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Synthesis of Heteroaryl 1,2-Diketones

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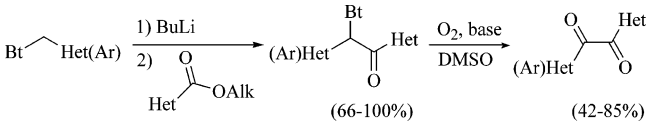
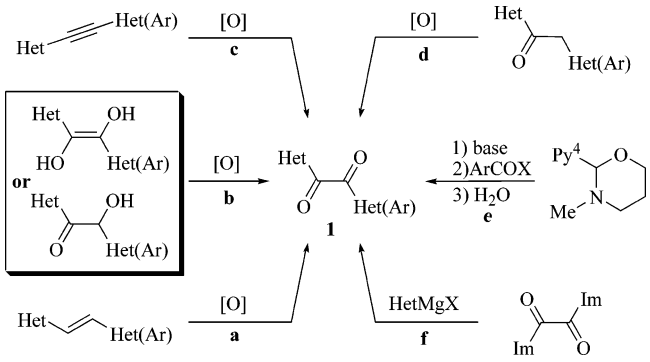


Reactions of lithiated heteroaryl- (or aryl-) methylbenzotriazoles **4a**−**e** with heteroaryl (or aryl) esters **5a**−**f** give α-benzotriazolyl ketones **6a**−**n** in average yields of 90−95%. Oxidation of ketones **6a**−**l** in aqueous DMSO in the presence of oxygen and sodium bicarbonate gave heteroaryl- (aryl-) 1,2-ethanediones **7a**−**l** in average yields of 60−80%.

Heteroaryl 1,2-diketones are of importance in organic synthesis and for their potential biological activity. Heteroaryl 1,2-diketones are precursors for the synthesis of heterocyclic compounds[1a−k] including compounds possessing pharmacological properties, such as antiinflammatory,[1a,e] antinociceptive,[1a] antipyretic,[1a] and antirheumatoid[1h] activities.

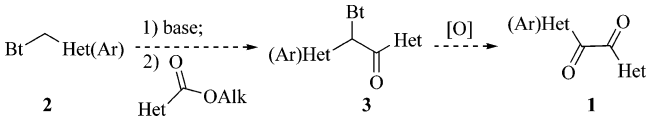
Popular methods for the preparation of heteroaryl/aryl 1,2-diketones **1** (Scheme 1) involve oxidation of various precursors: (a) olefins with selenium dioxide[1a,2] or potassium permanganate;[1b,e] (b) α-hydroxyketones or tautomeric 1,2-dihydroxyolefins by atmospheric oxygen,[1c,3] iodine,[1f,g,j,4] sodium hypobromite,[5] or triphenyl antimony dibromide;[6] (c) acetylenes with potassium permanganate,[7] NBS/DMSO,[1d] or $PdCl_2$/DMSO;[8] (d) methylene ketones by selenium dioxide,[1a,i,9] hypervalent iodine compounds,[10] hydrobromic acid/DMSO,[1a,h,k] bismuth nitrate−copper(II) acetate,[11] or oxygen in the presence of Fe(III)−EDTA.[12] Along non-oxidative methods, the substitution of imidazolyl group in 1,2-di(imidazol-1-yl)glyoxal by Grignard reagents (Scheme 1, route f)[13] and the reaction of lithiated 2-(pyridin-4-yl)-1,3-oxazine with acid chlorides and esters (Scheme 1, Route e)[14] were reported to give symmetrical 1,2-diketones and 1-aryl-2-(pyridin-4-yl)ethanediones, respectively.

SCHEME 1[a]



[a] Key: Het, heteroaryl; Ar, aryl; Het(Ar), heteroaryl or aryl; Py^4, pyridin-4-yl; Im, imidazol-1-yl.

SCHEME 2



The benzotriazolyl group possesses electron-withdrawing properties providing stabilization of an anion in the α-position to benzotriazole.[15] Lithiation of aryl- (or heteroaryl-) methylbenzotriazoles **2** (Scheme 2) followed by the reaction of the anion formed with heteroarylcarboxylic acid halides or esters should afford intermediates **3**. Oxidation of intermediate **3** by (a) metalation followed by reaction with molecular oxygen,[16] sodium,[17] or hydrogen[18] peroxide, (b) reaction with molecular oxygen in the presence of a base similar to oxidative decyanation of diarylacetonitriles,[19] or (c) reaction with DMSO in the

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presence of a base analogous to oxidation of α-haloketones[20] and alkyl halides and tosylates[21] should provide access to a diversity of heteroaryl- (or aryl-) diketones **1**.

