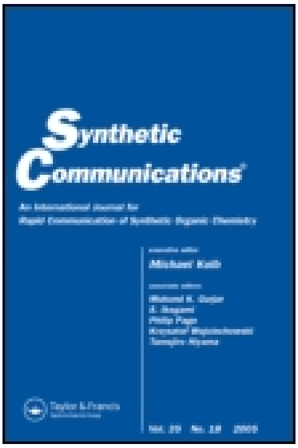

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Copper(I)-Catalyzed Tandem Cyclization/Condensation Reaction to Novel 4,5-Dihydropyrazolo[1,5-a]quinolines and Pyrazolo[1,5-a]indoles

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COPPER(I)-CATALYZED TANDEM CYCLIZATION/CONDENSATION REACTION TO NOVEL 4,5-DIHYDROPYRAZOLO[1,5-*a*]QUINOLINES AND PYRAZOLO[1,5-*a*]INDOLES

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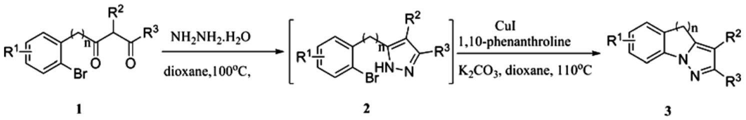
GRAPHICAL ABSTRACT



Abstract *A facile copper(I)-catalyzed tandem reaction for the synthesis of 4,5-dihydropyrazolo[1,5-*a*]quinolines and pyrazolo[1,5-*a*]indoles is reported here. High efficiency and good yields are displayed in this transformation under mild reaction conditions.*

Keywords Copper(I); 4,5-dihydropyrazolo[1,5-*a*]quinolines; 1,3-diketones; pyrazolo[1,5-*a*]indoles

INTRODUCTION

DNA topoisomerases are key enzymes that allow DNA strands or double helices to pass through each other, and they can solve all of the topological problems of DNA in replication, transcription, and other cellular transactions.[1] Hence, a number of anticancer agents take DNA topoisomerases as their targets.[2] It was first reported by Katayama that some quaternary salts of pyrazolo[1,5-*a*]indole derivatives, as represented by the structure **A** (Fig. 1), have fairly strong inhibitory activity against DNA topoisomerases I and II and have strong cytotoxic activity against cancer cells.[3] The structure–activity relationship (SAR) in these derivatives was briefly investigated, and the results showed that the size and polarity of the substituents were crucial for the activity and that poisonous activities against enzyme might be the reason for growth inhibition.[4] We have been involved in the synthesis of pyrazolo[1,5-*a*]indole derivatives,[5] as represented by the structure **B** (Fig. 1). The

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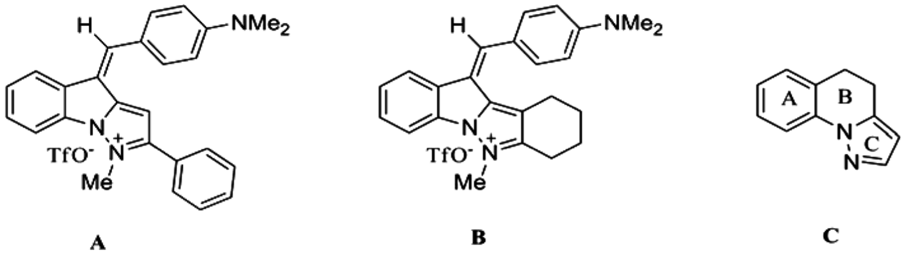
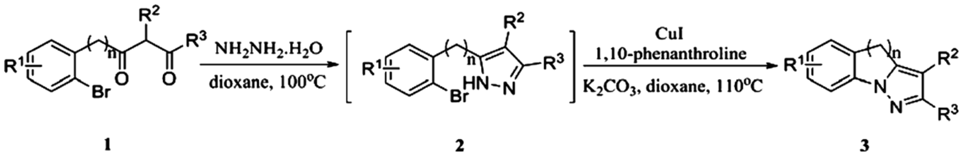


Figure 1. The active compounds and the designed skeleton.

in vitro antitumor activity of **B** was examined with leukemia K562 and HL-60 cells respectively. It showed that **B** can kill both leukemia K562 and HL-60 cells, with IC_{50} of 5.56 μg/ml for K562 cells and 1.33 μg/ml for HL-60 cells. The strong anticancer activity of **B** prompted us to figure out the structure of 4,5-dihydropyrazolo [1,5-*a*]quinoline **C** (Fig. 1) as a possible candidate with the hope to discover new biologically active compounds. There are few synthetic routes to 4,5-dihydropyrazolo [1,5-*a*]quinolines,[6–8] but their syntheses was cumbersome with poor yields of the products and harsh reaction conditions.

