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Three-component reaction for the C2-functionalization of 1-substituted imidazoles with acetylenic ketones and isocyanates

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ABSTRACT

An efficient method for the direct C2-amidation of 1-substituted imidazoles with acetylenic ketones and isocyanates is reported. This three-component procedure has the advantages of catalyst-free, operational simplicity, mild reaction conditions, and good to excellent yields.

1. Introduction

Functionalized imidazoles are an important class of heterocyclic compounds in organic chemistry because they are common structural units in a number of natural products and pharmaceuticals and useful building blocks for the construction of various biologically active molecules and functional materials.[1] Imidazole-based drugs, such as Cimetidine, Etomidate, and Ketoconazole are currently in clinical use.[2] Other applications of imidazole derivatives include the imidazole-tailored ionic liquids and stable nucleophilic carbenes.[3] Consequently, efforts are focused on the development of methods for the synthesis and functionalization of the imidazole nucleus.[4]

Multicomponent reactions (MCRs) have emerged as a powerful and bond-forming efficient tool in organic, combinatorial, and medicinal chemistry.[5] Using this strategy, C2-founctionalizations of 1-substituted imidazoles have been successfully performed.[6] Considering the continued importance of the imidazole derivatives in both biological and chemical fields, new direct approaches remain highly valuable to the contemporary collection of synthetic methods.

The reactions of zwitterionic adducts of nucleophiles for various organic transformations have received considerable attention.[7] Previously, we have utilized the Huisgen zwitterions to synthesize pyrazolines and triazolinones.[8] In continuation of our efforts to develop MCRs,[9] herein we report a multicomponent reaction strategy for the direct C2-amidation of 1-substituted imidazoles with acetylenic ketones and isocyanates.

2. Results and discussion

Exhaustive studies of the reaction conditions for the synthesis of imidazole **4a** from phenyl acetylenic ketone **1a** with phenylisocyanate **2a** and *N*-methylimidazole **3a** were conducted (Table 1). We first examined the reaction temperature and reaction time in dichloromethane (DCM), and found that the yield was slightly dependent upon the reaction temperature and the time (Table 1, entries 1–5). Furthermore, we examined several organic solvents and found that a remarkable solvent effect existed in this model reaction at room temperature. These results showed that DCM was the most suitable solvent for this transformation among others, such as acetonitrile, toluene, and chloroform (Table 1, entries 5–8). Thus, the most suitable reaction conditions for the formation of **4a** were stablished (Table 1, entry 5).

With the optimized reaction conditions in hand, we next explored the protocol with a variety of acetylenic ketones and isocyanates, and the results were presented in Table 2. From the results of Table 2, the protocol has proven to be useful multicomponent reaction of acetylenic ketones **1a**–**i** with isocyanates **2a**–**k** and imidazoles **3a**–**c** in DCM at room temperature in the absence of any catalyst to afford the corresponding products **4a**-**u** in 72–98%

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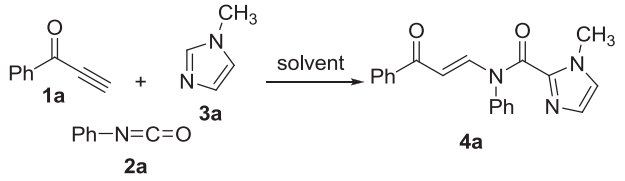
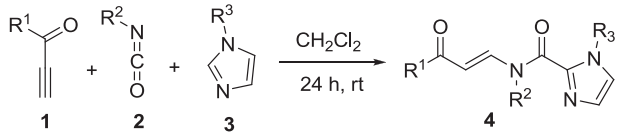
Table 1
Optimization of reaction conditions for the synthesis of **4a**[a]

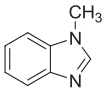


Entry	Temp (°C)	Solvent	Time (h)	Yield[b] (%)
1	0	CH_2Cl_2	24	71
2	Reflux	CH_2Cl_2	24	84
3	rt	CH_2Cl_2	1	72
4	rt	CH_2Cl_2	8	78
5	**rt**	**CH_2Cl_2**	**24**	**84**
6	rt	CH_3CN	24	67
7	rt	PhMe	48	57
8	rt	$CHCl_3$	24	23

Bold values in the table means the optimized reaction conditions.
[a] Reaction conditions: **1a** (1.0 mmol), **2a** (1.0 mmol), **3a** (1.0 mmol), the indicated solvent (5 mL).
[b] Yield of isolated product.

