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ORIGINAL PAPER

A simple new hydrazine-free synthesis of methyl 1,4,5-trisubstituted 1*H*-pyrazole-3-carboxylates

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Abstract Conditions for successful syntheses of polysubstituted pyrazole-3-carboxylates have been found. The methodology consists in mixing equimolar amounts of diazonium tetrafluoroborates and enaminoesters in presence of sodium acetate. 1-Methylpyrrolidone has appeared to be the solvent of choice. The compounds prepared have been characterized by means of nuclear magnetic resonance (NMR) spectroscopy, elemental analysis, and in two cases, also by X-ray diffraction. The advantage of the methodology is a simple implementation without necessity of working under inert atmosphere. The presence of other functional groups enables further synthetic transformations of the products.

Keywords NMR spectroscopy · Diazonium salts · X-ray structure determination · Enaminoesters · Heterocycles

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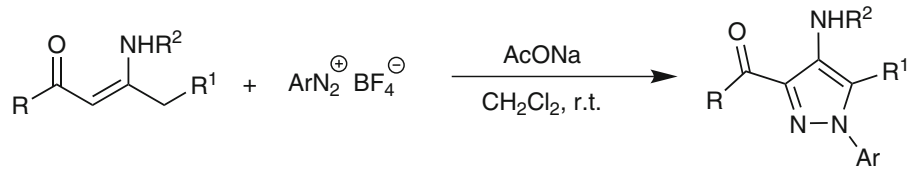
Introduction

Compounds containing pyrazole motif are relatively rare in nature. Among some exceptions rank withasomnine, isolated from the Indian plant *Withania somnifera* [1], or pyrazomycines that are very efficient antivirotics and antineoplastics, isolated from *Streptomyces candidus* [2]. Pyrazole derivatives have found broad applications as either pharmaceutics [3] [e.g., nonsteroidal anti-inflammatory drugs (NSAIDs), antivirotics, antineoplastics, etc.] or pesticides [4]. Synthesis of pyrazoles attracts great attention and is the subject of many reviews; for some of them see [5–12]. Probably the most widespread method for construction of the pyrazole skeleton is the reaction of 1,3-difunctional compounds with hydrazine derivatives. The drawbacks of this methodology are, on the one hand, the substantial toxicity of some hydrazines and, on the other hand, the possibility of the formation of regioisomers in case of using unsymmetrical starting compounds.

A few years ago we published a simple new method for synthesis of polysubstituted pyrazoles from β-enaminones [13] using diazonium salts as nitrogen source. This method is generally safer, as the risk upon working with stabilized diazonium salts is sometimes lower in comparison with hydrazines. Another advantage of the methodology is its regioselectivity. Only 3-acyl derivatives have been hitherto isolated (Scheme 1). As arylhydrazines are usually prepared from the corresponding diazonium salts, the methodology also shortens the synthesis. Later we successfully used the methodology for synthesis of some fluorinated pyrazoles [14].

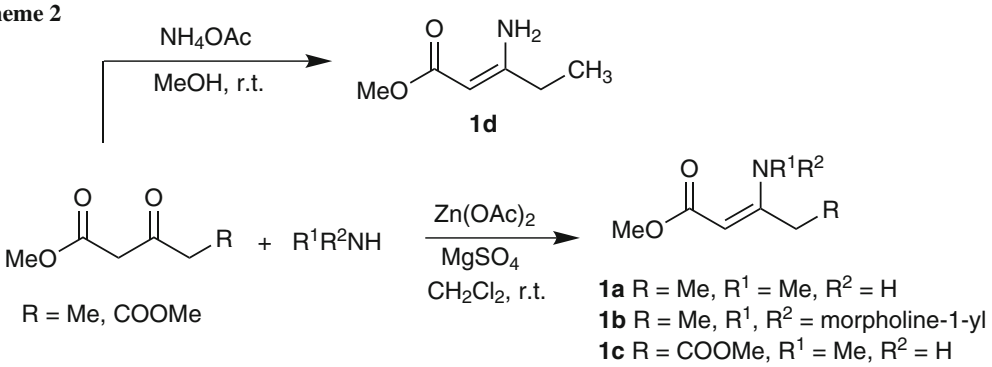
The products of the reaction represent, due to the presence of both carbonyl and amino group, useful precursors for further synthetic transformations. In addition to that, the above-mentioned protocol has considerable potential for

Scheme 1



R = Et, Ph, cycloPr
R^1 = Me, Ph
R^2 = H, Me, subst. Ph

Scheme 2



R = Me, COOMe

1a R = Me, R^1 = Me, R^2 = H
1b R = Me, R^1, R^2 = morpholine-1-yl
1c R = COOMe, R^1 = Me, R^2 = H

extension to other polarized ethylenes (enaminoesters, enaminoamides, enaminonitriles, etc.), which would enable access to other pyrazole derivatives. The goal of the present work is to find conditions for transformation of enaminoesters to the corresponding pyrazoles.

