Tetrahedron 69 (2013) 6083–6087

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

N-Tosylhydrazine-mediated deoxygenative hydrogenation of aldehydes and ketones catalyzed by Pd/C

Lei Zhou [a,b], Zhenxing Liu [a], Yizhou Liu [a], Yan Zhang [a,*], Jianbo Wang [a,*]

[a] *Beijing National Laboratory of Molecular Sciences (BNLMS) and Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China*
[b] *School of Chemistry and Chemical Engineering, Sun Yat-Sen University, Guangzhou 510275, China*

ARTICLE INFO

Article history:
Received 31 January 2013
Received in revised form 11 May 2013
Accepted 20 May 2013
Available online 23 May 2013

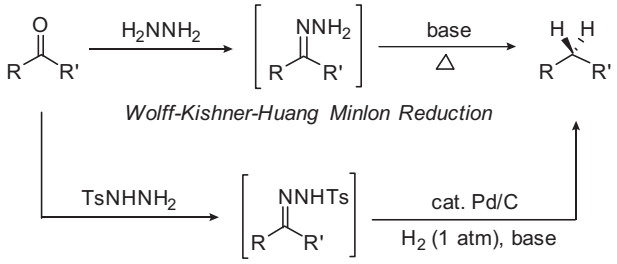
Keywords:
Reduction
Hydrogenation
Deoxygenation
N-Tosylhydrazone
Aldehydes
Ketones

ABSTRACT

A mild and efficient method for the deoxygenative hydrogenation of aldehydes and ketones has been developed. The reaction is mediated by *N*-tosylhydrazine with H_2 (1 atm) as the reductant and 10% Pd/C as the catalyst.

1. Introduction

The deoxygenative reduction of aldehydes and ketones to methyl or methylene derivatives is one of the fundamental processes in organic chemistry, which was first developed by Wolff and Kishner via hydrazone or semicarbazone cleavage in basic media[1] and Clemmensen by using Zn–Hg and HCl.[2] The original Wolff–Kishner reduction procedure was to mix the carbonyl compound with 100% H_2NNH_2 and potassium hydroxide in a sealed tube and heat the mixture at high temperature (160–200 °C) for days. Huang Minlon late modified this procedure by using 85% $H_2NNH_2 \cdot H_2O$ in a high boiling point solvent (ethylene glycol) (Scheme 1).[3] Over the many decades, the Wolff–Kishner–Huang Minlon reduction has been widely used in organic synthesis.[4,5] In the meantime, the original procedures have been modified in order to make the reaction conditions milder and more efficient.[6,7] Other methods involving the use of aluminum hydride,[8] boron hydride,[9] or hydrosilane[10] with a combination of protic acids or Lewis acids have been well studied. In addition, supercritical 2-propanol[11] and metallic selenium with CO and water[12] were also used for the deoxygenative reduction. Moreover, for the consideration of green chemistry and atom economy aspects, catalytic systems utilizing hydrogen as a clean hydrogen source for reduction of carbonyl compounds to hydrocarbons have also been reported, such as the reduction using H_2/Raney nickel,[13] catalytic hydrogenation with polyoxometalates,[14] Cu/SiO_2,[15] montmorillonite,[16] and hydrogenolysis over Pd in the presence of HCl.[17]



Scheme 1. Deoxygenative reduction of carbonyl compounds.

In the Wolff–Kishner–Huang Minlon reduction mechanism, the carbonyl compound is first converted to hydrazone. The hydrazone is then deprotonated under strong basic conditions to generate diimide intermediate. The diimide intermediate undergoes further deprotonation and loss of N_2 to form a carbanion, which is protonated to afford the final reduction product.[18] Recently, Furrow and Myers reported a modified reaction by using

* Corresponding authors. E-mail address: wangjb@pku.edu.cn (J. Wang).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.05.070

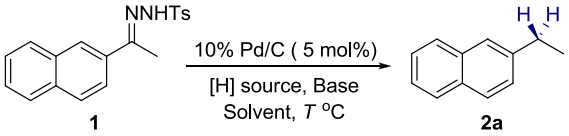
N-*tert*-butyldimethylsilylhydrazones (TBSHs) as alternatives to hydrazones in Wolff–Kishner–Huang Minlon reduction.[7] Subsequently, the same authors described the preparation of diazoalkanes by the oxidation of TBSHs with (difluoroiodo)benzene.[19] However, the use of freshly prepared dry solvents, the risk of detonation during the distillation of anhydrous TBSHs, and the tenuous operations might limit its applications in large scale synthesis.

On the other hand, it is known that diazoalkanes can be hydrogenated by H_2 with palladium catalyst.[20] It is also well established that diazoalkanes can be generated from *N*-tosylhydrazones by treatment with base (Bamford–Stevens reaction).[21,22] Based on this background, we have conceived that a mild method of deoxygenative reduction of carbonyl compounds may be developed by the combination of *N*-tosylhydrazone formation and diazo hydrogenation. Although the reduction of tosylhydrazones to hydrocarbons with other hydride donors have been developed,[23] the reactions suffered some drawbacks, such as the generation of a large amount of wastes and undesired by-products. Herein we wish to report a one-pot, two-step deoxygenation reaction converting carbonyl group to methyl or methylene group. This method employs hydrogen as the clean reductant with 10% Pd/C as the catalyst under weak base conditions (Scheme 1).

