2 Hz, 1 H, H_{Ar}), 6.61 (d, J = 8.5 Hz, 1 H, H_{Ar}), 5.35–5.50 (br s, 1 H, -CH=), 2.04 (s, 3 H, CH_3).

A 65% aq soln of $N_2H_4{\cdot}H_2O$ (5 mL) and glacial AcOH (0.021 mol) were added to a soln of **17d** (3.65 g, 0.016 mol) in EtOH (30 mL). The resulting mixture was heated at reflux for 5 h, cooled to r.t., and the volatiles were removed in vacuo. The resulting precipitate was suspended in H_2O (100 mL), filtered off, washed with more H_2O, air dried, and further dried in vacuo (60 °C, overnight) to provide **14d** (2.4 g, 74%) as an off-white solid; mp 95–97 °C.

IR (KBr): 3442, 3153, 1610 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 12.70–13.06 (br s, 1 H, $NH_{pyrazole}$), 10.03–11.40 (br s, 1 H, Ar-OH), 7.64 (s, 1 H, H_{Ar}), 7.10 (d, J = 8.5 Hz, 1 H, H_{Ar}), 6.87 (d, J = 8.5 Hz, 1 H, H_{Ar}), 6.63 (s, 1 H, $H_{pyrazole}$), 2.31 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 154.1, 158.0, 128.0, 125.9, 122.9, 119.1, 118.1, 100.7, 10.7.

Anal. Calcd for $C_{10}H_9ClN_2O$: C, 57.57; H, 4.35; N, 13.43. Found: C, 57.41; H, 4.35; N, 13.49.

2-(1*H*-Pyrazol-5-yl)phenol (14a)

White solid; yield: 1.78 g (84%); mp 128–131 °C.

IR (KBr): 3435, 3140, 1620 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 13.00–13.49 (br s, 1 H, $NH_{pyrazole}$), 10.73–11.08 (br s, 1 H, Ar-OH), 7.86 (s, 1 H, $H_{pyrazole}$), 7.72 (d, J = 7.9 Hz, 1 H, H_{Ar}), 7.17 (t, J = 7.5 Hz, 1 H, H_{Ar}), 6.79–6.95 (m, 3 H, H_{Ar}, $H_{pyrazole}$).

^{13}C NMR (DMSO-d_6, 300 K): δ = 155.3, 139.1, 128.6, 128.6, 126.7, 119.2, 119.1, 117.2, 116.4, 101.0.

Anal. Calcd for $C_9H_8N_2O$: C, 67.49; H, 5.03; N, 17.49. Found: C, 67.31; H, 5.04; N, 17.58.

2-(3-Methyl-1*H*-pyrazol-5-yl)phenol (14b)

White solid; yield: 1.4 g (76%); mp 128–131 °C.

IR (KBr): 3430, 3143, 1628 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 12.80–13.09 (br s, 1 H, $NH_{pyrazole}$), 10.97–11.21 (br s, 1 H, Ar-OH), 7.63 (d, J = 7.9 Hz, 1 H, H_{Ar}), 7.15 (t, J = 7.9 Hz, 1 H, H_{Ar}), 6.82–6.94 (m, 2 H, H_{Ar}), 6.59 (s, 1 H, $H_{pyrazole}$), 2.30 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 155.3, 128.6, 128.6, 126.6, 119.2, 119.1, 117.2, 116.4, 101.3, 10.6.

Anal. Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08. Found: C, 68.76; H, 5.79; N, 16.15.

2-(3-Ethyl-1*H*-pyrazol-5-yl)phenol (14c)
White solid; yield: 2.31 g (65%); mp 50–52 °C.