Results and discussion

The starting enaminoesters **1a**–**1c** were prepared by adoption of the method published by Vohra et al. [15]; the derivative **1d** with primary amino group was prepared using ammonium acetate as ammonia source (Scheme 2). Enaminoester **1b** is very unstable and undergoes decomposition even under cooling; hence, the crude reaction mixture was, after structure elucidation by NMR, used for the next step without further purification.

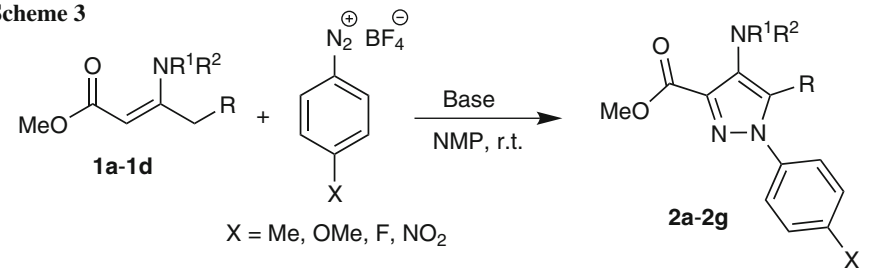
As the starting point we used the conditions successfully applied for synthesis of 1-aryl-4-(substituted amino)-5-acyl-1*H*-pyrazoles [13] (CH_2Cl_2, 2 eq. of diazonium salt, 6 eq. of AcONa). Only low yield (25 %) of pyrazole **2a** was isolated after time-consuming work-up of the reaction mixture.

Upon gradual change of the reaction parameters (base, solvent, and ratio of starting components), it was found that the key factor was solvent selection. 1-Methylpyrrolidone (NMP) turned out to be the most convenient one. Application of this solvent led to successful synthesis of derivatives **2a**–**2d** in moderate to low yields (Scheme 3, "Experimental"). Upon an attempt to prepare diester **2g**, application of sodium acetate failed, but success was achieved using tripotassium phosphate as the base.

The structure of the prepared compounds was confirmed using ^{1}H and ^{13}C NMR spectroscopy, elemental analysis, and in case of derivatives **2b** and **2e** also by means of X-ray diffraction (Figs. 1–3).

ORTEP [16] views of compounds **2b** and **2e** are shown in Figs. 1 and 3. Compound **2b** crystallizes in the orthorhombic space group $P2_12_12_1$ with four molecules within the unit cell without intermolecular hydrogen bonding. Only the intramolecular N(1)–H(1)···O(2) contact is present, along with other short contacts forming a three-dimensional (3D) structure (Fig. 2). In the molecule of **2b**, the interatomic angles within the central heterocyclic ring confirm that this ring is planar. The arrangement of the substituents of this ring led to self-assembly of the molecules, producing a helical superstructure in the solid state with chiral properties similar to, for example, in helicenes. Although a high degree of conjugation is observed through the molecule, C2–C3 and C1–N3 bonds are attributed as the multiple ones [17]. Direct comparison of the structure of **2b** with recently obtained structures of compounds with the same central ring (1-(4-methoxyphenyl)-4-(methylamino)-5-phenyl-1*H*-pyrazol-3-yl(phenyl)methanones [13]) could be made, with the exception that these structures do not reveal atropoisomerism. Similar structures of different heterocycles also exist [18–22].

