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New synthesis of 3-methoxy-4-substituted pyrazole derivatives

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Abstract—A simple and efficient protocol for the synthesis of 3-methoxy-4-arylmethylene- and 3-methoxy-4-heteroarylmethylene-pyrazoles has been developed. These derivatives are obtained *in one step* from alcohols **3** or **8a**–**b**.
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The pyrazole moiety is present in a wide variety of biologically active compounds.[1] Among them, Kess et al. have described a number of 3-hydroxy-4-benzylpyrazoles (Fig. 1), which represent a new class of antidiabetic compounds.[2] These pyrazoles seem to act as inhibitors of glucose renal reabsorption. The authors have described a wide number of derivatives with good hypoglycemic activities. In all cases, their syntheses proceeded in low yield from β-ketoesters (Fig. 1).

In the last few years, we have been interested in the reactivity and the biological activity of ethyl 3-hydroxy-1*H*-pyrazole-4-carboxylate. During these studies, reactions on N1, O3 and C5 positions and the in vivo hypoglycemic activity of these derivatives have been described.[3] In the present letter, we show a new and efficient synthesis of 4-arylmethylenepyrazole and 4-heteroarylmethylene-pyrazole derivatives. The methodology employed was based on a Friedel–Crafts-type reaction between carbocation **1** and aromatic species (Scheme 1). We postulated that this intermediate could be easily obtained by dehydration of alcohol **3**,[4] compound synthesized in quantitative yield by reduction of the ester function of pyrazole **2**.[3]

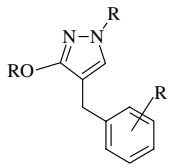
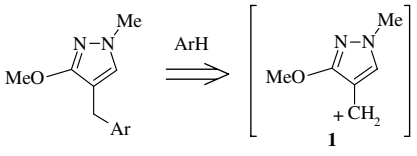


Figure 1. Structure of hypoglycemic pyrazoles.

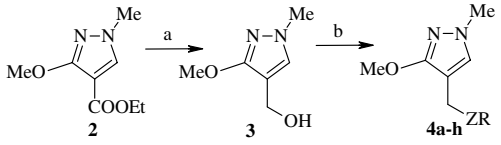
In order to examine the formation of carbocation **1** we decided to react pyrazolylmethanol **3** with nucleophilic species, such as an alcohol and a thiol.

Reactions were carried out with a catalytic quantity of camphorsulfonic acid using either dichloromethane or the alcohol as a solvent. This resulted in the formation of ether or thioether **4a**–**h** in moderate to excellent yields (Scheme 2, Table 1).[5]

During these reactions, bispyrazolylmethane **5** was obtained as a by-product (Table 1). According to the synthesis of bisbenzopyrazolylalkane described by Miki and collaborators,[6] we have proposed the following autocondensation mechanism. In acidic conditions, dehydration of pyrazolylmethanol **3** forms the intermediate **1**



Scheme 1. Reaction investigated for the synthesis of 4-benzyl-pyrazoles.



Scheme 2. Reagents and conditions: (a) $LiAlH_4$ (2 equiv), THF, rt, 2 h, 99%. (b) **4a**–**c** ROH (solvent), CSA (0.1 equiv), rt, 1 h **4d**–**h** RZH (3 equiv), CSA (0.1 equiv), CH_2Cl_2, rt, 1 h.

Keywords: Pyrazole; Benzylpyrazole; Friedel–Crafts.
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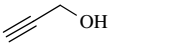
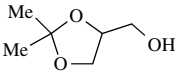
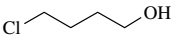
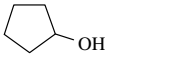
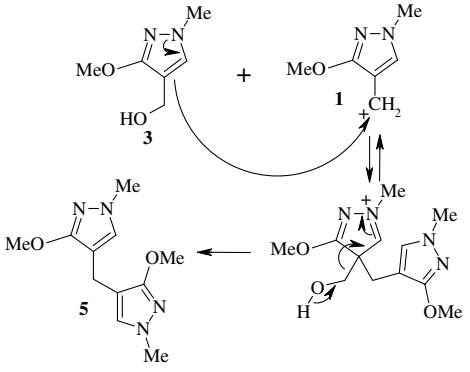
Table 1. Synthesis of ethers and thioether **4a–h**

