Tetrahedron Letters 51 (2010) 1434–1436

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Amino-functionalized carbon nanotubes as nucleophilic scavengers in solution phase combinatorial synthesis

Yongsheng Li [a,*], Yuzeng Zhao [b], Zhuo Zhang [a], Yaomin Xu [a]

[a] School of Materials Science and Engineering, Shanghai Institute of Technology, Shanghai 200235, China
[b] Department of Environmental Engineering, Shanghai University of Electric Power, Shanghai 200090, China

ARTICLE INFO

Article history:
Received 12 September 2009
Revised 5 January 2010
Accepted 8 January 2010
Available online 13 January 2010

Keywords:
Carbon nanotube
Functionalization
Nucleophilic scavenger
Parallel synthesis

ABSTRACT

A versatile method for fast scavenging a variety of electrophiles using carbon nanotubes functionalized by amino groups (CNT–NH_2) is reported. Following the scavenging event, CNT–NH_2 can be easily separated from the reaction mixture by filtration, leaving the desired products in excellent yields and purities.

The use of polymer-supported scavenger reagents plays an important role in solution phase combinatorial chemistry for the purification and isolation of target compounds.[1] These scavenger resins react selectively with excess reagents or side products in a crude reaction mixture to give polymer-bound products that can be removed readily by simple filtration, leaving the desired products in solution with high purities.[2] This revolutionary tool significantly simplifies work-up procedure and is widely employed.[3] However, most polymer-supported scavenging protocols require long reaction times because of the biphasic nature of the reaction systems and hindered access to functional groups within the resin cores.[4] To address this issue, some new strategies such as fluorous scavengers,[5] soluble polymer-supported scavengers[6] and ionic liquid scavengers[7] have been reported.

Multi-walled carbon nanotubes (CNTs) have now been industrially prepared with ton-scale. With the rapid development of produce technology, they will become a common type of raw material in the near future.[8] CNTs have excellent mechanical property, good chemical stability, small diameter and ample surface area.[9] They can be modified by attachment of organic molecules or polymers to their surface. Highly modified CNTs can be dissolved (or dispersed) in a variety of solvents and easily separated from the solvents by filtration.[10] Although CNTs and functionalized CNTs have been intensively investigated in many fields,[11] to the best of our knowledge, no reports to date have been published on the application of CNTs for the reaction purification in solution phase combinatorial chemistry. Herein, we report the preparation of amino-functionalized multi-walled CNTs (CNT–NH_2) and its application in scavenging excess electrophiles in solution phase parallel synthesis.

The general strategy for the preparation of CNT–NH_2 is described in Scheme 1.[12] Three steps are included: (1) CNTs were treated to attach carboxylic acid groups to their surface by oxidation of the crude CNTs with a mixture of sulfuric acid/nitric acid (3:1 by volume, respectively). (2) Carbonyl chloride groups-functionalized CNTs (CNT–COCl), the intermediate products for further chemical functionalization, were prepared via reaction of thionyl chloride with carboxyl-contained CNT (CNT–COOH). (3) Amino groups were introduced onto the surface of CNTs by reaction of CNT–COCl with triethylenetetramine or tetraethylenepentamine, generating CNT–NH_2 (**4a** or **4b**). The FTIR spectra of **4a** and **4b** are shown in Figure 1. The appearance of peaks at 3330, 1625 and 1384 cm^{-1} attributed to the N–H, C=O (corresponding to the amide carbonyl group) and CH_2 stretches, respectively, indicates that the amino groups were attached to the surface of CNTs. The TEM image of **4a** (Fig. 2) provides the direct evidence that CNT–NH_2 were well dispersed and the tube structures were kept. The TEM of **4b** also shows similar features. CNT–NH_2 exhibit well solubility (or dispersity) in DMF, H_2O, CH_2Cl_2 and $CHCl_3$. The amino functional loadings of **4a** and **4b** which were determined from the acid-base titration were 1.2 mmol/g and 1.3 mmol/g, respectively.[13]

Their applications as acyl chloride scavengers (see Scheme 2) in the benzoylation of an array of amines using excess benzoyl chloride or phenylacetyl chloride (Table 1, entries 1–8) were

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[*] Corresponding author. Tel./fax: +86 21 64942815.
E-mail address: yshli@sit.edu.cn (Y. Li).