We now report the preparation heteroaryl(aryl) diketones **7a**−**l** by the reaction of heteroaryl(aryl)methyl benzotriazoles **4a**−**e** with esters **5a**−**f** followed by oxidation of intermediates **6a**−**l** with oxygen in DMSO in the presence of sodium bicarbonate or potassium carbonate.

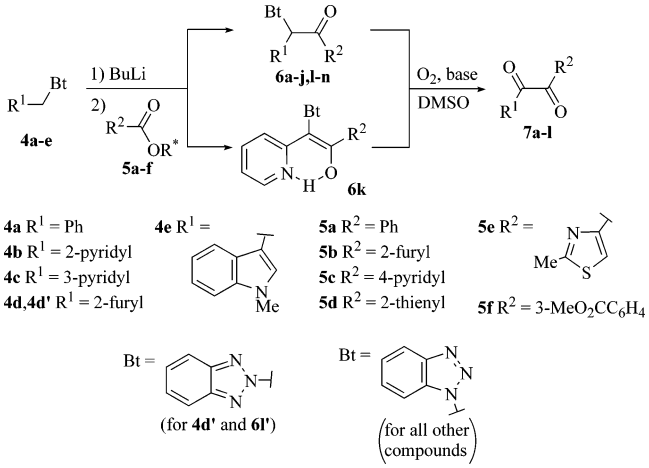
1-Benzylbenzotriazole **4a**[22] and 1-(1-methylindol-3-ylmethyl)benzotriazole **4e**[23] were prepared according to previously published procedures quoted. 2- and 3-(benzotriazolylmethyl)pyridines **4b**[24] and **4c**[25] were prepared by a new method from benzotriazole and 2- and 3-pyridylmethanols in 48% aqueous hydrobromic acid under reflux in 67% and 57% yields, respectively. 1- and 2-(2-furylmethyl)benzotriazoles **4d** and **4d′**[25] were prepared from 2-furylmethanol, thionyl chloride, and sodium benzotriazolate in 55% and 15% yields, respectively.

Compounds **4a**−**e** were treated with butyllithium (1.07 equiv) in THF at −78 °C for 1 h followed by the addition of esters **5a**−**f** (an equimolar amount of **5a**−**e** but a 2-fold excess of **5f** to curtail the bis substitution in diester **5f**) at the same temperature to give intermediate α-benzotriazolyl ketones **6a**−**n** in 52−100% yields (Scheme 3, Table 1). Structures **6a**−**n** are supported by their ^{1}H NMR and ^{13}C NMR spectra, which no longer showed distinctive singlets in the range 5.83−5.98 ppm in the ^{1}H spectra or signals in the range 44.0−53.8 ppm in the ^{13}C spectra corresponding to the methylene group in **4a**−**e**.[22−26] The ^{13}C NMR spectra of **6a**−**j**,**l**−**n** showed new signals in the range 60.7−68.6 and 179.7−193.3 ppm corresponding to a methine carbon α to benzotriazole and the carbonyl group, respectively. Unlike **6a**−**j**,**l**−**n**, the ^{13}C NMR spectrum of **6k** showed neither the signal of carbonyl group nor the signal of methine carbon. The signal at 100.6 ppm suggested the presence of a double bond and the existence of **6k** in tautomeric ethenol form resulting from the chelation of enol with pyridine nitrogen (Scheme 3);[9] enol tautomers were not detected for the other α-benzotriazolyl ketones.

The first attempted oxidation of **6a** with oxygen in a two-phase system[19b,d] of toluene or DMSO and 50% aqueous sodium hydroxide in the presence of phase-transfer catalyst at 20 °C gave no reaction. However, treatment of intermediates **6a**−**d**,**g**−**i**,**k** with oxygen in DMSO at 20 °C in the presence of potassium carbonate gave diketones **7a**−**d**,**g**−**i**,**k** in 19−69% yields and recovery of the corresponding intermediates **6a**−**d**,**g**−**i**,**k** (Table 1, method A), but attempts to convert intermediates **6m**,**n** into corresponding diketones **7m**,**n** failed and resulted in recovery of the ketones **6m**,**n**.