RXH	Solvent	Compound	**4** (%)[a]	**5** (%)[a]
EtOH	EtOH	**4a**	100	0
*i*PrOH	*i*PrOH	**4b**	100	0
*t*BuOH	*t*BuOH	**4c**	90	0
	CH_2Cl_2	**4d**	71	25
	CH_2Cl_2	**4e**	50	46
	CH_2Cl_2	**4f**	60	34
	CH_2Cl_2	**4g**	73	23
EtSH	CH_2Cl_2	**4h**	80	13

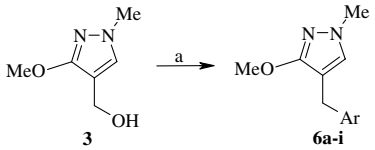
[a] Isolated yield.

which reacts with another alcohol to give, after loss of formaldehyde, pyrazole **5** (Scheme 3).

After optimizing the conditions for the formation of carbocation **1**, we investigated its reaction with aromatic and heteroaromatic species. To avoid the formation of bispyrazolylmethane **5**, reactions were carried out by adding pyrazolylmethanol **3** very slowly to a solution of the aromatic and a catalytic quantity of camphorsulfonic acid in dichloromethane. These reactions produced pyrazoles **6a–i**[7] in yields varying from 50% to 80% (Scheme 4, Table 2). Structure of these derivatives was assigned based on NMR (1D and 2D). For pyrazoles **6a–d**, the multiplicity of protons of phenyl rings indicates the substitution position. For compounds **6f–i**, NOESY experiments were needed, these show a correlation between the CH_2 and H3′ which confirms the substitution on C2 position of the heterocycle.

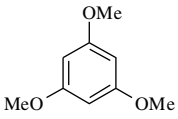
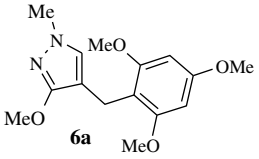
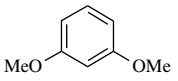
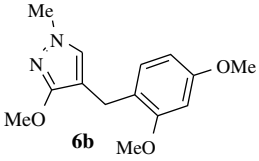
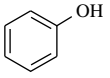
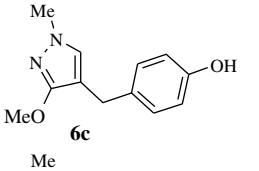
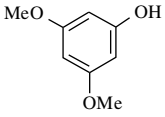
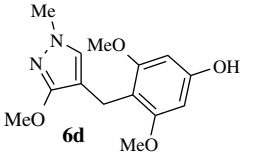
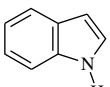
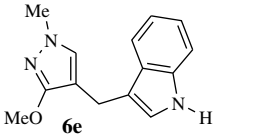
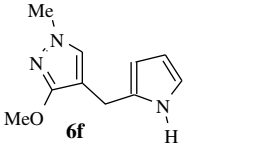
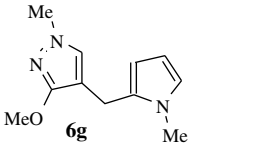
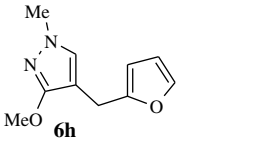
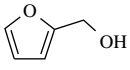
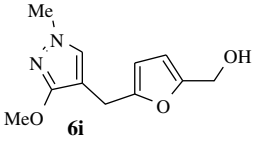


Scheme 3. Mechanism of the autocondensation of pyrazolylmethanol **3**.



Scheme 4. Reagents and conditions: (a) ArH (3 equiv), CSA (0.1 equiv), CH_2Cl_2, rt, 30 min.

