Tetrahedron 65 (2009) 3893–3899

Contents lists available at ScienceDirect

Tetrahedron

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

Selective mono- and di-N-alkylation of aromatic amines with alcohols and acylation of aromatic amines using Ph_3P/DDQ

Nasser Iranpoor *, Habib Firouzabadi *, Najmeh Nowrouzi †, Dariush Khalili

Department of Chemistry, College of Sciences, Shiraz University, Shiraz 71454, Iran

ARTICLE INFO

Article history:
Received 9 September 2008
Received in revised form 9 February 2009
Accepted 26 February 2009
Available online 5 March 2009

Keywords:
N-Monoalkylation
N,N-Dialkylation
Amide
Aromatic amine
Carboxylic acid
Triphenylphosphine
DDQ

ABSTRACT

Selective N-monoalkylation of aromatic amines with 1° and 2° alcohols and conversion of aromatic amines to amides are performed immediately and in excellent yields using triphenylphosphine (PPh_3) and 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in dichloromethane at room temperature. Symmetrical and unsymmetrical N,N-dialkylation of aromatic amines are also carried out in modest yield at room temperature by this reagent system.

1. Introduction

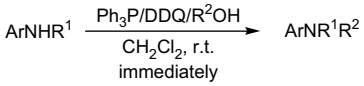
N-Alkylation of amines is an important reaction in organic synthesis. Amines and their derivatives are widely used as intermediates to prepare solvents, dyes, fine chemicals, biologically relevant molecules, pharmaceuticals, agrochemicals, and catalysts.[1] Although the conversion of primary amines to the corresponding secondary ones appears deceptively simple, this transformation continues to be a subject of investigation because in many cases N-monoalkylation of primary amines is not possible due to the difficulty in preventing over alkylation and exhibits often low chemical selectivity.

The alkylation of amines often involves their treatment with alkyl halides in the presence of a base[2] that is undesirable from an environmental point of view, reductive amination of aldehydes and ketones[3] that requires the use of strong reducing agents or hydrogen gas, and amide reduction.[4] Nevertheless, these conditions are not always selective and generate tertiary amines and/or quaternary ammonium salts as by-products. Some catalytic systems for N-alkylation of amines with alcohols have also been studied using Ni,[5] Ru,[6] and Rh[7] catalysts, most of which require high reaction temperature, which causes limitation for the use of alcohols and amines.

A number of techniques have been developed to overcome these problems[8] but the development of simple, mild, and selective methods for this conversion is still a major challenge in organic synthesis.

2. Results and discussion

In the course of our studies using a Ph_3P/DDQ system, we have reported that alcohols can be converted first into alkylating agents prior to their conversion into functionalities such as halides, azides, cyanides, and thiocyanides.[9] In order to develop a convenient reaction protocol for N-alkylation of amines, we studied the possibility of using this reagent system for alkylation of amines. In this work we report that the use of Ph_3P/DDQ provides a very efficient reagent system for the immediate and selective N-alkylation of primary and secondary aromatic amines with different alcohols in excellent yields (Scheme 1).



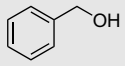
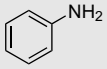
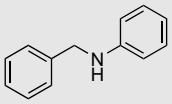
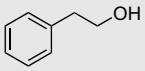
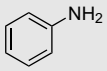
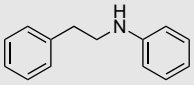
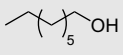
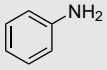
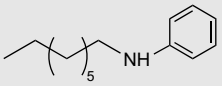
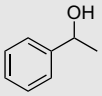
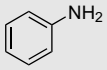
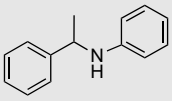
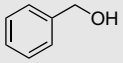
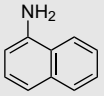
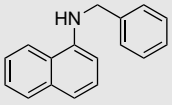
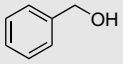
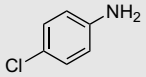
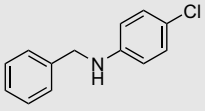
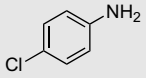
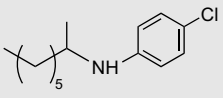
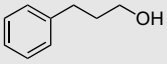
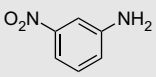
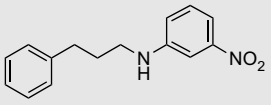
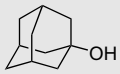
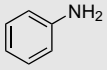
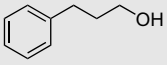
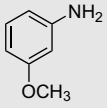
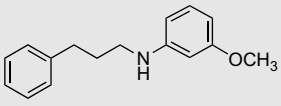
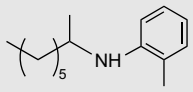
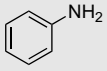
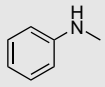
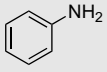
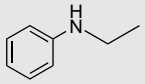
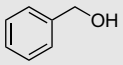
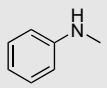
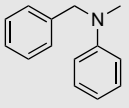
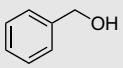
R^1= H or Alkyl or Aryl
R^2 = 1° or 2° Alkyl

