DOI: 10.1002/ejoc.201101346

Synthesis of α,β-Diketotriazoles by Aerobic Copper-Catalyzed Oxygenation with Triazole as an Intramolecular Assisting Group

Christophe Menendez,[a,b] Sylvain Gau,[a,b] Sonia Ladeira,[c] Christian Lherbet,*[a,b] and Michel Baltas*[a,b]

Keywords: Ketotriazoles / Diketotriazoles / Copper / Oxidation / Synthesis design

The catalytic oxidation of α-ketotriazoles to α,β-diketotriazoles was performed with $CuCl_2$ or CuI/2,9-dimethyl-1,10-phenanthroline in air at 80 °C in good yields. Studies showed that the triazole group participates in complexation to the copper and favors oxidation.

Introduction

1,2-Diketones have found widespread application as molecular building blocks for the synthesis of various biologically active heterocyclic compounds. Moreover, they are versatile building blocks for the synthesis of imidazoles,[1,2] quinoxalines,[3] triazines,[4] and other heterocycles. The 1,2-diketone framework can be prepared by different procedures, which have been described in the literature.[5] A typical method is the oxidation of alkynes to α-diketones in the presence of different catalysts.[6,7] For example, Ren et al. have reported the oxidation of alkynes to afford 1,2-diketones, which is catalyzed by $PdBr_2$ and $CuBr_2$.[8] Chen et al. have used a ruthenium complex for the first catalytic oxidation of alkenes at room temperature.[9] Another approach starts from 1,2-diols[10] with (2,2,6,6-tetramethylpiperidin-1-yl)oxyl as the catalyst and iodobenzene chloride as a stoichiometric oxidant or from 1,3-diols[11] using 2-iodoxybenzoic acid. Moghaddam et al. have reported the aerobic oxidation of aryl thioacetamides into the corresponding α-keto aryl thioamides in good yields with copper(II) chloride as a catalyst. 1,2-Diketones have also been prepared by the oxidation of α-hydroxy ketones with copper as, for example, copper-containing hydrotalcite[12] or the "copper(II)/cesium carbonate system"[13] in aerobic conditions. Zhang et al. have reported the synthesis of 1,2-diketones from 1,3-diketones with $FeCl_3$ as the catalyst and *tert*-butyl nitrite as the oxidant.[14]

We have recently reported the synthesis of α-ketotriazoles and related systems as potential inhibitors of InhA, an enoyl-ACP reductase enzyme of the type II fatty acid synthesis (FAS-II) system. During the synthesis of ketotriazole **2a** by click chemistry[15] starting from trimethylsilyl (TMS) ynone and benzyl azide under the conditions shown in Figure 1, we discovered the presence of a side product. Mass

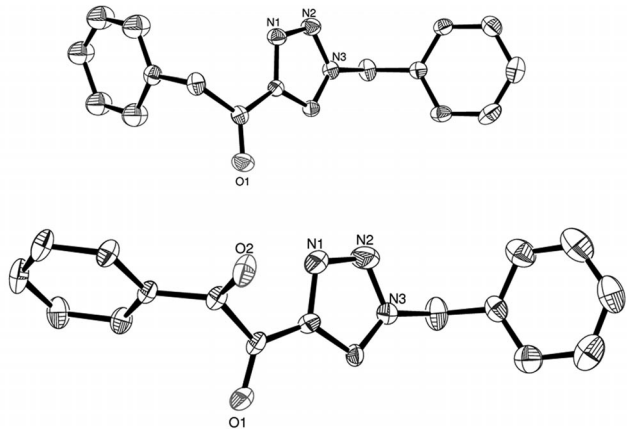
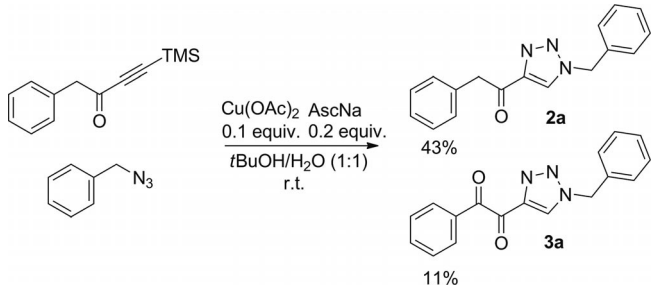


Figure 1. ORTEP[17] view of **2a** (top) and **3a** (bottom). Thermal ellipsoids are shown at 30% probability. Hydrogen atoms are omitted for clarity. Crystallographic data for **2a** and **3a** can be found in the Supporting Information.



Scheme 1. Side product observed during click chemistry.

[a] CNRS, Laboratoire de Synthèse et Physico-Chimie de Molécules d'Intérêt Biologique, SPCMIB, UMR-5068
118 Route de Narbonne, 31062 Toulouse cedex 9, France
Fax: +33-5-61556011
[b] Université de Toulouse, UPS, Laboratoire de Synthèse et Physico-Chimie de Molécules d'Intérêt Biologique, SPCMIB, 118 route de Narbonne, 31062 Toulouse cedex 9, France
[c] Institut de Chimie de Toulouse, FR2599
118 Route de Narbonne, 31062 Toulouse, France
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201101346.

spectrometric and NMR spectroscopic analysis indicated the possible oxidation of **2a** to afford the 1,2-diketone **3a** (Scheme 1).

In this paper, we wish to report our investigations on a copper-dependent method to produce α,β-diketotriazoles from α-ketotriazoles in air by employing triazole as an intramolecular assisting group.

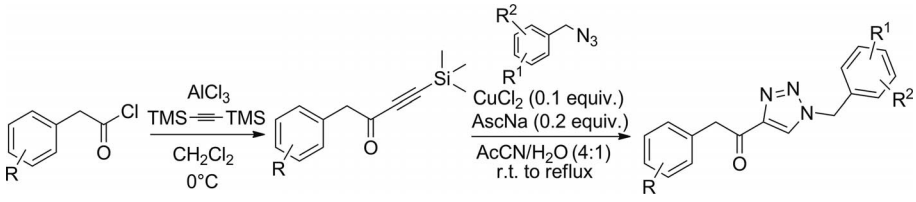
Results and Discussion

The starting materials were readily available from copper-catalyzed alkyne–azide cycloaddition reactions.[16] They were synthesized in a one-pot procedure by the in situ deprotection of TMS-ynone and cyclization with different azides (Scheme 2). The results are summarized in Table 1. The yields remained good regardless of the alkyl or benzyl groups, which bear various electron-donating or electron-withdrawing substituents.

In order to gain insight into the second transformation, we initiated our investigation using **2a** as the model substrate to establish a general procedure for the oxidation. A series of reaction conditions were screened, and the results are summarized in Table 2. The reaction was monitored by TLC until the disappearance of the starting material. We first conducted the reaction with copper(II) catalysts, such as $Cu(OAc)_2$ and $CuCl_2$, in the presence or absence of 1,10-phenanthroline derivatives (Table 2, Entries 1–3).

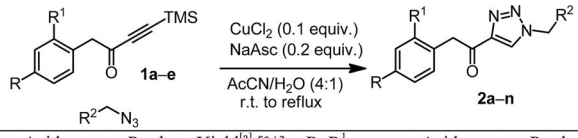
In preliminary experiments on the reaction conditions for the preparation of **2a**, we noted that with prolonged reaction times, a secondary product was formed, which was identified as the 1,2-diketone **3a**. Its structure was confirmed by X-ray crystallography, which showed that oxidation of the methylene occurred (Figure 1). To the best of our knowledge, this is the first reported synthesis of a α,β-diketotriazole framework.