Scheme 3



2a R = Me, R^1 = Me, R^2 = H, X = Me
2b R = Me, R^1 = Me, R^2 = H, X = NO_2
2c R = Me, R^1 = Me, R^2 = H, X = F
2d R = Me, R^1, R^2 = morpholine-1-yl, X = Me
2e R = Me, R^1, R^2 = morpholine-1-yl, X = OMe
2f R = Me, R^1, R^2 = H, X = Me
2g R = COOMe, R^1 = Me, R^2 = H, X = Me

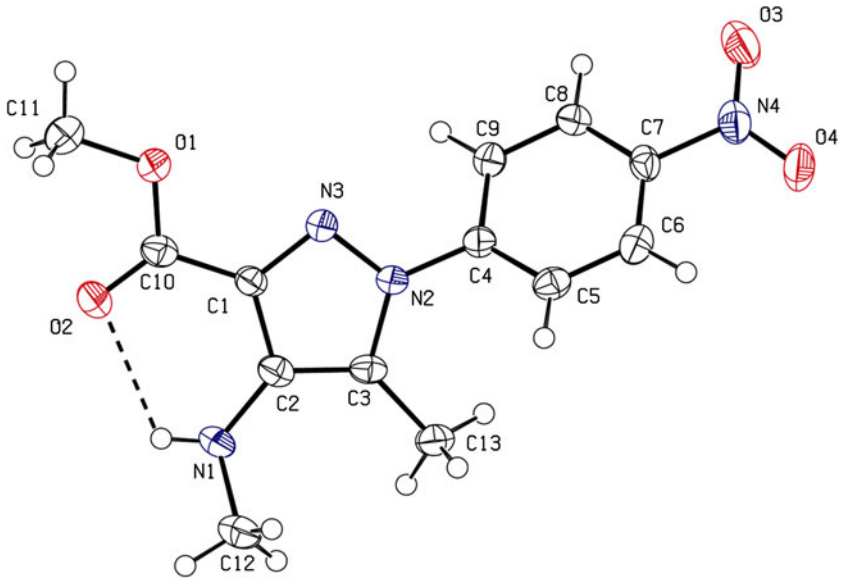


Fig. 1 Molecular structure of **2b** (ORTEP 50 % probability level) with H-bonding interaction [N(1)–H(1)···O(2), 2.875(3) Å]

Conclusions

Enaminoesters turned out to be much more challenging substrates for synthesis of pyrazoles by reaction with diazonium salts than corresponding enaminoketones. Upon gradual optimization, conditions for successful synthesis of polysubstituted pyrazole carboxylates were found. The advantage of the protocol is a simple implementation without the demand to work under inert atmosphere or to use hydrazine derivatives. Only pyrazole-3-carboxylates were isolated. Enaminoesters having primary as well as secondary or tertiary amino groups were successfully used. The method is applicable for diazonium salts bearing both electron-donating and electron-withdrawing groups. A certain drawback of the method is the moderate to low yield.

The method described here extends the synthetic arsenal for construction of the pyrazole moiety. Its extension to other polarized ethylenes is currently under research.

Experimental

Diazonium tetrafluoroborates were freshly prepared before use by standard procedures (dissolving the appropriate aniline in dilute hydrochloric acid, adding sodium nitrite solution, and subsequent treatment of the formed diazonium chloride by aqueous sodium tetrafluoroborate) and dried in vacuo. NMR spectra were measured in $CDCl_3$ at laboratory temperature using a Bruker AVANCE 400 spectrometer operating at 400.13 MHz (^{1}H), 376.46 MHz (^{19}F), and 100.62 MHz (^{13}C). The ^{1}H NMR spectra were calibrated on