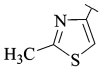
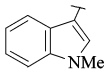
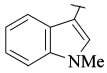
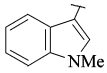
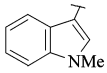
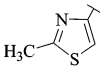
Surprisingly, a solution of **6d** in DMSO, which turned yellow prior to the addition of base and bubbling of

SCHEME 3[a]



[a] For designation of R^1, R^2 see Table 1. *For **5a**−**e**, R = Et; **5f**, R = Me.

TABLE 1. Preparation of Intermediates 6a−n and Diketones 7a−l

	R^1	R^2	Yields, %			
			6	**7**		
				A[a]	**B**[a]	Lit.
a	Ph	Ph	97	62	85	–[b]
b	Ph	2-furyl	94	61	73	94[6] 22[1c]
c	Ph	4-pyridyl	93	19	52	28[9]
d	Ph	2-thienyl	100	30	80	90[7] 35[1c]
e	Ph		81	–	64	–
f	Ph	$CH_3O_2CC_6H_4$	52	–	63	–
g		Ph	95	69	84	–
h		4-pyridyl	93	66	70	–
i		2-furyl	95	52	77	–
j			88	–	63	–
k	2-pyridyl	2-furyl	74	44	42	–
l	2-furyl	2-thienyl	95(93)[c]	–	43(42)[c]	–
m	2-furyl	4-pyridyl	87	0	0	–
n	3-pyridyl	2-furyl	66	0	0	–

[a] Methods: A, O_2, K_2CO_3, DMSO; B, O_2, $NaHCO_3$, DMSO. [b] Commercially available. [c] Yields in the parentheses are given for 2-substituted benzotriazole **6l′** and diketone **7l** obtained starting from 2-(furan-2-ylmethyl)benzotriazole (**4d′**).

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oxygen, produced diketone **7d** in low yields. Attempted variation of the temperature from 20 to 150 °C failed to provide complete conversion of intermediate **6d** and gave lower yields of diketone **7d**. Oxidation of **6d** in DMSO at 20 °C for 5 h in the presence of oxygen and saturated aqueous sodium bicarbonate instead of potassium carbonate increased the yield of **7d** to 80% (method B). Treatment of **6d** with DMSO in the presence of saturated aqueous sodium bicarbonate at 20 °C for 5 h without access of oxygen gave **7d** in 74% yield along with unidentified byproducts. We believe that the milder base, sodium bicarbonate, reduces side reactions and the presence of oxygen is also beneficial.

Application of method B was extended to oxidation of intermediates **6a**−**n** and gave generally clean reaction mixtures and better yields of the corresponding diketones **7a**−**l** (Table 1). Oxidation of 1- and 2-substituted benzotriazole intermediates **6l** and **6l′** gave the comparable yields of diketone **7l** (see Table 1 and the Experimental Section) that shows applicability of mixture of Bt^1/Bt^2 isomers **4d/4d′** for the preparation of diketones. However, attempted conversion of compounds **6m**,**n** into diketones **7m**,**n** resulted in the formation of complex sets of products; probably the furyl rings are susceptible to oxidative breakdown.

Structures **7a**−**l** are supported by their ^{1}H NMR and ^{13}C NMR spectra. Unlike **6a**−**l**, the ^{1}H NMR spectra of **7a**−**l** showed no characteristic signals for a *N*-substituted benzotriazolyl group in the range 7.2−8.1 ppm. The ^{13}C NMR spectra of **7a**−**l** also no longer showed typical signals assigned to carbons of the benzotriazole ring at ca. 120, 124, 133, 146 ppm nor any signals in the range 60.7−68.6 ppm (100.6 ppm for **6k**) corresponding to the α-carbon attached to benzotriazole in **6a**−**l**. The pairs of signals in ^{13}C NMR spectra of **7a**−**k** in the range 179.7−193.7 ppm confirmed the presence of two carbonyl groups.

An efficient and simple route to heteroaryl(aryl) 1,2-diketones **7a**−**l** has been established starting from readily available 1-[heteroaryl(or aryl)methyl]benzotriazoles **4a**−**e** and heteroaryl(or aryl) esters **5a**−**f**. This protocol affords synthesis of variety of unsymmetrical heteroaryl 1,2-diketones **7** in good overall yields under mild reaction conditions and should be a useful addition to synthetic methodology.