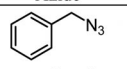
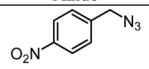
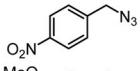
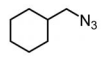
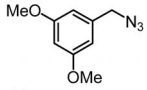
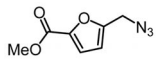
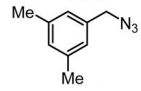
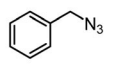
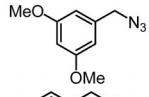
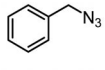
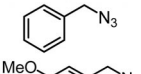
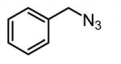
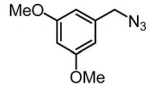
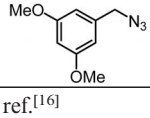
The best yield (55%) was obtained with $CuCl_2$ in the presence of 2,9-dimethyl-1,10-phenanthroline with heating



Scheme 2. Synthesis of α-ketotriazole derivatives **2a**–**n**.

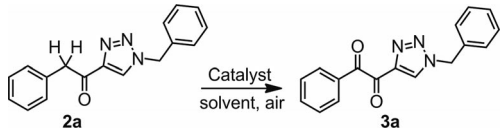
Table 1. Synthesis of triazoles.



R, R[1]	Azide	Product	Yield[a] [%]	R, R[1]	Azide	Product	Yield[a] [%]
H, H		**2a**	90[b]	Cl, Cl		**2i**	86[b]
H, H		**2b**	84[b]	Cl, Cl		**2j**	63
H, H		**2c**	63[b]	Cl, Cl		**2k**	73
H, H		**2d**	80[b]	NO_2, H		**2l**	79
H, H	Octyl azide	**2e**	69[b]	NO_2, H		**2m**	52
OMe, H		**2f**	57	H, OMe		**2n**	80
Cl, Cl		**2g**	86[b]	H, OMe		**2o**	74
Cl, Cl		**2h**	67[b]				

[a] Isolated yields. [b] Published in ref.[16]

Table 2. Screening of reaction conditions for the oxidation of α-ketotriazole.



2a 3a

Entry	Catalyst (equiv.)	Solvent	Conditions	Yield[a] [%]
1	$Cu(OAc)_2$ (0.1), 1,10-phenanthroline (0.2)	CH_3CN	reflux, 20 h	40
2	$CuCl_2$ (0.1), 1,10-phenanthroline (0.2)	CH_3CN	reflux, 20 h	43
3	$CuCl_2$ (0.1), 2,9-dimethyl-1,10-phenanthroline (0.2)	CH_3CN	reflux, 20 h	55
4	$CuCl_2$ (0.1), K_2CO_3 (1), 2,9-dimethyl-1,10-phenanthroline (0.2)	DMF	reflux, 2 h	32
5	$Cu(OAc)_2$ (0.1), Na ascorbate (0.2)	CH_3CN	r.t., 48 h	17
6	$Cu(OAc)_2$ (0.1), Na ascorbate (0.2)	CH_3CN	reflux, 3 h	39
7	CuI (0.1)	CH_3CN	reflux, 7 h	37
8	CuI (0.1), 2,9-dimethyl-1,10-phenanthroline (0.2)	CH_3CN	reflux, 2 h	55
9	CuCl (0.1), 2,9-dimethyl-1,10-phenanthroline (0.2)	CH_3CN	reflux, 2 h	52
10	CuI (0.1), K_2CO_3 (1), 2,9-dimethyl-1,10-phenanthroline (0.2)	CH_3CN	reflux, 2 h	53
11	CuI (0.1), 2,9-dimethyl-1,10-phenanthroline (0.2)	CH_3CN	60 °C, 2 h	34
12	CuI (0.1), O_2 balloon, 2,9-dimethyl-1,10-phenanthroline (0.2)	CH_3CN	reflux, 30 min	59

[a] Isolated yields.

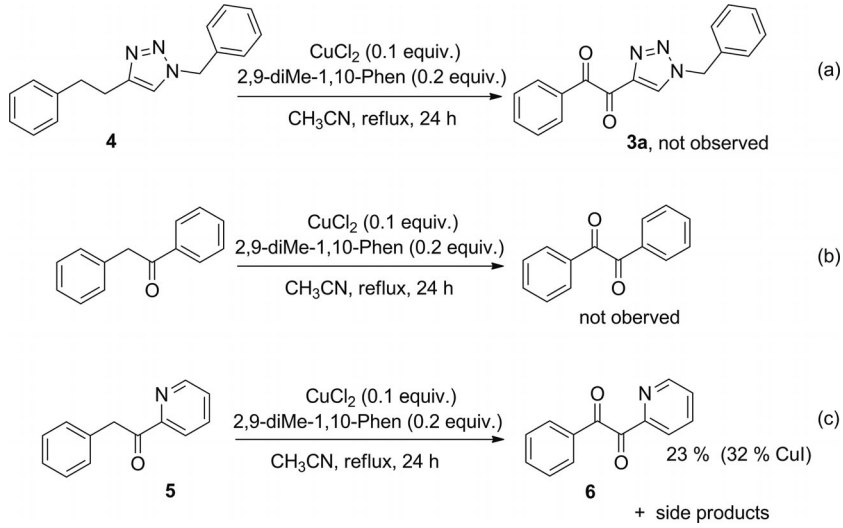
under reflux. The reaction was less efficient in *N*,*N*-dimethylformamide (DMF) in the presence of K_2CO_3 (Entry 4). For each reaction, side products were observed, a major one of which was identified as benzaldehyde.

Copper(I) was also investigated and was first generated in the presence of copper acetate and sodium ascorbate (NaAsc) at room temperature (Entries 5 and 6). Heating under reflux shortened the reaction time remarkably to 3 h to afford **3a** in 39% yield (Entry 6). When copper iodide alone was used as the Cu^I source, a 37% yield of **3a** was obtained after 7 h of heating to reflux. The introduction of 0.2 equiv. of 2,9-dimethyl-1,10-phenanthroline afforded a much better yield of **3a** in only 2 h with heating to reflux (Entry 8). The addition of CuCl instead of CuI (Entry 9) or base (Entry 10) did not improve the yield, even at a lower temperature (Entry 11) to avoid the formation of side products.

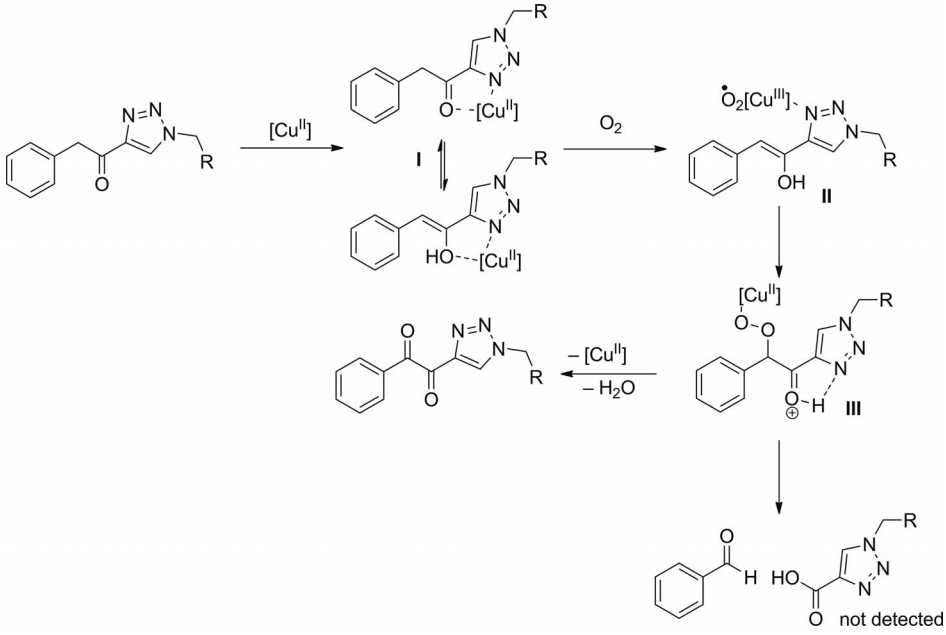
We have also performed the reaction under O_2. After 30 min of heating under reflux in acetonitrile, **3a** was obtained in 59% yield after silica gel purification (Entry 12). Finally, when the reaction was carried out under nitrogen, no product was observed, which demonstrates that oxygen has a direct effect on the process.

