A novel route to the synthesis of α,ω-diphenylalkanes

Hui Chen[a]*, Yancai Chen[a,b], Yinlong Zhang[a], Zhenqiang Yang[a], Ji Li[a,b], Ruina Yang[a] and Wenxin Wang[a]

[a]Institute of Chemistry, Henan Academy of Sciences, Zhengzhou 450002, P.R. China;
[b]College of Chemistry and Molecular Engineering, Zhengzhou University, Zhengzhou 450001, P.R. China

A novel route to the synthesis of α,ω-diphenylalkanes is reported. Toluene was metalated in the benzylic position by *n*-butyllithium with THF as an activating reagent, and then directly reacted with α,ω-dichloroalkanes to obtain the target product. This process provides a facile and efficient route to the synthesis of α,ω-diphenylalkanes.

Keywords: α,ω-diphenylalkane, toluene, benzylic metalation, tetrahydrofuran, α,ω-dichloroalkane

Recently, α,ω-diphenylalkanes have attracted attention because of their promising applications in the field of fluorescent probes.[1–3] They are also in demand as ligands for metal complexes,[4] as precursors for cyclophanes/calixarenes[5] and as polymerisation initiators[6]. In addition, α,ω-diphenylalkanes are important reagents for improving the viscosity index of lubricants, especially in high-temperature nuclear-radiation-resistant hydraulic fluids.[7]

Synthetic procedures to produce α,ω-diphenylalkanes have been described previously. For example, the preparation of α,ω-diphenylalkanes has been reported[8] by the Friedel–Crafts acylation of arenes using $ClOC(CH_2)_nCOCl$ in the presence of Lewis acid with a subsequent reduction. As another approach to the α,ω-diphenylalkanes, the coupling of Grignard reagents with α,ω-dihaloalkanes using a transition metal catalyst has been thoroughly studied.[9] Reduction of the corresponding ketones and α,β-enones is also a powerful way to obtain α,ω-diphenylalkanes.[10] Iridium-catalysed reactions of ω-phenylalkanols to form α,ω-diphenylalkanes have been reported recently.[11] However, these previous methods have some major drawbacks including multistep reactions, harsh reaction conditions, and/or the use of transition metal catalysts. The development of a facile, versatile, and waste-minimising method for preparing α,ω-diphenylalkanes from easily accessible chemicals is highly desirable.

In this paper, we report a novel synthetic method for producing α,ω-diphenylalkanes. At room temperature, toluene was metalated in the benzylic position by *n*-butyllithium with THF as an activating reagent, and then directly reacted with α,ω-dichloroalkanes to obtain the target products. To our knowledge, this has not been attempted previously. This reaction provides a simple and clean route to synthesis of α,ω-diphenylalkanes from easily available materials. α,ω-Diphenylalkanes **1a–d**, which contain different alkyl chains, were synthesised as shown in Scheme 1.

Results and discussion

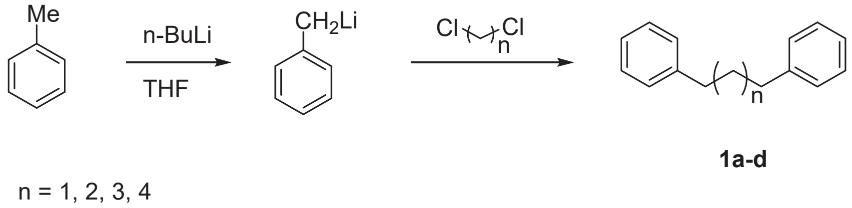
A series of experiments were carried out to optimise the reaction conditions. When we started our work, toluene was firstly metalated in the benzylic position by *n*-BuLi in hexane, and then CH_2Cl_2 was added to produce **1a**. Different activating reagents such as Et_2O, THF and tetramethylethylenediamine (TMEDA) were employed to evaluate the solvent effect under similar reaction conditions (Table 1). When no activating reagent was used in the reaction system, the reaction did not occur, which indicated that toluene was not activated by *n*-BuLi in hexane at room temperature. When Et_2O, THF were used, 1,3-diphenylpropane **1a** was generated in moderate yield. THF gave the best result (62% yield). However, when TMEDA as the traditional depolymersation reagent for *n*-BuLi was added, the yield was very low. The yield was also low when TMEDA was used in conjunction with Et_2O and THF. We considered that the low yield of **1a** may be caused by the high activity of the benzyl lithium intermediate, and hence the mild THF gave better results when reacted with CH_2Cl_2.

The promising outcome of the initial screening encouraged us to extend the observed amplification to a series of diphenylalkanes **1b–d**, and each gave satisfactory results. Along with increase of the alkyl chain of α,ω-dichloroalkanes, the yields of **1b–d** were increased from 67% to 78%. This result indicated that a decrease in steric hindrance was more favourable for the reaction.