IR (KBr): 3431, 3140, 1620 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 13.04–13.55 (br s, 1 H, $NH_{pyrazole}$), 10.86–11.18 (br s, 1 H, Ar-OH), 7.60 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 7.12 (t, *J* = 7.0 Hz, 1 H, H_{Ar}), 6.84 (m, 2 H, H_{Ar}), 6.53 (s, 1 H, $H_{pyrazole}$), 2.70 (m, 2 H, CH_2CH_3), 1.28 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 155.3, 128.6, 128.5, 126.6, 119.2, 119.1, 117.3, 116.4, 99.9, 18.5, 13.4.

Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.01; H, 6.44; N, 14.95.

4-Methyl-2-(3-methyl-1*H*-pyrazol-5-yl)phenol (14e)
White solid; yield: 1.6 g (63%); mp 61–63 °C.

IR (KBr): 3426, 3139, 1618 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 12.85–13.12 (br s, 1 H, $NH_{pyrazole}$), 10.71–11.22 (br s, 1 H, Ar-OH), 7.36 (s, 1 H, H_{Ar}), 6.91 (d, *J* = 6.6 Hz, 1 H, H_{Ar}), 6.73 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 6.47 (s, 1 H, $H_{pyrazole}$), 2.32 (s, 3 H, Ar-CH_3), 2.27 (s, 3 H, pyrazole-CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 153.3, 129.1, 129.1, 127.2, 126.9, 126.8, 116.9, 116.2, 101.1, 20.2, 10.7.

Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.98; H, 6.42; N, 14.91.

Methyl 2-Ethyldibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine-10-carboxylate (19g); Typical Procedure for the Synthesis of Compounds 19a–o
A mixture of **14c** (1.88 g, 10 mmol), methyl 4-chloro-3-nitrobenzoate (2.16 g, 10 mmol), and K_2CO_3 (1.15 g, 30 mmol) in anhyd DMF (15 mL) was stirred at 75 °C for 7 h, then cooled to r.t. and poured into H_2O (100 mL). The resulting precipitate was filtered off and crystallized (*i*-PrOH) to provide **19g** (1.92 g, 60%) as a white solid; mp 94–96 °C.

IR (KBr): 1744, 1623, 1219, 1201 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.01 (s, 1 H, H_{Ar}), 7.83–7.96 (m, 2 H, H_{Ar}), 7.69 (d, *J* = 7.9 Hz, 1 H, H_{Ar}), 7.57 (d, *J* = 8.2 Hz, 1 H, H_{Ar}), 7.49 (t, *J* = 7.2 Hz, 1 H, H_{Ar}), 7.33 (t, *J* = 7.2 Hz, 1 H, H_{Ar}), 6.87 (s, 1 H, $H_{pyrazole}$), 3.88 (s, 3 H, CO_2CH_3), 2.71 (m, 2 H, CH_2CH_3), 1.29 (t, *J* = 7.9 Hz, 3 H, CH_2CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 165.0, 157.1, 155.5, 149.1, 141.0, 136.5, 131.4, 129.2, 128.9, 127.2, 126.4, 123.4, 122.9, 121.6, 121.4, 106.1, 52.5, 21.1, 13.4.

Anal. Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.03; H, 5.04; N, 8.79.

Methyl Dibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine-10-carboxylate (19a)
White solid; yield: 0.78 g (66%); mp 173–175 °C (EtOH).

IR (KBr): 1745, 1619, 1223, 1200 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.02–8.05 (m, 2 H, H_{Ar}, $H_{pyrazole}$), 7.83–7.94 (m, 2 H, H_{Ar}), 7.68 (d, *J* = 7.3 Hz, 1 H, H_{Ar}), 7.56 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 7.51 (t, *J* = 7.0 Hz, 1 H, H_{Ar}), 7.35 (t, *J* = 7.5 Hz, 1 H, H_{Ar}), 6.10 (s, 1 H, $H_{pyrazole}$), 3.87 (s, 3 H, CO_2CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 165.0, 155.6, 151.4, 149.0, 141.1, 140.2, 136.5, 131.5, 129.2, 128.9, 127.2, 126.4, 123.4, 122.9, 121.4, 107.4, 52.5.