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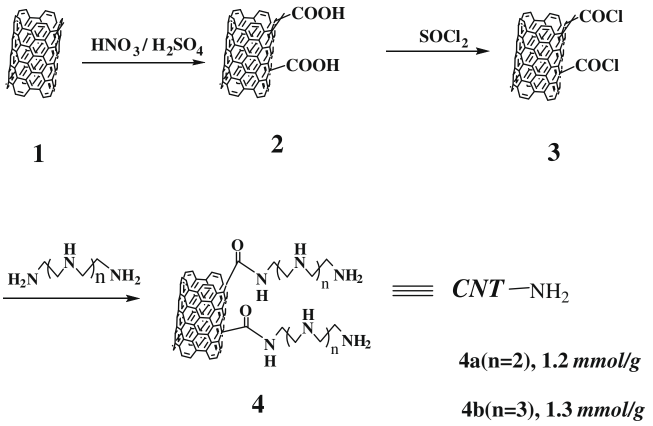
doi:10.1016/j.tetlet.2010.01.022



Scheme 1. Preparation of CNT–NH_2.

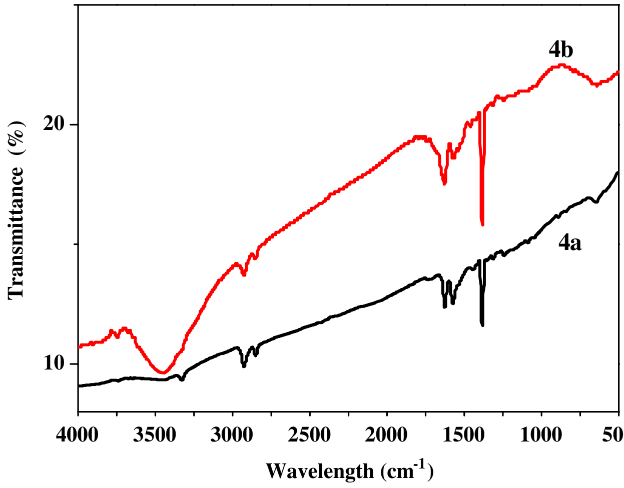


Figure 1. FTIR spectra of CNT–NH_2 (**4a** and **4b**).

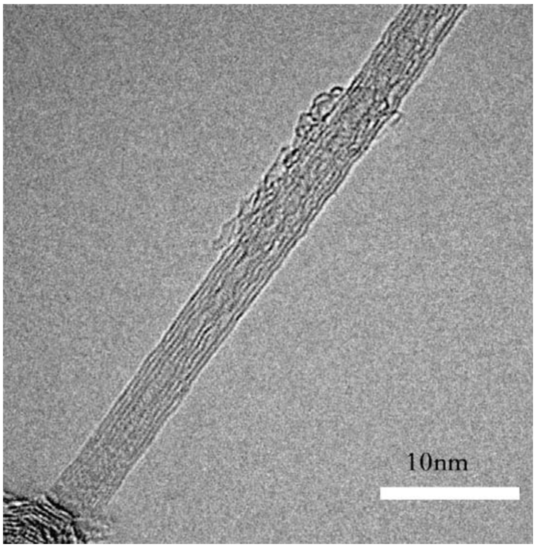
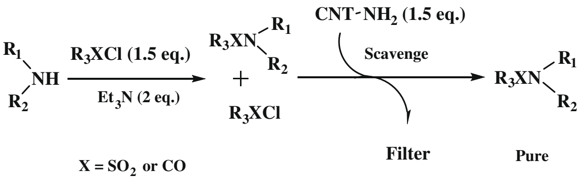


Figure 2. HRTEM image of the soluble CNT–NH_2 (**4a**).