Under the optimal experimental conditions, different α,ω-dibromoalkanes were also used to see if similar results were obtained (Scheme 2). It was surprising to find that α,ω-dibromoalkanes gave completely different results. When CH_2Br_2 was employed instead of CH_2Cl_2, only a trace of **1a** (1%) was

Table 1 The effect of reaction conditions on the yield of compound **1a**

Entry	Activating reagent	Yield of **1a** (%)
1	0	0
2	Et_2O	51
3	THF	62
4	TMEDA	23
5	Et_2O +TMEDA	47
6	THF +TMEDA	18

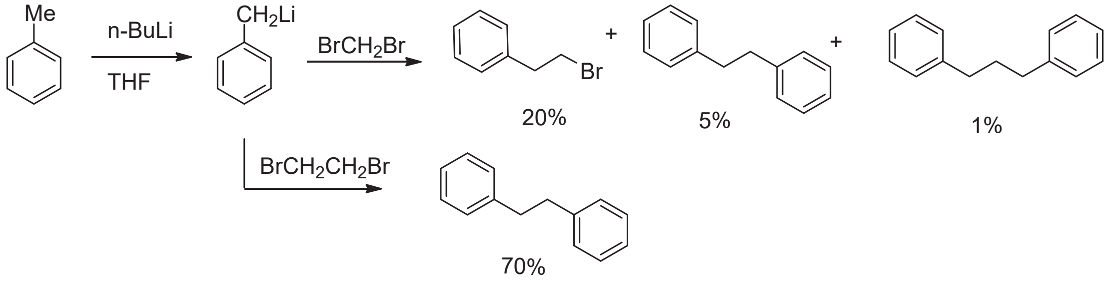


1a-d

Scheme 1

---

* Correspondent. E-mail: hchen@kingorgchem.com



Scheme 2

detected. It was accompanied by 20% of 1,2-diphenylethane and 5% of 2-bromoethylbenzene. When 1,2-dibromoethane was used, only 1,2-diphenylethane **1e** was obtained in relatively higher yield (70% yield). This suggested that here α,ω-dibromoalkane mainly played the role of oxidant.[12]

Conclusion

In summary, we have discovered a facile and efficient manner to synthesise α,ω-diphenylalkanes from toluene as a starting material. Regioselective metalation in the benzylic position with *n*-BuLi in THF could be used in conjunction with α,ω-dichloroalkane to allow direct access to the α,ω-diphenylalkanes in moderate yield. This one-pot synthetic operation did not require additional synthetic steps to preactivate the coupling partners or the use of transition metal catalysts. Moreover, the convenience and low costs associated with the process are worth highlighting.

Experimental

All experiments were performed under a dry argon atmosphere using standard Schlenk techniques. Column chromatography was performed in air, unless stated in text. All solvents and reagents were of reagent quality, purchased from commercial sources and used without further purification. Toluene, Et_2O, and THF were dried and distilled from sodium/benzophenone just before use. ^1H NMR spectra were recorded on Bruker AM400. ^1H chemical shifts were reported in parts per million (ppm) relative to $Si(CH_3)_4$ as external standard. High-resolution mass spectra were obtained on a Varian MAT 311 instrument. Elemental analysis was performed on a Carlo-Erba-1106 autoanalyser.

Synthesis of α,ω*-diphenylalkanes* (**1a–e**)*; general procedure*

n-Butyllithium (8 mL, 20 mmol, 2.5M in hexane) was added to toluene (10 mL) at r.t., and then THF (10 mL) was added dropwise to the mixture. After stirring for 3 h, the dihaloalkane (10 mmol) was added. The resulting suspension was allowed to stir at r.t. overnight, and then quenched with water. The resulting solution was extracted with ethyl acetate (20 × 3 mL). The extract was washed with brine (3 × 10 mL) and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography on silica (hexane) to give compound **1**.

1,3-Diphenylpropane (**1a**):[13] Colourless oil; 62% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 1.96–2.06 (t, *J* = 8.0 Hz, 2H), 2.66–2.74 (t, *J* = 8.0 Hz, 4H), 7.19–7.25 (m, 6H), 7.27–7.35 (m, 4H); MS (ESI) *m/z*: 197.1226 [M + H]$^+$; Anal. calcd for $C_{15}H_{16}$: C, 91.78; H, 8.22; found: C, 91.77: H, 8.23%.