Anal. Calcd for $C_{17}H_{12}N_2O_3$: C, 69.86; H, 4.14; N, 9.58. Found: C, 69.67; H, 4.16; N, 9.63.

Dibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine-10-carbonitrile (19b)
Light-yellow solid; yield: 1.3 g (79%); mp 196–196 °C (EtOH–DMF).

IR (KBr): 2239, 1615 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.34 (s, 1 H, H_{Ar}), 8.21 (d, *J* = 8.5 Hz, 1 H, H_{Ar}), 7.98–8.03 (m, 2 H, H_{Ar}, $H_{pyrazole}$), 7.63 (d, *J* = 7.4 Hz, 1 H, H_{Ar}), 7.42–7.60 (m, 2 H, H_{Ar}), 7.34 (t, *J* = 7.5 Hz, 1 H, H_{Ar}), 6.11 (s, 1 H, $H_{pyrazole}$).

^{13}C NMR (DMSO-d_6, 300 K): δ = 155.0, 151.6, 149.3, 141.3, 140.2, 136.8, 131.5, 130.3, 129.2, 126.5, 126.2, 124.1, 117.5, 110.2, 107.6.

Anal. Calcd for $C_{16}H_9N_3O$: C, 74.12; H, 3.50; N, 16.21. Found: C, 73.90; H, 3.51; N, 16.29.

10-Nitrodibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine (19c)
Dark-yellow solid; yield: 0.67 g (81%); mp 217–219 °C (EtOH–DMF).

IR (KBr): 1682, 1619, 1223, 1200 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.46 (s, 1 H, H_{Ar}), 8.24 (d, *J* = 8.5 Hz, 1 H, H_{Ar}), 8.00–8.13 (m, 2 H, H_{Ar}, $H_{pyrazole}$), 7.77 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 7.66 (d, *J* = 7.9 Hz, 1 H, H_{Ar}), 7.55 (t, *J* = 7.2 Hz, 1 H, H_{Ar}), 7.39 (t, *J* = 6.9 Hz, 1 H, H_{Ar}), 6.08 (s, 1 H, $H_{pyrazole}$).

^{13}C NMR (DMSO-d_6, 300 K): δ = 155.4, 153.0, 148.5, 145.9, 141.3, 140.2, 138.0, 131.7, 129.3, 126.7, 123.7, 121.9, 121.6, 121.4, 118.1, 108.2.

Anal. Calcd for $C_{15}H_9N_3O_3$: C, 64.52; H, 3.25; N, 15.05. Found: C, 64.32; H, 3.27; N, 15.12.

Methyl 2-Methyldibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine-10-carboxylate (19d)
White solid; yield: 1.64 g (77%); mp 146–148 °C (*i*-PrOH).

IR (KBr): 1741, 1622, 1220, 1205 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.01 (s, 1 H, H_{Ar}), 7.83–7.95 (m, 2 H, H_{Ar}), 7.67 (d, *J* = 7.2 Hz, 1 H, H_{Ar}), 7.55 (d, *J* = 7.9 Hz, 1 H, H_{Ar}), 7.50 (t, *J* = 6.9 Hz, 1 H, H_{Ar}), 7.34 (t, *J* = 7.5 Hz, 1 H, H_{Ar}), 6.82 (s, 1 H, $H_{pyrazole}$), 3.88 (s, 3 H, CO_2CH_3), 2.35 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 165.0, 155.5, 151.4, 149.0, 141.1, 136.5, 131.5, 129.2, 128.9, 127.2, 126.4, 123.4, 122.9, 121.4, 107.4, 52.5, 13.5.

Anal. Calcd for $C_{18}H_{14}N_2O_3$: C, 70.58; H, 4.61; N, 9.15. Found: C, 70.41; H, 4.60; N, 9.19.

2-Methyldibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine-10-carbonitrile (19e)
Light-yellow solid; yield: 1.1 g (81%); mp 208–209 °C (EtOH–DMF).

