

A new CuAl–hydrotalcite catalyzed homocoupling reaction of terminal alkynes at room temperature

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CuAl–LDH has been prepared and applied, for the first time, in the homocoupling reaction of a variety of terminal alkynes at room temperature. The Cu (II) in the host layers of the hydrotalcite exhibits high activity and the catalyst can be easily recovered and reused for eight cycles without depreciation of catalytic activity. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: hydrotalcite; copper (II); alkynes; glaser coupling; reusability

INTRODUCTION

Alkyne dimerization to give 1,3-diynes through oxidative homocoupling, so-called Glaser coupling reaction, is one of the few C–C bond forming reaction which takes place under mild conditions in the presence of oxygen. The Glaser coupling reaction is important for a number of applications, particularly in the construction of linearly π -conjugated acetylenic oligomers and polymers,^{1,2} natural products^{3,4} and molecular recognition processes.⁵ The Cu (I)-catalytic system has been widely employed^{6–8} to carry the homocoupling reaction first discovered by Glaser in 1869.⁹ Another commonly used catalyst system for the Glaser coupling reaction is the Pd-catalyzed system,^{10–17} which involves Cu (I) salts as co-catalyst. Although the Pd catalysts are effective for conducting the homocoupling reaction of terminal alkynes, they are more expensive than the easily available cupric salts and often require phosphine or amine reagents. Cu (II) salt-catalyzed oxidative acetylenic coupling^{18,19} has proved to be of great value since its discovery,²⁰ but it has not gained much attention in recent years. Jiang *et al.* reported the Cu(II)-promoted oxidative homocoupling reaction of terminal alkynes in supercritical carbon dioxide.^{21,22} This protocol requires special equipment, high CO₂ pressure and elevated reaction temperature, but from a practical point of view it is desirable to develop an operationally simple system, which has the ability to

operate at room temperature. Therefore, simpler but effective and environmentally benign Cu (II)-catalyzed homocoupling approaches are still a challenge.

Layered double hydroxides (LDHs), or hydrotalcites of general formula $[M^{II}_{1-x} M^{III}_x(OH)_2]^{x+}[A^{n-}_{x/n} \cdot yH_2O]^{x-}$, contain divalent and trivalent cations. These materials have been studied for many years as catalyst precursors,^{23,24} adsorbents,^{25,26} medicines²⁷ and flame retardants for polymer development.²⁸ In most catalytic applications, LDHs are used as support for palladium and other transition metals.^{29–34} It is of both scientific and practical interests to explore the possibility of using LDHs containing different transition metals in the brucite-like layers directly for some organic reactions. However, studies on the copper-containing hydrotalcites are scarce in the literature.^{35–37}

Herein we report the preparation and characterization of CuAl–LDHs and their application as a catalyst for the Glaser coupling reaction. It is the first time that the copper (II) in the host layers of the hydrotalcites has acted as an effective catalyst for the Cu (II) catalyzed homocoupling reactions. We anticipated that such a procedure would not only avoid the handling of expensive palladium catalysts and sensitive Cu (I) salts, but also allow the recovery and reuse of the catalyst.

RESULTS AND DISCUSSION

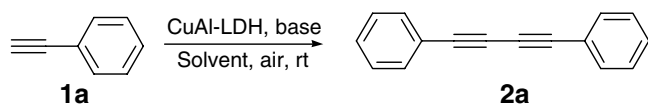
Initially, phenylacetylene was chosen as a model substrate for screening the catalysts and optimizing the reaction conditions. The results were presented in Table 1.

Stoichiometric amounts of Cu (II) salts were used as the catalyst for the coupling reaction. CuAl–LDH with Cu : Al molar ratios of 3 : 1 and 4 : 1 showed better performance

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Table 1. Effect of catalysts and reaction conditions on the oxidative coupling of phenyl acetylene^a

Entry	Catalyst	Base	Solvent	Yield (%) ^b
1	Cu(OAc) ₂ / MgAl-LDH	TMEDA	CH ₃ CN	81
2 ^c	CuAl-LDH	TMEDA	CH ₃ CN	87
3	CuAl-LDH	TMEDA	CH ₃ CN	88
4 ^d	CuAl-LDH	TMEDA	CH ₃ CN	87
5	CuAl-LDH	Et ₂ NH	CH ₃ CN	73
6	CuAl-LDH	Pyridine	CH ₃ CN	67
7	CuAl-LDH	^t BuNH ₂	CH ₃ CN	70
8	CuAl-LDH	NaOAc	CH ₃ CN	53
9	CuAl-LDH	—	CH ₃ CN	31
10	CuAl-LDH	TMEDA	H ₂ O	13
11	CuAl-LDH	TMEDA	Cyclohexane	55
12	CuAl-LDH	TMEDA	CH ₂ Cl ₂	70