Table 2
Scope of the reaction[a]



Entry	**1** (R^1)	**2** (R^2)	**3** (R^3)	Yield[b] (%)
1	**1a** (Ph)	**2a** (Ph)	**3a**(Me)	**4a**/87
2	**1b** (4-ClC_6H_4)	**2a**	**3a**	**4b**/91
3	**1c** (4-BrC_6H_4)	**2a**	**3a**	**4c**/93
4	**1d** (4-$MeOC_6H_4$)	**2a**	**3a**	**4d**/78
5	**1e** (4-$NO_2C_6H_4$)	**2a**	**3a**	**4e**/73
6	**1f** (4-MeC_6H_4)	**2a**	**3a**	**4f**/88
7	**1g** (Furan-2-)	**2a**	**3a**	**4g**/98
8	**1h** (*n*-C_6H_{13})	**2a**	**3a**	**4h**/72
9	**1i** (PhCH=CH)	**2a**	**3a**	**4i**/74
10	**1a**	**2b** (4-MeC_6H_4)	**3a**	**4j**/78
11	**1a**	**2c** (4-BrC_6H_4)	**3a**	**4k**/82
12	**1a**	**2d** (2-BrC_6H_4)	**3a**	**4l**/96
13	**1a**	**2e** (3-$AcOC_6H_4$)	**3a**	**4m**/90
14	**1a**	**2f** (4-$NO_2C_6H_4$)	**3a**	**4n**/74
15	**1a**	**2g** (4-$CH_3OC_6H_4$)	**3a**	**4o**/92
16	**1a**	**2h** (4-FC_6H_4)	**3a**	**4p**/97
17	**1a**	**2i** (3-ClC_6H_4)	**3a**	**4q**/76
18	**1a**	**2j** (EtOCOCH$_2$)	**3a**	**4r**/95
19	**1a**	**2k** (Cyclohexyl)	**3a**	**4s**/83
20	**1a**	**2a**	**3b** ($PhCH_2$)	**4t**/90
21	**1a**	**2a**	 **3c**	**4u**/82

[a] Reaction conditions: **1** (1.0 mmol), **2** (1.0 mmol), **3** (1.0 mmol), CH_2Cl_2 (5 mL), room temperature, 24 h.
[b] Yield of isolated products.

yields. It should be noted that the reactions with the alkyl acetylenic ketone **1i**, alkyl isocyanates **2j**–**k** or 1-methyl-1*H*-benzo[*d*]imidazole **3c** proceeded smoothly, leading to good yields of products **4** (Table 2, entries 8, 18, 19, and 21).

The structures of products **4a**–**u** were characterized by ^{1}H NMR, ^{13}C NMR, IR and HRMS spectra. The structure of compound **4c** (Table 2, entry 3) was unambiguously confirmed by single-crystal X-ray analysis (Fig. 1).[10]

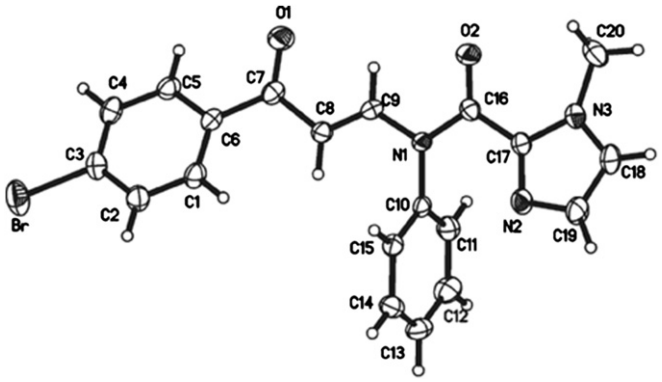
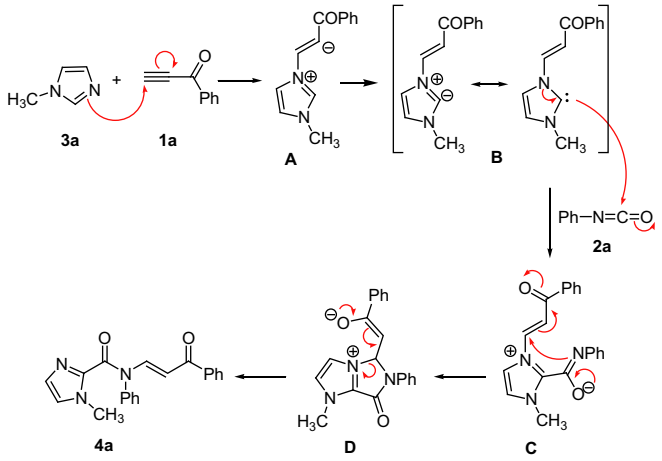