Scheme 2. Scavenging reaction.

investigated.[14] Facile amidation was completed in less than 1 h for amine in the presence of 1.5 equiv of benzoyl chloride and 2 equiv of base (Et_3N or pyridine). Upon completion of the reaction, scavenger (1.5 equiv) was added. The mixture was sonicated for 10 min (or stirred for 30 min), filtered through a Polytetrafluoroethylene membrane (0.22 μm pore size) and concentrated under reduced pressure to give the target products in excellent yields and purities. It is worthy to note that only 10 min (or 30 min under stir) was required to achieve satisfactory scavenging efficiency. In comparison, the conventional polymer-supported scavenging protocols often require several hours to achieve the quenching reaction (see Supplementary data).[1a,4d] We surmised that the short sequestration duration of CNT protocol was mainly due to the fact that functional groups were on the external wall surface of CNTs, and electrophiles could easily get access to them.

Scavenger **4a** and **4b** were further investigated in the sulfonation of a variety of amines with tosyl chloride present in excess (Table 1, entries 9–14). The desired products in similarly high yields and purities were achieved.

Table 1
Evaluation of the CNT–NH_2 (**4a** and **4b**) as reaction scavenger

Entry	R_3XCl[c]	R_1R_2NH	Scavenger	Base	Yield[a] (%)	Purity[b] (%)
1	Benzoyl chloride	Butylamine	**4a**	Et_3N	90	>95
2	Benzoyl chloride	Dibutylamine	**4a**	C_5H_5N	84	>95
3	Benzoyl chloride	Cyclohexylamine	**4b**	Et_3N	89	>95
4	Phenylacetyl chloride	Butylamine	**4a**	C_5H_5N	86	>95
5	Phenylacetyl chloride	Dibutylamine	**4a**	C_5H_5N	92	>95
6	Phenylacetyl chloride	Cyclohexylamine	**4a**	Et_3N	91	>95
7	Phenylacetyl chloride	Butylamine	**4b**	Et_3N	87	>95
8	Phenylacetyl chloride	Dibutylamine	**4b**	C_5H_5N	86	>95
9	Tosyl chloride	Cyclohexylamine	**4a**	C_5H_5N	93	>95
10	Tosyl chloride	Butylamine	**4a**	C_5H_5N	91	>95
11	Tosyl chloride	Butylamine	**4b**	Et_3N	91	>95
12	Tosyl chloride	Butylamine	**4a**	Et_3N	91	>95
13	Tosyl chloride	Dibutylamine	**4a**	C_5H_5N	93	>95
14	Tosyl chloride	Dibutylamine	**4b**	C_5H_5N	91	>95

[a] Measured by weight after scavenging with the CNT–NH_2.
[b] Determined by ^1H NMR analysis(see Supplementary data).
[c] X = CO or SO_2.

In summary, CNTs were modified by the attachment of amino groups to their surface. The resulting CNT–NH$_2$ can be dissolved (or dispersed) in a variety of solvents and separated from the solvents by filtration. The utility of CNT–NH$_2$ for fast scavenging of an assortment of electrophiles has been demonstrated. However, the amino functional loadings of CNT–NH$_2$ are slightly lower than that of conventional Polystyrene-supported scavengers.[15] Increasing the amino functional group content on CNTs and expanding applications of this method are now underway.

Acknowledgements

Financial support from Shanghai Education Commission (06OZ025), Shanghai Institute of Technology (Yj-2006-19) and Shanghai Leading Academic Discipline Project (P1502) are gratefully acknowledged.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.01.022.