Experimental Section

General Procedure for the Preparation of α-Benzotriazolyl Ketones 6a−n. To a stirred solution of **4a**−**e** (6 mmol) in anhydrous THF (70 mL) was added *n*-butyllithium (4.0 mL, 6.4 mmol, 1.6 M in hexanes) at −78 °C under nitrogen. The reaction mixture was stirred at −78 °C for 1 h, and the appropriate ester **5a**−**f** (6 mmol; 12 mmol of **5f**) was then added dropwise. The reaction mixture was stirred at −78 °C for 2 h and was allowed to warm to room temperature overnight. Saturated aqueous ammonium chloride was added, and product was extracted with ethyl acetate. The extract was washed with brine and dried over magnesium sulfate. The solvent was removed under reduced pressure to give the crude product **6a**−**n**, which was purified by column chromatography using mixture ethyl acetate/hexanes as an eluent.

2-(1*H*-Benzotriazol-1-yl)-1-(2-furyl)-2-phenyl-1-ethanone (6b): plates from ethyl acetate/hexanes (94%); mp 169−170 °C; ^{1}H NMR δ 8.04 (m, 1H), 7.66 (s, 1H), 7.57 (s, 1H), 7.40−7.26 (m, 9H), 6.56−6.53 (m, 1H); ^{13}C NMR δ 181.3, 150.8, 147.7, 146.5, 133.0, 132.5, 129.3, 129.1, 128.8, 127.5, 123.9, 119.9, 119.8, 113.0, 111.4, 67.5. Anal. Calcd for $C_{18}H_{13}N_3O_2$: C, 71.28; H, 4.32; N, 13.85. Found: C, 71.21; H, 4.17; N, 13.96.

2-(1*H*-Benzotriazol-1-yl)-2-phenyl-1-(4-pyridinyl)-1-ethanone (6c): needles from ethyl acetate/hexanes (93%); mp 168−170 °C; ^{1}H NMR δ 8.79−8.77 (m, 2 H), 8.34 (s, 1 H), 8.09 (d, J = 8.4 Hz, 1 H), 7.88−7.83 (m, 3 H), 7.60−7.40 (m, 7 H); ^{13}C NMR δ 193.3,150.9, 145.2, 140.8, 133.0, 132.9, 129.6, 129.3, 129.1, 127.9, 124.4, 121.6, 119.4, 110.9, 66.8. Anal. Calcd for $C_{19}H_{14}N_4O$: C, 72.60; H, 4.49; N, 17.82. Found: C, 72.34; H, 4.39; N, 17.78.

2-(1*H*-Benzotriazol-1-yl)-2-phenyl-1-(2-thienyl)-1-ethanone (6d): needles from ethyl acetate/hexanes (100%); mp 163−165 °C; ^{1}H NMR δ 8.06−8.00 (m, 1H), 7.73 (d, J = 3.9 Hz, 1H) 7.71−7.69 (m, 2H), 7.45−7.37 (m, 5H), 7.34−7.26 (m, 3H), 7.09 (t, J = 4.7 Hz, 1H); ^{13}C NMR δ 185.4, 146.6, 141.3, 135.7, 134.0, 133.0, 132.9, 129.4, 129.2, 128.9, 128.6, 127.6, 123.9, 119.9, 111.5, 68.6. Anal. Calcd for $C_{18}H_{13}N_3OS$: C, 67.69; H, 4.10; N, 13.16. Found: C, 67.61; H, 3.96; N, 13.18.

2-(1*H*-Benzotriazol-1-yl)-1-(2-methyl-1,3-thiazol-4-yl)-2-phenyl-1-ethanone (6e): needles from ethyl acetate/hexanes (81%); mp 119−120 °C; ^{1}H NMR δ 8.18 (s, 1H), 8.06 (s, 1H), 8.01 (d, J = 7.7 Hz, 1H), 7.46−7.44 (m, 2H), 7.34−7.25 (m, 6H), 2.58 (s, 3H); ^{13}C NMR δ 187.1, 166.6, 152.0, 146.2, 133.2, 132.7, 129.2, 129.0, 128.8, 128.0, 127.2, 123.7, 119.7, 111.2, 68.0, 19.0. Anal. Calcd for $C_{18}H_{14}N_4OS$: C, 64.65; H, 4.22; N, 16.75. Found: C, 64.96; H, 4.24; N, 16.71.

Methyl 3-[2-(1*H*-benzotriazol-1-yl)-2-phenylacetyl]benzoate (6f): microcrystals from ethyl acetate (52%); mp 159−161 °C; ^{1}H NMR δ 8.66 (s, 1H), 8.23 (d, J = 7.8, 1H), 8.17 (d, J = 7.8 Hz, 2H), 8.05−8.02 (m, 1H), 7.89 (s, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.40−7.21 (m, 8H), 3.90 (s, 3H); ^{13}C NMR δ 192.0, 165.7, 146.6, 134.9, 134.8, 133.1, 132.8, 132.5, 131.2, 129.9, 129.6, 129.4, 129.3, 129.1, 127.5, 123.9, 120.0, 111.2, 68.1, 52.4. Anal. Calcd for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.61; N, 11.31. Found: C, 70.80; H, 4.62; N, 11.24.