Fig. 1. X-ray crystal structure of **4c**.

Furthermore, a tentative mechanism for this three-component reaction is proposed in Scheme 1. Firstly, the zwitterion **A** is derived from initial nucleophilic addition of imidazole **3a** to acetylenic ketone **1a**.[4,5] Then, the imidazole carbene intermediate **B** forms via proton transfer from position 2 of the imidazole ring to the carbanionic center of **A**. Then, the imidazole carbene intermediate **B** nucleophilically attacks the central carbon of isocyanate **2a** to form the zwitterionic adduct **C**, which undergoes an intramolecular conjugated addition–elimination to yield the final product **4a**.



Scheme 1. Possible mechanism for the formation of **4**.

3. Conclusion

In summary, we have developed an efficient method for the direct C2-amidation of 1-substituted imidazoles via a three-component reaction of 1-substituted imidazoles with acetylenic ketones and isocyanates under mild conditions. The major features of this procedure include: (1) high synthetic efficiency, (2) atom economics, and (3) catalyst-free.

4. Experimental section

4.1. General experimental

Infrared spectra were obtained on an FTIR spectrometer. ^{1}H NMR spectra were recorded on 400 MHz spectrometer unless noted otherwise and the chemical shifts were reported relative to internal standard TMS (0 ppm). The following abbreviations are used to describe peak patterns where appropriate: br=broad, s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet. Coupling constants

are reported in hertz (Hz). ^{13}C NMR were recorded on 100 MHz unless noted otherwise and referenced to the internal solvent signals (central peak is 77.0 ppm for $CDCl_3$ or 40.0 ppm for DMSO-d_6). MS and HRMS were obtained using EI ionization. Melting points were measured with micro melting point apparatus.

DCM was distilled from phosphorous pentoxide, and CH_3CN was distilled from CaH_2, while THF and toluene were distilled from Na/benzophenone, respectively. The propynones were prepared via the nucleophilic addition of ethynylmagnesium bromides to aldehydes and then oxidation with IBX.[11]

4.2. General procedure for the synthesis of imidazoles 4

To a solution of acetylenic ketone **1** (1.0 mmol) and *N*-alkylimmidazole **3** (1.0 mmol) in DCM (5 mL) was slowly added isocyanate **2** (1.0 mmol) through a syringe under nitrogen atmosphere over 3–5 min. The reaction mixture was stirred at room temperature for 24 h. After the solvent was removed under reduced pressure, the residue was subject to flash chromatography on silica gel (petroleum ether/ethyl acetate, 2:1 to 1:1) to afford pure **4**.

*4.2.1. (E)-1-Methyl-N-(3-oxo-3-phenylprop-1-enyl)-N-phenyl-1H-imidazole-2-carboxamide (**4a**).* Yellow solid, mp 149–151 °C; IR: 1646, 1570, 1402, 1251, 1168, 1040, 954, 643 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.35 (d, J=13.6 Hz, 1H), 7.75–7.73 (m, 2H), 7.54–7.49 (m, 2H), 7.47–7.45 (m, 2H), 7.39–7.37 (m, 2H), 7.30–7.28 (m, 2H), 7.13 (s, 1H), 7.03 (s, 1H), 5.96 (d, J=13.6 Hz, 1H), 3.93 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.4, 160.1, 147.0, 138.4, 138.1, 132.2, 129.9, 129.1, 128.9, 128.3, 128.2, 128.1, 125.9, 107.6, 35.7 ppm; HRMS (EI): m/z calcd for $C_{20}H_{17}N_3O_2$ ([M]$^+$): 331.1321; found: 331.1324.