2. Results and discussion

At the outset, we investigated the reduction of *N*-tosylhydrazone **1** under Pd/C-catalyzed reaction conditions (Table 1). In the initial experiment, we used triethylsilane (TES-H) as the hydride donor. In the presence of 10% Pd/C (5 mol %) and *t*-BuOLi (3 equiv) in dichloroethane (DCE) at 80 °C, we were pleased to observe that the expected reduction product **2a** was formed in 72% GC yield (Table 1, entry 1). With MeOH as solvent, the reaction afforded sightly higher yield (Table 1, entry 2). In the absence of TES-H, **2a** could only be detected in trace amount (Table 1, entry 3). The Pd/C catalyst was also proved indispensable (Table 1, entry 4). To our delight, when H_2 (1 atm) was used to replace TES-H as hydrogen source, **2a** could be formed in 90% yield (Table 1, entry 5). Furthermore, we observed that ^{t}BuOLi could be replaced by inexpensive K_2CO_3, although the yields were slightly diminished (Table 1, entries 6–8). Based on these experiments, we concluded following optimized reaction conditions: 10% Pd/C (5 mol %), H_2 (1 atm), K_2CO_3 (4.0 equiv), MeOH, 65 °C, 24 h.

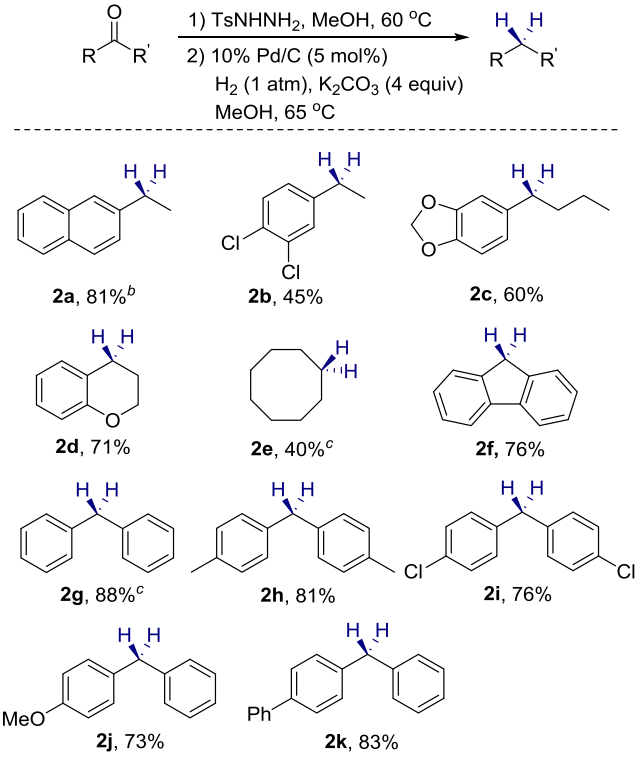
Table 1
Optimization experiments



Entry	Base (equiv)	Solvent	*T* (°C)	[H]	**2a** Yield[a] (%)
1	^{t}BuOLi	DCE	80	TES-H (2 equiv)	72
2	^{t}BuOLi	MeOH	80	TES-H (2 equiv)	84
3	^{t}BuOLi	MeOH	80	—	Trace
4[b]	^{t}BuOLi	MeOH	80	TES-H (2 equiv)	6
5	^{t}BuOLi	MeOH	80	H_2 (1 atm)	90
6	K_2CO_3	MeOH	80	H_2 (1 atm)	77
7	K_2CO_3	MeOH	65	H_2 (1 atm)	63
8	K_2CO_3 (3)	MeOH	65	H_2 (1 atm)	75
9	K_2CO_3 (4)	MeOH	65	H_2 (1 atm)	85

[a] The yield was determined by GC with dodecane as internal standard.
[b] In the absence of Pd/C.