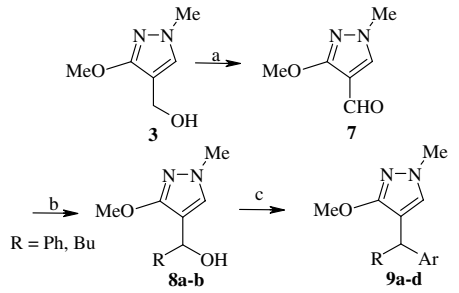
Table 2. Synthesis of 3-methoxy-4-substituted pyrazoles **6a–i**

ArH	Compound	Yield (%)[a]
	 **6a**	50
	 **6b**	64
	 **6c**	71
	 **6d**	50
	 **6e**	75
	 **6f**	80
	 **6g**	85
	 **6h**	78
	 **6i**	60

[a] Isolated yield.

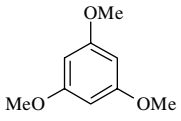
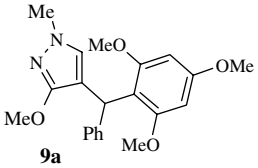
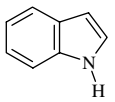
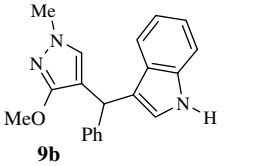
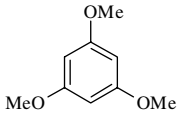
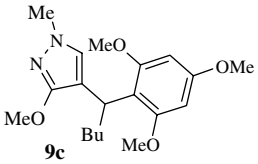
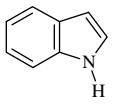
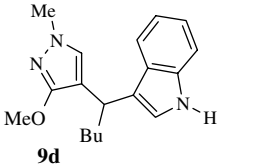
This reaction is compatible with activated benzene derivatives and neutral oxygen and nitrogen heteroaromatic species. In the case of less activated benzene derivatives, such as anisole and toluene, this reaction yielded pyrazole **5**.

To further diversify our synthetic library, we extended this reaction to substituted pyrazolylmethanol. Alcohols **8a** and **8b**[8] were synthesized in good yields by the addition of organolithium species to aldehyde **7** (Scheme 5).[9]



Scheme 5. Reagents and conditions: (a) MnO_2 (10 equiv), $CHCl_3$, 20 h, rt, 99%. (b) RLi (2.5 equiv), THF, −30 °C, 3 h, (**8a**: R = Ph 87%; **8b**: R = Bu 83%). (c) ArH (3 equiv), CSA (0.1 equiv), CH_2Cl_2, rt, 30 min.

Table 3. Synthesis of pyrazoles **9a–d**

R	ArH	Compound	Yield (%)[a]
Ph		 **9a**	68
Ph		 **9b**	83
Bu		 **9c**	67
Bu		 **9d**	86

[a] Isolated yield.

As this aldehyde could not be obtained by the reduction of ester **2**, this was carried out in quantitative yield by the reaction of alcohol **3** with MnO_2. Reactions of these alcohols with aromatic and heteroaromatic species in the same conditions as described before gave the 4-substituted pyrazoles **9a–d** in good yields (Table 3).[10]

In summary, we have developed a new and efficient synthesis of 3-methoxy-4-substituted pyrazoles **4**, **6** and **9**. These derivatives are synthesized in mild conditions starting from alcohols **3** and **8a–b**.