Scheme 1.

* Corresponding authors. Tel.: +98 711 2280926; fax: +98 711 2286008.
E-mail addresses: iranpoor@chem.susc.ac.ir (N. Iranpoor), firouzabadi@chem.susc.ac.ir (H. Firouzabadi).
† Present address: Chemistry Department, Faculty of Sciences, Persian Gulf University, Bushehr, Iran.

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.02.078

Table 1
N-Monoalkylation of aromatic amines with alcohols using Ph_3P/DDQ[a] in CH_2Cl_2 at room temperature[b]

Entry	Alcohol	Amine	Product	Yield[c] (%)[ref]
1				92[10]
2				92[11]
3				88[12]
4				82[13]
5				95[14]
6				90[12]
7				90[15]
8				91[-]
9			—	—[d]
10				94[-]
11				89[15]
12	CH_3OH			93[10]
13	C_2H_5OH			91[10]
14				91[10]
15				86

[a] The molar ratio of Ph_3P/DDQ/amine/ROH is 1.2:1.2:1.2:1.0.
[b] All reactions are completed within 1 min.
[c] Isolated yield.
[d] No product was produced even under reflux condition in acetonitrile.

The obtained results from this study are summarized in Table 1. As the results show, the reactions occur in dichloromethane immediately and different *N*-alkylated anilines are obtained in excellent yields at room temperature.

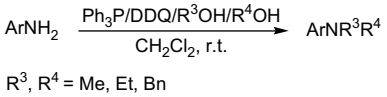
The effect of substituents on the aromatic ring has also been studied. It was observed that anilines having electron-donating or electron-withdrawing substituents react very fast under our reaction conditions and the overall yield in all cases is very high (Table 1, entries 8 and 10).

Since the reaction occurs at room temperature, methanol and ethanol as low boiling point alcohols can also be used for alkylation of anilines. *N*-Methyl and *N*-ethyl aniline were obtained in 93 and 91% yields, respectively (Table 1, entries 12 and 13). Primary and secondary alcohols were generally applicable to this methodology. As predicted, tertiary alcohols were resistant to alkylation even under reflux condition in acetonitrile. This is probably due to steric effects. *N*-Methyl aniline, a secondary aromatic amine, reacts with benzyl alcohol immediately (Table 1, entry 14) to gives a benzylated tertiary amine in excellent yield.

One crucial feature embedded in this protocol is the excellent chemoselectivity of the method. In these reactions, only monoalkylated anilines are produced as a single product without any dialkylation. The reaction is clean and high yielding and the only by-product is Ph_3PO.

We also examined the alkylation of primary aliphatic amines (e.g., benzyl amine and 1-octyl amine). Our attempts to alkylate these amines were unsuccessful. These results are explicable based on the pK_a value of amines. In order for this reaction to succeed, the amines have to be deprotonated for generation of the reactive nucleophile. Similar results have been reported for the Mitsunobu reaction, which generally requires the nucleophile to have a pK_a less than 11 for satisfactory alkylation to occur.[16] In most cases, for the success of Mitsunobu reaction it is important to protect amines as the acidic compound of the reaction in the form of amides, phthalimides, *N*-alkylsulfonamides, etc. So, aliphatic amines are also resistant toward N-alkylation under Mitsunobu conditions.

We also used this method for synthesis of tertiary amines via symmetrical and unsymmetrical N,N-dialkylation of primary amines using different alcohols. For this purpose, we chose the aromatic amine as the limiting agent. For symmetrical N,N-dialkylation, we used 2 equiv of one alcohol, however, in the case of unsymmetrical N,N-dialkylation, two different alcohols were used (Scheme 2).