*4.2.2. (E)-N-(3-(4-Chlorophenyl)-3-oxoprop-1-enyl)-1-methyl-N-phenyl-1H-imidazole-2-carboxamide (**4b**).* Yellow solid, mp 157–159 °C; IR: 1659, 1583, 1397, 1249, 1203, 1149, 1029, 971 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.35 (d, J=13.2 Hz, 1H), 7.67 (d, J=8.8 Hz, 2H), 7.54–7.41 (m, 2H), 7.48–7.44 (m, 1H), 7.32 (d, J=8.4 Hz, 2H), 7.28–7.25 (m, 2H), 7.13 (s, 1H), 7.03 (s, 1H), 5.88 (d, J=13.2 Hz, 1H), 3.92 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 189.4, 160.3, 147.8, 138.8, 138.3, 137.0, 130.2, 129.9, 129.4, 129.3, 128.9, 128.4, 126.3, 107.2, 36.1 ppm; HRMS (EI): m/z calcd for $C_{20}H_{16}ClN_3O_2$ ([M]$^+$): 365.0931; found: 365.0934.

*4.2.3. (E)-N-(3-(4-Bromophenyl)-3-oxoprop-1-enyl)-1-methyl-N-phenyl-1H-imidazole-2-carboxamide (**4c**).* Light yellow solid, mp 175–177 °C; IR: 1659, 1580, 1395, 1288, 1202, 1149, 1028, 817 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.36 (d, J=13.6 Hz, 1H), 7.60 (d, J=8.0 Hz, 2H), 7.55–7.45 (m, 5H), 7.29–7.25 (m, 2H), 7.13 (s, 1H), 7.04 (s, 1H), 5.87 (d, J=13.6 Hz, 1H), 3.93 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 189.6, 160.3, 147.9, 138.3, 138.2, 137.5, 131.9, 130.2, 130.0, 129.4, 129.3, 128.4, 127.4, 126.3, 107.2, 36.1 ppm; HRMS (EI): m/z calcd for $C_{20}H_{16}BrN_3O_2$ ([M]$^+$): 409.0426; found: 409.0434.

*4.2.4. (E)-N-(3-(4-Methoxyphenyl)-3-oxoprop-1-enyl)-1-methyl-N-phenyl-1H-imidazole-2-carboxamide (**4d**).* Light yellow solid, mp 177–178 °C; IR 1657, 1583, 1399, 1251, 1152, 1015, 817 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.31 (d, J=13.2 Hz, 1H), 7.76 (d, J=9.2 Hz, 2H), 7.57–7.46 (m, 3H), 7.31 (d, J=8.0 Hz, 2H), 7.15 (s, 1H), 7.04 (s, 1H), 6.87 (d, J=8.8 Hz, 2H), 5.99 (d, J=13.2 Hz, 1H), 3.95 (s, 3H), 3.83 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 188.9, 163.3, 160.4, 146.4, 138.6, 138.5, 131.6, 130.6, 130.1, 129.3, 129.1, 128.5, 126.0, 113.8, 107.6, 55.6, 35.9 ppm; HRMS (EI): m/z calcd for $C_{21}H_{19}N_3O_3$ ([M]$^+$): 361.1426; found, 361.1425.

*4.2.5. (E)-1-Methyl-N-(3-(4-nitrophenyl)-3-oxoprop-1-enyl)-N-phenyl-1H-imidazole-2-carboxamide (**4e**).* Yellow solid, mp 170–172 °C; IR: 1674, 1595, 1513, 1420, 1264, 1178, 1074, 849 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.48 (d, J=13.6 Hz, 1H), 8.23 (d, J=8.8 Hz, 2H), 7.89 (d, J=8.8 Hz, 2H), 7.59–7.49 (m, 3H), 7.30 (d, J=7.2 Hz, 2H), 7.16 (s, 1H), 7.08 (s, 1H), 5.88 (d, J=13.6 Hz, 1H), 3.97 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 189.2, 160.1, 150.0, 149.2, 143.8, 138.1, 138.0, 130.3, 129.5, 129.4, 129.3, 128.3, 126.6, 123.8, 107.2, 36.2 ppm; HRMS (EI): m/z calcd for $C_{20}H_{16}N_4O_4$ ([M]$^+$): 376.1172; found: 376.1176.