^a Phenyl acetylene (2.0 mmol), base (2.0 mmol), solvent (10 ml), Cu(II) catalyst (2.2 mmol), CuAl-LDH with Cu:Al molar ratio of 4:1, at 25 °C for 4 h.

^b Isolated yields.

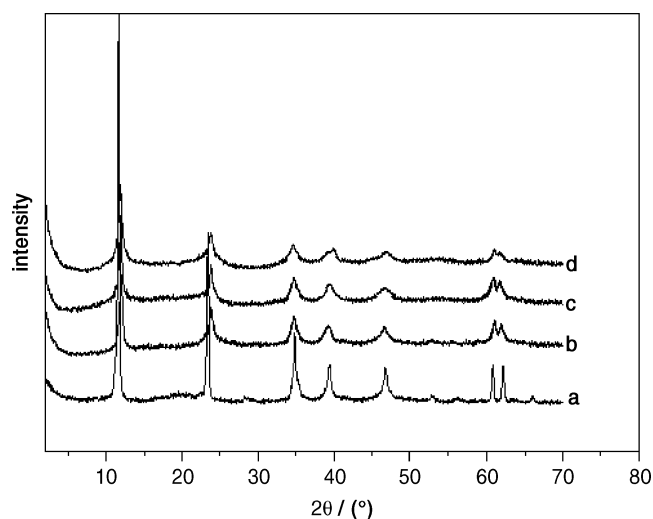
^c Cu:Al molar ratio is 3:1.

^d The reaction temperature is 50 °C.

than Cu(OAc)₂/MgAl-LDH (Table 1, entries 1–3). The bases showed significant influence on the yield of 1,4-diphenylbuta-1,3-diyne. Among the bases tested, amines gave better results than solid base NaOAc, and TMEDA (*N,N,N',N'*-tetramethyl ethylenediamine) was most effective (Table 1, entries 5–8). The reaction gave only 31% yield of diyne without addition of amines (Table 1, entry 9). The coupling reaction provided a low yield using H₂O instead of CH₃CN as the solvent (Table 1, entry 10). When cyclohexane and CH₂Cl₂ were used as the solvent, the diyne was obtained in 55 and 70% yields, respectively (Table 1, entries 11 and 12). All the reactions took place at room temperature. When elevating the reaction temperature up to 50 °C, the yield of the product almost kept at constant value (Table 1, entries 3 and 4).

According to the above results, the optimized reaction conditions for the homocoupling reaction of terminal alkynes using CuAl-LDH as catalyst were determined to be TMEDA as the base in CH₃CN at room temperature.

Under the optimized conditions, we examined the substrate scope of this reaction. Our experiments revealed that a variety of functional groups could be tolerated in this reaction. As shown in Table 2, the diynes were isolated in 74–89% yields, which were approximately the same compared with the results in literature. Dimerization of terminal alkyne **1b–1i** all resulted in homocoupling to give the corresponding diynes **2b–2i** in excellent yields (Table 2, entries 1–8). Structurally complex terminal alkynes, such as

**Figure 1.** XRD patterns of different hydrotalcites. (a) Cu(OAc)₂/MgAl-LDH; (b) CuAl-LDH; (c) CuAl-LDH after the third cycle; (d) CuAl-LDH after the eighth cycle.

1j and **1k**, can also be dimerized in good yield under the same reaction conditions (Table 2, entries 9 and 10).