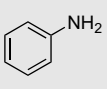
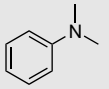
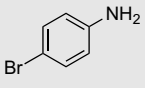
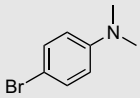
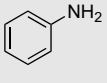
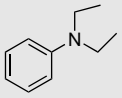
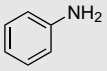
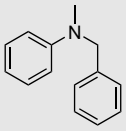
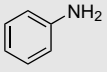
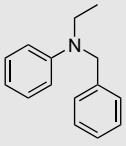
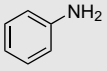
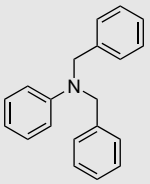
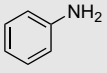
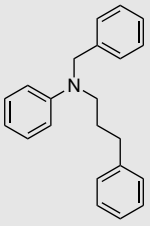
Scheme 2.

The results of this study are tabulated in Table 2.

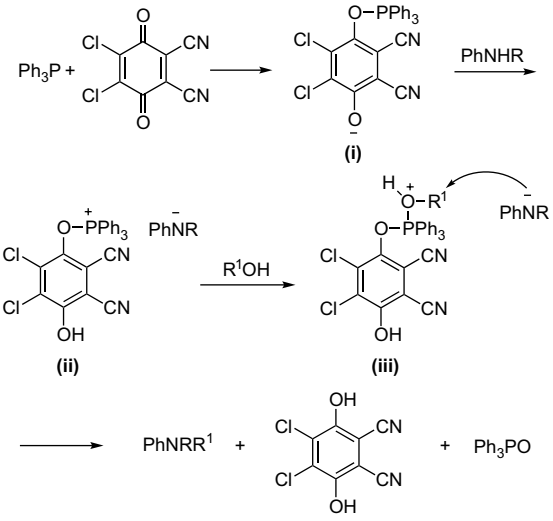
Most of the methods in the literature for this conversion employ a strong base, however, in this method no additional base is required.[8b,8d,12,17] The suggested mechanism to explain this transformation involves the initial formation of the known quaternary phosphonium salts (**i**) through the addition of DDQ to Ph_3P. The negatively charged oxygen in the hydroquinone part of this adduct can act as a base to deprotonate the amine and therefore no additional base is required for generation of an amine anion. The resulting complex (**ii**) reacts with the alcohol to give the alkoxyphosphonium salt (**iii**), which undergoes an S_N type displacement to give the desired alkylated amine (Scheme 3).

In addition to the formation of Ph_3PO and dihydro-DDQ, in order to have more evidence in support of the proposed mechanism, we performed a ^1H NMR study of the reaction mixture of PPh_3, DDQ, and *N*-methylaniline prior to the addition of alcohol. The presence

Table 2
Synthesis of tertiary amines from primary amines in the presence of Ph_3P/DDQ system

Entry	Alcohol	Amine	Product	Yield[a] (%)[ref]
1	CH_3OH[b]			66[10]
2	CH_3OH			60[10]
3	C_2H_5OH			60[10]
4	CH_3OH $PhCH_2OH$			55[10]
5	C_2H_5OH $PhCH_2OH$			53[10]
6	$PhCH_2OH$			10[c]
7	$PhCH_2OH$ $Ph(CH_2)_3OH$			10[c]

[a] Isolated yield.
[b] The molar ratio of Ph_3P/DDQ/amine/ROH is 3.0:3.0:1.0:3.0.
[c] Reflux conditions.



Scheme 3.

of phenolic hydrogen at 8.53 ppm and disappearance of the amine hydrogen supports the intermediacy of (**ii**) in the proposed mechanism.

As shown in Table 2, *N*,*N*-dialkylaniline derivatives were obtained in moderate yields under our reaction conditions. In the case of using two different alcohols, for example, methanol and benzyl alcohol, we added methanol (low molecular weight alcohol) first in the reaction mixture to obtain a better yield. As shown in entry 6, we cannot obtain *N*,*N*-dibenzyl aniline from benzyl alcohol in good yield even under reflux condition possibly due to steric effects. We also added extra equivalents of benzyl alcohol but only 10% product was obtained after a long reaction time.