2-(1*H*-Benzotriazol-1-yl)-2-(1-methyl-1*H*-indol-3-yl)-1-phenyl-1-ethanone (6g): needles from ethyl acetate/hexanes (95%); mp 166−168 °C; ^{1}H NMR δ 8.22 (s, 1H), 8.07 (d, J = 7.2 Hz, 2H), 8.00−7.97 (m, 1H), 7.59−7.49 (m, 2H), 7.42 (t, J = 7.8 Hz, 2 H), 7.37−7.20 (m, 5H), 7.16 (s, 1H), 7.10−7.05 (m, 1H), 3.73 (s, 3H); ^{13}C NMR δ 192.9, 146.7, 137.1, 134.4, 134.1, 133.3, 129.6, 129.0, 128.9, 127.0, 126.6, 123.6, 122.8, 120.5, 119.7, 118.6, 111.9, 109.7, 106.0, 61.5, 33.1. Anal. Calcd for $C_{23}H_{18}N_4O$: C, 75.39; H, 4.95; N, 15.29. Found: C, 74.99; H, 4.98; N, 15.44.

2-(1*H*-Benzotriazol-1-yl)-2-(1-methyl-1*H*-indol-3-yl)-1-(4-pyridinyl)-1-ethanone (6h): microcrystals from ethyl acetate/hexanes (93%); mp 142−144 °C; ^{1}H NMR δ 8.78 (d, J = 6.0 Hz, 2H), 8.12 (s, 1H), 8.03−7.99 (m, 1H), 7.82−7.80 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H), 7.36−7.26 (m, 5H), 7.15−7.11 (m, 2H), 3.77 (s, 3H); ^{13}C NMR δ 192.5, 151.2, 146.7, 140.4, 137.2, 133.2, 129.5, 127.3, 126.4, 123.8, 123.2, 121.5, 120.9, 120.0, 118.5, 111.4, 109.9, 104.9, 61.6, 33.3. Anal. Calcd for $C_{22}H_{17}N_5O$: C, 71.92; H, 4.66; N, 19.06. Found: C, 72.24; H, 4.72; N, 19.07.

2-(1*H*-Benzotriazol-1-yl)-1-(2-furyl)-2-(1-methyl-1*H*-indol-3-yl)-1-ethanone (6i): prisms from ethyl acetate/hexanes (95%); mp 166−168 °C; ^{1}H NMR δ 8.01 (s, 1H), 7.98−7.95 (m, 1H), 7.54 (d, J = 0.9 Hz, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.44−7.38 (m, 2H), 7.29−7.13 (m, 5H), 7.08−7.03 (m, 1H), 6.49 (dd, J = 1.5, 3.6 Hz), 3.72 (s, 3H); ^{13}C NMR δ 181.6, 150.6, 147.8, 146.6, 137.1, 133.2, 129.5, 127.2, 126.9, 123.7, 122.7, 120.4, 119.9, 119.7, 118.7, 112.9, 111.9, 109.8, 105.5, 60.7, 33.1. Anal. Calcd for $C_{21}H_{16}N_4O_2$: C, 70.77; H, 4.53; N, 15.72. Found: C, 70.71; H, 4.46; N, 15.76.

2-(1*H*-Benzotriazol-1-yl)-2-(1-methyl-1*H*-indol-3-yl)-1-(2-methyl-1,3-thiazol-4-yl)-1-ethanone (6j): microcrystals from ethyl acetate/hexanes (88%); mp 168−170 °C; ^{1}H NMR δ 8.51 (s, 1H), 8.21 (d, J = 1.1 Hz, 1H), 8.04−8.01 (m, 1H), 7.61 (d, J

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= 7.8 Hz, 1H), 7.50 (d, J = 7.9 Hz, 1H), 7.31−7.22 (m, 5H), 7.12−7.07 (m, 1H), 3.70 (s, 3H), 2.64 (d, J = 0.9 Hz, 3H); ^{13}C NMR δ 187.1, 166.5, 151.9, 146.2, 136.9, 133.2, 129.7, 127.8, 126.9, 126.8, 123.4, 122.3, 120.0, 119.4, 118.9, 111.5, 109.5, 105.3, 61.1, 32.8, 19.0. Anal. Calcd for $C_{21}H_{17}N_5OS$: C, 65.10; H, 4.42; N, 18.07. Found: C, 64.99; H, 4.33; N, 17.84.