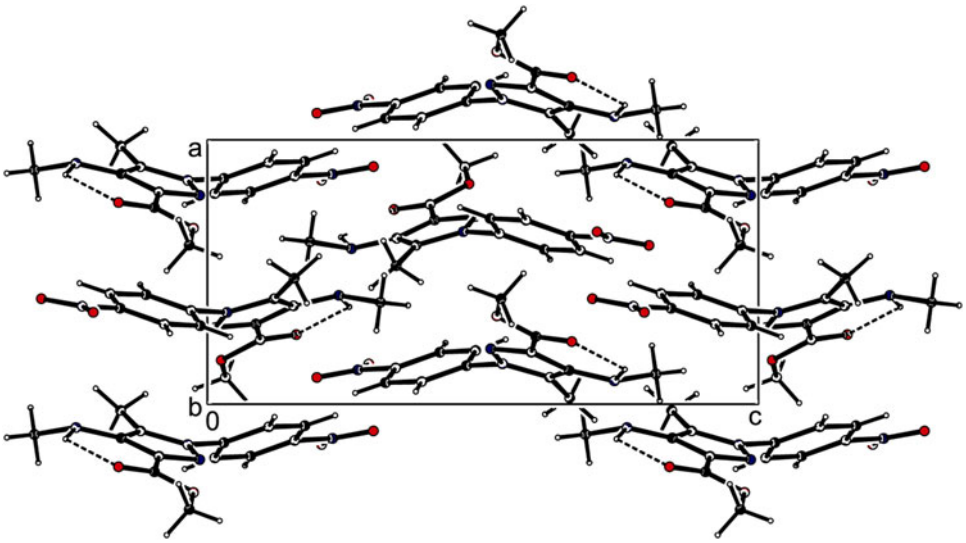


Fig. 2 Supramolecular architecture of **2b**, view along the *b*-axis

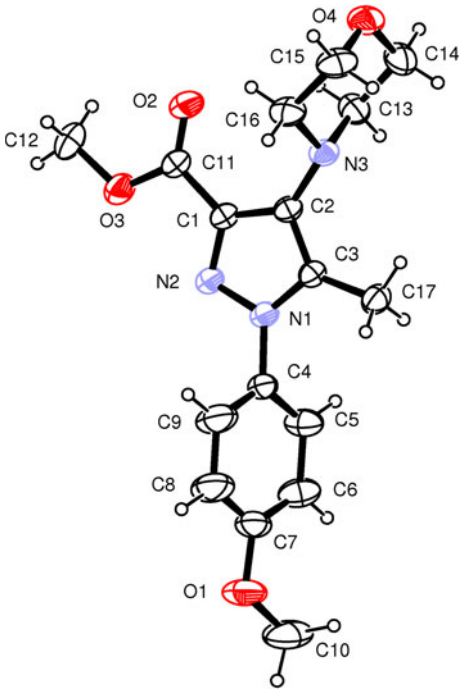


Fig. 3 ORTEP view of **2e** showing the thermal ellipsoids at 30 % level of probability

tetramethylsilane (TMS, $\delta = 0.0$ ppm). The ^{13}C NMR spectra were measured in the standard way and by attached proton test (APT) pulse sequence, and calibrated on the central signal of the solvent multiplet ($\delta = 77.16$ ppm). ^{19}F NMR spectra were measured using Waltz-16 proton decoupling and were standardized against fluorobenzene as the secondary external standard ($\delta = -113.1$ against $CFCl_3$ as primary standard [23]). Elemental analyses were performed on a Flash 2000 CHNS elemental analyzer. Melting points were measured on a Kofler hot-stage microscope (Boetius PHMK 80/2644).

Crystallography

X-ray data were collected on a Nonius Kappa charge-coupled device (CCD) diffractometer with Mo K_α radiation ($\lambda = 0.71073$ Å), a graphite monochromator, and the ϕ and χ scan mode. Data for orange single crystal of **2b** were obtained at 150 K using an Oxford Cryostream low-temperature device and for compound **2e** at laboratory temperature (295 K). Data reductions were performed with DENZO-SMN [24]. The absorption was corrected by integration methods [25]. The structures were solved by direct methods (SIR92 [26] for **2b** or SIR97 [28] for **2e**) and refined by full matrix least-squares based on F^2 (SHELXL97) [27]. Hydrogen atoms were mostly localized on a difference Fourier map; however, to ensure uniformity of treatment of crystal, all hydrogens were recalculated into idealized positions (riding model) and assigned temperature factors $H_{iso}(H) = 1.2U_{eq}$ (pivot atom) or $1.5U_{eq}$ for the methyl moiety with C–H = 0.96 and 0.93 Å for methyl and hydrogen atoms in aromatic ring, respectively. The hydrogen atom of N–H group was placed according to appropriate maxima on Fourier difference map.

Crystallographic data for structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC 913069 for **2b** and CCDC 900893 for **2e**. Copies of this information may be obtained, free of charge, from The Director, CCDC, 12 Union Road, Cambridge CB2 1EY, UK (fax: + 44(0)-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or via http://www.ccdc.cam.ac.uk/conts/retrieving.html).