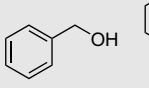
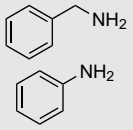
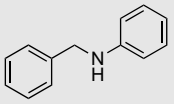
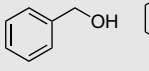
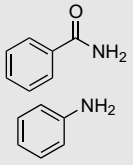
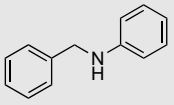
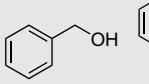
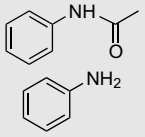
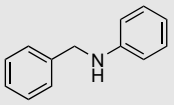
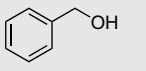
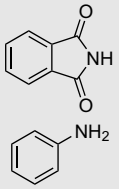
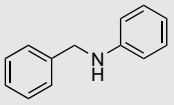
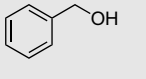
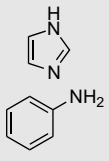
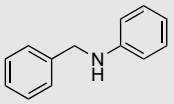
The conversion of amides, phthalimide, and imidazole into their corresponding alkylated products was unsuccessful, which makes this method very selective for amines. This is most probably due to the low nucleophilicity of the produced anions after deprotonation by (**i**).

In order to have more insight into the applicability, selectivity, and limitations of this new method, we studied the possibility of the conversion of aromatic amines in the presence of some other functional groups in binary mixtures (1:1) using the same stoichiometry of the reagents to substrate as before. The results of this study are presented in Table 3.

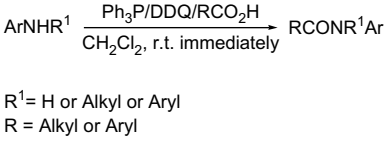
The most important point about the selectivity of this method is that, aromatic amines can be converted to their corresponding alkylated products in binary mixtures in excellent selectivity.

Due to the importance of biological properties[18] and industrial applications[19] of amides, amidation is an important reaction in organic chemistry. Since carboxylic acids usually show low

Table 3
Selective reaction of different binary mixtures with Ph_3P/DDQ[a,b,c]

Entry	Alcohol	Binary mixture	Product	Isolated yield (%)
1				90
2				93
3				93
4				89
5				92

[a] The molar ratio of Ph_3P/DDQ/binary mixture/alcohol is 1.2:1.2:1.2:1.2:1.0.
[b] Room temperature.
[c] All reactions are completed within 1 min.



Scheme 4.

reactivity, attachment of different leaving groups to the acyl carbon of the acid, or in situ activation of carboxylic group to allow attack by amino groups is necessary in this transformation.[20] Conversion to acyl chlorides is one of the easiest method to activate an acid, but an additional base is required to trap the formed HCl, because some substrates are acid sensitive and require non-acidic conditions and also to avoid the conversion of the amine into its unreactive HCl salt. The acyl azide route is another way for activation of carboxylic acids. In this case, an occasional side reaction is a Curtius rearrangement, leading to the formation of the unwanted corresponding isocyanate.[21] Carbonyl diimidazole (CDI), anhydrides, and activated esters such as aromatic esters are frequently used for amide formation.[22] Although, as was mentioned, different methodologies have been reported in the literature for this transformation, there is still considerable interest in the synthesis of amides by direct combination of acids and amines under mild reaction conditions.

Having success for immediate alkylation of aromatic amines using Ph_3P/DDQ reagent system, we sought to extend this methodology to the direct conversion of aromatic amines to amides (Scheme 4). It was observed that the reaction of carboxylic acids with aromatic amines with stoichiometry ratios of Ph_3P/DDQ/amine/RCO_2H (1.2:1.2:1.2:1.0) in dichloromethane occurred at room temperature almost immediately (1 min) to give excellent yields of the corresponding amides.

Using this reagent system, reaction of aliphatic and aromatic carboxylic acids with primary and secondary aromatic amines occurs efficiently. The presence of electron-donating or electron-withdrawing groups has no pronounced effect on the rate and yield of the reaction (Table 4).

The results shown in Table 4 demonstrate that the direct reaction of aromatic amines with aromatic and non-aromatic carboxylic acids performs efficiently with this reagent system.

The results from the above reactions clearly demonstrate that the direct amidation was successful only in the case of aromatic amines and not with aliphatic ones. Using primary and secondary aliphatic amines such as benzyl amine or octyl amine or *N*-methyl cyclohexyl amine (Table 4, entries 11, 12, and 13) resulted in unsuccessful reaction similar to the results of amination.