(*E*)-2-(1*H*-Benzotriazol-1-yl)-1-(2-furyl)-2-(2-pyridinyl)-1-ethenol (6k): microcrystals from ethyl acetate (74%); mp 159−161 °C; ^{1}H NMR δ 8.20−8.17 (m, 2H), 7.53−7.33 (m, 4H), 7.16 (d, J = 0.9 Hz, 1H), 7.01−6.97 (m, 1H), 6.14 (dd, J = 3.6, 1.5 Hz, 1H), 6.00 (d, J = 8.7 Hz, 1H), 5.68 (d, J = 3.6 Hz, 1H); ^{13}C NMR δ 163.9, 155.2, 149.0, 145.9, 144.5, 139.2, 139.1, 135.0, 128.2, 124.2, 120.0, 117.4, 117.2, 113.8, 111.5, 109.8, 100.6. Anal. Calcd for $C_{17}H_{12}N_4O_2$: C, 67.10; H, 3.97; N, 18.41. Found: C, 67.17; H, 3.98; N, 18.28.

2-(1*H*-Benzotriazol-1-yl)-2-(2-furyl)-1-(2-thienyl)-1-ethanone (6l): microcrystals from ethyl acetate/hexanes (95%); mp 116−117 °C; ^{1}H NMR δ 8.03 (d, J = 8.2 Hz, 1H), 7.80−7.77 (m, 2H), 7.71 (d, J = 5.0 Hz, 1H), 7.48−7.27 (m, 4H), 7.10 (t, J = 4.4 Hz, 1H), 6.65 (d, J = 3.4 Hz, 1H), 6.42 (dd, J = 3.4, 1.9 Hz, 1H); ^{13}C NMR δ 182.5, 146.4, 145.5, 144.2, 140.4, 135.9, 134.0, 132.9, 128.6, 127.7, 124.0, 119.8, 112.5, 111.4, 111.2, 62.7. Anal. Calcd for $C_{16}H_{11}N_3O_2S$: C, 62.12; H, 3.58; N, 13.58. Found: C, 62.23; H, 3.53; N, 13.53.

2-(2*H*-Benzotriazol-2-yl)-2-(2-furyl)-1-(2-thienyl)-1-ethanone (6l′): needles from ethyl acetate/hexanes (93%); mp 102−103 °C; ^{1}H NMR δ 7.92−7.86 (m, 2H), 7.70−7.67 (m, 2H), 7.55 (s, 2H), 7.40−7.35 (m, 2H), 7.10−7.07 (m, 1H), 6.77 (d, J = 3.3 Hz, 1H), 6.49 (dd, J = 3.2, 1.9 Hz, 1H); (DMSO-d_6) 8.39 (s, 1H), 8.15 (dd, J = 4.9, 1.1 Hz, 1H), 8.02 (dd, J = 3.9, 1.1 Hz, 1H), 7.99−7.92 (m, 2H), 7.84 (dd, J = 1.9, 0.8 Hz, 1H), 7.49−7.46 (m, 2H), 7.27 (dd, J = 5.0, 3.7 Hz, 1H), 6.83 (d, J = 3.4 Hz, 1H), 6.59 (dd, J = 3.4, 1.9 Hz, 1H); ^{13}C NMR δ 181.5, 145.2, 144.7, 144.4, 140.5, 135.5, 133.6, 128.5, 126.8, 118.4, 113.1, 111.4, 68.5. Anal. Calcd for $C_{16}H_{11}N_3O_2S$: C, 62.12; H, 3.58; N, 13.58. Found: C, 62.21; H, 3.35; N, 13.52.

2-(1*H*-Benzotriazol-1-yl)-2-(2-furyl)-1-(4-pyridinyl)-1-ethanone (6m): microcrystals from ethyl acetate/hexanes (87%); mp 145−147 °C; ^{1}H NMR δ 8.77 (d, J = 5.9 Hz, 2H), 8.04 (d, J = 8.1 Hz, 1H), 8.01 (s, 1H), 7.75 (d, J = 6.1 Hz, 2H), 7.46−7.31 (m, 4H), 6.63 (d, J = 3.4 Hz, 1H), 6.43−6.42 (m, 1H); ^{13}C NMR δ 189.6, 150.9, 146.2, 144.3, 144.3, 139.8, 132.8, 127.8, 123.9, 121.2, 119.8, 112.9, 111.4, 110.7, 62.3. Anal. Calcd for $C_{17}H_{12}N_4O_2$: C, 67.10; H, 3.97; N, 18.41. Found: C, 67.05; H, 3.94; N, 18.33.