*4.2.6. (E)-1-Methyl-N-(3-oxo-3-p-tolylprop-1-enyl)-N-phenyl-1H-imidazole-2-carboxamide (**4f**).* Yellow solid, mp 142–144 °C; IR: 1658, 1583, 1399, 1250, 1148, 1030, 973, 815 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.33 (d, J=13.6 Hz, 1H), 7.67 (d, J=8.0 Hz, 2H), 7.56–7.46 (m, 3H), 7.30 (d, J=7.6 Hz, 2H), 7.18 (d, J=8.4 Hz, 2H) 7.14 (s, 1H), 7.04 (s, 1H), 5.98 (d, J=13.6 Hz, 1H), 3.94 (s, 3H), 2.36 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 189.8, 160.1, 146.5, 142.9, 138.2, 138.1, 135.8, 129.8, 129.0, 128.9, 128.8, 128.2, 128.1, 125.8, 107.5, 35.6, 21.5 ppm; HRMS (EI): m/z calcd for $C_{21}H_{19}N_3O_2$ ([M]$^+$): 345.1477; found: 345.1479.

*4.2.7. (E)-N-(3-(Furan-2-yl)-3-oxoprop-1-enyl)-1-methyl-N-phenyl-1H-imidazole-2-carboxamide (**4g**).* Yellow solid, mp 188–190 °C; IR: 1644, 1569, 1490, 1410, 1251, 1173, 1080, 1034 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.38 (d, J=14.0 Hz, 1H), 7.56–7.47 (m, 4H), 7.29 (d, J=7.5 Hz, 2H), 7.15 (s, 1H), 7.07–7.06 (m, 2H), 6.47–6.46 (m, 1H), 5.89 (d, J=14.0 Hz, 1H), 3.95 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 178.5, 160.3, 153.7, 146.2, 146.0, 138.3, 138.2, 130.0, 129.3, 129.0, 128.3, 126.2, 116.6, 112.4, 107.1, 35.9 ppm; HRMS (EI): m/z calcd for $C_{18}H_{15}N_3O_2$ ([M]$^+$): 321.1113; found: 321.1118.

*4.2.8. (E)-1-Methyl-N-(3-oxooct-1-enyl)-N-phenyl-1H-imidazole-2-carboxamide (**4h**).* Colorless oil; IR: 1651, 1626, 1456, 1402, 1277, 1248, 1156, 968 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.21 (d, J=14.4 Hz, 1H), 7.43–7.32 (m, 3H), 7.13–7.11 (m, 2H), 7.03 (s, 1H), 6.95 (s, 1H) 5.14 (d, J=14.0 Hz, 1H), 3.86 (s, 3H), 2.38 (t, J=7.6 Hz, 2H), 1.54–1.47 (m, 2H), 1.24–1.17 (m, 4H), 0.80–0.77 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.2, 159.7, 144.8, 138.2, 137.8, 129.8, 128.8, 128.7, 128.2, 125.8, 112.1, 40.5, 35.8, 31.5, 24.3, 22.4, 13.9 ppm; HRMS (EI): calcd for $C_{19}H_{23}N_3O_2$ ([M]$^+$): 325.1790; found: 325.1784.

*4.2.9. 1-Methyl-N-((1E,4E)-3-oxo-5-phenylpenta-1,4-dienyl)-N-phenyl-1H-imidazole-2-carboxamide (**4i**).* Yellow oil; IR: 1669, 1610, 1568, 1405, 1248, 1162, 1093, 728 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.36 (d, J=13.5 Hz, 1H), 7.51–7.31 (m, 6H), 7.29–7.25 (m, 3H), 7.22–7.20 (m, 2H), 7.08 (s, 1H), 7.00 (s, 1H), 6.82 (d, J=15.5 Hz, 1H), 5.46 (d, J=13.5 Hz, 1H), 3.87 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 188.5, 159.8, 145.8, 142.0, 138.1, 138.0, 134.9, 130.2, 129.9, 129.0, 128.9, 128.8, 128.7, 128.2, 126.1, 125.4, 111.5, 35.9 ppm; HRMS (EI): m/z calcd for $C_{22}H_{19}N_3O_2$ ([M]$^+$): 357.1477; found: 357.1470.