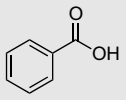
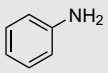
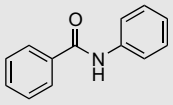
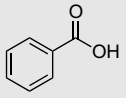
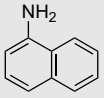
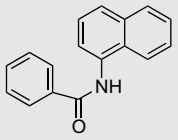
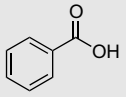
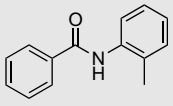
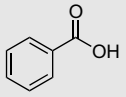
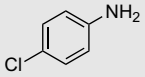
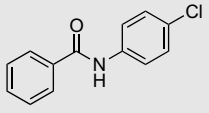
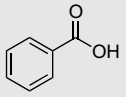
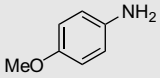
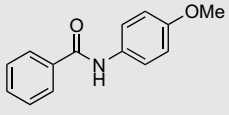
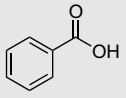
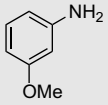
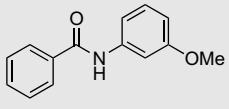
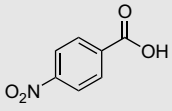
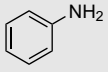
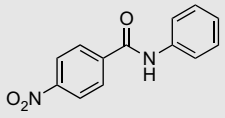
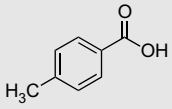
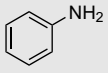
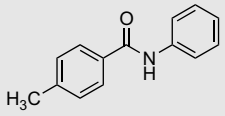
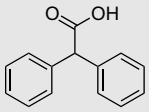
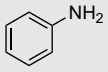
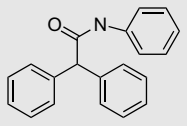
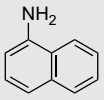
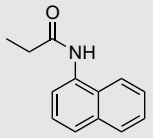
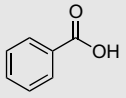
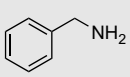
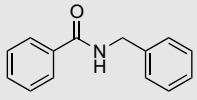
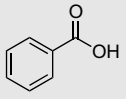
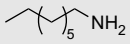
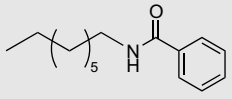
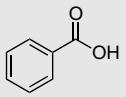
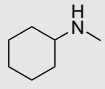
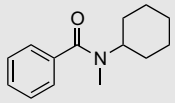
In conclusion, we have developed a new, efficient, neutral, and mild method for immediate and selective N-monoalkylation and also symmetrical or unsymmetrical N,N-dialkylation of aromatic amines with alcohols. The immediate and high yielding conversion of aromatic amines to amides is also possible using this method. High yields, short reaction times, mild reaction conditions, and absence of base in the reaction medium could make this newly method of broad synthetic utility.

3. Experimental section

3.1. General

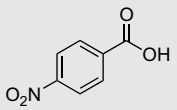
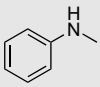
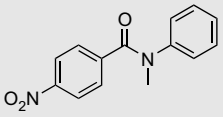
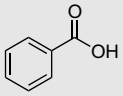
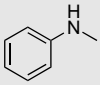
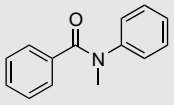
All the solvents and reagents were purchased from Fluka or Merck chemical companies. The products were purified by column or prep. TLC techniques and identified by comparison of their spectral data with those of known compounds. FTIR spectra were recorded on a Shimadzu DR-8001 spectrometer. NMR spectra were recorded on a Brucker Avance DPX 250 MHz instrument.

Table 4
Conversion of aromatic amines to amides in CH_2Cl_2 at room temperature[a]

Entry	Acid	Amine	Product	Yield[b] (%)[ref]
1				90[10]
2				87[23]
3				91[24]
4				90[25]
5				94[26]
6				88[26]
7				92[27]
8				89[28]
9				90[23]
10				94[23]
11				—
12				—
13				—

(*continued on next page*)

Table 4 (*continued*)

Entry	Acid	Amine	Product	Yield[b] (%)[ref]
14				93[23]
15				90[23]

[a] All the reactions were finished in 1 min.
[b] Isolated yield.

3.1.1. Typical procedure for N-benzylation of 4-amino-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one

To a flask containing a stirred mixture of Ph_3P (1.2 mmol, 0.314 g) and DDQ (1.2 mmol, 0.272 g) in dichloromethane (5 mL) was added 4-amino-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one (1.2 mmol, 0.244 g) at room temperature. Benzyl alcohol (1.0 mmol, 0.1 mL) was then added to the reaction mixture. TLC monitoring showed the completion of the reaction after 1 min. The solvent was evaporated and the residue was chromatographed on a silica gel column using *n*-hexane/ethyl acetate (4:1) as eluent. 4-(*N*-Benzylamino)-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one was obtained in 86% yield (0.30 g). IR (neat) 3403, 3054, 2986, 2928, 1662, 1594, 1455, 1359 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ (ppm)=1.86 (3H, s), 2.06 (1H, s), 2.60 (3H, s), 5.18 (2H, s), 7.07–7.42 (10H, m); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm)=9.75, 36.32, 57.81, 113.45, 123.34, 126.04, 126.82, 127.65, 127.93, 128.10, 128.82, 129.00, 139.83, 154.59. Anal. Calcd for $C_{18}H_{19}N_3O$: C, 73.69; H, 6.53; N, 14.32%. Found: C, 73.46; H, 6.57; N, 14.22%.