In order to verify the generality of our method, we extended it to different α-ketotriazoles with different substituents on the aromatic moieties (Table 3).[18] As with the results shown in Table 2, the reaction was monitored by looking at the disappearance of the starting material by TLC. Two different sources of copper, $CuCl_2$ and CuI, were used for comparison.

In general, the yields for the reactions performed in the presence of CuI are similar or better except for Entries 7 and 9 (Table 3). The substrate with a benzylic group that bears an electron-rich *p*-methoxy substituent seems to be oxidized in a way similar to that of the parent benzylic group (Entry 6 compared to Entry 1). In the case of substrates with electron-poor substituents, oxidation to the corresponding 1,2-diketone is quite similar (Entries 12 and 13).



Scheme 3. Investigations on the reaction mechanism.



Scheme 4. Possible mechanism for the oxidation reaction.

The presence of substituents in the 2-position on the aryl moiety seems to favor oxidation. Indeed, when chloro or methoxy substituents are present, α,β-diketones were obtained in good yields (Entries 7, 8, 14, and 15). In all cases, either with copper(II) or copper(I), substituted benzaldehydes were observed by ^{1}H NMR spectroscopy in the crude mixtures. For example, *p*-methoxybenzaldehyde was obtained as a major byproduct in 25% yield for Entry 6 with copper(II) and *p*-nitrobenzaldehyde in 20 and 33% yield for Entries 12 and 13, respectively (Table 3).

We conducted further studies in order to gain insights into the mechanism (Scheme 3). First, **3a** was not obtained from **4**, which bears a methylene group instead of a carbonyl group. The same result was obtained with deoxybenzoin. Under copper-mediated conditions, no trace of product was observed. Finally, and most interestingly, when phenylacetylpyridine **5** was used as a substrate, the corresponding diketone **6** was observed in 32% yield with CuI as catalyst, which strongly suggests that nitrogen participates in the oxidation reaction through copper chelation.

Aerobic oxidation reactions that use transition metals are receiving considerable attention, and directing group assisted inter/intramolecular C–H functionalization is considered to be one of the most promising approaches for new C–C (or heteroatom) bond formation. Recently, Ohno et al. have reported Cu^{II}-mediated oxidative intermolecular functionalization, which uses tetrahydropyrimidine as a directing group for the introduction of oxygen or nitrogen at the *ortho* position on the aromatic ring.[19] The results indicated that this reaction is sensitive to the presence of electron-withdrawing groups on the aromatic ring.

Zhu et al. have reported direct access to formyl-substituted imidazoles and other aromatic N-heterocycles through an intramolecular dehydrogenerative aminooxygenation via a proposed pyridine–Cu^{III} intermediate in the presence of oxygen.[20] Chiba et al. have reported the first copper-catalyzed benzylic C–H oxygenation under oxygen with N–H imines as intramolecular directing groups and a proposed iminyl–Cu^{III} intermediate.[21]

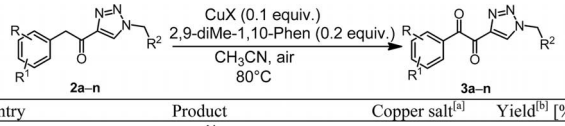
Taking into account the suggested mechanisms cited above, a possible mechanism is depicted in Scheme 4. The process is initiated by the coordination of the α-ketotriazole, which is considered as a bidentate ligand, to Cu^{II} through the triazole moiety and the oxygen atom of the carbonyl group or its enol form. The triazole frame may act as an internal directing group. The copper species is oxidized with O_2 to form the peroxy copper(III) species **II**. The benzylic moiety is converted into the peroxy copper(II) species **III** through a benzylic radical. This intermediate may either lead to benzaldehyde, which is obtained in low yield in some cases, and triazolo acid (not observed) through the cleavage of the carbon–carbon bond, or deliver the α,β-diketotriazole product as described in Tables 2 and 3.

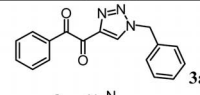
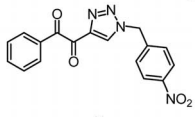
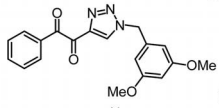
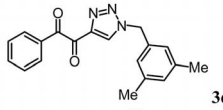
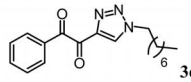
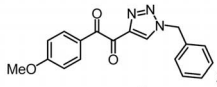
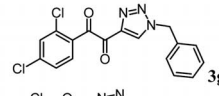
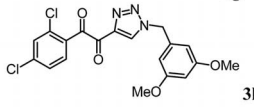
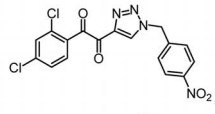
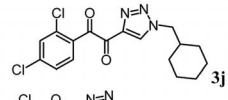
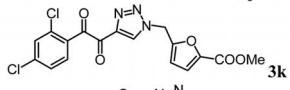
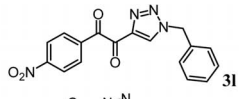
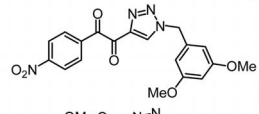
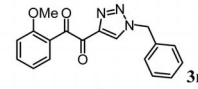
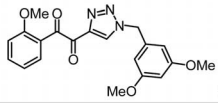
The broad synthetic utility of these α,β-diketo products was demonstrated by carrying out the subsequent synthesis of quinoxalines (Scheme 5a) or imidazoles (Scheme 5b and c). These derivatives are prevalent in a number of natural products and pharmacologically active compounds.[22,23] Quinoxaline **7** was obtained in 97% yield from 4,5-dimethylbenzene-1,2-diamine. Imidazoles **8** and **9** were prepared by known procedures (Scheme 5).[2,24] The exact structure of **9** was determined by X-ray crystallography.

Conclusions

We have developed a new approach for the synthesis of α,β-diketotriazoles from α-ketotriazoles in the presence of 10 mol-% copper(I) or -(II) and 20 mol-% 2,9-dimethyl-

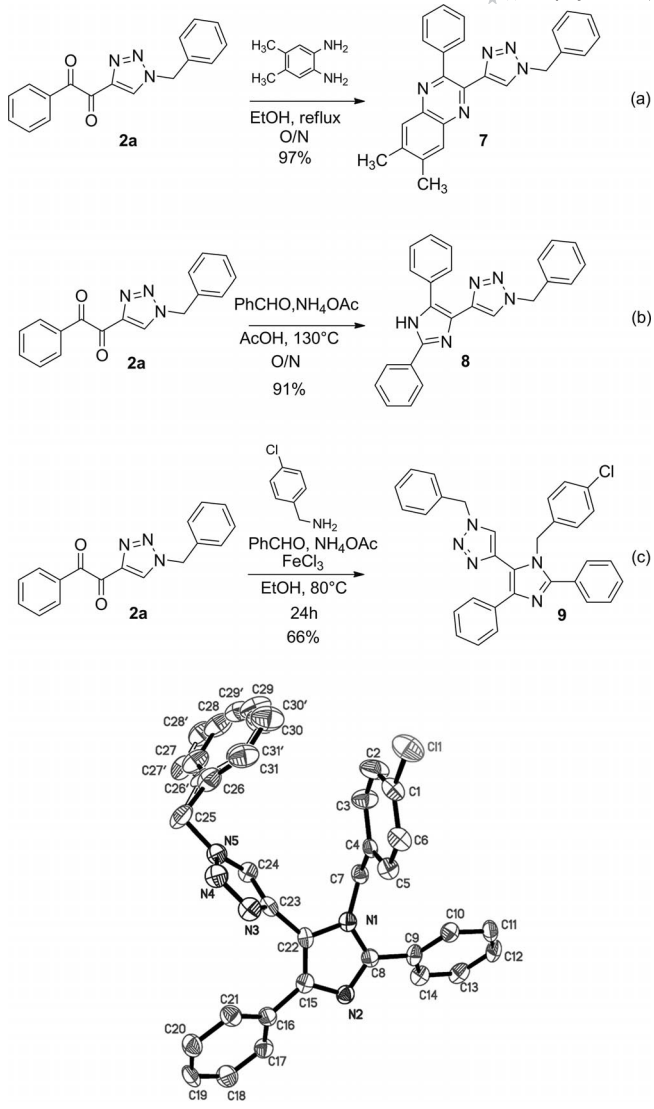
Table 3. Synthesis of α,β-diketotriazoles from α-ketotriazoles.