References and notes

1. Elguero, J.; Goya, P.; Jagerovic, N.; Silva, A. M. S. *Targets Heterocycl. Syst.* **2002**, *6*, 52.
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3. (a) Cottineau, B.; Chenault, J. *Synlett* **2002**, 769; (b) Cottineau, B.; Toto, P.; Marot, C.; Pipaud, A.; Chenault, J. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 2105.
4. Synthesis of compound **3**: To a stirred suspension of $LiAlH_4$ (4.1 g, 108.4 mmol) in 30 mL of dry THF, cooled to 0 °C, was added slowly a solution of compound **2** (10 g, 54.2 mmol) in 50 mL of dry THF. The reaction mixture was stirred for 2 h at rt and cooled to 0 °C. Then, 4.1 mL of water, 4.1 mL of 15% NaOH solution and 12.3 mL of water were added successively. The resulting mixture was stirred for 1 h at rt and filtered off on Celite. The filtrate was dried over $MgSO_4$ and concentrated under vacuum to give a colourless oil (7.6 g, 99%). ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.55 (s, 3H); 3.75 (s, 3H); 4.25 (s, 2H); 6.95 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 38.7, 56.2, 58.2, 105.4, 131.4, 161.3. MS: 143 5$[M+H]^+$. IR (NaCl) 3100 cm^{-1}.
5. (a) Synthesis of compounds **4a–c**, general procedure: To a stirred solution of CSA (23 mg, 0.1 mmol) in 5 mL of alcohol was added pyrazole **3** (140 mg, 1 mmol). The resulting mixture was stirred at rt for 1 h, then 15 mL of a saturated $NaHCO_3$ solution and 15 mL of CH_2Cl_2 were added. The organic layer was separated, dried over $MgSO_4$ and concentrated under vacuum to give a colourless oil. Synthesis of compounds **4d–h**, general procedure: To a stirred solution of CSA (23 mg, 0.1 mmol) and alcohol or thiol (3 mmol) in 5 mL of CH_2Cl_2 was added pyrazole **3** (140 mg, 1 mmol). The resulting mixture was stirred at rt for 1 h, then 15 mL of a saturated $NaHCO_3$ solution and 15 mL of CH_2Cl_2 were added. The organic layer was separated, dried over $MgSO_4$ and concentrated under vacuum to give a colourless oil.
(b) Spectral data for compounds **4a–h**. Compound **4a**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.15 (t, $J = 6.8$ Hz, 3H); 3.44 (q, $J = 6.8$ Hz, 2H); 3.65 (s, 3H); 3.85 (s, 3H); 4.21 (s, 2H); 7.11 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 15.5; 39.2; 56.4; 61.5; 65.5; 102.7; 132.0; 162.0. MS: 172 $[M+H]^+$. Compound **4b**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.12 (d, $J = 6.2$ Hz, 2H); 3.55–3.68 (m, 4H); 3.85 (s, 3H); 4.21 (s, 2H); 7.11 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 21.9; 38.5; 55.9; 58.4; 70.0; 102.6; 131.3; 161.3. MS: 185 $[M+H]^+$. Compound **4c**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.23 (s, 9H); 3.66 (s, 3H); 3.87 (s, 3H); 4.18 (s, 2H); 7.12 (s,1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 29.3; 40.4; 54.8; 57.7; 74.7; 105.1; 132.9; 162.8. MS: 199 $[M+H]^+$. Compound **4d**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.39 (t, $J = 2.35$ Hz, 1H); 3.62 (s, 3H); 3.82 (s, 3H); 4.04 (d, $J = 2.35$ Hz, 2H); 4.29 (s, 2H); 7.11 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 37.6; 54.9; 55.1; 58.8; 73.1; 78.6; 99.8; 130.7; 160.6. MS: 181 $[M+H]^+$. Compound **4e**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.37 (s, 3H); 1.44 (s, 3H); 3.59 (dd, $J = 5.0$ and 11.6 Hz, 1H); 3.65–3.80 (m, 5H); 3.90 (s, 3H); 4.05 (dd, $J = 6.6$, 8.2 Hz, 1H); 4.20–4.25 (m, 1H); 4.28 (s, 2H); 7.17 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 23.7; 25.2; 37.3; 54.6; 58.5; 61.5; 64.3; 74.7; 100.7; 107.8; 130.3; 160.3. MS: 257 $[M+H]^+$. Compound **4f**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.57–1.81 (m, 4H); 3.38 (t, $J = 6.1$ Hz, 2H); 3.46 (d, $J = 6.5$ Hz, 2H); 3.63 (s, 3H); 3.83 (s, 3H); 4.18 (s, 2H); 7.08 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 29.0; 31.5; 40.9; 47.0; 58.1; 63.3; 70.7; 104.2; 133.6; 163.7. MS: 232–234 $[M+H]^+$. Compound **4g**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.40–1.80 (m, 4H); 3.65 (s, 3H); 3.86 (s, 3H); 3.90–4.00 (m, 1H); 4.18 (s, 2H); 7.11 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 24.0; 33.0; 39.3; 56.6; 59.8; 80.8; 103.2; 132.0; 162.1. MS: 211 $[M+H]^+$. Compound **4h**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.23 (t, $J = 7.3$ Hz, 3H); 2.48 (q, $J = 7.3$ Hz, 2H); 3.47 (s, 2H); 3.68 (s, 3H); 3.88 (s, 3H); 7.06 (s, 1H). ^{13}C NMR(63 MHz, $CDCl_3$) δ 14.6; 23.0; 25.7; 39.0; 56.3; 102.2; 130.8; 161.4. MS: 187 $[M+H]^+$.