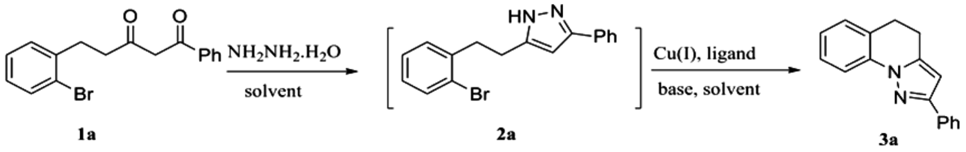
It is well recognized that the development of tandem reactions is an important pursuit from the view of operational simplicity and assembly efficiency.[9] We noticed that 1,3-diketones were converted in situ into pyrazoles by the addition of hydrazine easily,[10] but the difficulties exist in isolation and purification of pyrazoles. Also, in the past few years, the elaboration of heterocycles through copper-catalyzed coupling reactions has been well developed.[11] Inspired by these findings, we planned to explore a novel and facile method to construct pyrazoloheterocycles starting with 1,3-diketones via tandem process (Scheme 1). The method may fit the preparation of 4,5-dihydropyrazolo[1,5-*a*]quinoline as well as pyrazolo[1,5-*a*]indole derivatives as shown in Scheme 1.

Our group has been involved in the studies of copper(I)-catalyzed coupling reactions and has reported some intramolecular amination reactions via copper(I) catalysis.[5,12,13] Compound **1a** was used as a model to achieve and optimize the desired tandem reaction for the formation of **3a**. The results are summarized in Table 1. As a base, K_2CO_3 provided better yield than Cs_2CO_3. Ligand is essential, and 1,10-phenanthroline (PHAN) was found to be better than ethylenediamine (EDA). As a catalyst, CuBr was usable but yield was less than with CuI. Without catalyst, no reaction was observed. The optimal reaction condition for the coupling of pyrazole **2a** required CuI, PHAN, and K_2CO_3 in dioxane as a solvent. To have an effective tandem reaction, the conversion of 1,3-diketones to pyrazoles should be



Scheme 1. The tandem reaction route.

Table 1. Screening of reaction conditions for the tandem reactions of **1a**[a]



Entry	Solvent (mL)	Temp (°C)[b]	R Time (h)[b]	Catalyst[b]	Ligand[c]	Base	Yield (%)[d]
1	Dioxane (2)	rt[b]	6	CuI	PHAN	K_2CO_3	39
2	Dioxane (2)	100	6	CuI	PHAN	K_2CO_3	73
3	Dioxane (0.5)	100	1	CuI	PHAN	K_2CO_3	92
4	Dioxane (0.5)	100	1	CuI	PHAN	$CsCO_3$	79
5	Dioxane (0.5)	100	1	CuI	EDA	K_2CO_3	44
6	Dioxane (0.5)	100	1	CuBr	PHAN	K_2CO_3	83
7	Toluene (0.5)	100	1	CuI	PHAN	K_2CO_3	38
8	Dioxane (0.5)	100	1	CuI	—	K_2CO_3	40
9	Dioxane (0.5)	100	1	—	PHAN	K_2CO_3	0

[a] Reaction conditions: **1a** (1 mmol) and $N_2H_4 \cdot H_2O$ (1.2 mmol) were dissolved in solvent and stirred for 1 h. Then catalyst (0.05 mmol), ligand (0.1 mmol), and base (2.5 mmol) were added subsequently, and the reaction mixture was refluxed for 20 h.

[b] Temp., reaction temperature; rt, room temperature.