Entry	Product	Copper salt[a]	Yield[b] [%]
1	 **3a**	$CuCl_2$/CuI	55/55
2	 **3b**	$CuCl_2$/CuI	40/51
3	 **3c**	$CuCl_2$/CuI	48/49
4	 **3d**	$CuCl_2$/CuI	48/47
5	 **3e**	$CuCl_2$/CuI	40/48
6	 **3f**	$CuCl_2$/CuI	50/58
7	 **3g**	$CuCl_2$/CuI	72/53
8	 **3h**	CuI	57
9	 **3i**	$CuCl_2$/CuI	71/58
10	 **3j**	$CuCl_2$	52
11	 **3k**	$CuCl_2$	57
12	 **3l**	$CuCl_2$/CuI	39/63
13	 **3m**	$CuCl_2$/CuI	49/60
14	 **3n**	CuI	71
15	 **3o**	CuI	68

[a] Reactions with $CuCl_2$ were performed for 20 h and those with CuI for 2–4 h depending on the starting material. [b] Isolated yields.

1,10-phenanthroline under air. Our study showed the importance of the triazole as an intramolecular directing group for the oxidation of the benzylic moiety. This method



Scheme 5. Application to the synthesis of quinoxaline **7** or imidazoles **8** and **9**. Crystallographic data for **9** can be found in the Supporting Information.

provides access to a variety of α,β-diketotriazole compounds, which could be of importance in medicinal chemistry. The investigation of further applications of this reaction is underway.

Experimental Section

General Information: All chemicals were obtained from Aldrich or Acros Organics and used without further purification. NMR spectra were recorded with a Bruker AC 300 spectrometer (^1H and ^{13}C NMR). ^1H NMR spectra were recorded at 300 MHz with $CDCl_3$ (δ = 7.26 ppm) as an internal standard. ^{13}C NMR spectra were recorded at 75.0 MHz and are referenced against the central line of the $CDCl_3$ triplet at δ = 77.0 ppm. MS data were obtained with a ThermoQuest TSQ 7000 spectrometer, and HRMS was performed with a ThermoFinnigan MAT 95 XL spectrometer by using ESI methods. IR spectra were recorded with a Perkin–Elmer 1725.

Representative Procedure for the Synthesis of TMS-Ynone Derivatives: These compounds were prepared according to a reported pro-

cedure.[25] The analytical data for the compounds synthesized were compared with those previously reported (**1a** and **1b**).[25]

1-(2,4-Dichlorophenyl)-4-(trimethylsilyl)but-3-yn-2-one (1c): Yellow oil. Yield 92%. ^{1}H NMR ($CDCl_3$): δ = 0.19 (s, 9 H), 3.95 (s, 2 H), 7.17 (d, J = 8.2 Hz, 1 H), 7.24 (dd, J = 8.2, J = 2.1 Hz, 1 H), 7.42 (d, J = 2.1 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –0.9, 48.2, 100.5, 101.1, 127.2, 129.4, 130.2, 132.6, 134.1, 135.6, 182.9 ppm. HRMS: calcd. for $C_{13}H_{15}Cl_2OSi$ $[M]^+$ 285.0269; found 285.0272.

1-(4-Nitrophenyl)-4-(trimethylsilyl)but-3-yn-2-one (1d): Gummy yellow solid. Yield 38%. ^{1}H NMR ($CDCl_3$): δ = 0.20 (s, 9 H), 3.96 (s, 2 H), 7.41 (d, J = 8.7 Hz, 2 H), 8.20 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –1.0, 51.3, 101.2, 101.3, 123.7, 130.8, 140.1, 147.3, 182.7 ppm. HRMS: calcd. for $C_{13}H_{16}N_3OSi$ $[M]^+$ 262.0899; found 262.0883.

1-(2-Methoxyphenyl)-4-(trimethylsilyl)but-3-yn-2-one (1e): Yellow oil. Yield 75%. ^{1}H NMR ($CDCl_3$): δ = 0.16 (s, 9 H), 3.80 (s, 3 H), 3.82 (s, 2 H), 6.88 (d, J = 8.2 Hz, 1 H), 6.93 (td, J = 7.4, J = 1.0 Hz, 1 H), 7.15 (dd, J = 7.4, J = 1.5 Hz, 1 H), 7.28 (td, J = 8.1, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –0.9, 46.5, 53.5, 98.5, 101.7, 110.4, 120.5, 122.2, 128.8, 131.4, 157.7, 185.4 ppm. HRMS: calcd. for $C_{14}H_{19}O_2Si$ $[M]^+$ 247.1154; found 247.1155.

Representative Procedure for the Synthesis of α-Ketotriazole Derivatives: To a solution of 1-trimethylsilyl-1-alkynyl ketone (1 equiv.) and azide (1.2 equiv.) in CH_3CN/H_2O (4:1), was added $CuCl_2$ (0.1 equiv.) and sodium ascorbate (0.2 equiv.) at room temperature. The reaction mixture was warmed to 80 °C for 45–60 min. After cooling to room temperature, H_2O was added, and the mixture was extracted with EtOAc. The organic layer was washed with brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The product was purified by flash chromatography (petroleum ether/EtOAc). The compounds **2a**–**e**, **2g**, **2i** have identical analytical data to those reported.[15]

Representative Procedure for the Synthesis of α,β-Diketotriazole Derivatives: To a solution of α-ketotriazole (1 equiv.) in CH_3CN (3 mL) were added $CuCl_2$ (0.1 equiv.) and 2,9-dimethyl-1,10-phenanthroline (0.2 equiv.) at room temperature. The reaction mixture was warmed to reflux with stirring under air for 20 h. The solvent was evaporated under reduced pressure, and the residue was dissolved in EtOAc. The organic layer was washed with water (3 × 20 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-2-phenylethane-1,2-dione (3a): Yellow solid obtained upon standing. M.p. 115 °C. Yields ($CuCl_2$/CuI) 55/55%. ^{1}H NMR ($CDCl_3$): δ = 5.61 (s, 2 H), 7.31 (m, 2 H), 7.41 (m, 3 H), 7.50 (t, J = 7.6 Hz, 2 H), 7.66 (t, J = 7.4 Hz, 1 H), 8.02 (d, J = 8.4 Hz, 2 H), 8.19 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 54.5, 128.4, 128.9, 129.3, 129.4, 130.2, 132.2, 133.3, 134.9, 185.5, 191.9 ppm. IR (neat): $\tilde{\nu}$ = 1677, 1594, 1526 cm^{-1}. HRMS: calcd. for $C_{17}H_{14}N_3O_2$ $[M + H]^+$ 292.1086; found 292.1087.