6. (a) Miki, Y.; Tomii, O.; Nakao, H.; Kubo, M.; Hachiken, H.; Takemura, S.; Ikeda, M. *J. Heterocycl. Chem.* **1988**, *25*, 327; (b) Miki, Y.; Nakamura, N.; Hachiken, H.; Takemura, S. *J. Heterocycl. Chem.* **1989**, *26*, 1739.

7. (a) Synthesis of compounds **6a–i**, general procedure: To a stirred solution of CSA (23 mg, 0.1 mmol) and the aromatic (3 mmol) in 5 mL of CH_2Cl_2 was added slowly (1 h) pyrazole **3** (140 mg, 1 mmol) in 5 mL of CH_2Cl_2. The resulting mixture was stirred at rt for 1 h, then 15 mL of a saturated $NaHCO_3$ solution and 15 mL of CH_2Cl_2 were added. The organic layer was separated, dried over $MgSO_4$ and concentrated under vacuum. Compounds were purified by column chromatography on silica gel; (b) Spectral data for compounds **6a–i**. Compound **6a**: (white solid) mp: 118 °C ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.55 (s, 5H); 3.75 (s, 6H); 3.77 (s, 3H); 3.90 (s, 3H); 6.64 (s, 2H); 6.88 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 15.5; 39.0; 55.4; 56.0; 56.4; 91.2; 105.3; 110.3; 130.5; 158.9; 159.7; 161.2. MS: 293 $[M+H]^+$. Compound **6b**: (colourless oil) ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.56 (s, 2H); 3.63 (s, 3H); 3.75 (s, 3H); 3.78 (s, 3H); 3.89 (s, 3H); 6.38 (dd, $J = 2.4$ Hz, 8.1 Hz, 1H); 6.42 (d, $J = 2.4$ Hz, 1H); 6.81 (s, 1H); 7.0 (d, $J = 8.1$ Hz, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 20.7; 37.6; 55.2; 55.0; 97.4; 102.8; 103.2; 120.9; 128.8; 129.6; 156.9; 158.2; 160.3. MS: 263 $[M+H]^+$. Compound **6c**: (white solid) mp: 102 °C ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.60 (s, 2H); 3.66 (s, 3H); 3.92 (s, 3H); 6.77 (d, $J = 8.3$ Hz, 2H); 6.86 (s, 1H); 7.07 (d, $J = 8.3$ Hz, 2H); 8.53 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 27.8; 38.9; 56.8; 55.0; 106.0; 115.8; 129.8; 131.4; 132.7; 155.3; 161.6. MS: 219 $[M+H]^+$ IR (KBr) 3000–3300 cm^{-1}. Compound **6d**: (white solid) mp: 180 °C ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.51 (s, 3H); 3.65 (s, 8H); 3.75 (s, 3H); 6.04 (s, 2H); 6.71 (s, 1H); 8.28 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 27.8; 39.2; 55.7; 56.4; 91.2; 105.3; 110.3; 130.5; 155.9; 158.7; 161.2. MS: 279 $[M+H]^+$. IR (KBr) 3000–3300 cm^{-1}. Compound **6e**: (white solid) mp<40 °C ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.57 (s, 3H); 3.78 (s, 2H); 3.93 (s, 3H); 6.78 (s, 1H); 6.90 (s, 1H); 7.00–7.15 (m, 2H); 7.27 (d, $J = 7.5$ Hz, 1H); 7.56 (d, $J = 7.5$ Hz, 1H); 8.23 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 16.2; 36.8; 54.3; 102.8; 109.3; 113.5; 117.2; 