General procedure for preparation of enaminoesters ***1a–1c***

An appropriate β-ketoester (30 mmol), 0.33 g zinc acetate dihydrate (1.5 mmol, 5 mol %), and 0.72 g anhydrous

$MgSO_4$ (6 mmol, 20 mol %) were added into a flask equipped with a calcium chloride drying tube and suspended in 40 cm^3 dichloromethane. A corresponding amine (30 mmol) was then added in one portion, and the reaction mixture was stirred at room temperature for 16 h. Subsequently, another portion of 0.72 g $MgSO_4$ was added into the mixture and the suspension was stirred for 2 days. Solid compounds were then filtered off, and the filtrate was evaporated in vacuo to give products **1a**–**1c**. All products were used in next steps without further purification unless otherwise stated.

Methyl 3-(methylamino)pent-2-enoate (**1a**)

Prepared from methyl 3-oxopentanoate and 8 M ethanolic solution of methylamine. Yellow oily compound, 92 % yield. ^{1}H NMR (400.13 MHz): $\delta = 8.51$ (br s, 1H), 4.48 (s, 1H), 3.62 (s, 3H), 2.91 (d, $J = 5.3$ Hz, 3H), 2.23 (q, $J = 7.5$ Hz, 2H), 1.14 (t, $J = 7.5$ Hz, 3H) ppm.

Methyl 3-(morpholin-4-yl)pent-2-enoate (**1b**)

Prepared from methyl 3-oxopentanoate and morpholine. An unstable brown oily compound was obtained, which was used immediately for the next reaction step.

Dimethyl 3-(methylamino)pent-2-enedioate (**1c**)

Prepared from dimethyl 3-oxopentanedioate and 8 M ethanolic solution of methylamine. The isolated yellow oil crystallized using an ultrasonic bath. The crude product was washed thoroughly with diethyl ether, and the resulting white solid **1c** was isolated in 62 % yield. M.p.: 83–88 °C (Ref. [29] 83–90 °C).

Methyl 3-aminopent-2-enoate (**1d**)

Methyl 3-oxopentanoate (2.5 cm^3, 20 mmol) was introduced under argon atmosphere to the clear solution of 7.71 g ammonium acetate (100 mmol) in 25 cm^3 methanol and stirred at room temperature for 3 days. The solvent was then evaporated in vacuo, and 30 cm^3 chloroform was added. The resulting solid was then filtered off and washed with chloroform (2 × 15 cm^3). The combined filtrate was washed with 15 cm^3 water and 15 cm^3 brine, dried over Na_2SO_4, and evaporated in vacuo to give **1d** (2.25 g) as yellow oil in 87 % yield. The ^{1}H NMR spectrum was found to agree with the one described in Ref. [30].

General procedure for preparation of pyrazoles ***2a–2g***

The corresponding enaminoester **1a**–**1d** (2 mmol), 0.98 g sodium acetate (12 mmol), and 5 cm^3 dry NMP were added to a dried flask equipped with a calcium chloride drying tube. The mixture was then ice-cooled, and an appropriate benzenediazonium tetrafluoroborate (4 mmol) was added stepwise (during 20 min). The reaction temperature was then spontaneously raised to laboratory value, and the mixture was stirred for 4 days. Subsequently, the reaction mixture was diluted with 25 cm^3 ethyl acetate and filtered through Celite®. The clear filtrate was extracted with 20 cm^3 50 % brine, 20 cm^3 water, and concd. brine (2 × 20 cm^3). The organic layer was dried over Na_2SO_4 and evaporated in vacuo. The crude product was suspended in 10 cm^3 diluted (1:1) aqueous HCl and was well shaken. Undissolved solids were filtered off, and the filtrate was extracted with diethyl ether (4 × 10 cm^3). The aqueous phase was then neutralized with solid $NaHCO_3$. Precipitated products **2a**, **2b**, and **2d** were collected by filtration; compounds **2c** and **2e**–**2g** were isolated by extraction with dichloromethane (2 × 20 cm^3), drying of the organic layer over Na_2SO_4, and evaporating in vacuo. The resulting oils solidified on standing.

Methyl 5-methyl-4-(methylamino)-1-(4-methylphenyl)-1H-pyrazole-3-carboxylate (**2a**, $C_{14}H_{17}N_3O_2$)
Light-yellow solid; yield 49 %; m.p.: 80–85 °C; ^{1}H NMR (400.13 MHz): $\delta = 7.28$–7.32 (m, 2H), 7.23–7.28 (m, 2H), 4.42 (br s, 1H), 3.92 (s, 3H), 2.90 (s, 3H), 2.40 (s, 3H), 2.31 (s, 3H) ppm; ^{13}C NMR (100.62 MHz): $\delta = 164.6$, 138.5, 136.9, 136.6, 131.6, 129.7, 127.2, 125.4, 51.7, 35.0, 21.2, 11.6 ppm.