1-[1-(4-Nitrobenzyl)-1*H*-1,2,3-triazol-4-yl]-2-phenylethane-1,2-dione (3b): Yellow powder. M.p. 139 °C. Yields ($CuCl_2$/CuI) 40/51%. ^{1}H NMR ($CDCl_3$): δ = 5.74 (s, 2 H), 7.5 (m, 4 H), 7.67 (t, J = 7.4 Hz, 1 H), 8.03 (d, J = 8.5 Hz, 2 H), 8.26 (d, J = 8.6 Hz, 2 H), 8.33 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 53.5, 124.5, 128.6, 129.0, 130.3, 132.2, 135.1, 140.2, 144.7, 148.4, 184.9, 191.6 ppm. IR (neat): $\tilde{\nu}$ = 1687, 1591, 1523, 1343 cm^{-1}. HRMS: calcd. for $C_{17}H_{13}N_4O_4$ $[M]^+$ 337.0937; found 337.0924.

1-[1-(3,5-Dimethoxybenzyl)-1*H*-1,2,3-triazol-4-yl]-2-phenylethane-1,2-dione (3c): Yellow powder. M.p. 90 °C. Yields ($CuCl_2$/CuI) 48/49%. ^{1}H NMR ($CDCl_3$): δ = 3.78 (s, 6 H), 5.51 (s, 2 H), 6.45 (m, 3 H), 7.51 (t, J = 7.4 Hz, 2 H), 7.66 (tt, J = 7.5, J = 1.3 Hz, 1 H), 8.03 (d, J = 8.3 Hz, 2 H), 8.21 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.7, 54.7, 55.5, 100.8, 106.5, 128.3, 128.9, 130.2, 132.3, 134.9, 135.2, 144.4, 161.5, 185.5, 191.9 ppm. IR (neat): $\tilde{\nu}$ = 1681, 1600, 1531, 1346 cm^{-1}. HRMS: calcd. for $C_{19}H_{18}N_3O_4$ $[M + H]^+$ 352.1297; found 352.1312.

1-[1-(3,5-Dimethylbenzyl)-1*H*-1,2,3-triazol-4-yl]-2-phenylethane-1,2-dione (3d): Yellow powder. M.p. 97 °C. Yields ($CuCl_2$/CuI) 48/47%. ^{1}H NMR ($CDCl_3$): δ = 2.31 (s, 6 H), 6.93 (s, 2 H), 7.02 (s, 1 H), 7.50 (t, J = 7.6 Hz, 2 H), 7.65 (t, J = 7.4 Hz, 1 H), 8.00 (d, J = 7.2 Hz, 2 H), 8.18 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.2, 54.6, 126.2, 128.2, 128.9, 130.2, 130.9, 132.3, 133.0, 134.9, 139.2, 144.4, 185.6, 192.0 ppm. IR (neat): $\tilde{\nu}$ = 1681, 1600, 1531, 1346 cm^{-1}. HRMS: calcd. for $C_{19}H_{18}N_3O_2$ $[M]^+$ 320.1399; found 320.1394.

1-(1-Octyl-1*H*-1,2,3-triazol-4-yl)-2-phenylethane-1,2-dione (3e): Yellow gel. Yields ($CuCl_2$/CuI) 40/48%. ^{1}H NMR ($CDCl_3$): δ = 0.85 (t, J = 6.9 Hz, 3 H), 1.29 (m, 10 H), 1.95 (m, 2 H), 4.44 (t, J = 7.26 Hz, 2 H), 7.52 (t, J = 7.4 Hz, 2 H), 7.66 (t, J = 7.4 Hz, 1 H), 8.04 (dd, J = 8.3, J = 1.3 Hz, 2 H), 8.29 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.6, 26.4, 28.8, 29.0, 30.1, 31.6, 128.1, 128.9, 130.2, 132.4, 134.9, 144.1, 185.7, 192.1 ppm. IR (neat): $\tilde{\nu}$ = 2928, 1679, 1597, 1531, 1376 cm^{-1}. HRMS: calcd. for $C_{18}H_{24}N_3O_2$ $[M]^+$ 314.1869; found 314.1877.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-2-(4-methoxyphenyl)ethanone (2f): Yellow powder. M.p. 116 °C. Yield 80%. ^{1}H NMR ($CDCl_3$): δ = 3.79 (s, 3 H), 4.38 (s, 2 H), 5.56 (s, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 7.31 (m, 4 H), 7.40 (m, 3 H), 8.01 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 45.0, 54.4, 55.1, 113.9, 125.8, 128.3, 129.0, 129.2, 130.8, 133.5, 158.5, 192.4 ppm. IR (neat): $\tilde{\nu}$ = 1683, 1612, 1513, 1362 cm^{-1}. HRMS: calcd. for $C_{18}H_{18}N_3O_2$ $[M]^+$ 308.1399; found 308.1387.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-2-(4-methoxyphenyl)ethane-1,2-dione (3f): Yellow powder. M.p. 122 °C. Yields ($CuCl_2$/CuI) 50/58%. ^{1}H NMR ($CDCl_3$): δ = 3.88 (s, 6 H), 5.60 (s, 2 H), 6.96 (d, J = 9.0 Hz, 2 H), 7.33 (m, 2 H), 7.39 (m, 3 H), 8.01 (d, J = 9.0 Hz, 2 h), 8.19 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 54.5, 55.6, 114.3, 125.3, 128.3, 128.4, 129.3, 129.4, 132.8, 133.3, 144.5, 165.1, 185.6, 190.3 ppm. IR (neat): $\tilde{\nu}$ = 1681, 1597, 1513, 1322 cm^{-1}. HRMS: calcd. for $C_{18}H_{16}N_3O_3$ $[M]^+$ 322.1192; found 322.1183.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-2-(2,4-dichlorophenyl)ethane-1,2-dione (3g): Yellow powder. M.p. 115 °C. Yields ($CuCl_2$/CuI) 72/53%. ^{1}H NMR ($CDCl_3$): δ = 5.62 (s, 2 H), 7.34 (m, 2 H), 7.42 (m, 5 H), 7.82 (d, J = 8.3 Hz, 1 H), 8.21 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 54.6, 127.8, 128.3, 128.5, 129.3, 129.4, 130.5, 131.5, 133.0, 133.2, 135.0, 140.6, 143.8 ppm. IR (neat): $\tilde{\nu}$ = 1686, 1582, 1532, 1465, 1378 cm^{-1}. HRMS: calcd. for $C_{17}H_{12}Cl_2N_3O_2$ $[M]^+$ 360.0300; found 360.0307.

1-[1-(3,5-Dimethoxybenzyl)-1*H*-1,2,3-triazol-4-yl]-2-(2,4-dichlorophenyl)ethane-1,2-dione (3h): Yellow gummy solid. Yield 57%. ^{1}H NMR ($CDCl_3$): δ = 3.75 (s, 6 H), 5.52 (s, 2 H), 6.43 (s, 3 H), 7.38 (dd, J = 8.3, J = 1.9 Hz, 1 H), 7.42 (d, J = 1.8 Hz, 1 H), 7.79 (d, J = 8.3 Hz, 1 H), 8.26 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 54.5, 55.4, 100.7, 106.4,127.8, 128.4, 130.4, 131.4, 132.9, 134.9, 135.2, 140.5, 143.6, 161.4, 183.3, 190.9 ppm. IR (neat): $\tilde{\nu}$ = 1686, 1598, 1465, 1357 cm^{-1}. HRMS: calcd. for $C_{19}H_{16}Cl_2N_3O_4$ $[M]^+$ 420.0518; found 420.0518.