120.0; 125.4; 128.8; 134.6; 159.3. MS: 242 $[M+H]^+$. IR (KBr) 3300 cm^{-1}. Compound **6f**: (white solid) mp<40 °C ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.67 (s, 3H); 3.96 (s, 3H); 5.95 (m, 1H); 6.11 (m, 1H); 6.66 (m, 1H); 6.93 (s, 1H); 8.53 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 20.1; 38.0; 55.6; 102.4; 104.3; 107.2; 116.0; 129.7; 130.6; 160.4. MS: 192 $[M+H]^+$. IR (KBr) 3333 cm^{-1}. Compound **6g**: (white solid) mp: 90 °C ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.51 (s, 3H); 3.62 (s, 2H), 3.68 (s, 3H); 3.94 (s, 3H); 5.89 (m, 1H); 6.05 (m, 1H); 6.55 (m, 1H); 6.82 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 19.9; 34.0; 39.2; 56.5; 103.3; 106.8; 106.9; 121.7; 131.0; 132.2; 161.3. MS: 206 $[M+H]^+$. Compound **6h**: (colourless oil) ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.68 (s, 5H); 3.89 (s, 3H); 5.98 (m, 1H); 6.25 (m, 1H); 6.98 (s, 1H); 7.28 (m, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 20.5; 38.1; 55.4; 100.5; 104.5; 109.5; 129.8; 140.3; 153.8; 160.5. MS: 193 $[M+H]^+$. Compound **6i**: (colourless oil) ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.63 (s, 2H); 3.65 (s, 3H); 3.86 (s, 3H); 4.50 (s, 2H); 5.88 (d, $J = 3.1$ Hz, 1H); 6.12 (d, $J = 3.1$ Hz, 1H); 6.98 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 21.7; 39.1; 56.5; 57.7; 101.4; 106.4; 108.9; 131.1; 153.1; 155.0; 161.5. MS: 223 $[M+H]^+$. IR (KBr) 3150 cm^{-1}.

8. (a) Synthesis of alcohols **8a–b**, general procedure: Under nitrogen, to a stirred solution of compound **7** (1.4 g, 10 mmol) in 30 mL of dry THF, was added at −30 °C the organolithium (30 mmol). The resulting mixture was stirred at −30 °C for 3 h then 30 mL of water was added. After extraction with ethyl acetate, the organic layer was dried over $MgSO_4$ and concentrated under vacuum. Then, the residue was purified by flash chromatography on silica gel to give a colourless oil; (b) Spectral data for compounds **8a–b**. Compound **8a**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.56 (s, 3H); 3.61 (s, 3H); 5.31 (s, 1H); 6.84 (s, 1H); 7.23–7.42 (m, 5H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 38.9; 56.2; 73.9; 107.6; 126.5; 127.2; 128.3; 130.6; 142.5; 161.0. MS: 219 $[M+H]^+$. Compound **8b**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.80 (t, $J = 6.9$ Hz, 3H); 1.13–1.37 (m, 4H); 1.52–1.83 (m, 2H); 3.64 (s, 3H); 3.81 (s, 3H); 4.10 (t, $J = 6.9$ Hz, 1H); 7.0 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1; 22.6; 28.2; 36.1; 38.9; 56.1; 72.1; 106.8; 129.8; 161.5. MS: 199 $[M+H]^+$.