3.1.2. Typical procedure for the conversion of aniline to N,N-dimethylaniline

To a stirred solution of Ph_3P (3.0 mmol, 0.78 g), DDQ (3.0 mmol, 0.68 g), and aniline (1.0 mmol, 0.09 mL) in dichloromethane (5 mL) at room temperature was added methanol (3.0 mmol, 0.12 mL). The reaction was monitored by TLC. After 30 min, the solvent was evaporated. Column chromatography of the crude mixture on silica gel using *n*-hexane/ethyl acetate (3:1) as eluent gave *N*,*N*-dimethylaniline in 66% yield (0.08 g) (bp 193 °C, lit.[10] bp 194.15 °C). IR (neat) 3025, 2888, 2809, 1605, 1513, 1440, 1341, 753 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ (ppm)=3.07 (s, 6H), 7.00–7.05 (m, 2H), 7.24–7.28 (m, 1H), 7.70–7.74 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ (ppm)=29.30, 111.17, 116.08, 127.39, 148.40. Anal. Calcd for $C_8H_{11}N$: C, 79.29; H, 9.15; N, 11.56%. Found: C, 79.16; H, 9.20; N, 11.40%.

3.1.3. Typical procedure for the conversion of aniline to N-benzyl-N-methylaniline

Methanol (0.04 mL, 1.0 mmol) was added to a mixture of triphenylphosphine (0.314 g, 1.2 mmol), DDQ (0.272 g, 1.2 mmol), and aniline (0.09 mL, 1.0 mmol) in dichloromethane (5 mL). The reaction was stirred at room temperature. After 15 min, this mixture was added to a flask containing Ph_3P (0.392 g, 1.5 mmol) and DDQ (0.34 g, 1.5 mmol) in CH_2Cl_2 (4 mL). Benzyl alcohol (1.0 mmol, 0.1 mL) was then added to this flask. After 10 min, the solvent was evaporated. The crude product was purified by column chromatography using *n*-hexane/ethyl acetate (3:1) as eluent to give *N*-benzyl-*N*-methylaniline in 55% yield (0.1 g). IR (neat) 3033, 2892, 1594, 1506, 1443, 1361, 751, 693 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ (ppm)=2.93 (s, 3H), 4.45 (s, 2H), 6.66–6.80 (m, 4H), 7.16–7.35 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ (ppm)=38.54, 60.54, 112.45, 116.64, 126.88, 127.03, 128.55, 128.67, 129.18, 135.98. Anal. Calcd for $C_{14}H_{15}N$: C, 85.24; H, 7.66; N, 7.10%. Found: C, 85.10; H, 7.70; N, 7.02%.

3.1.4. Typical procedure for the conversion of benzoic acid to benzanilide

To a stirred solution of Ph_3P (1.2 mmol, 0.314 g) and DDQ (1.2 mmol, 0.272 g) in 5 mL dichloromethane at room temperature was added aniline (1.2 mmol, 0.11 mL) and benzoic acid (1 mmol, 0.122 g) successively. After completion of the reaction, the residue was washed with 4% aq HCl to remove the excess of aniline and dried with anhydrous Na_2SO_4. Evaporation of the solvent followed by column chromatography of the crude mixture on silica gel using *n*-hexane/ethyl acetate (3:1) as eluent gave benzanilide in 90% yield (0.177 g) (mp 161 °C, lit.[10] mp 163 °C). IR (neat) 3350, 2933, 2869, 1654, 1603, 1456, 1434, 720 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ (ppm)=7.15–8.08 (11H, Complex); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm)=120.26, 124.57, 127.04, 128.44, 128.76, 131.83, 133.56, 137.90, 165.85. Anal. Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10%. Found: C, 79.07; H, 5.59; N, 7.13%.

Acknowledgements

We are thankful to the Organization of Management and Planning of Iran and Shiraz University Research Council for the support of this work.