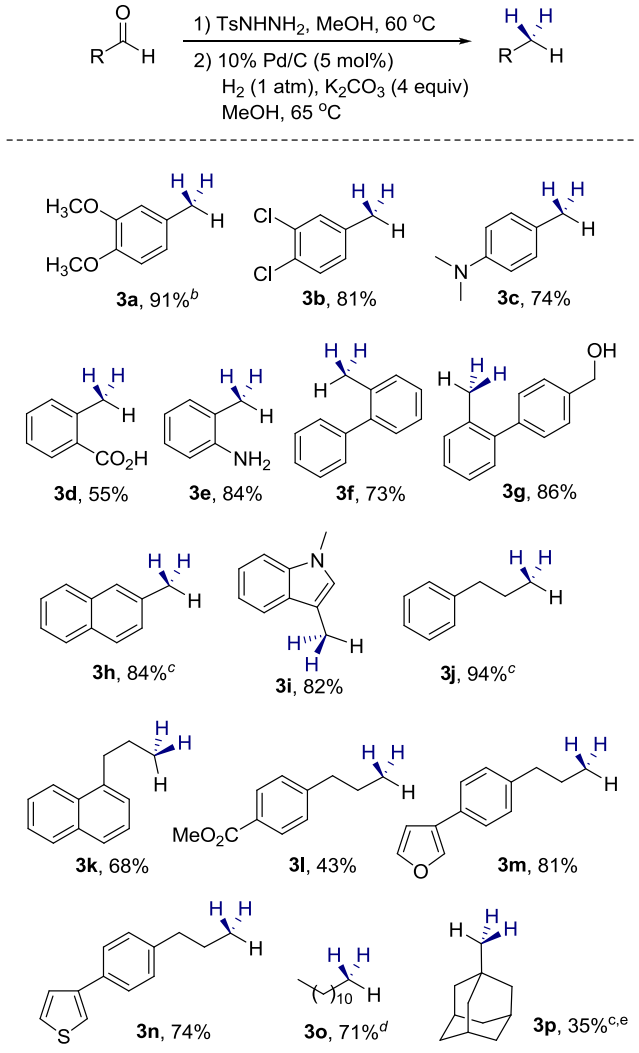
With the optimal reaction conditions in hand, we then examined the possibility of the formation of *N*-tosylhydrazone and the subsequent deoxygenative hydrogenation in a single reaction vessel. To our delight, 1-(naphthalen-2-yl)ethanone could be deoxygenated successfully in good yield without isolation of *N*-tosylhydrazone, affording the corresponding product **2a** in 81% isolated yield (Scheme 2, **2a**). Reduction of other three aryl–alkyl ketones gave the corresponding hydrocarbons **2b**–**d** in moderate to good yields. In the case of cyclooctanone, the product cyclooctane **2e** was only obtained in 40% yield. The diminished yield in this case may be attributed to the relatively high stability of *N*-tosylhydrazone generated from cyclooctanone. For aryl–aryl ketones, the reduction of 9*H*-fluoren-9-one and benzophenone proceeded smoothly in 76% and 88% (GC) yields, respectively. The methyl, chloro, methoxy, or phenyl substituted benzophenones were also converted to the corresponding methylene compounds **2h**–**k** in good yields.



[a] Reaction conditions: ketone (0.5 mmol), $TsNHNH_2$ (1.05 equiv), MeOH (10 mL), stirring at 60 °C until the disappearance of the ketone; then 10% Pd/C (5% mol), K_2CO_3 (4 equiv), H_2 (1 atm) at 65 °C for 24 h; [b] Isolated yield by column chromatography if not otherwise noted. [c] Due to the product volatility, the yield was determined by GC with dodecane as the internal standard.

Scheme 2. Deoxygenative hydrogenation of ketones.[a]

The present catalytic system was further applied to the deoxygenation of aldehydes. As shown in Scheme 3, various substituted benzaldehydes were smoothly reduced to their substituted toluene derivatives in good yields (Scheme 3, **3a**–**g**). Functional groups, such as methoxy, chloro, carboxyl, amino, and hydroxy were well tolerated in the reaction. The electronic property and position of the substituent on the aromatic ring does not significantly affect the reaction. The aldehyde group on the naphthalene and *N*-methyl indole was readily converted to the corresponding methyl group in good yields (**3h**,**i**). The reduction of aliphatic aldehydes also proceeded well (**3j**–**o**). A low yield was observed in the deoxygenation of 1-adamantanealdehyde, which may be attributed to the poor solubility of corresponding *N*-tosylhydrazone in MeOH (**3p**).

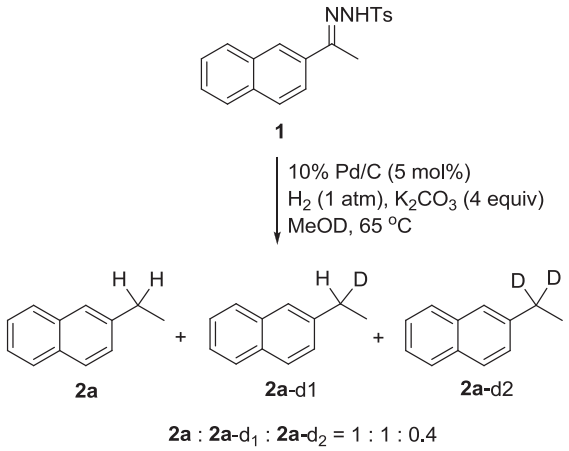


[a] Reaction conditions: aldehyde (0.5 mmol), $TsNHNH_2$ (1.05 equiv), MeOH (5 mL), stirring at 60 °C until the disappearance of the ketone; then 10% Pd/C (5% mol), K_2CO_3 (4 equiv), H_2 (1 atm) at 65 °C for 24 h. [b] Isolated yield by column chromatography if not otherwise noted. [c] Due to the product volatility, the yield was determined by GC with dodecane as the internal standard. [d] Yield was determined by GC with bromobenzene as the internal standard. [e] The *N*-tosylhydrazone was prepared and separated, then it was directly used for the reduction.