Methyl 5-methyl-4-(methylamino)-1-(4-nitrophenyl)-1H-pyrazole-3-carboxylate (**2b**, $C_{13}H_{14}N_4O_4$)
Red solid; yield 46 %; m.p.: 154–156 °C; ^{1}H NMR (400.13 MHz): $\delta = 8.33$–8.39 (m, 2H), 7.60–7.72 (m, 2H), 4.69 (br s, 1H), 3.95 (s, 3H), 2.94 (s, 3H), 2.44 (s, 3H) ppm; ^{13}C NMR (100.62 MHz): $\delta = 164.2$, 146.9, 144.2, 137.9, 133.5, 126.6, 125.3, 124.8, 52.0, 34.9, 12.2 ppm.

Crystallographic data for **2b**: $C_{13}H_{14}N_4O_4$, $M = 290.28$, orthorhombic, space group $P2_12_12_1$, $a = 7.4490(4)$ Å, $b = 11.6130(7)$ Å, $c = 15.5131(10)$ Å, $\beta = 90°$, $Z = 4$, $V = 1341.96(14)$ Å^3, $D_c = 1.437$ g cm^{-3}; $\theta_{max} = 27.49°$; 3,035 independent reflections measured, 2,294 reflections observed with $I > 2\sigma(I)$, 190 parameters, $S = 1.184$, *R1* (obs. data) = 0.0536, *wR2* (all data) = 0.0956.

Selected interatomic distances (Å) and angles (°): C1–C2 1.418(3), C2–C3 1.376(4), C3–N2 1.390(3), N2–N3 1.344(3), C1–N3 1.340(3), O1–C10 1.333(3), O2–C10 1.211(3), C2–N1 1.387(3), N1–C12 1.451(3), C7–N4 1.468(3), N4–O3 1.228(3), N4–O4 1.224(3); C1–C2–C3 105.2(2), C2–C3–N2 105.1(2), C3–N2–N3 113.7(2), N2–N3–C1 103.68(19), N3–C1–C2 112.3(2), C1–C2–N1 125.5(2), C2–N1–C12 121.4(2), C1–C10–O2 123.0(2), N3–C1–C10 122.6(2), O1–C10–O2 123.0(3), C7–N4–O3 118.6(2), O3–N4–O4 123.4(2).

Methyl 1-(4-fluorophenyl)-5-methyl-4-(methylamino)-1H-pyrazole-3-carboxylate (**2c**, $C_{13}H_{14}FN_3O_2$)
The isolated compound was purified by column chromatography (silica gel/AcOEt) and obtained as yellow solid in 41 % yield. M.p.: 94–98 °C; ^{1}H NMR (400.13 MHz): $\delta = 7.42$–7.49 (m, 2H), 7.14–7.18 (m, 2H), 4.72 (br s, 1H), 3.93 (s, 3H), 2.91 (s, 3H), 2.31 (s, 3H) ppm; ^{13}C NMR (100.62 MHz): $\delta = 164.4$, 162.3 (d, $^1J_{CF} = 249.0$ Hz), 136.8, 135.4 (d, $^4J_{CF} = 3.3$ Hz), 131.9, 127.4 (d, $^3J_{CF} = 8.8$ Hz), 127.1, 116.1 (d, $^2J_{CF} = 22.7$ Hz), 51.7, 34.9, 11.5 ppm; ^{19}F NMR (376.46 MHz): $\delta = -112.4$ ppm.

Methyl 5-methyl-1-(4-methylphenyl)-4-(morpholin-4-yl)-1H-pyrazole-3-carboxylate (**2d**, $C_{17}H_{21}N_3O_3$)
Brown-red solid; yield 23 %; m.p.: 98–104 °C; ^{1}H NMR (400.13 MHz): $\delta = 7.29$–7.34 (m, 2H), 7.24–7.29 (m, 2H), 3.94 (s, 3H), 3.86–3.77 (m, 4H), 3.17–3.08 (m, 4H), 2.41 (s, 3H), 2.26 (s, 3H) ppm; ^{13}C NMR (100.62 MHz): $\delta = 163.1$, 138.7, 138.6, 137.1, 137.0, 135.0, 129.8, 125.2, 68.1, 52.1, 51.5, 21.3, 10.6 ppm.