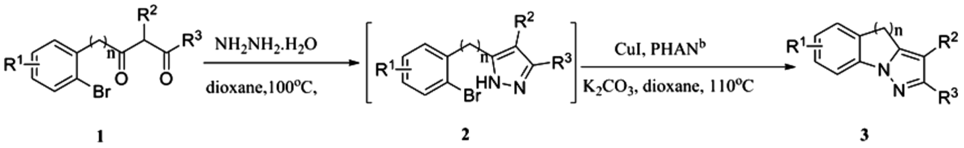
[c] Isolated yields after silica-gel chromatography.

[d] PHAN, 1,10-phenanthroline; EDA, ethylenediamine, 0.3 mmol.

completed prior copper(I)-catalyzed intramolecular C-N coupling reaction, but it was reported that pyrazoles could be formed in aqueous conditions from 1,3-diketones and hydrazine in the presence of dodeca-tungstophosphoric acid.[14] Thus, the effect of a dehydrating agent at the initial stage of the tandem reaction was investigated as follows. When 5-(2-bromophenyl)-1-phenylpentane-1,3-diketone **1a** (1 mmol) and hydrazine hydrate (1.2 equiv) in 1,4-dioxane (2 mL) were reacted in the presence of molecular sieves 4A (330 mg) and $MgSO_4$ (1 equiv) at room temperature, the yield of the desired product **2a** was low (as monitored by thin-layer chromatography, TLC), but temperature elevation up to 100 °C increased the yield of **2a** with longer reaction time (6 h). When the solvent was reduced to 0.5 mL, the tandem reaction completed within 1 h, and the isolated yield of 2-phenyl-4,5-dihydropyrazolo[1,5-*a*]quinoline **3a** became 92%. This result indicated that solvent volume and temperature were crucial to the desired tandem reaction. The optimal reaction conditions were applied to the synthesis of a variety of 4,5-dihydropyrazolo[1,5-*a*]quinolines. We have found that our method is versatile and the yields were generally good to excellent. This method was also applicable for the synthesis of pyrazolo[1,5-*a*]indoles. The results are summarized in Table 2.

A wide range of functional groups in both rings A and C were tolerated in the reaction. The yields of 4,5-dihydropyrazolo[1,5-*a*]quinolines (entries 1–9) were in general better those that of pyrazolo[1,5-*a*]indoles (entries 10–18), presumably because of the steric reason. Methyl substituent *ortho* to bromine atom required prolonged reaction time (entries 4 and 18). Yields were insensitive to the introduction of substitution at ring C.

Table 2. Synthesis of 4,5-dihydropyrazolo[1,5-*a*]quinolines and pyrazolo[1,5-*a*]indoles via a copper-catalyzed tandem reaction[a]



Entry	Starting material[c]	N	R^1	R^2	R^3	Yield (%)[d]
1	**1a**	2	H	H	Ph	**3a** (92)
2	**1b**	2	5-MeO	H	Ph	**3b** (93)
3	**1c**	2	5-F	H	Ph	**3c** (91)
4	**1d**	2	3-Me	H	Ph	**3d** (80)[e]
5	**1e**	2	H	H	4-MeOC_6H_4	**3e** (86)
6	**1f**	2	H	H	$4\text{-NO}_2C_6H_4$	**3f** (94)
7	**1g**	2	H		$\text{-(CH}_2)_4\text{-}$	**3g** (87)
8	**1h**	2	5-MeO		$\text{-(CH}_2)_4\text{-}$	**3h** (89)
9	**1i**	2	5-F		$\text{-(CH}_2)_4\text{-}$	**3i** (74)
10	**1j**	1	H	H	Ph	**3j** (90)
11	**1k**	1	5-MeO	H	Ph	**3k** (91)
12	**1l**	1	5-F	H	Ph	**3l** (89)
13	**1m**	1	H	H	4-MeOC_6H_4	**3m** (79)
14	**1n**	1	H	H	$4\text{-NO}_2C_6H_4$	**3n** (89)
15	**1o**	1	H		$\text{-(CH}_2)_4\text{-}$	**3o** (85)
16	**1p**	1	5-MeO		$\text{-(CH}_2)_4\text{-}$	**3p** (86)
17	**1q**	1	5-F		$\text{-(CH}_2)_4\text{-}$	**3q** (70)
18	**1r**	1	3-Me		$\text{-(CH}_2)_4\text{-}$	**3r** (55)[d]

[a] Reaction conditions: A solution of **1** (1 mmol) and N_2H_4 H_2O (1.2 mmol) in 0.5 mL dioxane was stirred for 1 h. Then CuI (0.05 mmol), PHAN (0.1 mmol), K_2CO_3 (2.5 mmol), and dioxane (2 mL) were added, and the resulting solution was refluxed for 20 h.