IR (KBr): 2241, 1606 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.36 (s, 1 H, H_{Ar}), 8.20 (d, *J* = 8.8 Hz, 1 H, H_{Ar}), 7.99 (d, *J* = 9.0 Hz, 1 H, H_{Ar}), 7.67 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 7.43–7.60 (m, 2 H, H_{Ar}), 7.34 (t, *J* = 7.5 Hz, 1 H, H_{Ar}), 6.80 (s, 1 H, $H_{pyrazole}$), 2.38 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 155.4, 151.8, 149.2, 141.3, 136.8, 131.5, 130.3, 129.2, 126.5, 126.2, 124.1, 117.5, 110.2, 107.7, 13.3.

Anal. Calcd for $C_{17}H_{11}N_3O$: C, 74.71; H, 4.06; N, 15.38. Found: C, 74.79; H, 4.07; N, 15.45.

2-Methyl-10-nitrodibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine (19f)
Dark-yellow solid; yield: 0.88 g (68%); mp 237–239 °C (EtOH–DMF).

IR (KBr): 1680, 1617, 1352 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.42 (s, 1 H, H_{Ar}), 8.21 (d, *J* = 8.9 Hz, 1 H, H_{Ar}), 7.99 (d, *J* = 9.2 Hz, 1 H, H_{Ar}), 7.71 (d, *J* = 7.9 Hz, 1 H, H_{Ar}), 7.63 (d, *J* = 8.2 Hz, 1 H, H_{Ar}), 7.53 (t, J = 7.5 Hz, 1 H, H_{Ar}),

7.37 (t, J = 7.9 Hz, 1 H, H_{Ar}), 6.89 (s, 1 H, $H_{pyrazole}$), 2.37 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 155.1, 152.2, 148.6, 145.9, 141.3, 138.0, 131.7, 129.3, 126.7, 123.7, 121.8, 121.6, 121.2, 118.1, 108.1, 13.5.

Anal. Calcd for $C_{16}H_{11}N_3O_3$: C, 65.53; H, 3.78; N, 14.33. Found: C, 65.38; H, 3.77; N, 14.40.

2-Ethyldibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine-10-carbonitrile (19h)
Light-yellow solid; yield: 1.07 g (73%); mp 178–181 °C (EtOH–DMF).

IR (KBr): 2235, 1610 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.01 (s, 1 H, H_{Ar}), 7.93 (d, J = 8.5 Hz, 1 H, H_{Ar}), 7.76 (d, J = 8.5 Hz, 1 H, H_{Ar}), 7.67 (d, J = 7.9 Hz, 1 H, H_{Ar}), 7.43–7.51 (m, 2 H, H_{Ar}), 7.33 (t, J = 7.0 Hz, 1 H, H_{Ar}), 6.81 (s, 1 H, $H_{pyrazole}$), 2.74 (m, 2 H, CH_2CH$_3$), 1.32 (t, J = 7.4 Hz, 3 H, CH$_2$CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 155.0, 151.7, 149.2, 141.1, 136.8, 131.5, 130.3, 129.2, 126.5, 126.2, 124.1, 117.51 110.2, 107.7, 20.9, 13.3.

Anal. Calcd for $C_{18}H_{13}N_3O$: C, 75.25; H, 4.56; N, 14.63. Found: C, 75.03; H, 4.57; N, 14.70.

2-Ethyl-10-nitrodibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine (19i)
Dark-yellow solid; yield: 0.92 g (85%); mp 221–223 °C (EtOH–DMF).