Methyl 1-(4-methoxyphenyl)-5-methyl-4-(morpholin-4-yl)-1H-pyrazole-3-carboxylate (**2e**, $C_{17}H_{21}N_3O_4$)
The isolated compound was purified by column chromatography (silica gel/AcOEt) and obtained as brown-red solid in 15 % yield. M.p.: 121–126 °C; ^{1}H NMR (400.13 MHz): $\delta = 7.31$–7.37 (m, 1H), 6.94–7.00 (m, 1H), 3.93 (s, 1H), 3.86 (s, 2H), 3.79–3.83 (m, 2H), 3.10–3.17 (m, 2H), 2.24 (s, 1H) ppm; ^{13}C NMR (100.62 MHz): $\delta = 163.0$, 159.7, 138.5, 137.2, 134.8, 132.6, 126.8, 114.3, 68.1, 55.7, 52.1, 51.6, 10.5 ppm.

Crystallographic data for **2e**: $C_{17}H_{21}N_3O_4$; $M = 331.37$, triclinic, space group *P-1*, $a = 5.9674(2)$ Å, $b = 10.3939(3)$ Å, $c = 14.7099(5)$ Å, $\alpha = 102.623(1)°$, $\beta = 92.262(1)°$, $\gamma = 103.969(2)°$, $V = 859.88(5)$ Å^3, $Z = 2$, $D_c = 1.280$ g cm^{-3}; $\theta_{max} = 28.0°$; 4,093 independent reflections measured, 3,153 reflections observed with $I > 2\sigma(I)$, 220 parameters, $S = 1.044$, *R1* (obs. data) = 0.0645, *wR2* (all data) = 0.1858.

Selected interatomic distances (Å): C1–C2 = 1.420(2), C1–N2 = 1.339(2), C2–C3 = 1.383(2), N1–C3 = 1.362(2), N1–N2 = 1.349(2).

Methyl 4-amino-5-methyl-1-(4-methylphenyl)-1H-pyrazole-3-carboxylate (**2f**, $C_{13}H_{15}N_3O_2$)
The isolated compound was purified by column chromatography (silica gel/AcOEt) and obtained as orange solid in 14 % yield. M.p.: 88–92 °C; ^{1}H NMR (400.13 MHz): $\delta = 7.28$–7.33 (m, 2H), 7.22–7.28 (m, 2H), 3.94 (s, 3H), 2.41 (s, 3H), 2.18 (s, 3H) ppm; ^{13}C NMR (100.62 MHz): $\delta = 164.5$, 138.5, 137.0, 132.2, 130.8, 129.8, 125.3, 125.1, 51.8, 21.3, 10.0 ppm.

Dimethyl 4-(methylamino)-1-(4-methylphenyl)-1H-pyrazole-3,5-dicarboxylate (**2g**, $C_{15}H_{17}N_3O_4$)
Enaminoester **1c** (373 mg, 2 mmol), 1.27 g tripotassium phosphate (6 mmol), and 5 cm^3 dry NMP were added to a dried flask equipped with a calcium chloride drying tube. The mixture was then ice-cooled and 826 mg 4-methylbenzenediazonium tetrafluoroborate (4 mmol) was added stepwise (during 15 min). The reaction temperature was then spontaneously raised to r.t. and the mixture was stirred for 2 days. Subsequently, the reaction mixture was diluted with 25 cm^3 ethyl acetate and filtered through Celite®. The clear filtrate was extracted with 20 cm^3 50 % brine, 20 cm^3 water, and concd. brine (2 × 20 cm^3). The organic layer was dried over Na_2SO_4 and evaporated in vacuo. The crude product was purified by column chromatography (silica gel/AcOEt) and obtained as brown-yellow solid in 26 % yield. M.p.: 114–116 °C; ^{1}H NMR (400.13 MHz): $\delta = 7.23$–7.27 (m, 2H), 7.19–7.23 (m, 2H), 3.93 (s, 3H), 3.70 (s, 3H), 3.04 (s, 3H), 2.40 (s, 3H) ppm; ^{13}C NMR (100.62 MHz): $\delta = 163.6$, 160.4, 143.6, 139.0, 138.6, 130.8, 129.3, 125.6, 119.3, 52.2, 51.8, 34.4, 21.4 ppm.