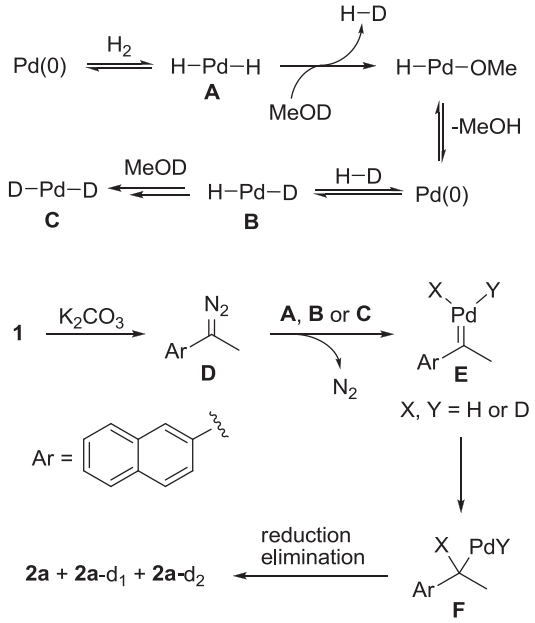
Scheme 3. Deoxygenative hydrogenation of aldehydes.[a]

To gain insight into the reaction mechanism, we have carried out the reduction of *N*-tosylhydrazone **1** under Pd/C-catalyzed reaction conditions in MeOD (Scheme 4). The reaction was complete in 24 h and we observed the formation of **2a**, **2a**-d_1 and **2a**-d_2 in a ratio of 1:1:0.4, based on the analysis of the product with GC–MS and ^{1}H NMR.

The observed scrambling of the deuterium in the product can be rationalized by the proposed reaction mechanism shown in Scheme 5. First, the Pd(II) species **A**, **B** and **C** can be formed in equilibrium by exchange of deuterium and hydrogen though the process shown in the Scheme. In the presence of base, the *N*-tosylhydrazone **1** is converted to diazo intermediate **D**, which reacts with **A**, **B** or **C** to form Pd carbene intermediate **E**. Migratory insertion of hydrogen or deuterium from Pd to generate intermediate **F**,[24] which is followed by reductive elimination to afford the final product.



Scheme 4. The reduction of *N*-tosylhydrazone **1** in MeOD.



Scheme 5. Proposed reaction mechanism.

3. Summary

In summary, we have developed a one-pot, two-step deoxygenation reaction of carbonyl to methyl or methylene, which employs hydrogen as the clean reductant with 10% Pd/C as the catalyst. Various functional groups are tolerated to this reduction system. This mild deoxygenative hydrogenation provides an alternative method for converting a carbonyl group into CH_2, which is one of the most important functional group transformations in organic synthesis.

4. Experimental section

4.1. General

All reactions were performed under a nitrogen atmosphere in a flame-dried reaction flask. All solvents were distilled prior to use. THF and toluene was dried over Na before use. For chromatography, 200–300 mesh silica gel was employed. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in parts per million using tetramethylsilane (TMS) as the internal

standard. IR spectra are reported in wave numbers, cm^{-1}. For HRMS measurements, the mass analyzer is FT-ICR. Substrates **3f**–**g**,[25] **3k**–**n**,[26] and **3p**[27] were prepared according to the references. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. The identity and purity of all products were confirmed via spectroscopic (^1H and/or ^{13}C NMR) or analytical GC against commercial standards.

4.2. General procedure for the *N*-tosylhydrazine mediated reductive deoxygenation of aldehydes and ketones with Pd/C–H_2

The aldehyde or ketone (0.5 mmol), *N*-tosylhydrazine (98 mg, 1.05 equiv), and MeOH (10 mL) were placed in a 50 mL two-necked round bottle equipped with magnetic stirring bar and condenser. The reaction was heated at 60 °C until aldehyde or ketone was completely consumed. (For diarylmethanones, the preparation of corresponding *N*-tosylhydrazines often need 1 mol % $TsOH\cdot H_2O$ as catalyst.) After cooling to the room temperature, 10% w/w of Pd/C (26.5 mg, 5 mol %) and K_2CO_3 (276 mg, 4 equiv) were added. The mixture was degassed by 'pump-freeze-thaw' cycles (×3) and flushed with hydrogen. The resulting solution was heated at 65 °C for 24 h under 1 atm of hydrogen atmosphere. Resulting product mixture was filtered through a short path of silica gel, eluting with ethyl acetate. The volatile compounds were removed in vacuo and the crude residue was purified by column chromatography (SiO_2, hexane) or analyzed by GC.

*4.2.1. 2-Ethylnaphthalene (**2a**).*[28] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, J=7.6, 14.7 Hz, 3H), 7.56 (s, 1H), 7.41–7.28 (m, 3H), 2.75 (q, J=7.6 Hz, 2H), 1.28 (t, J=7.6 Hz, 3H).

*4.2.2. 1,2-Dichloro-4-ethylbenzene (**2b**).*[9f] Colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J=8.2 Hz, 1H), 7.27 (t, J=1.8 Hz, 1H), 7.02 (d, J=1.9, 8.2 Hz, 1H), 2.60 (q, J=6.0 Hz, 2H), 1.22 (t, J=7.6 Hz, 3H).

*4.2.3. 5-Butylbenzo[d][1,3]dioxole (**2c**).*[29] Colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 6.64–6.52 (m, 3H), 5.82 (s, 2H), 2.44 (t, J=7.6 Hz, 2H), 1.50–1.43 (m, 2H), 1.30–1.20 (m, 2H), 0.83 (t, J=7.2 Hz, 3H).