References and notes

1. Seayad, A. M. A.; Klein, H.; Jackstell, R.; Gross, T.; Beller, M. *Science* **2002**, *297*, 1676.
2. Smith, M. B.; March, J. *Advanced Organic Chemistry*, 5th ed.; Wiley: New York, NY, 2001; p 499.
3. (a) Smith, M. B.; March, J. *Advanced Organic Chemistry*, 5th ed.; Wiley: New York, NY, 2001; p 1187; (b) Abdel-Magid, A. F.; Carson, K. G.; Harris, B. D.; Maryanoff, C. A.; Shah, R. D. *J. Org. Chem.* **1996**, *61*, 3849; (c) Firouzabadi, H.; Iranpoor, N.; Alinejhad, H. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 143.
4. Salomaa, S. In *The Chemistry of Carbonyl Group*; Patai, S., Ed.; Wiley: New York, NY, 1966; Vol. 1, pp 177–210.
5. Rice, R. G.; Kohn, E. J. *J. Am. Chem. Soc.* **1955**, *77*, 4052.
6. (a) Watanabe, Y.; Tsuji, Y.; Ohsugi, Y. *Tetrahedron Lett.* **1981**, *22*, 2667; (b) Murahashi, S. I.; Kondo, K.; Hakata, T. *Tetrahedron Lett.* **1982**, *23*, 229; (c) Watanabe, Y.; Tsuji, Y.; Ige, H.; Ohsugi, Y.; Ohta, T. *J. Org. Chem.* **1984**, *49*, 3359; (d) Bitsi, G.; Schleiffer, E.; Antoni, F.; Jenner, G. *J. Organomet. Chem.* **1989**, *373*, 343; (e) Watanabe, Y.; Moriaki, Y.; Kondo, T.; Mitsudo, T. *J. Org. Chem.* **1996**, *61*, 4214; (f) Jun, C.; Hwang, D.; Na, S. *Chem. Commun.* **1998**, 1405.
7. Grigg, R.; Mitchell, T. R. B.; Sutthivaiyakit, S.; Tongpenyai, N. *J. Chem. Soc., Chem. Commun.* **1981**, 611.
8. (a) Siswanto, C.; Rathman, J. F. *J. Colloid Interface Sci.* **1997**, *196*, 99; (b) Salvatore, R. N.; Nagle, A. S.; Schmidt, S. E.; Jung, K. W. *Org. Lett.* **1999**, 1893; (c) Earle, M. J.; McCormac, P. B.; Seddon, K. R. *Chem. Commun.* **1998**, 2245; (d) Johnstone, R. A. W.; Payling, D. W.; Thomas, C. *J. Chem. Soc.* **1969**, 2223; (e) Chiappe, C.; Pieraccini, D. *Green Chem.* **2003**, *5*, 193; (f) Valot, F.; Fache, F.; Jacquot, R.; Spagnol, M.; Lemaire, M. *Tetrahedron Lett.* **1999**, *40*, 3689.
9. (a) Iranpoor, N.; Firouzabadi, H.; Aghapour, Gh.; Vaes Zadeh, A. R. *Tetrahedron* **2002**, *58*, 8689; (b) Iranpoor, N.; Firouzabadi, H.; Akhlaghinia, B.; Nowrouzi, N. *J. Org. Chem.* **2004**, *69*, 2562; (c) Iranpoor, N.; Firouzabadi, H.; Akhlaghinia, B.; Nowrouzi, N. *Tetrahedron Lett.* **2004**, *45*, 3291; (d) Iranpoor, N.; Firouzabadi, H.; Nowrouzi, N. *Tetrahedron* **2006**, *62*, 5498; (e) Iranpoor, N.; Firouzabadi, H.; Akhlaghinia, B.; Azadi, R. *Synthesis* **2004**, 92; (f) Iranpoor, N.; Firouzabadi, H.; Nowrouzi, N. *Tetrahedron Lett.* **2006**, 8247; (g) Iranpoor, N.; Firouzabadi, H.; Nowrouzi, N.; Firouzabadi, D. *Tetrahedron Lett.* **2006**, 6879.
10. *CRC Handbook of Chemistry and Physics*, 87th ed.; Lide, D. R., Ed.; CRC: London, 2006–2007.
11. Hamid, M. S. A.; Williams, J. M. J. *Chem. Commun.* **2007**, 725.