References

1. Schröter HB, Neumann D, Katritzky AR, Swinbourne FJ (1966) Tetrahedron 22:2895
2. Doyle Daves G, Cheng CC (1976) In: Ellis GP, West GB (eds) Progress in Medicinal Chemistry, vol 13. North-Holland, Amsterdam, p 327
3. Orth RE (1968) J Pharm Sci 57:537
4. Lamberth C (2007) Heterocycles 71:1467
5. Stanovnik B, Svete J (2002) In: Neier R (ed) Science of Synthesis, vol 12. Thieme, Stuttgart, p 15
6. Schmidt A, Dreger A (2011) Curr Org Chem 15:1423
7. Schmidt A, Dreger A (2011) Curr Org Chem 15:2897
8. Fustero S, Simón-Fuentes A, Sanz-Cervera JF (2009) Org Prep Proced Int 41:253
9. Elguero J (1996) In: Katritzky AR, Scriven EFV (eds) Comprehensive Heterocyclic Chemistry II, vol 3. Elsevier, Oxford
10. Makino K, Kim HS, Kurasawa Y (1999) J Heterocycl Chem 36:321
11. Fustero S, Sanchez-Rosello M, Barrio P, Simon-Fuentes A (2011) Chem Rev 111:6984
12. Bekhit AA, Hymete A, Bekhit AEA, Damtew A, Aboul-Enein HY (2010) Mini-Rev Med Chem 10:1014
13. Šimůnek P, Svobodová M, Bertolasi V, Macháček V (2008) Synthesis 2008(11):1761–1766
14. Šimůnek P, Svobodová M, Macháček V (2009) J Heterocycl Chem 46:650
15. Vohra RK, Renaud JL, Bruneau C (2005) Collect Czech Chem Commun 70:1943
16. Burnett MN, Johnson CK (1996) ORTEP III, Report ORNL-6895. Oak Ridge National Laboratory, Oak Ridge
17. Allen FH, Kennard O, Watson DG, Brammer L, Orpen AG, Taylor R (1987) J Chem Soc Perkin Trans 2:S1
18. Gieren A, Lamm V (1982) Acta Crystallogr Sect B 38:844
19. El-Abadelah MM, Sabri SS, Khanfar MA, Voelter W, Maichle-Moessmer C (1999) Z Naturforsch B 54:1323

20. Boyd M, Atwell GJ, Denny WA (1993) Acta Crystallogr Sect C 49:1429
21. Brady T, Khang V, Barber JR, Chung Ng S, Zhou Y (2009) Tetrahedron Lett 50:6223
22. Ibrahim HM, Behbehani H, Makhseed S, Elnagdi MH (2011) Molecules 16:3723
23. Berger S, Braun S, Kalinowski HO (1997) NMR Spectroscopy of the Non-metallic Elements. Wiley, Chichester
24. Otwinowski Z, Minor W (1997) Processing of X-ray diffraction data collected in oscillation mode. In: Carter CW, Sweet RM (eds) Methods in Enzymology, vol 276, part A. London pp 307–326
25. Coppens P (1970) In: Ahmed FR, Hall SR, Huber CP (eds) Crystallographic Computing. Munksgaard, Copenhagen, p 255
26. Altomare A, Cascarano G, Giacovazzo C, Guagliardi A (1994) J Appl Crystal 27:1045
27. Sheldrick GM (2008) SHELXL-97. University of Göttingen, Göttingen
28. Altomare A, Burla MC, Camalli M, Cascarano GL, Giacovazzo C, Guagliardi A, Moliterni AGG, Polidori G, Spagna R (1999) J Appl Crystallogr 32:115
29. Augustine RL, Bellina RF, Gustavsen AJ (1968) J Org Chem 33:1287
30. Ohashi T, Oguro Y, Tanaka T, Shiokawa Z, Tanaka Y, Shibata S, Sato Y, Yamakawa H, Hattori H, Yamamoto Y, Kondo S, Miyamoto M, Nishihara M, Ishimura Y, Tojo H, Baba A, Sasaki S (2012) Bioorg Med Chem 20:5507