9. Synthesis of aldehyde **7**. To a stirred solution of alcholol **3** (1.4 g, 10 mmol) in 40 mL of $CHCl_3$ was added MnO_2 (8.9 g, 100 mmol). The resulting mixture was stirred at rt for 20 h and filtered off, the filtrate was dried over $MgSO_4$ and concentrated under vacuum to give a slighly yellow solid (140 mg, 99%). ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.74 (s, 3H); 3.94 (s, 3H); 7.64 (s, 1H); 9.67 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 40.3; 56.6; 109.6; 134.4; 164.0; 183.2 MS: 141 $[M+H]^+$. IR (KBr) 1734 cm^{-1}.

10. (a) Synthesis of compounds **9a–d**, general procedure: To a stirred solution of CSA (0.1 mmol) and the aromatic (3 mmol) in 5 mL of CH_2Cl_2 was added slowly (1 h) pyrazole **8** (1 mmol) in 5 mL of CH_2Cl_2. The resulting mixture was stirred at rt for 1 h, then 15 mL of a saturated $NaHCO_3$ solution and 15 mL of CH_2Cl_2 were added. The organic layer was separated, dried over $MgSO_4$ and concentrated under vacuum. Compounds were purified by column chromatography on silica gel.
(b) Spectral data for compounds **9a–d**. Compound **9a**: (white solid) mp: 78 °C ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.58 (s, 6H); 3.65 (s, 3H); 3.75 (s, 3H); 3.84 (s, 3H); 5.84 (s, 1H); 6.13 (s, 2H); 6.99 (s, 1H); 7.08–7.15 (m, 5H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 32.9; 38.8; 55.2; 55.9; 56.2; 91.9; 106.4; 114.8; 124.8; 127.5; 132.1; 144.9; 158.8; 159.8; 161.6. MS: 369 $[M+H]^+$. Compound **9b**: (white solid) mp: 92 °C ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.63 (s, 3H); 3.85 (s, 3H); 5.44 (s, 1H); 6.67–6.69 (m, 1H); 6.71 (s, 1H); 6.95–7.02 (m, 1H); 7.11–7.34 (m, 8H); 7.97 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 37.2; 39.0; 56.3; 108.5; 111.1; 119.4; 120.0; 122.1; 123.2; 126.2; 126.9; 128.3; 128.4; 131.4; 136.9; 144.1; 160.9. MS: 318 $[M+H]^+$ IR (KBr) 3315 cm^{-1}. Compound **9c**: (white solid) mp: 52 °C ^{1}H NMR (250 MHz, CCl_3) δ 0.82 (t, $J = 6.9$ Hz, 3H); 1.10–1.31 (m, 4H); 1.85–2.12 (m, 2H); 3.63 (s, 3H); 3.77 (s, 9H); 3.86 (s, 3H); 4.41 (dd, $J = 6.9$, 9.42 Hz, 1H); 6.13 (s, 2H); 6.96 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1; 22.7; 28.5; 30.5; 33.2; 38.7; 55.1; 55.8; 56.2; 91.5; 109.3; 113.7; 130.6; 159.2; 159.3; 161.2. MS: 349 $[M+H]^+$. Compound **9d**: (white solid) mp: 45 °C ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.83–0.88 (m, 3H); 1.25–1.35 (m, 4H); 1.93–2.05 (m, 2H); 3.59 (s, 3H); 3.91 (s, 3H); 4.03 (t, $J = 7.7$ Hz, 1H); 6.82 (s, 1H); 6.96 (d, $J = 2.5$ Hz, 1H); 7.03–7.17 (m, 2H); 7.28 (d, $J = 7.8$ Hz, 1H); 7.59 (d, $J = 7.85$ Hz, 1H); 8.26 (s, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1; 22.7; 30.3; 31.1; 35.6; 38.7; 56.2; 109.8; 111.2; 119.0; 119.6; 120.1; 121.1; 126.9; 129.9; 136.6; 161.1. MS: 298 $[M+H]^+$. IR (KBr) 3305 cm^{-1}.