*4.2.10. (E)-1-Methyl-N-(3-oxo-3-phenylprop-1-enyl)-N-p-tolyl-1H-imidazole-2-carboxamide (**4j**).* Yellow solid, mp 139–141 °C; IR: 1647, 1561, 1508, 1404, 1247, 1211, 1015, 768 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.35 (d, J=13.6 Hz, 1H), 7.78–7.76 (m, 2H), 7.50–7.46 (m, 1H), 7.41–7.33 (m, 4H), 7.19–7.15 (m, 3H), 7.04 (s, 1H), 6.00 (d, J=13.6 Hz, 1H), 3.94 (s, 3H) 2.44 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.7, 160.4, 147.4, 139.1, 138.7, 138.4, 135.5, 132.4, 130.8, 129.3, 128.5, 128.3, 128.0, 126.1, 107.7, 35.9, 21.5 ppm; HRMS (EI): m/z calcd for $C_{21}H_{19}N_3O_2$ ([M]$^+$): 345.1477; found: 345.1479.

*4.2.11. (E)-N-(4-Bromophenyl)-1-methyl-N-(3-oxo-3-phenylprop-1-enyl)-1H-imidazole-2-carboxamide (**4k**).* Yellow solid, mp 159–161 °C; IR: 1649, 1563, 1420, 1247, 1158, 1012, 798, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.31 (d, J=13.6 Hz, 1H), 7.78–7.76 (m, 2H), 7.68–7.66 (m, 2H), 7.51–7.37 (m, 3H), 7.20 (d, J=8.8 Hz, 2H),

7.14 (s, 1H), 7.06 (s, 1H), 5.91 (d, J=13.6 Hz, 1H), 3.94 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.1, 159.6, 146.4, 138.3, 137.8, 137.2, 133.2, 132.4, 130.0, 129.0, 128.4, 128.1, 126.1, 122.9, 107.6, 35.8 ppm; HRMS (EI): m/z calcd for $C_{20}H_{16}BrN_3O_2$ ($[M]^+$): 409.0426; found: 409.0419.

*4.2.12. (E)-N-(2-Bromophenyl)-1-methyl-N-(3-oxo-3-phenylprop-1-enyl)-1H-imidazole-2-carboxamide (**4l**).* White solid, mp 141–143 °C; IR: 1684, 1654, 1564, 1405, 1247, 1160, 1014, 778 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.25 (br s, 1H), 7.76–7.71 (m, 3H), 7.51–7.48 (m, 3H), 7.40–7.33 (m, 3H), 7.07–7.03 (m, 2H), 5.84 (d, J=14.0 Hz, 1H), 3.95 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.5, 158.8, 138.4, 137.7, 137.2, 133.8, 132.3, 130.6, 130.5, 129.0, 128.5, 128.3, 128.2, 125.8, 125.7, 122.6, 107.8, 35.8 ppm; HRMS (EI): m/z calcd for $C_{20}H_{16}BrN_3O_2$ ($[M]^+$): 409.0426; found: 409.0436.

*4.2.13. (E)-N-(3-Acetylphenyl)-1-methyl-N-(3-oxo-3-phenylprop-1-enyl)-1H-imidazole-2-carboxamide (**4m**).* Dark yellow solid, mp 178–180 °C; IR: 1660, 1565, 1442, 1252, 1170, 1015, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.38 (d, J=13.2 Hz, 1H), 8.07 (d, J=5.6 Hz, 1H), 7.88 (s, 1H), 7.75–7.65 (m, 3H), 7.54–7.46 (m, 2H), 7.40–7.36 (m, 2H), 7.13 (s, 1H), 7.05 (s, 1H), 5.91 (d, J=13.2 Hz, 1H), 3.94 (s, 3H), 2.62 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.4, 160.3, 159.6, 147.3, 138.5, 138.2, 132.2, 130.6, 129.1, 129.0, 128.3, 128.1, 125.8, 115.1, 107.4, 55.5, 35.7 ppm; HRMS (EI): m/z calcd for $C_{22}H_{19}N_3O_3$ ($[M]^+$): 373.1426; found: 373.1434.