References and notes

1. (a) Kaldor, S. W.; Siegel, M. G.; Fritz, J. E.; Dressman, B. A.; Hahn, P. J. *Tetrahedron Lett.* **1996**, *37*, 7193–7196; (b) Sanna, M.; White, P. D.; Chan, W. C. *Tetrahedron Lett.* **2008**, *49*, 6160–6162; (c) Storer, R. I.; Takemoto, T.; Jackson, P. S.; Brown, D. S.; Baxendale, I. R.; Ley, S. V. *Chem. Eur. J.* **2004**, *10*, 2529–2547; (d) Wang, Z.; Luo, J.; Zhu, X. X.; Jin, S.; Tomaszewski, M. J. *J. Comb. Chem.* **2004**, *6*, 961–966; (e) Luo, J.; Pardin, C.; Zhu, X. X.; Lubell, W. D. *J. Comb. Chem.* **2007**, *9*, 582–591.
2. (a) Booth, R. J.; Hodges, J. C. *J. Am. Chem. Soc.* **1997**, *119*, 4882–4886; (b) Booth, R. J.; Hodges, J. C. *Acc. Chem. Res.* **1999**, *32*, 18–26.
3. (a) Curran, D. P. *Angew. Chem., Int. Ed.* **1998**, *37*, 1174–1196; (b) Herpel, R. H.; Vedantham, P.; Flynn, D. L.; Hanson, P. R. *Tetrahedron Lett.* **2006**, *47*, 6429–6432; (c) Eames, J.; Watkinson, M. *Eur. J. Org. Chem.* **2001**, 1213–1224; (d) An, H.; Cook, P. D. *Chem. Rev.* **2000**, *100*, 3311–3340.
4. (a) Ghanem, N.; Martinez, J.; Stien, D. *Tetrahedron Lett.* **2002**, *43*, 1693–1695; (b) Ghanem, N.; Martinez, J.; Stien, D. *Eur. J. Org. Chem.* **2004**, 84–89; (c) Radi, M.; Saletti, S.; Botta, M. *Tetrahedron Lett.* **2008**, *49*, 4464–4466; (d) Dallinger, D.; Gorobets, N. Y.; Kappe, C. O. *Org. Lett.* **2003**, *5*, 1205–1208.
5. (a) Studer, A.; Hadida, S.; Ferritto, R.; Kim, S.-Y.; Jeger, P.; Wipf, P.; Curran, D. P. *Science* **1997**, *275*, 823–826; (b) Matsugi, M.; Suganuma, M.; Yoshida, S.; Hasebe, S.; Kunda, Y.; Hagihara, K.; Oka, S. *Tetrahedron Lett.* **2008**, *49*, 6573–6574; (c) Zhang, W.; Chen, C. H.-T.; Nagashima, T. *Tetrahedron Lett.* **2003**, *44*, 2065–2068; (d) Linclau, B.; Sing, A. K.; Curran, D. P. *J. Org. Chem.* **1999**, *64*, 2835–2842.
6. (a) Moore, J. D.; Herpel, R. H.; Lichtsinn, J. R.; Flynn, D. L.; Hanson, P. R. *Org. Lett.* **2003**, *5*, 105–107; (b) Moore, J. D.; Byrne, R. J.; Vedantham, P.; Flynn, D. L.; Hanson, P. R. *Org. Lett.* **2003**, *5*, 4241–4244.
7. (a) Song, G.; Cai, Y.; Peng, Y. *J. Comb. Chem.* **2005**, *7*, 561–566; (b) Lei, M.; Tao, X.-L.; Wang, Y.-G. *Helv. Chim. Acta* **2006**, *89*, 532–536; (c) Cai, Y.; Zhang, Y.; Peng, Y.; Lu, F.; Huang, X.; Song, G. *J. Comb. Chem.* **2006**, *8*, 636–638.
8. (a) Gao, C.; He, H.; Zhou, L.; Zheng, X.; Zhang, Y. *Chem. Mater.* **2009**, *21*, 360–370; (b) http://www.nanotubes.com.cn/.
9. For review, see: (a) Zhao, Y.-L.; Stoddart, J. F. *Acc. Chem. Res.* **2009**, *42*, 1161–1171; (b) Prato, M.; Kostarelos, K.; Bianco, A. *Acc. Chem. Res.* **2008**, *41*, 60–68; (c) Tasis, D.; Tagmatarchis, N.; Bianco, A.; Prato, M. *Chem. Rev.* **2006**, *106*, 1105–1136; (d) Khabashesku, V. N.; Billups, W. E.; Margrave, J. L. *Acc. Chem. Res.* **2002**, *35*, 1087–1095; (e) Ajayan, P. M. *Chem. Rev.* **1999**, *99*, 1787–1800.