[b] PHAN, 1,10-phenanthroline.

[c] The structure of 1,3-diketone is not keto-form but enol-form, as indicated by the spectral data.

[d] Isolated yields after silica-gel chromatography.

[e] Reaction time was prolonged to 40 h.

In summary, a novel method for the synthesis of 4,5-dihydropyrazolo[1,5-*a*] quinolines and pyrazolo[1,5-*a*]indoles has been developed by a tandem copper(I)-catalyzed cyclization/condensation reaction of 1,3-diketones. This method provides a general, facile, and convenient route to the synthesis of pharmacologically attractive compounds. High efficiency and good yields are displayed in this transformation under mild reaction conditions. A more detailed investigation on the potential biologically active compounds is ongoing in our laboratory.

EXPERIMENTAL

A solution of compound **1** (1.0 mmol) and hydrazine monohydrate (0.058 mL, 60 mg, 1.2 mmol) in anhydrous 1,4-dioxane (0.5 mL) was stirred at 100 °C for 1 h. Then, CuI (10 mg, 0.05 mmol), 1,10-phenanthroline (18 mg, 0.1 mmol), K_2CO_3 (345 mg, 2.5 mmol), and anhydrous 1,4-dioxane (2 mL) were added. The mixture was refluxed at 110 °C for 20 h under the protection of argon and filtered through a pad of celite. After the filtrate was evaporated under reduced pressure, the residue was purified by chromatography (silica gel H 10 g, solvents: petroleum ether/ethyl acetate) to give **3** as a solid.

SPECTRAL DATA

2-Phenly-4,5-dihydropyrazolo[1,5-*a*]quinoline 3a

White solid (EtOAc), mp 77.7–78.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.01–2.93 (m, 2H), 3.09-3.01 (m, 2H), 6.48 (s, 1H), 7.17–7.11 (m, 1H), 7.24 (d, $J = 6.87$ Hz, 1H), 7.38–7.30 (m, 2H), 7.46–7.38 (m, 2H), 7.91 (d, $J = 7.62$ Hz, 2H), 8.01 (d, $J = 7.95$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.0, 21.1, 97.1, 111.5, 120.5, 121.4 (×2), 122.2, 123.5, 123.9, 124.2 (×2), 129.0, 132.2, 135.4, 147.6, 153.3. HRMS (EI): calcd. for $C_{17}H_{14}N_2$ 246.1157 [M+]; found 246.1159.

7-Methoxy-2-phenyl-4,5-dihydropyrazolo[1,5-*a*]quinoline 3b

White solid (EtOAc), mp 111.1–112.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.95 (t, $J = 7.58$ Hz, 2H), 3.04 (t, $J = 7.52$ Hz, 2H), 3.83 (s, 3H), 6.46 (s, 1H), 6.80 (s, 1H), 6.87 (d, $J = 8.78$ Hz, 1H), 7.36–7.29 (m, 1H), 7.46–7.38 (m, 2H), 7.95-7.86 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7, 26.2, 55.8, 101.4, 112.7, 114.2, 117.3, 125.9 (×2), 128.0, 128.2, 128.8 (×2), 130.9, 133.7, 139.3, 151.7, 157.2. HRMS (ESI): calcd. for $C_{18}H_{17}N_2O$ 276.1263 [M+]; found 276.1258.