2-(1*H*-Benzotriazol-1-yl)-1-(2-furyl)-2-(3-pyridinyl)-1-ethanone (6n): microcrystals from ethyl acetate/hexanes (66%); mp 138−139 °C; ^{1}H NMR δ 8.73 (d, J = 2.0 Hz, 1H), 8.62 (dd, J = 4.8, 1.4 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H), 7.82−7.79 (m, 1H), 7.61 (s, 1H), 7.55 (d, J = 1.0 Hz, 1H), 7.42−7.30 (m, 5H), 6.53 (dd, J = 3.7, 1.6 Hz, 1H); ^{13}C NMR δ 179.7, 150.4, 150.3, 149.7, 147.9, 146.1, 136.5, 132.6, 128.6, 127.9, 124.1, 123.7, 120.2, 120.0, 113.1, 110.3, 64.7. Anal. Calcd for $C_{17}H_{12}N_4O_2$: C, 67.10; H, 3.97; N, 18.41. Found: C, 67.26; H, 3.99; N, 18.28.

General Procedures for the Preparation of Diketones 7a−l. Method A (Diketones 6a−d,g−i,k). To a solution of **6a−d**,**g−i**,**k** (2 mmol) in DMSO (20 mL) was added 4 M aqueous potassium carbonate (1.5 mL, 6 mmol) at 20−25 °C. Then oxygen gas was bubbled through the reaction mixture with vigorous stirring at 20−25 °C for 12 h. The product was extracted with ethyl acetate. The extract was washed with brine and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by column chromatography to give **7a−d**,**g−i**,**k** (yields are given in Table 1).

Method B. To a solution of **6a−l** (1 mmol) in DMSO (10 mL) was added saturated aqueous sodium bicarbonate (1 mL) at 20−25 °C. Then oxygen gas was bubbled through the reaction mixture with vigorous stirring at 20−25 °C for 6 h. Water (20 mL) was added to the mixture, and the product was extracted with ethyl acetate. The extract was washed with brine and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by column chromatography to give **7a−l**.

1-(2-Methyl-1,3-thiazol-4-yl)-2-phenyl-1,2-ethanedione (7e): needles from ethyl acetate/hexanes (64%); mp 99−100 °C; ^{1}H NMR δ 8.26 (s, 1H), 8.00−7.97 (m, 2H), 7.68−7.62 (m, 1H), 7.53−7.47 (m, 2H), 2.74 (s, 3H); ^{13}C NMR δ 193.1, 186.6, 167.6, 151.0, 134.7, 132.4, 131.7, 129.9, 128.8, 19.1. Anal. Calcd for $C_{12}H_9NO_2S$: C, 62.32; H, 3.92; N, 6.06. Found: C, 62.70; H, 3.95; N, 6.04.

Methyl 3-(2-oxo-2-phenylacetyl)benzoate (7f): oil (63%); ^{1}H NMR δ 8.61 (s, 1H), 8.32 (d, J = 7.8 Hz, 1H), 8.18 (d, J = 7.8 Hz, 1H), 8.00−7.97 (m, 2H), 7.70−7.50 (m, 4H), 3.94 (s, 3H); ^{13}C NMR δ 193.7, 193.3, 165.7, 135.4, 135.0, 133.7, 133.3, 132.8, 131.2, 130.9, 129.9, 129.2, 129.0, 52.4. Anal. Calcd for $C_{16}H_{12}O_4$: C, 71.63; H, 4.51. Found: C, 71.22; H, 4.57.

1-(1-Methyl-1*H*-indol-3-yl)-2-phenyl-1,2-ethanedione (7g): needles from ethyl acetate/hexanes (84%); mp 91−92 °C; ^{1}H NMR δ 8.47−8.44 (m, 1H), 8.09−8.05 (m, 2H), 7.76 (s, 1H), 7.63−7.57 (m, 1H), 7.49−7.43 (m, 2H), 7.40−7.33 (m, 3H), 3.76 (s, 3H); ^{13}C NMR δ 193.7, 187.5, 139.5, 137.6, 134.2, 133.3, 130.2, 128.6, 126.2, 124.1, 123.4, 122.5, 112.7, 110.0, 33.6. Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.73; H, 5.01; N, 5.39.