*4.2.14. (E)-1-Methyl-N-(4-nitrophenyl)-N-(3-oxo-3-phenylprop-1-enyl)-1H-imidazole-2-carboxamide (**4n**).* Yellow solid, mp 185–187 °C; IR: 1647, 1565, 1517, 1400, 1252, 1173, 1035, 670 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.28 (d, J=14.0 Hz, 1H), 8.40 (d, J=8.5 Hz, 2H), 7.75 (d, J=7.5 Hz, 2H), 7.51–7.50 (m, 3H), 7.40 (t, J=7.5 Hz, 2H), 7.10 (s, 1H), 7.07 (s, 1H), 5.98 (d, J=14.0 Hz, 1H), 3.97 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 190.0, 159.5, 147.8, 145.8, 144.5, 138.3, 137.6, 132.8, 129.9, 129.6, 128.7, 128.3, 126.7, 125.5, 108.0, 36.2 ppm; HRMS (EI): m/z calcd for $C_{20}H_{16}N_4O_4$ ($[M]^+$): 376.1172; found: 376.1175.

*4.2.15. (E)-N-(4-Methoxyphenyl)-1-methyl-N-(3-oxo-3-phenylprop-1-enyl)-1H-imidazole-2-carboxamide (**4o**).* Light yellow solid, mp 150–151 °C; IR: 1650, 1565, 1408, 1251, 1168, 1014, 776, 639 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.33 (d, J=13.6 Hz, 1H), 7.76–7.74 (m, 2H), 7.48–7.35 (m, 3H), 7.20–7.04 (m, 3H), 7.04–7.02 (m, 3H), 5.99 (d, J=13.6 Hz, 1H), 3.91 (s, 3H) 3.85 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.3, 1630.3, 159.5, 147.3, 138.4, 138.1, 132.2, 130.5, 129.1, 129.0, 128.3, 128.1, 125.8, 115.1, 1107.3, 55.4, 35.7 ppm; HRMS (EI): m/z calcd for $C_{21}H_{19}N_3O_3$ ($[M]^+$): 361.1426; found: 361.1430.

*4.2.16. (E)-N-(4-Fluorophenyl)-1-methyl-N-(3-oxo-3-phenylprop-1-enyl)-1H-imidazole-2-carboxamide (**4p**).* White solid, mp 180–181 °C; IR: 1647, 1567, 1504, 1399, 1249, 1170, 1013, 778 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.35 (d, J=13.2 Hz, 1H), 7.78–7.75 (m, 2H), 7.51–7.38 (m, 3H), 7.31–7.21 (m, 4H), 7.14 (s, 1H), 7.05 (s, 1H), 5.97 (d, J=13.2 Hz, 1H), 3.95 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.2, 160.0, 146.9, 138.3, 137.9, 134.0, 132.3, 130.1, 130.0, 129.1, 128.3, 128.1, 126.1, 117.1, 107.4, 35.8 ppm; HRMS (EI): m/z calcd for $C_{20}H_{16}FN_3O_2$ ($[M]^+$): 349.1227; found: 349.1227.

*4.2.17. (E)-N-(3-Chlorophenyl)-1-methyl-N-(3-oxo-3-phenylprop-1-enyl)-1H-imidazole-2-carboxamide (**4q**).* White solid, mp 199–201 °C; IR: 1646, 1569, 1402, 1253, 1216, 1042, 1019, 755 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.34 (d, J=13.6 Hz, 1H), 7.78 (d, J=7.2 Hz, 2H), 7.52–7.47 (m, 3H), 7.43–7.32 (m, 3H), 7.25–7.22 (m, 1H), 7.16 (s, 1H), 7.07 (s, 1H), 5.97 (d, J=13.6 Hz, 1H), 3.96 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.2, 159.7, 146.6, 139.2, 138.3, 137.8, 135.3, 132.3, 130.8, 129.3, 129.2, 128.6, 128.4, 128.2, 126.6, 126.2, 107.6, 35.8 ppm; HRMS (EI): m/z calcd for $C_{20}H_{16}ClN_3O_2$ ($[M]_+$): 365.0931; found: 365.0936.