7-Fluoro-2-phenyl-4,5-dihydropyrazolo[1,5-*a*]quinoline 3c

White solid (EtOAc), mp 111.7–112.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.96 (t, $J = 7.67$ Hz, 2H), 3.05 (t, $J = 7.73$ Hz, 2H), 6.47 (s, 1H), 6.96 (dd, $J = 2.18$, 8.63 Hz, 1H), 7.04 (dt, $J = 2.30$, 8.62 Hz, 1H), 7.37–7.29 (m, 1H), 7.47-7.38 (m, 2H), 7.88 (d, $J = 7.85$ Hz, 2H), 7.99–7.92 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 26.0, 101.7, 114.4 and 114.7, 115.2 and 115.5, 117.7 and 117.8, 126.0 (×2), 128.2, 128.6 and 128.7, 128.9 (×2), 133.2 and 133.5, 139.5, 152.2, 158.6 and 161.8. HRMS (ESI): calcd. for $C_{17}H_{13}FN_2$ 264.1063 [M+]; found 264.1055.

9-Methyl-2-phenyl-4,5-dihydropyrazolo[1,5-*a*]quinoline 3d

White solid (EtOAc), mp 99.1–100.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.86 (s, 3H), 2.95–2.89 (m, 2H), 3.01–2.95 (m, 2H), 6.47 (s, 1H), 7.07–7.01 (m, 1H), 7.10 (d, $J = 7.04$ Hz, 1H), 7.19 (d, $J = 7.42$ Hz, 1H), 7.35–7.28 (m, 1H), 7.46–7.39 (m, 2H), 7.90 (d, $J = 7.61$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0, 22.1, 27.5, 100.1, 124.9, 125.5 (×2), 126.1, 127.7, 128.4, 128.6 (×2), 129.0, 131.8, 133.6, 135.4, 141.7, 150.5. HRMS (ESI): calcd. for $C_{18}H_{16}N_2$ 260.1313 [M+]; found 260.1301.

2-(4-Methoxyphenyl)-4,5-dihydropyrazolo[1,5-*a*]quinoline 3e

White solid (EtOAc), mp 125.1–126.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.01–2.94 (m, 2H), 3.10–3.01 (m, 2H), 3.85 (s, 3H), 6.41 (s, 1H), 6.96 (d, $J = 8.75$ Hz, 2H), 7.17–7.08 (m, 1H), 7.28–7.21 (m, 1H), 7.39-7.30 (m, 1H), 7.83 (d, *J* = 8.75 Hz, 2H), 7.98 (d, *J* = 7.99 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 25.6, 55.3, 101.0, 114.0 (×2), 115.8, 124.7, 126.1, 126.3, 127.0 (×2), 127.7, 128.2, 136.7, 139.7, 151.9, 159.5. HRMS (ESI): calcd. for $C_{18}H_{16}N_2O$ 276.1263 [M+]; found 276.1257.

2-(4-Nitrophenyl)-4,5-dihydropyrazolo[1,5-*a*]quinoline 3f

Yellow solid (EtOAc), mp 174.2–175.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.05–2.97 (m, 2H), 3.12–3.05 (m, 2H), 6.57 (s, 1H), 7.22–7.16 (m, 1H), 7.32–7.24 (m, 1H), 7.43–7.34 (m, 1H), 8.01 (d, *J* = 7.95 Hz, 1H), 8.05 (d, *J* = 8.91 Hz, 2H), 8.28 (d, *J* = 8.92 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 25.7, 102.5, 116.3, 124.2 (×2), 125.9, 126.3 (×2), 126.8, 128.1, 128.6, 136.5, 139.9, 140.6, 147.3, 149.7. HRMS (EI): calcd. for $C_{17}H_{13}N_3O_2$ 291.1008 [M+]; found 291.1006.

5,6,7,8,9,10-Hexahydroindazolo[2,3-*a*]quinoline 3g

White solid (EtOAc), mp 72.7–73.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.89–1.75 (m, 4H), 2.50 (t, *J* = 5.80 Hz, 2H), 2.79 (t, *J* = 5.94 Hz, 2H), 2.98–2.83 (m, 4H), 7.11–7.06 (m, 1H), 7.21 (d, *J* = 7.40 Hz, 1H), 7.33–7.27 (m, 1H), 7.86 (d, *J* = 7.95 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.5, 15.5, 18.8, 18.9, 19.1, 21.1, 108.8, 110.8, 119.7, 121.5, 123.1, 123.7, 130.1, 132.3, 146.1. HRMS (EI): calcd. for $C_{15}H_{16}N_2$ 224.1313 [M+]; found 224.1315.