IR (KBr): 1689, 1620, 1347 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.42 (s, 1 H, H_{Ar}), 8.22 (d, J = 8.9 Hz, 1 H, H_{Ar}), 7.99 (d, J = 9.2 Hz, 1 H, H_{Ar}), 7.72 (d, J = 7.2 Hz, 1 H, H_{Ar}), 7.63 (d, J = 7.5 Hz, 1 H, H_{Ar}), 7.53 (t, J = 7.5 Hz, 1 H, H_{Ar}), 7.37 (t, J = 7.2 Hz, 1 H, H_{Ar}), 6.94 (s, 1 H, $H_{pyrazole}$), 2.74 (m, 2 H, CH_2CH$_3$), 1.30 (t, J = 7.5 Hz, 3 H, CH$_2$CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 155.8, 155.1, 148.6, 145.8, 141.2, 138.1, 131.6, 129.2, 126.7, 123.7, 121.8, 121.5, 121.3, 118.1, 106.7, 21.1, 13.2.

Anal. Calcd for $C_{17}H_{13}N_3O_3$: C, 66.24; H, 4.26; N, 13.67. Found: C, 66.28; H, 4.27; N, 13.74.

Methyl 5-Chloro-2-methyldibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine-10-carboxylate (19j)
Grey solid; yield: 0.73 g (74%); mp 192–195 °C (DMF).

IR (KBr): 1745, 1620, 1224, 1205 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.00 (s, 1 H, H_{Ar}), 7.85–7.93 (m, 2 H, H_{Ar}), 7.70 (s, 1 H, H_{Ar}), 7.55 (d, J = 9.5 Hz, 1 H, H_{Ar}), 7.48 (d, J = 9.4 Hz, 1 H, H_{Ar}), 6.85 (s, 1 H, $H_{pyrazole}$), 3.89 (s, 3 H, CO_2CH_3), 2.37 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 165.0, 154.3, 151.5, 148.8, 139.8, 136.3, 130.8, 130.4, 129.4, 128.3, 127.2, 123.4, 123.2, 122.8, 108.1, 52.3, 13.3.

Anal. Calcd for $C_{18}H_{13}ClN_2O_3$: C, 63.44; H, 3.85; N, 8.22. Found: C, 63.27; H, 3.87; N, 8.26.

5-Chloro-2-methyldibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine-10-carbonitrile (19k)
Light-yellow solid; yield: 1.52 g (83%); mp 215–217 °C (DMF).

IR (KBr): 2241, 1604 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.02 (s, 1 H, H_{Ar}), 7.91 (d, J = 8.5 Hz, 1 H, H_{Ar}), 7.77 (d, J = 8.5 Hz, 1 H, H_{Ar}), 7.71 (s, 1 H, H_{Ar}), 7.44–7.55 (m, 2 H, H_{Ar}), 6.88 (s, 1 H, $H_{pyrazole}$), 2.37 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 153.7, 151.9, 148.7, 139.8, 136.5, 131.2, 130.8, 130.6, 128.5, 126.5, 124.1, 123.3, 123.1, 117.6, 110.1, 104.7, 13.5.

Anal. Calcd for $C_{17}H_{10}ClN_3O$: C, 66.35; H, 3.28; N, 13.65. Found: C, 66.14; H, 3.31; N, 13.72.

5-Chloro-2-methyl-10-nitrodibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine (19l)
Brown solid; yield: 1.06 g (85%); mp 224–226 °C (DMF).

IR (KBr): 1681, 1615, 1341 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.39 (s, 1 H, H_{Ar}), 8.21 (d, J = 8.5 Hz, 1 H, H_{Ar}), 7.99 (d, J = 9.2 Hz, 1 H, H_{Ar}), 7.73 (s, 1 H, H_{Ar}), 7.62 (d, J = 8.5 Hz, 1 H, H_{Ar}), 7.51 (d, J = 8.5 Hz, 1 H, H_{Ar}), 6.92 (s, 1 H, $H_{pyrazole}$), 2.38 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 153.8, 152.3, 148.4, 146.2, 140.0, 137.9, 131.0, 130.7, 128.3, 123.7, 123.3, 123.1, 121.7, 117.9, 108.7, 13.3.