*4.2.4. Chroman (**2d**).*[30] Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.00–6.94 (m, 2H), 6.77–6.70 (m, 2H), 4.11 (t, J=6.8 Hz, 2H), 2.71 (t, J=8.4 Hz, 2H), 1.93 (dd, J=2.0, 6.8 Hz, 2H).

*4.2.5. 9H-Fluorene (**2f**).*[31] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J=7.5 Hz, 2H), 7.52 (d, J=7.3 Hz, 2H), 7.36 (t, J=7.4 Hz, 2H), 7.29 (t, J=7.4 Hz, 2H), 3.88 (s, 2H).

*4.2.6. Di p-tolylmethane (**2h**).*[32] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.06 (m, 8H), 3.80 (s, 2H), 2.29 (s, 6H).

*4.2.7. Bis(4-chlorophenyl)methane (**2i**).*[33] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J=8.4 Hz, 4H), 7.08 (d, J=8.4 Hz, 4H), 3.91 (s, 2H).

*4.2.8. 1-Benzyl-4-methoxybenzene (**2j**).*[34] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.29–7.24 (m, 2H), 7.19–7.16 (m, 3H), 7.10 (d, J=8.8 Hz, 2H), 6.82 (d, J=8.8 Hz, 2H), 3.92 (s, 2H), 3.77 (s, 3H).

*4.2.9. 4-Benzylbiphenyl (**2k**).*[35] White solid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 -7.21 (m, 14H), 4.02 (s, 2H).

*4.2.10. 1,2-Dimethoxy-4-methylbenzene (**3a**).*[35] Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 6.75–6.70 (m, 3H), 3.86–3.82 (m, 6H), 2.30 (s, 3H).

*4.2.11. 1,2-Dichloro-4-methylbenzene (**3b**).*[36] Colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.26–7.20 (m, 2H), 6.95–6.92 (m 1H), 2.25 (s, 3H).

*4.2.12. N,N,4-Trimethylaniline (**3c**).*[37] Yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, J=8.2 Hz, 2H), 6.67 (d, J=8.2 Hz, 2H), 2.87 (s, 6H), 2.24 (s, 3H).

*4.2.13. 2-Methylbenzoic acid (**3d**).*[38] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 12.44 (br, s, 1H), 8.09–8.07 (m, 1H), 7.47–7.43 (m 1H), 7.27 (q, J=7.5 Hz, 2H), 2.69 (s, 3H).

*4.2.14. o-Toluidine (**3e**).*[39] Yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.05–7.00 (m, 2H), 6.72–6.55 (m, 2H), 3.59 (br, 2H), 2.16 (s, 3H).

*4.2.15. 2-Methylbiphenyl (**3f**).*[40] Colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.38 (m, 2H), 7.33–7.30 (m, 3H), 7.26–7.22 (m, 4H), 2.26 (s, 3H).

*4.2.16. (2′-Methylbiphenyl-4-yl)methanol (**3g**).* Colorless oil. IR (film) 3333, 2924, 1483, 1456, 1406, 1207, 1006, 908, 821, 759, 728, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J=8.0 Hz, 2H), 7.31 (d, J=8.0 Hz, 2H), 7.26–7.20 (m, 4H), 4.72 (s, 2H), 2.26 (s, 3H), 1.97 (br, s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 141.4, 139.4, 135.4, 130.4, 129.8, 129.4, 127.3, 126.8, 125.8, 65.2, 20.5. HRMS (ESI) calcd for $C_{14}H_{14}ONa$ [$(M+Na)^+$] 221.0939, found: 221.0938.

*4.2.17. 1,3-Dimethyl-1H-indole (**3i**).*[41] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J=8.0 Hz, 1H), 7.26–7.18 (m, 3H), 7.11–7.07 (m, 1H), 6.79 (s, 1H), 3.70 (s, 3H), 2.31 (s, 3H).

*4.2.18. 1-Propylnaphthalene (**3k**).*[42] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J=8.0 Hz, 1H), 7.84 (d, J=8.0 Hz, 1H), 7.70 (d, J=8.0 Hz, 1H), 7.51–7.43 (m, 2H), 7.38 (t, J=7.6 Hz, 1H), 7.31 (d, J=6.8 Hz, 1H), 3.04 (t, J=7.6 Hz, 2H), 1.83–1.74 (m, 2H), 1.03 (t, J=7.3 Hz, 3H).

*4.2.19. Methyl 4-propylbenzoate (**3l**).*[43] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J=7.6 Hz, 2H), 7.24 (d, J=7.6 Hz, 2H), 3.90 (s, 3H), 2.64 (s, 2H), 1.70–1.61 (m, 2H), 0.94 (t, J=7.2 Hz, 3H).

*4.2.20. 3-(4-Propylphenyl)furan (**3m**).*[44] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.47–7.45 (m, 1H), 7.33 (d, J=8.0 Hz, 2H), 7.26–7.13 (m, 2H), 6.68 (s, 1H), 2.61–2.57 (m, 2H), 1.69–1.60 (m, 2H), 0.95 (t, J=7.2 Hz, 3H).