2-Methoxy-7,8,9,10,11,12-hexahydroquinoline[1,2-*b*]indazole 3h

White solid (EtOAc), mp 78.5–79.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.88–1.72 (m, 4H), 2.47 (t, *J* = 5.98 Hz, 2H), 2.75 (t, *J* = 6.11 Hz, 2H), 2.92–2.79 (m, 4H), 3.79 (s, 3H), 6.75 (d, *J* = 2.65 Hz, 1H), 6.81 (dd, *J* = 8.75, 2.74 Hz, 1H), 7.72 (d, *J* = 8.75 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.5, 20.5, 23.8, 23.9, 24.0, 26.4, 55.9, 112.6, 113.3, 114.5, 116.7, 128.1, 131.3, 134.4, 150.5, 156.8. HRMS (EI): calcd. for $C_{16}H_{18}N_2O$ 254.1419 [M+]; found 254.1419.

2-Fluoro-7,8,9,10,11,12-hexahydroquinoline[1,2-*b*]indazole 3i

White solid (EtOAc), mp 101.1–101.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.91–1.73 (m, 4H), 2.48 (t, *J* = 5.97 Hz, 2H), 2.77 (t, *J* = 6.06 Hz, 2H), 2.96-2.83 (m, 4H), 6.93 (dd, *J* = 2.61, 8.64 Hz, 1H), 6.98 (dt, *J* = 2.73, 8.61 Hz, 1H), 7.83–7.77 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.3, 15.5, 18.7, 18.9, 19.0, 21.1, 108.8, 109.4 and 109.7, 110.4 and 110.7, 112.1 and 112.2, 123.4 and 123.5, 128.6 and 128.6, 129.6, 146.1, 153.4 and 156.6. HRMS (ESI): calcd. for $C_{15}H_{15}FN_2$ 242.1219 [M+]; found 242.1226.

REFERENCES

1. Wang, J. C. Cellular roles of DNA topoisomerases: A molecular perspective. *Nat. Rev. Mol. Cell Bio.* **2002**, *3*, 430–440.