Anal. Calcd for $C_{16}H_{10}ClN_3O_3$: C, 58.64; H, 3.08; N, 12.82. Found: C, 58.64; H, 3.10; N, 12.89.

Methyl 2,5-Dimethyldibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine-10-carboxylate (19m)
White solid; yield: 1.44 g (76%); mp 131–133 °C (*i*-PrOH).

IR (KBr): 1741, 1622, 1221, 1200 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 7.97 (s, 1 H, H_{Ar}), 7.89 (d, J = 8.4 Hz, 1 H, H_{Ar}), 7.65 (d, J = 7.0 Hz, 1 H, H_{Ar}), 7.49 (s, 1 H, H_{Ar}), 7.27–7.42 (m, 2 H, H_{Ar}), 6.79 (s, 1 H, $H_{pyrazole}$), 3.88 (s, 3 H, CO_2CH_3), 2.35 (s, 3 H, Ar-CH_3), 2.32 (s, 3 H, pyrazole-CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 165.0, 153.1, 151.7, 149.2, 141.3, 136.7, 135.9, 131.9, 130.5, 129.3, 127.5, 126.3, 124.1, 121.0, 120.9, 117.7, 52.3, 20.3, 13.5.

Anal. Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.12; H, 5.05; N, 8.71.

2,5-Dimethyldibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine-10-carbonitrile (19n)
Light-yellow solid; yield: 0.63 g (69%); mp 182–185 °C (EtOH–DMF).

IR (KBr): 2241, 1608 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.08 (s, 1 H, H_{Ar}), 7.90 (d, J = 8.5 Hz, 1 H, H_{Ar}), 7.79 (d, J = 7.9 Hz, 1 H, H_{Ar}), 7.50 (s, 1 H, H_{Ar}), 7.27–7.42 (m, 2 H, H_{Ar}), 6.83 (s, 1 H, $H_{pyrazole}$), 2.35 (s, 3 H, Ar-CH_3), 2.32 (s, 3 H, pyrazole-CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 153.2, 151.7, 149.2, 141.3, 136.7, 135.9, 132.0, 130.4, 129.3, 126.3, 124.1, 121.0, 120.9, 117.7, 109.9, 107.6, 20.3, 13.5.

Anal. Calcd for $C_{18}H_{13}N_3O$: C, 75.25; H, 4.56; N, 14.63. Found: C, 75.11; H, 4.56; N, 14.68.

2,5-Dimethyl-10-nitrodibenzo[*b*,*f*]pyrazolo[1,5-*d*][1,4]oxazepine (19o)
Dark-grey solid; yield: 1.38 g (80%); mp 207–209 °C (EtOH–DMF).

IR (KBr): 1685, 1619, 1354 cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 K): δ = 8.39 (s, 1 H, H_{Ar}), 8.21 (d, J = 8.9 Hz, 1 H, H_{Ar}), 7.99 (d, J = 8.9 Hz, 1 H, H_{Ar}), 7.47–7.56 (m, 2 H, H_{Ar}), 7.33 (d, J = 8.5 Hz, 1 H, H_{Ar}), 6.87 (s, 1 H, $H_{pyrazole}$), 2.36 (s, 3 H, Ar-CH_3), 2.33 (s, 3 H, pyrazole-CH_3).

^{13}C NMR (DMSO-d_6, 300 K): δ = 153.1, 152.1, 148.8, 145.8, 141.4, 138.1, 136.1, 132.1, 129.3, 123.7, 121.7, 121.2, 120.8, 118.0, 107.9, 20.3, 13.5.

Anal. Calcd for $C_{17}H_{13}N_3O_3$: C, 66.44; H, 4.26; N, 13.67. Found: C, 66.25; H, 4.23; N, 13.71.

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(14) Crystallographic data (excluding structure factors) for the structure **19h** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 871488. Copies of the data can be obtained free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(1223)336033 or e-mail: deposit@ccdc.cam.ac.uk].
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