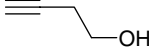
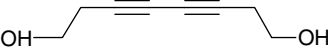
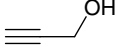
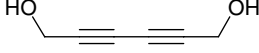
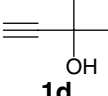
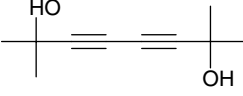
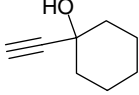
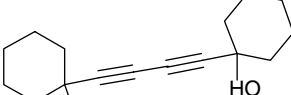
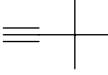
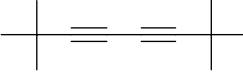
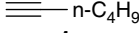
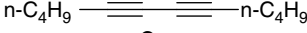
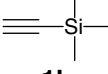
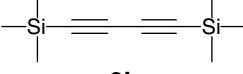
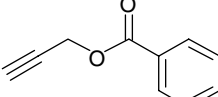
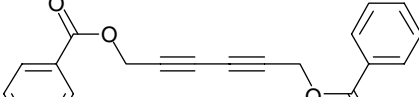
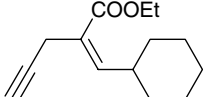
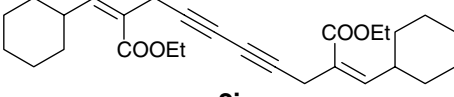
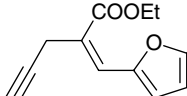
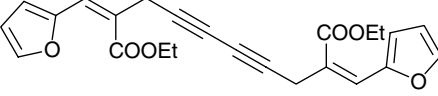
The use of heterogenous catalyst makes the workup procedure strikingly simple. The CuAl-LDH catalyst can be easily removed from the reaction mixture by simple filtration. The recovered catalyst was then reused for the oxidative dimerisation of Phenyl acetylene under the same conditions as those of the first run (Table 3). The catalysts were recycled up to nine times, and the yields dropped slightly only after the eighth cycle. For comparison, we also examined the recyclability of the supported Cu(OAc)₂/MgAl-LDH catalyst. The yield dramatically declined from 87 to 38% after the second cycle. The decrease in catalytic activity may be attributed to the loss of copper from the MgAl-LDH support.

The X-ray diffraction (XRD) patterns showed that the CuAl-LDH catalyst almost retained the same crystallized hydrotalcite structure after recycling in the coupling reaction, which explicated the fact that the CuAl-LDH catalyst could be reused with stable catalytic activity (Fig. 1).

CONCLUSIONS

In summary, we have demonstrated a novel and efficient protocol for the synthesis of conjugated diynes through oxidative dimerization of terminal alkynes that is catalytic in CuAl-LDH at room temperature. The Cu (II) in the host layers of the hydrotalcite acted as effective catalyst and the catalyst could be reused for eight cycles with consistent activity. The extremely mild experimental conditions, low cost and reusability of CuAl-LDH catalyst constructed a green strategy for the synthesis of 1,3-conjugated diynes with great potential for commercial applications.

Table 2. Oxidative coupling of different kinds of alkynes^a

Entry	Alkyne	Product	Yield (%) ^b
	$\text{R}-\text{C}\equiv\text{C}-\text{H} \xrightarrow[\text{CH}_3\text{CN, air, rt}]{\text{CuAl-LDH, TMEDA}} \text{R}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{R}$		
1	 1b	 2b	80
2	 1c	 2c	86
3	 1d	 2d	87
4	 1e	 2e	89
5	 1f	 2f	83
6	 1g	 2g	84
7	 1h	 2h	74
8	 1i	 2i	82
9	 1j	 2j	76
10	 1k	 2k	73

^a Acetylene (2.0 mmol), TMEDA (2.0 mmol), CH₃CN (10 ml), CuAl-LDH with Cu:Al molar ratio of 4:1 (2.2 mmol), at 25 °C for 4 h.^b Isolated yields.

EXPERIMENTAL

¹H and ¹³C NMR spectra were recorded on a Bruker Avance Digital 400 (400 MHz for ¹H NMR; 100MHz for ¹³C NMR) spectrometers with TMS as the internal standard; chemical

shifts were quoted in ppm and *J* values were given in Hz. Mass spectra (EI, 70 eV) were recorded on a HP5989B mass spectrometer. Infrared spectra in KBr were recorded on a Shimadzu IR-408 spectrometer. The X-ray diffraction (XRD) was performed using a RigakuD/max-rA rotating anode

Table 3. Recyclability of the CuAl-LDH for oxidative dimerization of phenyl acetylene^a

Catalyst	Yield (%) ^b Cycles									
	0	1	2	3	4	5	6	7	8	9
CuAl-LDH	88	87	89	88	91	88	92	89	86	76
Cu(OAc) ₂ /MgAl-LDH	81	71	38	—	—	—	—	—	—	—

^a Acetylene (2.0 mmol), TMEDA (2.0 mmol), CH₃CN (10 ml), CuAl-LDH with Cu:Al molar ratio of 4:1 (2.2 mmol), at 25 °C for 4 h.