1-(1-Methyl-1*H*-indol-3-yl)-2-(4-pyridinyl)-1,2-ethanedione (7h): needles from ethyl acetate/hexanes (70%); mp 145−147 °C; ^{1}H NMR δ 8.84−8.82 (m, 2H), 8.47−8.43 (m, 1H), 7.89−7.87 (m, 3H), 7.42−7.39 (m, 3H), 3.85 (s, 3H); ^{13}C NMR δ 192.0, 184.8, 150.8, 139.9, 139.5, 137.7, 126.3, 124.4, 123.7, 122.7, 122.6, 112.3, 110.1, 33.8. Anal. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60. Found: C, 73.02; H, 4.57; N, 10.47.

1-(2-Furyl)-2-(1-methyl-1*H*-indol-3-yl)-1,2-ethanedione (7i): needles from ethyl acetate/hexanes (77%); mp 113−114 °C; ^{1}H NMR δ 8.47−8.43 (m, 1H), 8.10 (s, 1H), 7.74−7.73 (m, 1H), 7.65 (d, J = 3.6 Hz, 1H), 7.38−7.35 (m, 3H), 6.60 (dd, J = 3.6, 1.6 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR δ 184.0, 179.7, 150.1, 148.6, 140.2, 137.3, 126.7, 124.0, 123.9, 123.4, 122.5, 112.7, 111.9, 109.9, 33.7. Anal. Calcd for $C_{15}H_{11}NO_3$: C, 71.14; H, 4.38; N, 5.53. Found: C, 71.40; H, 4.39; N, 5.92.

1-(1-Methyl-1*H*-indol-3-yl)-2-(2-methyl-1,3-thiazol-4-yl)-1,2-ethanedione (7j): microcrystals from ethyl acetate/hexane (63%); mp 114−116 °C; ^{1}H NMR δ 8.74−8.43 (m, 2H), 8.00 (s, 1H), 7.35−7.34 (m, 3H), 3.81 (s, 3H), 2.78 (s, 3H); ^{13}C NMR δ 185.4, 184.8, 167.0, 150.8, 140.1, 137.5, 132.3, 126.6, 124.0, 123.3, 122.5, 112.1, 109.9, 33.6, 19.2. Anal. Calcd for $C_{15}H_{12}N_2O_2S$: C, 63.36; H, 4.25; N, 9.85. Found: C, 63.74; H, 4.41; N, 9.80.

1-(2-Furyl)-2-(2-pyridinyl)-1,2-ethanedione (7k): microcrystals from ethyl acetate/hexanes (42%); mp 90−91 °C; ^{1}H NMR δ 8.70 (d, J = 4.5 Hz, 1H), 8.17 (d, J = 7.8 Hz, 1H), 7.94 (td, J = 7.7, 1.7 Hz, 1H), 7.71 (d, J = 1.1 Hz, 1H), 7.57−7.53 (m, 1H), 7.33 (d, J = 3.7 Hz, 1H), 6.63 (dd, J = 3.6, 1.7 Hz, 1H); ^{13}C NMR δ 192.4, 182.7, 151.1, 150.0, 149.7, 148.6, 137.2, 128.1, 123.5, 121.5, 112.8. Anal. Calcd for $C_{11}H_7NO_3$: C, 65.67; H, 3.51; N, 6.96. Found: C, 65.86; H, 3.45; N, 6.81.

1-(2-Furyl)-2-(2-thienyl)-1,2-ethanedione (7l): microcrystals from ethyl acetate/hexanes (43% from **6l**, 42% from **6l′**); mp 88−90 °C; ^{1}H NMR δ 8.07 (dd, J = 3.8 Hz, 1H), 7.85 (dd, J = 5.0, 1.0 Hz, 1H), 7.79 (d, J = 1.0 Hz, 1H), 7.63 (d, J = 3.7 Hz, 1H), 7.21 (t, J = 4.7 Hz, 1H), 6.64 (dd, J = 3.7, 1.5 Hz, 1H); ^{13}C NMR δ 182.0, 177.4, 149.5, 149.4, 138.8, 137.3, 137.2, 128.7, 124.6, 113.0. Anal. Calcd for $C_{10}H_6O_3S$: C, 58.24; H, 2.93. Found: C, 58.44; H, 2.94.

Supporting Information Available: Characterization data for compounds **4b−d**, **6a**, and **7a−d**.[27,28] This material is available free of charge via the Internet at http://pubs.acs.org.

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