1,4-Diphenylbutane (**1b**):[14] White solid; 67% yield; m.p. 51.2–52.7 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.65–1.73 (m, 4H), 2.61–2.68 (t, *J* = 8.0 Hz, 4H), 7.14–7.22 (m, 6H), 7.25–7.32 (m, 4H); MS (ESI) *m/z*: 211.1488 [M + H]$^+$; Anal. calcd for $C_{16}H_{18}$: C, 91.37; H, 8.63; found: C, 91.36; H, 8.64%.

1,5-Diphenylpentane (**1c**):[15] Colourless oil; 75% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 1.35–1.45 (m, 2H), 1.61–1.70 (m, 4H), 2.58–2.63 (t, *J* = 8.0 Hz, 4H), ,7.15–7.20 (m, 6H), 7.25–7.31 (m, 4H); MS (ESI) *m/z*: 225.1646 [M + H]$^+$; Anal. calcd for $C_{17}H_{20}$: C, 91.01; H, 8.99; found: C, 91.02; H, 8.98%.

1,6-Diphenylhexane (**1d**):[16] Colourless oil; 78% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 1.33–1.49 (m, 4H), 1.60–1.71 (m, 4H), 2.58–2.69 (t, *J* = 8.0 Hz, 4H), 7.17–7.23 (m, 5H), 7.24–7.35 (m, 5H); MS (ESI) *m/z*: 239.1798 [M + H]$^+$; Anal. calcd for $C_{18}H_{22}$: C, 90.70; H, 9.30; found: C, 90.71; H, 9.29%.

1,2-Diphenylethane (**1e**):[17] White solid; 70% yield; m.p. 51.8–53.5 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 2.99 (s, 4H), 7.22–7.30 (m, 6H), 7.35–7.40 (m, 4H); MS (ESI) *m/z*: 183.1172 [M + H]$^+$; Anal. calcd for $C_{14}H_{14}$: C, 92.26; H, 7.74; found: C, 92.25; H, 7.75%.

Acknowledgements

We thank the Natural Science Foundation of China (Project No. 21502045) and Outstanding Youth Foundation for Scientific and Technological Innovation of Henan Province (174100510018) for the financial support.

Received 2 May 2017; accepted 14 July 2017
Paper 1704738
https://doi.org/10.3184/174751917X15009724013088

References

1 K. Tani, Y. Tohda, H. Takemura, H. Ohkita, S. Ito and M. Yamamoto, *Chem. Commun.*, 2001, 1914.
2 M. Yamaji, H. Tsukada, J. Nishimura, H. Shizuka and S. Tobita, *Chem. Phys. Lett.*, 2002, **357**, 137.
3 T. Ikeda, B. Lee, S. Kurihara, S. Tazuke, S. Ito and M. Yamamoto, *J. Am. Chem. Soc.*, 1988, **110**, 8299.
4 T. Kato, H. Iwama, N. Iwama, Y. Osano and T. Sugano, *Stud. Surf. Catal.*, 1999, **121**, 473.
5 T. Yamato, K. Fujita, K. Futatsuki and H. Tsuzuki, *Can. J. Chem*., 2000, **78**, 1089.
6 W.G. Skene, J.C. Scaiano and G.P.A. Yap, *Macromolecules*, 2000, **33**, 3536.
7 D.R.Wilgus, A.C. Ettling and M.A. Pino, *J. Chem. Eng. Data*, 1961, **6**, 106.
8 W. Borsche and J. Wollemann, *Ber. Dtsch. Chem. Ges.,* 1912, **45**, 3713.
9 M. Uemura, H. Yorimitsu and K. Oshima, *Chem. Commun*., 2006, 4726.
10 A. Mori, T. Mizusaki, M. Kawase, T. Maegawa, Y. Moriguchi, S. Takao, Y. Takagi and H. Sajiki, *Adv. Synth. Catal*., 2008, **350**, 406
11 Y. Obora, Y. Anno, R. Okamoto, T. Matsu-ura and Y. Ishii, *Angew. Chem. Int. Ed*., 2011, **50**, 8618.
12 M. Blangetti, P. Fleming and D.F. O'Shea, *J. Org. Chem*., 2012, **77**, 2870.
13 L. Guo-Bin, Z. Hong-Yun, L. Daia, T. Thiemann, H. Tashiroc and M. Tashiro, *J. Chem. Res*., 2009, 579.
14 K.T. Serijan and P.H. Wise, *J. Am. Chem. Soc*., 1951, **73**, 4766.
15 K.T. Serijan and P.H. Wise, *J. Am. Chem. Soc*., 1952, **74**, 365.
16 K.T. Serijan and P.H. Wise, *J. Am. Chem. Soc*., 1951, **73**, 5191.
17 D. Papa, E. Schwenk and B. Whitman, *J. Org. Chem*., 1942, **7**, 587.