2. (a) Pontmesil, M.; Kohn, K. W. *DNA Topoisomerases in Cancer*; Oxford University Press: New York, 1991; (b) Halicka, H. D.; Ozkaynak, M. F.; Levendoglu-Tugal, O.; Sandoval, C.; Seiter, K.; Kajstura, M.; Traganos, F.; Jayabose, S.; Darzynkiewicz, Z. DNA damage response as a biomarker in treatment of leukemias. *Cell Cycle* **2009**, *8*, 1720–1724; (c) Ishimaru, C.; Yonezawa, Y.; Kuriyama, I.; Nishida, M.; Yoshida, H.; Mizushina, Y. Inhibitory effects of cholesterol derivatives on DNA polymerase and topoisomerase activities, and human cancer cell growth. *Lipids* **2008**, *43*, 373–382.
3. Katayama, H.; Kawada, Y.; Kaneko, K.; Oshiyama, T.; Takatsu, N. Synthetic inhibitors of DNA topoisomerase I and II. *Chem. Pharm. Bull.* **1999**, *47*, 48–53.
4. (a) Katayama, H.; Kiryu, Y.; Kaneko, K.; Ohshima, R. Anti-cancer activities of pyrazolo[1,5-*a*]indole derivatives. *Chem. Pharm. Bull.* **2000**, *48*, 1628–1633 (b) Umemura, K.; Mizushima, T.; Katayama, H.; Kiryu, Y.; Yamori, T.; Andoh, T. Inhibition of DNA topoisomerases II and/or I by pyrazolo[1,5-a]indole derivatives and their growth inhibitory activities. *Mol. Pharmacol.* **2002**, *62*, 873–880.
5. Zhu, Y.-M.; Qin, L.-N.; Liu, R.; Ji, S.-J.; Katayama, H. Synthesis of pyrazolo[1,5-*a*]indoles via copper(I)-catalyzed intramolecular amination. *Tetrahedron Lett.* **2007**, *48*, 6262–6266.
6. Deshayes, C.; Gelin, S. Photocyclization of 5-(1-alkenyl)-1-phenylpyrazoles: A convenient synthesis of 4,5-dihydropyrazolo[1,5-*a*]quinolines. *Tetrahedron Lett.* **1983**, *24*, 4679–4682.
7. Gotthardt, H.; Reiter, F. Lichtinduzierte reaktionen der sydnone in gegenwart von mehrfachbindungssystemen. *Chem. Ber.* **1979**, *112*, 1206–1225.
8. Winters, G.; Odasso, G.; Conti, M.; Tarzia, G.; Galliani, G. Synthesis and pregnancy terminating activity of pyrazolo[1,5-*a*]indoles and quinolines. *Eur. J. Med. Chem.* **1984**, *19*, 215–218.
9. (a) Eilbracht, P.; Barfacker, L.; Buss, C.; Hollman, C.; Kitsos-Rzychon, B. E.; Kranemann, C. L.; Rische, T.; Roggenbuck, R.; Schmidt, A. Tandem reaction sequences under hydroformylation conditions: New synthetic applications of transition metal catalysis. *Chem. Rev.* **1999**, *99*, 3329–3365; (b) Ji, K.-G.; Shu, X.-Z.; Chen, J.; Zhao, S.-C.; Zheng, Z.-J.; Lu, L.; Liu, X.-Y.; Liang, Y.-M. $PtCl_2$-catalyzed tandem triple migration reaction toward (*Z*)-1,5-dien-2-yl eaters. *Org. Lett.* **2008**, *10*, 3919–3922; (c) Kabalka, G. W.; Tejedor, D.; Li, N.-S.; Malladi, R. R.; Trotman, S. An unprecedented, tandem aldol–Grob reaction sequence. *J. Org. Chem.* **1998**, *63*, 6438–6439; (d) Liu, Y.-K.; Ma, C.; Jiang, K.; Liu, T.-Y.; Chen, Y.-C. Asymmetric tandem Michael addition–Witting reaction to cyclohexenone annulation. *Org. Lett.* **2009**, *11*, 2848–2851.
10. Heller, S. T.; Natarajan, S. R. 1,3-Diketones from acid chlorides and ketones: A rapid and general one-pot synthesis of pyrazoles. *Org. Lett.* **2006**, *8*, 2675–2678.
11. (a) Maiti, D.; Buchwald, S. T. Orthogonal Cu- and Pd-based catalyst systems for the O- and N-arylation of aminophenols. *J. Am. Chem. Soc.* **2009**, *131*, 17423–17429; (b) Kwong, F. Y.; Buchwald, S. T. Mild and efficient copper-catalyzed amination of aryl bromides with primary alkylamines. *Org. Lett.* **2003**, *5*, 793–796; (c) Yuan, Q.-L.; Ma, D.-W. A one-pot coupling/hydrolysis/condensation process to pyrrolo[1,2-*a*]quinoxaline. *J. Org. Chem.* **2008**, *73*, 5159–5162; (d) Liu, F.; Ma, D.-W. Assembly of conjugated enynes and substituted indoles via CuI/amino acid-catalyzed coupling of 1-alkynes with vinyl iodides and 2-bromotrifluoroacetanilides. *J. Org. Chem.* **2007**, *72*, 4844–4850.
12. Liu, R.; Zhu, Y.-M.; Qin, L.-N.; Ji, S.-J. Efficient synthesis of 1-aryl-1*H*-indazole derivatives via copper(I)-catalyzed intramolecular amination reaction. *Synth. Commun.* **2008**, *38*, 249–254.
13. Liu, R.; Zhu, Y.-M.; Qin, L.-N.; Ji, S.-J.; Katayama, H. Synthesis of 2-aryl-2*H*-indazoles via copper(I)-catalyzed intramolecular amination reaction. *Heterocycles* **2007**, *71*, 1755–1763.
14. Chen, X.; She, J.; Shang, Z.; Wu, J.; Wu, H.; Zhang, P. Synthesis of pyrazoles, diazepines, enaminones, and enamino esters using 12-tungstophosphoric acid as a reusable catalyst in water. *Synthesis* **2008**, *21*, 3478–3486.