1-[1-(4-Nitrobenzyl)-1*H*-1,2,3-triazol-4-yl]-2-(2,4-dichlorophenyl)ethanone (2i): Yellow powder. M.p. 97 °C. Yield 86%. ^{1}H NMR ($CDCl_3$): δ = 4.58 (s, 2 H), 5.70 (s, 2 H), 7.23 (d, J = 1.1 Hz, 2 H), 7.39 (s, 1 H), 7.45 (t, J = 8.6 Hz, 2 H), 8.18 (s, 1 H), 8.23 (t, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 43.6, 54.5, 124.5, 126.0,

127.2, 128.9, 129.3, 130.9, 132.8, 133.8, 135.4, 140.4, 147.8, 190.1 ppm. IR (neat): $\tilde{\nu}$ = 1693, 1603, 1524, 1347 cm^{-1}. HRMS: calcd. for $C_{17}H_{13}Cl_2N_4O_3$ $[M]^+$ 391.0365; found 391.0371.

1-[1-(4-Nitrobenzyl)-1*H*-1,2,3-triazol-4-yl]-2-(2,4-dichlorophenyl)ethane-1,2-dione (3i): Yellow powder. M.p. 87 °C. Yields ($CuCl_2$/CuI) 71/58%. ^1H NMR ($CDCl_3$): δ = 5.76 (s, 2 H), 7.43 (dd, J = 8.3, J = 1.9 Hz, 1 H), 7.46 (d, J = 1.8 Hz, 1 H), 7.50 (d, J = 8.7 Hz, 2 H), 7.82 (d, J = 8.3 Hz, 1 H), 8.27 (d, J = 8.7 Hz, 2 H), 8.35 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 53.5, 124.6, 128.0, 128.6, 129.0, 130.5, 131.4, 133.0, 134.9, 140.2, 140.8, 144.0, 182.9, 190.8 ppm. IR (neat): $\tilde{\nu}$ = 1685, 1582, 1524, 1348 cm^{-1}. HRMS: calcd. for $C_{17}H_{11}Cl_2N_4O_4$ $[M]^+$ 405.0157; found 405.0166.

2-(2,4-Dichlorophenyl)-1-[1-(cyclohexylmethyl)-1*H*-1,2,3-triazol-4-yl]ethanone (2j): White powder. M.p. 119 °C. Yield 63%. ^1H NMR ($CDCl_3$): δ = 1.04–1.92 (m, 11 H), 4.24 (d, J = 6.9 Hz, 2 H), 4.60 (s, 2 H), 7.23 (d, J = 0.9 Hz, 2 H), 7.43 (s, 1 H), 8.02 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 25.4, 25.9, 30.3, 38.6, 43.5, 56.8, 126.2, 127.1, 129.3, 131.2, 132.8, 133.6, 135.5, 190.4 ppm. IR (neat): $\tilde{\nu}$ = 2928, 1692, 1589, 1531, 1381 cm^{-1}. HRMS: calcd. for $C_{17}H_{20}Cl_2N_3O$ $[M]^+$ 352.0983; found 352.0985.

2-(2,4-Dichlorophenyl)-1-[1-(cyclohexylmethyl)-1*H*-1,2,3-triazol-4-yl]ethane-1,2-dione (3j): Yellow powder. M.p. 121 °C. Yield 52%. ^1H NMR ($CDCl_3$): δ = 1.11 (m, 5 H), 1.66 (m, 5 H), 1.94 (m, 1 H), 4.28 (d, J = 7.2 Hz, 2 H), 7.42 (dd, J = 8.3, J = 1.9 Hz, 1 H), 7.45 (d, J = 1.9 Hz, 1 H), 7.84 (d, J = 8.3 Hz, 1 H), 8.28 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 25.3, 25.9, 30.3, 38.5, 56.9, 127.8, 128.8, 130.5, 131.6, 133.0, 135.0, 140.5, 143.3, 183.5, 191.0 ppm. IR (neat): $\tilde{\nu}$ = 2926, 1684, 1581, 1532, 1379 cm^{-1}. HRMS: calcd. for $C_{17}H_{18}Cl_2N_3O_2$ $[M]^+$ 366.0776; found 352.0759.

Methyl 4-[(4-{2-(2,4-Dichlorophenyl)acetyl}-1*H*-1,2,3-triazol-1-yl)methyl]furan-3-carboxylate (2k): White powder. M.p. 108 °C. Yield 73%. ^1H NMR ($CDCl_3$): δ = 3.87 (s, 3 H), 4.54 (s, 2 H), 5.64 (s, 2 H), 6.56 (d, J = 3.5 Hz, 1 H), 7.13 (d, J = 3.5 Hz, 1 H), 7.19 (s, 2 H), 7.38 (s, 1 H), 8.22 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 43.5, 46.8, 52.1, 112.5, 118.6, 126.0, 127.0, 129.2, 131.0, 132.7, 133.6, 135.4, 145.5, 147.5, 150.1, 158.5, 190.0 ppm. IR (neat): $\tilde{\nu}$ = 1721, 1691, 1595, 1534, 1474 cm^{-1}. HRMS: calcd. for $C_{17}H_{14}Cl_2N_3O_4$ $[M]^+$ 394.0361; found 394.0355.

Methyl 4-[(4-{2-(2,4-Dichlorophenyl)-2-oxoacetyl}-1*H*-1,2,3-triazol-1-yl)methyl]furan-3-carboxylate (3k): Yellow gummy solid. Yield 57%. ^1H NMR ($CDCl_3$): δ = 3.90 (s, 3 H), 5.70 (s, 2 H), 6.62 (d, J = 3.5 Hz, 1 H), 7.16 (d, J = 3.4 Hz, 1 H), 7.42 (dd, J = 8.3, J = 1.9 Hz, 1 H), 7.45 (d, J = 1.9 Hz, 1 h), 7.82 (d, J = 8.3 Hz, 1 H), 8.43 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 46.9, 52.2, 112.9, 118.7, 127.9, 128.6, 130.5, 131.5, 133.0, 135.0, 140.6, 143.9, 145.7, 149.8, 158.5, 183.1, 190.8 ppm. IR (neat): $\tilde{\nu}$ = 1730, 1683, 1582, 1534, 1438, 1380 cm^{-1}. HRMS: calcd. for $C_{17}H_{12}Cl_2N_3O_5$ $[M]^+$ 408.0154; found 408.0136.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-2-(4-nitrophenyl)ethanone (2l): White powder. M.p. 142 °C. Yield 79%. ^1H NMR ($CDCl_3$): δ = 4.53 (s, 2 H), 5.57 (s, 2 H), 7.30 (m, 2 H), 7.38 (m, 3 H), 7.52 (d, J = 8.8 Hz, 2 H), 8.00 (s, 1 H), 8.16 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 45.6, 54.6, 123.6, 126.1, 128.4, 129.4, 130.8, 133.3, 141.4, 147.3, 190.6 ppm. IR (neat): $\tilde{\nu}$ = 1685, 1601, 1531, 1510, 1341 cm^{-1}. HRMS: calcd. for $C_{17}H_{15}N_4O_3$ $[M]^+$ 323.1144; found 323.1133.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-2-(4-nitrophenyl)ethane-1,2-dione (3l): Yellow powder. M.p. 130 °C. Yields ($CuCl_2$/CuI) 39/63%. ^1H NMR ($CDCl_3$): δ = 5.63 (s, 2 H), 7.34 (m, 2 H), 7.41 (m, 3 H), 8.19 (d, J = 9.0 Hz, 2 H), 8.28 (s, 1 H), 8.33 (d, J = 9.0 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 54.7, 123.9, 128.4, 128.5, 129.4, 129.5, 131.2, 133.1, 136.8, 144.0, 151.1, 184.1, 189.8 ppm. IR (neat): $\tilde{\nu}$ = 1678, 1596, 1517, 1345 cm^{-1}. HRMS: calcd. for $C_{17}H_{13}N_4O_4$ $[M]^+$ 337.0937; found 337.0926.