^b Isolated yields.

X-ray diffractometer equipped with a Cu K α tube and Ni filter ($\lambda = 0.1542$ nm). The scan speed was 5 deg/min at 40 kV and 30 mA. Melting points are uncorrected. All the alkynes and other reagents were used without further purification.

The preparation of CuAl-LDH

CuAl-LDH with different Cu:Al ratios was synthesized by co-precipitation. An aqueous solution (200 ml) containing appropriate amounts of Cu(NO₃)₂·6H₂O and Al(NO₃)₃·9H₂O was added dropwise with vigorous stirring into 100 ml of 0.5 M Na₂CO₃ solution. The addition took about 1 h. In the course of synthesis, the temperature was maintained at 25 °C and pH at about 10 by a simultaneous addition of a 3 M NaOH solution. The resulting suspension was then maintained at 30 °C, with stirring, for 36 h. The product was filtered off and washed several times with distilled water and dried overnight at 80 °C in air.

General synthetic procedure and recycling process

A mixture of terminal alkyne (2 mmol), TMEDA (2 mmol), CuAl-LDH (2.2 mmol) in CH₃CN (10 ml) was stirred in air at ambient temperature for 4 h. After completion of the reaction, as indicated by TLC, the reaction mixture was filtered and washed with CH₃CN. The combined CH₃CN eluents were concentrated *in vacuo* and the resulting product was directly charged on a small silica gel column and eluted with *n*-hexane to afford pure symmetrical diyne. The remaining CuAl-LDH was dried at 80 °C for 6 h before the next run.

1,4-Diphenyl Buta-1,3-diyne (2a)

White solid, m.p.: 87–88 °C. ¹H NMR (CD₃Cl) δ 7.57–7.55 (m, 4H), 7.40–7.34 (m, 6H); ¹³C NMR (CD₃Cl) δ 132.4, 129.2, 128.4, 121.7, 81.5, 73.9; MS *m/z* 202 (M⁺); IR ν_{\max} (cm⁻¹) 3339, 2928, 2853, 2487, 2147, 1923, 1699, 1615, 1561, 1278, 984, 712.

Octa-3,5-diyne-1,8-diol (2b)

¹H NMR (CD₃COCD₃) δ 4.09 (t, *J* = 5.6 Hz, 2H), 3.60 (dd, *J*₁ = 6.4 Hz, *J*₂ = 5.6 Hz, 4H), 2.41 (t, *J* = 6.4 Hz, 4H); ¹³C NMR (CD₃COCD₃) δ 75.9, 66.8, 60.9, 23.9; MS *m/z* 138 (M⁺); IR ν_{\max} (cm⁻¹) 3333, 2946, 2889, 2258, 2156, 1654, 1417, 1184, 1044, 845.

Hexa-2,4-diyne-1,6-diol (2c)

White solid, m.p.: 98–100 °C. ¹H NMR (DMSO-*d*₆) δ 5.36 (s, 2H), 4.16 (s, 4H); ¹³C NMR (DMSO-*d*₆) δ 79.6, 68.0, 49.4; MS *m/z* 110 (M⁺); IR ν_{\max} (cm⁻¹) 3300, 2929, 2126, 1636, 1475, 1445, 1352, 1219, 1031, 914, 677, 555.

2,7-Dimethyl-3,5-octadiyne-2,7-diol (2d)

White solid, m.p.: 132–134 °C. ¹H NMR (CD₃COCD₃) δ 4.47 (s, 2H), 1.40 (s, 12H); ¹³C NMR (CD₃COCD₃) δ 85.6, 66.1, 65.1, 31.5; MS *m/z* 168 (M⁺); IR ν_{\max} (cm⁻¹) 3572, 3220, 2982, 2935, 2514, 2256, 2144, 1685, 1449, 1364, 1211, 1170, 954, 889, 841, 732.

1,4-Bis(1-hydroxycyclohexyl)-1,3-butadiyne (2e)

White solid, mp: 174–176 °C. ¹H NMR (DMSO-*d*₆) δ 5.49 (s, 2H), 1.76–1.17 (m, 20H); ¹³C NMR (DMSO-*d*₆) δ 84.5, 67.03, 66.96, 39.2, 24.7, 22.5; MS *m/z* 246 (M⁺); IR ν_{\max} (cm⁻¹) 3277, 2932, 2857, 1636, 1445, 1348, 1278, 1258, 1164, 1065, 1031, 965, 904, 852, 709, 609, 524.