*4.2.21. 3-(4-Propylphenyl)thiophene (**3n**).* Colorless oil. IR (film) 2958, 2927, 1503, 1463, 1260, 908, 775, 733, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52–7.50 (m, 2H), 7.41–7.40 (m, 1H), 7.37–7.36 (m, 2H), 7.21–7.19 (m, 2H), 2.60 (t, J=7.6 Hz, 2H), 1.71–1.62 (m, 2H), 0.98–0.94 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 141.7, 133.4, 128.9, 126.4, 126.3, 126.0, 119.7, 37.7, 24.5, 13.9. HRMS (ESI) calcd for $C_{13}H_{15}S$ [$(M+H)^+$] 203.0889, found: 203.0891.

*4.2.22. 1-Methyl adamantane (**3p**).*[45] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 1.92 (s, 3H), 1.70–1.59 (m, 6H), 1.45–1.44 (m, 6H), 0.76 (s, 3H).

Acknowledgements

Financial support from Sun Yat-Sen University, Beijing National Laboratory of Molecular Sciences (BNLMS) is gratefully acknowledged, National Basic Research Program of China (973 Program, No. 2009CB825300) and Natural Science Foundation of China (21272010).

Supplementary data

Copies of ^{1}H and/or ^{13}C spectra for isolated products. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.05.070.