1-[1-(3,5-Dimethoxybenzyl)-1*H*-1,2,3-triazol-4-yl]-2-(4-nitrophenyl)ethanone (2m): White powder. M.p. 166 °C. Yield 52%. ^1H NMR ($CDCl_3$): δ = 3.76 (s, 6 H), 4.53 (s, 2 H), 5.47 (s, 2 H), 6.40 (d, J = 2.1 Hz, 2 H), 6.44 (t, J = 2.1 Hz, 1 H), 7.52 (d, J = 8.7 Hz, 2 H), 8.01 (s, 1 H), 8.16 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 45.6, 54.7, 55.4, 100.6, 106.5, 123.6, 126.1, 130.8, 135.3, 141.4, 147.2, 161.5, 190.5 ppm. IR (neat): $\tilde{\nu}$ = 1687, 1602, 1504, 1347 cm^{-1}. HRMS: calcd. for $C_{19}H_{18}N_4O_5$ $[M]^+$ 383.1355; found 383.1330.

1-[1-(3,5-Dimethoxybenzyl)-1*H*-1,2,3-triazol-4-yl]-2-(4-nitrophenyl)ethane-1,2-dione (3m): Yellow needles. M.p. 133 °C. Yields ($CuCl_2$/CuI) 49/60%. ^1H NMR ($CDCl_3$): δ = 3.78 (s, 6 H), 5.53 (s, 2 H), 6.45 (m, 3 H), 8.20 (d, J = 8.9 Hz, 2 H), 8.29 (s, 1 H), 8.33 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 54.8, 55.5, 100.7, 106.5, 124.0, 128.6, 131.2, 135.1, 136.8, 144.0, 151.1, 161.5, 184.0, 189.8 ppm. IR (neat): $\tilde{\nu}$ = 1684, 1602, 1522, 1348 cm^{-1}. HRMS: calcd. for $C_{19}H_{17}N_4O_6$ $[M]^+$ 397.1148; found 397.1143.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-2-(2-methoxyphenyl)ethanone (2n): White powder. M.p. 127 °C. Yield 86%. ^1H NMR ($CDCl_3$): δ = 3.73 (s, 3 H), 4.44 (s, 2 H), 5.54 (s, 2 H), 6.87 (d, J = 8.2 Hz, 1 H), 6.92 (td, J = 7.4, J = 1.1 Hz, 1 H), 7.22–7.34 (m, 4 H), 7.41 (m, 3 H), 8.03 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 40.9, 54.3, 55.3, 110.4, 120.4, 123.0, 125.6, 128.3, 128.4, 129.0, 129.2, 131.4, 133.7, 147.9, 157.5, 192.0 ppm. IR (neat): $\tilde{\nu}$ = 1692, 1602, 1528, 1495, 1358 cm^{-1}. HRMS: calcd. for $C_{18}H_{18}N_3O_2$ $[M]^+$ 308.1399; found 308.1396.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-2-(2-methoxyphenyl)ethane-1,2-dione (3n): Yellow powder. M.p. 121 °C. Yield 71%. ^1H NMR ($CDCl_3$): δ = 3.59 (s, 3 H), 5.60 (s, 2 H), 6.93 (d, J = 8.4 Hz, 1 H), 7.10 (td, J = 7.8, J = 0.7 Hz, 1 H), 7.29–7.40 (m, 5 H), 7.58 (td, J = 7.4, J = 1.8 Hz, 1 H), 7.97 (dd, J = 7.8, J = 1.8 Hz, 1 H), 8.12 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 54.5, 55.8, 112.3, 121.3, 123.2, 127.1, 128.3, 129.2, 129.3, 130.7, 133.5, 136.5, 144.4, 160.4, 185.6, 192.8 ppm. IR (neat): $\tilde{\nu}$ = 1688, 1598, 1535, 1467, 1354 cm^{-1}. HRMS: calcd. for $C_{18}H_{16}N_3O_3$ $[M]^+$ 322.1192; found 322.1197.

1-[1-(3,5-Dimethoxybenzyl)-1*H*-1,2,3-triazol-4-yl]-2-(2-methoxyphenyl)ethanone (2o): Light yellow oil. Yield 74%. ^1H NMR ($CDCl_3$): δ = 3.73 (s, 3 H), 3.76 (s, 6 H), 4.43 (s, 2 H), 5.45 (s, 2 H), 6.41 (d, J = 2.1 Hz, 2 H), 6.44 (t, J = 2.2 Hz, 1 H), 6.87 (d, J = 8.2 Hz, 1 H), 6.91 (td, J = 7.4, J = 1.0 Hz, 1 H), 7.19 (dd, J = 7.4, J = 1.6 Hz, 1 H), 7.25 (td, J = 8.0, J = 1.3 Hz, 1 H), 8.00 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 40.9, 54.4, 55.3, 55.4, 100.6, 106.3, 110.4, 120.4, 123.0, 125.6, 128.4, 131.4, 135.7, 147.9, 157.5, 161.3, 192.0 ppm. IR (neat): $\tilde{\nu}$ = 1687, 1610, 1529, 1465, 1322 cm^{-1}. HRMS: calcd. for $C_{20}H_{22}N_3O_4$ $[M]^+$ 368.1610; found 368.1617.

1-[1-(3,5-Dimethoxybenzyl)-1*H*-1,2,3-triazol-4-yl]-2-(2-methoxyphenyl)ethane-1,2-dione (3o): White powder. M.p. 120 °C. Yield 68%. ^1H NMR ($CDCl_3$): δ = 3.60 (s, 3 H), 3.76 (s, 6 H), 5.50 (s, 2 H), 6.42 (m, 3 H), 6.92 (d, J = 8.4 Hz, 1 H), 7.09 (t, J = 7.3 Hz, 1 H), 7.57 (t, J = 7.4 Hz, 1 H), 7.96 (dd, J = 7.8, J = 1.7 Hz, 1 H), 8.13 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 54.5, 55.4, 55.8, 100.7, 106.3, 112.3, 121.5, 123.2, 127.2, 130.6, 135.5, 136.5, 144.4, 160.4, 161.4, 185.6, 192.8 ppm. IR (neat): $\tilde{\nu}$ = 1686, 1655, 1597, 1463, 1301 cm^{-1}. HRMS: calcd. for $C_{20}H_{20}N_3O_5$ $[M]^+$ 382.1403; found 382.1419.

1-Phenyl-2-(pyridin-2-yl)ethane-1,2-dione (6): Phenylacetylpyridine **5** was synthesized as described previously.[26] The same protocol for α,β-diketotriazoles was then used to prepare **6**. Spectroscopic data for **6** are identical to those previously reported.[27]

2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-6,7-dimethyl-3-phenylquinoxaline (7): α,β-Diketotriazole (1 equiv.) and 4,5-dimethylbenzene-1,2-diamine (1 equiv.) were dissolved in EtOH (2 mL). The reaction mixture was heated to reflux overnight, concentrated under reduced pressure, dissolved in EtOAc, and washed with water and brine. The residue was purified by flash chromatography to afford **7** as a light brown powder. M.p. 180 °C. Yield 91%. ^{1}H NMR ($CDCl_3$): δ = 2.50 (s, 6 H), 5.45 (s, 2 H), 6.99 (s, 1 H), 7.16 (m, 2 H), 7.34 (m, 6 H), 7.44 (m, 2 H), 7.87 (s, 1 H), 7.98 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.4, 54,1, 124.3, 128.0, 128.1, 128.4, 128.7, 128.9, 129.0, 129.2, 134.2, 138.9, 140.1, 140.2, 140.9, 141.2, 143.0, 146.2, 152.4 ppm. IR (neat): $\tilde{\nu}$ = 2923, 1731, 1629, 1534, 1456 cm^{-1}. HRMS: calcd. for $C_{25}H_{21}N_5$ $[M]^+$ 392.1875; found 392.1874.