10. (a) Sun, Y.-P.; Fu, K.; Lin, Y.; Huang, W. *Acc. Chem. Res.* **2002**, *35*, 1096–1104; (b) Pompeo, F.; Resasco, D. E. *Nano. Lett.* **2002**, *2*, 369–373; (c) Huang, W.; Fernando, S.; Allard, L. F.; Sun, Y.-P. *Nano. Lett.* **2003**, *3*, 565–568; (d) Zhao, B.; Hu, H.; Haddon, R. C. *Adv. Funct. Mater.* **2004**, *14*, 71–76; (e) Liang, F.; Beach, J. M.; Rai, P. K.; Guo, W.; Hauge, R. H.; Pasquali, M.; Smalley, R. E.; Billups, W. E. *Chem. Mater.* **2006**, *18*, 1520–1524.
11. (a) Hata, K.; Futaba, D. N.; Mizuno, K.; Namai, T.; Yumura, M.; Iijima, S. *Science* **2004**, *306*, 1362–1364; (b) Su, M.; Zheng, B.; Liu, J. *Chem. Phys. Lett.* **2000**, *322*, 321–326; (c) Li, Y.; Liu, J.; Wang, Y.; Wang, Z. L. *Chem. Mater.* **2001**, *13*, 1008–1014; (d) Villa, A.; Tessonnier, J.-P.; Majoulet, O.; Su, D. S.; Schlögl, R. *Chem. Commun.* **2009**, 4405–4407.
12. Preparation of scavenger CNT–NH$_2$ (**4a**): (a) 0.5 g of as-received multi-walled CNTs was added to 400 mL of a mixture of sulfuric acid/nitric acid (3:1 by volume, respectively). The mixture was treated with ultrasonic bath (40 kHz) for 10 min, and then stirred for 8 h in reflux, followed by filtering through a Polytetrafluoroethylene membrane (0.22 µm pore size), and washed with water until no residual acid was present. The filtered solid was dried under vacuum for 12 h at 60 °C, giving CNT–COOH (0.3205 g). (b) 0.3205 g of CNT–COOH was suspended in 20 mL of SOCl$_2$. The mixture was stirred at room temperature for 12 h. The solid was then separated by filtration and dried under vacuum for 6 h, obtaining CNT–COCl (0.2825 g). (c) 0.2825 g of as-prepared CNT–COCl was mixed with 5.0 mL of Triethylenetetramine and stirred at room temperature for 24 h. The solid was separated by filtering and washed with THF. The resulting solid was dried overnight in vacuum, obtaining 0.3135 g of CNT–NH$_2$ (**4a**).
13. The titration was based on a procedure reported by Su and coworkers,[11d] and typical procedure see supplementary material (S1).
14. A typical procedure for amide formation and purification is as fellow: Benzoyl chloride (0.13 g, 0.75 mmol, 1.5 equiv) was added to a solution of butylamine (0.05 mL, 0.5 mmol, 1 equiv), Et$_3$N (0.14 mL, 1 mmol, 2 equiv) and CH$_2$Cl$_2$ (5 mL). After stirring for 1 h, CNT–NH$_2$ (0.32 g, 0.38 mmol, 1.5 equiv) was added. The mixture was treated with ultrasonic bath (40 kHz) for 10 min. The reaction was then filtered and washed with CH$_2$Cl$_2$. The filtrates were evaporated under reduced pressure to afford the desired products.
15. (a) http://www.biotage.com/.; (b) Stoianova, D. S.; Yao, L.; Rolfe, A.; Samarakoon, T.; Hanson, P. R. *Tetrahedron Lett.* **2008**, *49*, 4553–4555; (c) http://www.glschina.com/.