2,2,7,7-Tetramethylocta-3,5-diyne (2f)

White solid, mp: 106–109 °C. ¹H NMR (CD₃Cl) δ 1.22 (s, 18H); ¹³C NMR (CD₃Cl) δ 86.2, 63.7, 30.6, 27.9; MS *m/z* 162 (M⁺); IR ν_{\max} (cm⁻¹) 3449, 2927, 2856, 2140, 1630, 1456, 1116, 1069, 618.

Dodeca-5,7-diyne (2g)

¹H NMR (CD₃Cl) δ 2.26–2.22 (t, 4H), 1.52–1.46 (m, 4H), 1.43–1.38 (m, 4H), 0.92–0.88 (t, 6H); ¹³C NMR (CD₃Cl) δ 77.3, 65.3, 30.4, 21.9, 18.8, 13.5; MS *m/z* 162 (M⁺); IR ν_{\max} (cm⁻¹) 2958, 2928, 2859, 2139, 1464, 1379, 1319, 1259, 1104, 754.

1,4-Bis(trimethylsilyl)-1,3-butadiyne (2h)

White solid, mp: 110–113 °C. ¹H NMR (CD₃Cl) δ 0.16 (s, 18H); ¹³C NMR (CD₃Cl) δ 88.1, 85.6, -0.552; MS *m/z* 194 (M⁺); IR ν_{\max} (cm⁻¹) 3448, 2925, 2858, 2143, 1628, 1457, 1254, 1115, 847.

1,6-Bisbenzoxylhexa-2,4-diyne (2i)

White solid, m.p.: 73–75 °C. ¹H NMR (CD₃Cl) δ 8.06–8.04 (m, 4H), 7.59–7.55 (t, 2H), 7.46–7.42 (q, 4H), 4.98 (s, 4H); ¹³C NMR (CD₃Cl) δ 165.5, 133.4, 129.8, 129.1, 128.4, 73.7, 70.5, 52.7; MS *m/z* 318 (M⁺); IR ν_{\max} (cm⁻¹) 2942, 1731, 1599, 1451, 1425, 1367, 1314, 1259, 1087, 1067, 1027, 980, 924, 708, 683, 570.

2,9-Bis-cyclohexylmethylene-deca-4,6-diyne-2,9-dioic acid diethyl ester(2j)

¹H NMR (CD₃Cl) δ 6.64 (d, *J* = 10.0 Hz, 2H), 4.16 (q, *J* = 7.2 Hz, 4H), 3.22 (s, 4H), 2.34 (q, *J* = 10.0 Hz, 2H), 1.72–1.62 (m, 10H), 1.29 (t, *J* = 7.2 Hz, 6H), 1.24–1.10 (m, 10H); ¹³C NMR (CD₃Cl) δ 166.6, 149.5, 124.8, 74.7, 64.8, 60.7, 37.9, 31.6, 25.6, 25.3, 16.9, 14.1; MS *m/z* 438 (M⁺); IR ν_{\max} (cm⁻¹) 3357, 2927, 2852, 1710, 1648, 1448, 1369, 1277, 1202, 1150, 1069, 1020, 970, 761.

2,9-Bis-furan-2-ylmethylene-deca-4,6-diyne-2,9-dioic acid diethyl ester (2k)

¹H NMR (CD₃Cl) δ 7.57–7.56 (d, 2H), 7.46 (s, 2H), 6.74–6.73 (d, 2H), 6.51–6.50 (q, 2H), 4.26 (q, *J* = 7.6 Hz, 4H), 3.67 (s, 4H),

1.33 (t, $J = 7.6$ Hz, 6H); ^{13}C NMR (CD_3Cl) δ 166.8, 150.5, 144.9, 126.9, 122.5, 116.6, 112.2, 74.1, 64.8, 61.2, 18.3, 14.2; MS m/z 406 (M^+); IR ν_{max} (cm^{-1}) 3448, 3145, 2986, 1696, 1633, 1467, 1412, 1391, 1368, 1271, 1211, 1089, 1027, 919, 767, 754, 593.

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