References and notes

1. (a) Kishner, N. *Russ. Phys. Chem. Soc.* **1911**, *43*, 582; (b) Wolff, L. *Justus Liebigs Ann. Chem.* **1912**, *394*, 86.
2. Clemmensen, E. *Chem. Ber.* **1913**, *46*, 1837.
3. (a) Huang, M. *J. Am. Chem. Soc.* **1946**, *68*, 2487; (b) Huang, M. *J. Am. Chem. Soc.* **1949**, *71*, 3301.
4. For reviews see: (a) Hutchins, R. O.; Hutchins, M. K. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, UK, 1991; Vol. 8, pp 327–362; (b) Fieser, L. F.; Fieser, M. *Topics in Organic Chemistry*; Reinhold: New York, NY, 1963258; (c) Todd, D. *Org. React.* **1948**, *4*, 378; (d) Buu-Hoï, N. P.; Hoán, N.; Xuong, N. D. *Recl. Trav. Chim. Pays-Bas* **1952**, *71*, 285; (e) Huang, M. *Sci. Sinica* **1961**, *10*, 711; (f) Reusch, W. In *Reduction*; Augustine, R. L., Ed.; Dekker: New York, NY, 1968; pp 171–211.
5. For recent examples of Wolff–Kishner–Huang Minlon reduction in organic synthesis, see: (a) Toyota, M.; Wada, T.; Ihara, M. *J. Org. Chem.* **2000**, *65*, 4565; (b) Marino, J. P.; Rubio, M. B.; Gao, G.; de Dios, A. *J. Am. Chem. Soc.* **2002**, *124*, 13398; (c) Miyaoka, H.; Kajiwara, Y.; Hara, Y.; Yamada, Y. *J. Org. Chem.* **2001**, *66*, 1429.
6. (a) Barton, D. H. R.; Ives, D. A. J.; Thomas, B. R. *J. Chem. Soc., Abstr.* **1955**, 2056; (b) Cram, D. J.; Sahyun, M. R. V.; Knox, G. R. *J. Am. Chem. Soc.* **1962**, *84*, 1734; (c) Grundon, M. F.; Henbest, H. B.; Scott, M. D. *J. Chem. Soc., Abstr.* **1963**, 1855; (d) Nagata, W.; Itazaki, H. *Chem. Ind.* **1964**, 1194; (e) Barth, M. M.; Binet, J. L.; Thomas, D. M.; de Fornel, D. C.; Samreth, S.; Schuber, F. J.; Renaut, P. P. *J. Med. Chem.* **1996**, *39*, 2302; (f) Parquet, E.; Lin, Q. *J. Chem. Educ.* **1997**, *74*, 1225; (g) Gadhwal, S.; Baruah, M.; Sandhu, J. S. *Synlett* **1999**, 1573; (h) Eisenbraun, E. J.; Payne, K. W.; Bymaster, J. S. *Ind. Eng. Chem. Res.* **2000**, *39*, 1119; (i) Chattopadhyay, S.; Banerjee, S. K.; Mitra, A. K. *J. Indian Chem. Soc.* **2002**, *79*, 906; (j) Jaisankar, P.; Pal, B.; Giri, V. S. *Synth. Commun.* **2002**, *32*, 2569.
7. Furrow, M. E.; Myers, A. G. *J. Am. Chem. Soc.* **2004**, *126*, 5436.
8. (a) Broome, J.; Brown, B. R.; Roberts, A.; White, A. M. S. *J. Chem. Soc.* **1960**, 1406; (b) Zieger, H. E.; Dixon, J. A. *J. Am. Chem. Soc.* **1960**, *82*, 3702; (c) Brewster, J. H.; Osman, S. F.; Bayer, H. O.; Hopps, H. B. *J. Org. Chem.* **1964**, *29*, 121; (d) Cormier, R. A. *Synth. Commun.* **1981**, *11*, 295; (e) Suzuki, H.; Masuda, R.; Kubota, H.; Osuka, A. *Chem. Lett.* **1983**, 909; (f) Eisch, J. J.; Liu, Z. R.; Boleslawski, M. P. *J. Org. Chem.* **1992**, *57*, 2143.
9. (a) Breuer, E. *Tetrahedron Lett.* **1967**, *20*, 1849; (b) Gribble, G. W.; Leese, R. M. *Synthesis* **1977**, 172; (c) Satoh, T.; Mitsuo, N.; Nishiki, M.; Nanba, K.; Suzuki, S. *Chem. Lett.* **1981**, 1029; (d) Lau, C. K.; Dufresne, C.; Bélanger, P. C.; Piétré, S.; Scheigetz, J. *J. Org. Chem.* **1986**, *51*, 3038; (e) Ono, A.; Suzuki, N.; Kamimura, J. *Synthesis* **1987**, 736; (f) Lau, C. K.; Tardif, S.; Dufresne, C.; Scheigetz, J. *J. Org. Chem.* **1989**, *54*, 491; (g) Srikrishna, A.; Sattigeri, J. A.; Viswajanani, R.; Yelamaggad, C. V. *Synlett* **1995**, 93; (h) Dehmlow, E. D.; Niemann, T.; Krafts, A. *Synth. Commun.* **1996**, *26*, 1467.
10. (a) Kursanov, D. N.; Parnes, Z. N.; Bassova, G. I.; Loim, N. M.; Zdanovich, V. I. *Tetrahedron* **1967**, *23*, 2235; (b) Doyle, M. P.; West, C. T.; Donnelly, S. J.; McOsker, C. C. *J. Organomet. Chem.* **1976**, *117*, 129; (c) Fry, J. L.; Orfanopoulos, M.; Adlington, M. G.; Dittman, W. R.; Silverman, S. B. *J. Org. Chem.* **1978**, *43*, 374; (d) West, C. T.; Donnelly, S. J.; Kooistra, D. A.; Doyle, M. P. *J. Org. Chem.* **1978**, *38*, 2675; (e) Orfanopoulos, M.; Smonou, I. *Synth. Commun.* **1988**, *18*, 833; (f) Olah, G. A.; Wang, Q.; Prakash, G. K. S. *Synlett* **1992**, 647; (g) Smonou, I. *Tetrahedron Lett.* **1994**, *35*, 2071; (h) Gevorgyan, V.; Rubin, M.; Liu, J.-X.; Yamamoto, Y. *J. Org. Chem.* **2001**, *66*, 1672; (i) Chandrasekhar, S.; Reddy, C. R.; Babu, B. N. *J. Org. Chem.* **2002**, *67*, 9080; (j) Wei, T.; Lan, Y.; Xu, J. *Heteroat. Chem.* **2005**, *16*, 2; (k) Dal Zotto, C.; Virieux, D.; Campagne, J.-M. *Synlett* **2009**, 276; (l) Xu, S.; Toyama, T.; Nakamura, J.; Arimoto, H. *Tetrahedron Lett.* **2010**, *51*, 4534.
11. Nishiyama, Y.; Hamanaka, S.; Ogawa, A.; Kambe, N.; Sonoda, N. *J. Org. Chem.* **1988**, *53*, 1326.
12. Hatano, B.; Tagaya, H. *Tetrahedron Lett.* **2003**, *44*, 6331.