1-Benzyl-4-(2,4-diphenyl-1*H*-imidazol-5-yl)-1*H*-1,2,3-triazole (8): α,β-Diketotriazole (1 equiv.), benzaldehyde (1.1 equiv.), and ammonium acetate (2.5 equiv.) were dissolved in HOAc (2 mL). The reaction mixture was heated to 130 °C overnight, concentrated under reduced pressure, dissolved in EtOAc, and washed with water and brine. The residue was purified by flash chromatography to give **8** as a yellow solid upon standing. M.p. 142 °C. Yield 91%. ^{1}H NMR ($CDCl_3$): δ = 5.46 (s, 2 H), 7.19–7.39 (m, 11 H), 7.60 (dd, J = 7.7, J = 1.3 Hz, 2 H), 7.62 (s, 1 H), 7.92 (dd, J = 7.8, J = 1.3 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 54.2, 120.4, 125.6, 127.7, 127.8, 128.1, 128.4, 128.7, 128.9, 129.0, 129.3, 130.1, 134.3, 140.3, 146.6 ppm. IR (neat): $\tilde{\nu}$ = 1739, 1670, 1602, 1488, 1460 cm^{-1}. HRMS: calcd. for $C_{24}H_{20}N_5$ $[M]^+$ 378.1719; found 378.1724.

4-[1-(4-Chlorobenzyl)-2,4-diphenyl-1*H*-imidazol-5-yl]-1-benzyl-1*H*-1,2,3-triazole (9): α,β-Diketotriazole (1 equiv.), benzaldehyde (1.1 equiv.), 4-chlorobenzylamine (1.1 equiv.), ammonium acetate (2.5 equiv.), and $FeCl_3$ (0.1 equiv.) were dissolved in EtOH (2 mL). The reaction mixture was heated to 80 °C for 24 h, concentrated under reduced pressure, dissolved in EtOAc, and washed with water and brine. The residue was purified by flash chromatography to give **9** as a white solid. M.p. 145 °C. Yield 66%. ^{1}H NMR ($CDCl_3$): δ = 5.41 (s, 2 H), 5.45 (s, 2 H), 6.73 (d, J = 8.5 Hz, 2 H), 7.06 (m, 3 H), 7.09 (m, 1 H), 7.13 (s, 1 H), 7.23 (m, 3 H), 7.35 (m, 3 H), 7.43 (m, 3 H), 7.55–7.63 (m, 4 H) ppm. IR (neat): $\tilde{\nu}$ = 1671, 1599, 1491, 1454, 1396 cm^{-1}. HRMS: calcd. for $C_{31}H_{25}N_5Cl$ $[M]^+$ 502.1798; found 502.1833.

CCDC-807295 (for **2a**), CCDC-807296 (for **3a**), and CCDC-836436 (for **9**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Crystallographic data for **2a**, **3a**, and **9**, copies of NMR spectra.

Acknowledgments

The authors are grateful to the Ministère de l'Enseignement et de la Recherche Scientifique for financial support.

[1] X. Deng, N. S. Mani, *Org. Lett.* **2006**, *8*, 269–272.
[2] S. E. Wolkenberg, D. D. Wisnoski, W. H. Leister, Y. Wang, Z. Zhao, C. W. Lindsley, *Org. Lett.* **2004**, *6*, 1453.
[3] F. Rong, S. Chow, S. Yan, G. Larson, Z. Hong, J. Wu, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1663–1666.
[4] Z. Zhao, W. H. Leister, K. Strauss, D. D. Wisnoski, C. W. Lindsley, *Tetrahedron Lett.* **2003**, *44*, 1123–1127.
[5] P. Nowak, D. Malwitz, D. C. Cole, *Synth. Commun.* **2010**, *40*, 2164–2171, and references herein.
[6] Z. Wan, C. D. Jones, D. Mitchell, J. Y. Pu, T. Y. Zhang, *J. Org. Chem.* **2006**, *71*, 826–828.
[7] M. Niu, H. Fu, Y. Jiang, Y. Zhao, *Synthesis* **2008**, 2879–2882.
[8] W. Ren, Y. Xia, S.-J. Ji, Y. Zhang, X. Wan, J. Zhao, *Org. Lett.* **2009**, *11*, 1841–1844.
[9] S. Chen, Z. liu, E. Shi, L. Chen, W. Wie, H. Li, Y. Cheng, X. Wan, *Org. Lett.* **2011**, *13*, 2274–2277.
[10] X.-F. Zhao, C. Zhang, *Synthesis* **2007**, 551–557.
[11] J. S. Yadav, S. K. Biswas, R. Srinivas, *Synthesis* **2006**, 4237–4241.
[12] D. Sachdev, M. A. Naik, A. Dubey, B. G. Mishra, *Catal. Commun.* **2010**, *11*, 684–688.
[13] L. Liang, G. Rao, H.-L. Sun, J.-L. Zhang, *Adv. Synth. Catal.* **2010**, *352*, 2371–2377.
[14] L. Huang, K. Cheng, B. Yao, Y. Xie, Y. Zhang, *J. Org. Chem.* **2011**, *76*, 5732–5737.
[15] a) K. B. Sharpless, V. V. Fokin, L. G. Green, V. V. Rostovtsev, *Angew. Chem.* **2002**, *114*, 2126; *Angew. Chem. Int. Ed.* **2002**, *41*, 2024–2711; b) M. Meldal, C. Christensen, C. W. Tornoe, *J. Org. Chem.* **2002**, *67*, 3057–3064.
[16] C. Menendez, S. Gau, C. Lherbet, F. Rodriguez, M. R. Pasca, M. Baltas, *Eur. J. Med. Chem*. 2011, DOI: 10.1016/j.ejmech.2011.09.013.
[17] ORTEP3: L. J. Farrugia, *J. Appl. Crystallogr.* **1997**, *30*, 565–565.
[18] The same reaction was performed with 1-(1-benzyl-1*H*-1,2,3-triazol-4-yl)-3-phenylpropan-1-one. The starting material was totally recovered, even after prolonged reaction times.
[19] T. Mizuhara, S. Inuki, S. Oishi, N. Fujii, H. Ohno, *Chem. Commun.* **2009**, 3413–3415.
[20] H. Wang, Y. Wang, D. Liang, L. liu, J. Zhang, Q. Zhu, *Angew. Chem. Int. Ed.* **2011**, *50*, 5678–5681.
[21] L. Zhang, G. Y. Ang, S. Chiba, *Org. Lett.* **2011**, *13*, 1622–1625.
[22] D. E. Frantz, L. Morency, A. Soheili, J. A. Murry, E. J. J. Grabowski, R. D. Tillyer, *Org. Lett.* **2004**, *6*, 843–846 and references therein.
[23] C. Venkatesh, B. Singh, P. K. Mahata, H. Ila, H. Junjappa, *Org. Lett.* **2005**, *7*, 2169–2172, and references therein.
[24] M. M. Heravi, F. Derikvand, M. Haghighi, *Monatsh. Chem.* **2008**, *139*, 31–33.
[25] Y. Yamauchi, M. Yuki, Y. Tanabe, Y. Miyake, Y. Inada, S. Uemura, Y. Nishibayashi, *J. Am. Chem. Soc.* **2008**, *130*, 2908–2909.
[26] J. Easmon, G. Pürstinger, K.-S. Thies, G. Heinisch, J. Hofmann, *J. Med. Chem.* **2006**, *49*, 6343–6350.
[27] V. Mamane, E. Aubert, Y. Fort, *J. Org. Chem.* **2007**, *72*, 7294–7300.

Received: September 15, 2011
Published Online: November 14, 2011