*4.2.18. (E)-Ethyl 2-(1-methyl-N-(3-oxo-3-phenylprop-1-enyl)-1H-imidazole-2-carboxamido)acetate (**4r**).* White solid, mp 102–103 °C; IR: 1738, 1649, 1588, 1568, 1409, 1275, 1198, 1133 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.19 (br s, 1H), 7.88 (d, J=7.2 Hz, 2H), 7.51–7.42 (m, 3H), 7.15 (s, 1H), 7.02 (s, 1H), 6.31 (d, J=14.0 Hz, 1H), 4.78 (br s, 2H), 4.24 (q, J=7.6 Hz, 2H), 3.93 (s, 3H), 1.28 (t, J=7.2 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.2, 167.5, 159.9, 138.5, 137.6, 132.2, 129.0, 128.4, 128.2, 126.1, 105.1, 76.5, 61.8, 35.8, 14.1 ppm; HRMS (EI): m/z calcd for $C_{18}H_{19}N_3O_4$ ($[M]^+$): 341.1376; found: 341.1368.

*4.2.19. (E)-N-Cyclohexyl-1-methyl-N-(3-oxo-3-phenylprop-1-enyl)-1H-imidazole-2-carboxamide (**4s**).* White solid, mp 141–143 °C; IR: 1642, 1549, 1409, 1255, 1203, 1042, 1116, 781 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.53 (d, J=14.0 Hz, 1H), 7.90 (d, J=8.0 Hz, 2H), 7.52–7.41 (m, 3H), 7.12 (s, 1H), 7.00 (s, 1H), 6.69 (d, J=14.0 Hz, 1H), 4.22–4.15 (m, 1H), 3.88 (s, 3H), 2.25–2.16 (m, 2H), 1.88–1.69 (m, 5H), 1.42–1.22 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.7, 161.9, 146.1, 138.9, 138.8, 132.1, 128.8, 128.3, 128.1, 125.6, 104.7, 58.4, 35.8, 29.2, 26.3, 25.3 ppm; HRMS (EI): m/z calcd for $C_{20}H_{23}N_3O_2$ ($[M]^+$): 337.1790; found: 337.1790.

*4.2.20. (E)-1-Benzyl-N-(3-oxo-3-phenylprop-1-enyl)-N-phenyl-1H-imidazole-2-carboxamide (**4t**).* White solid, mp 179–180 °C; IR: 1649, 1561, 1420, 1250, 1206, 1158, 1009, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.18 (d, J=13.2 Hz, 1H), 7.76–7.74 (m, 2H), 7.51–7.44 (m, 4H), 7.40–7.32 (m, 5H), 7.22–7.07 (m, 6H), 5.96 (d, J=13.6 Hz, 1H), 5.50 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.2, 160.2, 146.2, 138.4, 138.1, 136.2, 132.2, 129.8, 129.1, 128.9, 128.3, 128.2, 128.1, 128.0, 127.7, 124.5, 107.8, 51.4 ppm; HRMS (EI): m/z calcd for $C_{26}H_{21}N_3O_2$ ($[M]^+$): 407.1634; found: 407.1635.

*4.2.21. (E)-1-Methyl-N-(3-oxo-3-phenylprop-1-enyl)-N-phenyl-1H-benzo[d]imidazole-2-carboxamide (**4u**).* White solid, mp 185–186 °C; IR: 1647, 1563, 1484, 1296, 1225, 1163, 1020, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.21 (d, J=13.6 Hz, 1H), 7.85–7.77 (m, 3H), 7.58–7.48 (m, 4H), 7.44–7.35 (m, 7H), 6.06 (d, J=13.6 Hz, 1H), 4.03 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.4, 161.1, 145.9, 142.8, 141.5, 138.2, 137.6, 135.8, 132.3, 130.0, 129.2, 128.4, 128.2, 128.1, 125.4, 123.6, 121.6, 110.2, 108.8, 31.7 ppm; HRMS (EI): m/z calcd for $C_{24}H_{19}N_3O_2$ ($[M]^+$): 381.1477; found: 381.1476.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.08.069.

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10. CCDC 807582 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif
11. Propynones were prepared according to the literature method Kueny-Stotz, M.; Isorez, G.; Chassaing, S.; Brouillard, R. *Synlett* **2007**, 1226.