13. (a) Cook, P. L. *J. Org. Chem.* **1962**, *27*, 3873; (b) Schwenk, E.; Whitman, B. *J. Org. Chem.* **1942**, *7*, 587.
14. Kogan, V.; Aizenshtat, Z.; Neumann, R. *Angew. Chem., Int. Ed.* **1999**, *38*, 3331.
15. Zaccheria, F.; Ravasio, N.; Ercolic, M.; Allegrinic, P. *Tetrahedron Lett.* **2005**, *46*, 7743.
16. Torok, B.; London, G.; Bartok, M. *Synlett* **2000**, 631.
17. (a) Hartung, W. H.; Crossley, F. S. *J. Am. Chem. Soc.* **1934**, *56*, 158; (b) Horning, E. C.; Reisner, D. B. *J. Am. Chem. Soc.* **1949**, *71*, 1036; (c) Lee, W. Y.; Park, C. H.; Kim, H. J.; Kim, S. *J. Org. Chem.* **1994**, *59*, 878; (d) Studer, M.; Burkhardt, S.; Indolese, A. F.; Blaser, H.-U. *Chem. Commun.* **2000**, 1327.
18. (a) Szmant, H. H. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 120; (b) Szmant, H. H.; Alciaturi, C. E. *J. Org. Chem.* **1977**, *42*, 1081; (c) Szmant, H. H.; Birke, A.; Lau, M. P. *J. Am. Chem. Soc.* **1977**, *99*, 1863; (d) Brecknell, D. J.; Carman, R. M.; Schumann, R. C. *Aust. J. Chem.* **1989**, *42*, 527; (e) Taber, D. F.; Stachel, S. J. *Tetrahedron Lett.* **1992**, *33*, 903.
19. Furrow, M. E.; Myers, A. G. *J. Am. Chem. Soc.* **2004**, *126*, 12222.
20. Pellicciari, R.; Natalini, B.; Cecchetti, S.; Fringuelli, R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 493.
21. Bamford, W. R.; Stevens, T. S. *J. Chem. Soc.* **1952**, 4735.
22. For recent reviews on the applications of N-tosylhydrazones in diazo-related transformations, see: (a) Fulton, J. R.; Aggarwal, V. K.; de Vicente, J. *Eur. J. Org. Chem.* **2005**, 1479; (b) Barluenga, J.; Valdés, C. *Angew. Chem., Int. Ed.* **2011**, *50*, 7486; (c) Shao, Z. H.; Zhang, H. B. *Chem. Soc. Rev.* **2011**, *41*, 560; (d) Zhang, Y.; Wang, J. *Top. Curr. Chem.* **2012**, *327*, 239; (e) For the seminal report of the generation of diazo alkanes from aliphatic ketones and aldehydes see: Taber, D. F.; Guo, P. *J. Org. Chem.* **2008**, *73*, 9479.
23. For the reports on the reduction of N-tosylhydrazones with lithium aluminium hydride or borohydride as the hydride sources, see: (a) Caglioti, L.; Magi, M. *Tetrahedron* **1963**, *19*, 1127; (b) Kabalka, G. W.; Baker, J. D., Jr. *J. Org. Chem.* **1975**, *40*, 1834; (c) Kabalkaa, G. W.; Chandler, J. H. *Synth. Commun.* **1979**, *9*, 275; (d) Kabalka, G. W.; Summers, S. T. *J. Org. Chem.* **1981**, *46*, 1217; (e) Iida, T.; Chang, F. C. *J. Org. Chem.* **1982**, *47*, 2966; (f) Kim, S.; Oh, C. H.; KO, J. S.; Ahn, K. H.; Kim, Y. J. *J. Org. Chem.* **1985**, *50*, 1927.
24. (a) Zhang, Y.; Wang, J. *Eur. J. Org. Chem.* **2011**, 1015; (b) Xiao, Q.; Zhang, Y.; Wang, J. *Acc. Chem. Res.* **2013**, *46*, 236.
25. Ye, F.; Shi, Y.; Zhou, L.; Xiao, Q.; Zhang, Y.; Wang, J. *Org. Lett.* **2011**, *13*, 5020.
26. Gesinski, M. R.; Tadpetch, K.; Rychnovsky, S. D. *Org. Lett.* **2009**, *11*, 5342.
27. Braverman, S.; Pechenick-Azizi, T.; Gottlieb, H. E.; Sprecher, M. *Synthesis* **2011**, 1741.
28. Chan, L. Y.; Lim, J. S. K.; Kim, S. *Synlett* **2011**, 2862.
29. Takashi, S.; Kazuyoshi, M.; Masanori, U.; Akira, T. *Tetrahedron Lett.* **1987**, *28*, 3817.
30. Pathak, T. P.; Sigman, M. S. *J. Org. Chem.* **2011**, *76*, 9210.
31. Parisien, M.; Valette, D.; Fagnou, K. *J. Org. Chem.* **2005**, *70*, 7578.
32. Gordon, P. E.; Fry, A. G. *Tetrahedron Lett.* **2001**, *42*, 831.
33. Endo, K.; Ishioka, T.; Ohkubo, T.; Shibata, T. *J. Org. Chem.* **2012**, *77*, 7223–7231.
34. Schmink, J. R.; Leadbeater, N. E. *Org. Lett.* **2009**, *11*, 2575.
35. Kirste, A.; Elsler, B.; Schnakenburg, G.; Waldvogel, S. R. *J. Am. Chem. Soc.* **2012**, *134*, 3571.
36. Matsubara, H.; Yasuda, S.; Sugiyama, H.; Ryu, I.; Fujii, Y.; Kita, K. *Tetrahedron* **2002**, *58*, 4071.
37. Chen, W.-X.; Shao, L.-X. *J. Org. Chem.* **2012**, *77*, 9236.
38. Brunet, J.-J.; Sidot, C.; Caubere, P. *J. Org. Chem.* **1983**, *48*, 1166.
39. Eren, R. N.; Plante, A.; Meunier, A.; Laventure, A.; Huang, Y.; Briard, J. G.; Pellerin, C.; Soldera, A.; Label, O. *Tetrahedron* **2012**, *66*, 10130.
40. Wei, J.-F.; Jiao, J.; Feng, J.-J.; Lv, J.; Zhang, X.-R.; Shi, X.-Y.; Chen, Z.-G. *J. Org. Chem.* **2009**, *74*, 6283.
41. Xu, X.-H.; Liu, G.-K.; Azuma, A.; Tokunaga, E.; Shibata, N. *Org. Lett.* **2011**, *13*, 4854.
42. Grissom, J. W.; Klingberg, D. *J. Org. Chem.* **1993**, *58*, 6559.
43. Minami, T.; Nishimura, K.; Hirao, I. *J. Org. Chem.* **1982**, *47*, 2360.
44. Bender, S. L.; Castelhano, A. L.; Chong, W. K. M.; Abreo, M. A.; Billedeau, R. J.; Chen. J. J.; Deal, J. J. PCT Int. Appl. 19880430, 1998.
45. Aoyama, M.; Hara, S. *Tetrahedron* **2009**, *65*, 3682.