12. Fujita, K.; Li, Z.; Ozeki, N.; Yamaguchi, R. *Tetrahedron Lett.* **2003**, *44*, 2687.
13. Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 4397.
14. Buchwald, S. L.; Klapars, A.; Kwong, F. Y. *Org. Lett.* **2002**, *4*, 581.
15. Khedkar, V.; Tillack, A.; Beller, M. *Org. Lett.* **2003**, *5*, 4767.
16. (a) Mitsunobu, O. *Synthesis* **1981**, 1; (b) Hughes, D. L. *Org. React.* **1992**, *42*, 335; (c) Tsunoda, T.; Yamamiya, Y.; Ito, S. *Tetrahedron Lett.* **1993**, *34*, 1639.
17. (a) Tanigawa, Y.; Murahashi, S.; Moritani, I. *Tetrahedron Lett.* **1975**, 471; (b) Srivastava, S. K.; Chauhan, P. M. S.; Bhaduri, A. P. *Synth. Commun.* **1999**, 2085; (c) Mohri, K.; Suzuki, K.; Usui, M.; Isobe, K.; Tsuda, Y. *Chem. Pharm. Bull.* **1995**, *43*, 159; (d) Suga, K.; Watanabe, S.; Fujita, T.; Pan, T. P. *Bull. Chem. Soc. Jpn.* **1969**, 3606; (e) Hayat, S.; Rahman, A.; Choudhary, M. I.; Khan, K. M.; Schumann, W.; Bayer, E. *Tetrahedron* **2001**, 9951.
18. (a) Mrozik, H.; Jones, H.; Friedman, J.; Schwartzkopf, G.; Schardt, R. A.; Patchett, A. A.; Holff, D. R.; Yakstis, J. J.; Riek, R. F.; Ostlind, D. A.; Plischker, G. A.; Butler, R. W.; Cuckler, A. C.; Campbell, W. C. *Experientia* **1996**, 883; (b) White, G. A. *Pestic. Biochem. Physiol.* **1989**, *34*, 255; (c) Yalcin, I.; Kaymakcioglu, B. K.; Oren, I.; Sener, E.; Temiz, O.; Akin, A.; Altanlar, N. *Farmaco* **1997**, *52*, 685; (d) Pradhan, K. J.; Variyar, P. S.; Bandekar, J. R. *Lebensm.-Wiss. Technol.* **1999**, *32*, 121.
19. (a) Mabermann, C. E. *Encyclopedia of Chemical Technology*; Wiley: New York, NY, 1991; Vol. 1, pp 251–266; (b) Lipp, D. *Encyclopedia of Chemical Technology*; Wiley: New York, NY, 1991; Vol. 1, pp 266–287; (c) Opsahl, R. *Encyclopedia of Chemical Technology*; Wiley: New York, NY, 1991; Vol. 2, pp 346–356.
20. Montalbetti, C. A. G. N.; Falque, V. *Tetrahedron* **2005**, *61*, 10827.
21. (a) Klausner, Y.; Bodansky, M. *Synthesis* **1974**, 549; (b) Curtius, T. *Chem. Ber.* **1890**, *23*, 3023; (c) Curtius, T. *J. Prakt. Chem. [2]* **1894**, *50*, 275; (d) Smith, P. A. S. *Org. React.* **1946**, *3*, 337.
22. (a) Paul, R.; Anderson, W. *J. Am. Chem. Soc.* **1960**, *82*, 4596; (b) Mikolajczyk, M.; Kielbasinski, P. *Tetrahedron* **1981**, *37*, 233; (c) Gangwar, G. M.; Pauletti, T.; Siahaan, J.; Stella, V. J.; Borchardt, R. T. *J. Org. Chem.* **1997**, *62*, 1356; (d) Rajappan, V. P.; Hosmane, R. S. *Synth. Commun.* **1998**, *28*, 753; (e) Kisfaludy, L.; Schon, I. *Synthesis* **1983**, 325; (f) Carpino, L. A. *J. Am. Chem. Soc.* **1993**, *115*, 4397.
23. www.chemfinder.com.
24. Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 6043.
25. Wu, X.; Hu, L. *Tetrahedron Lett.* **2005**, *46*, 8401.
26. Rodriguez, J.; Martin-Villamil, R.; Ramos, S. *New J. Chem.* **1998**, 865.
27. Khalafi-Nezhad, A.; Parhami, A.; Soltani Rad, M. N.; Zareaa, A. *Tetrahedron Lett.* **2005**, *46*, 6879.
28. Cai, M.; Song, C.; Huang, X. *Synth. Commun.* **1997**, *27*, 361.