Tetrahedron 65 (2009) 2436–2442

Contents lists available at ScienceDirect

Tetrahedron

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

An efficient method for the synthesis of α-arylated nitroalkanes and α-arylated hydroximoyl chlorides mediated by $AlCl_3$

Zhijay Tu, B. Rama Raju, Tzuo-Rung Liou, Veerababurao Kavala, Chun-Wei Kuo, Yaochung Jang, Yu-Hsuan Shih, Chun-Chao Wang, Ching-Fa Yao *

Department of Chemistry, National Taiwan Normal University, 88, Sec. 4, Tingchow Road, Taipei 116, Taiwan, ROC

ARTICLE INFO

Article history:
Received 25 September 2008
Received in revised form 8 January 2009
Accepted 20 January 2009
Available online 23 January 2009

ABSTRACT

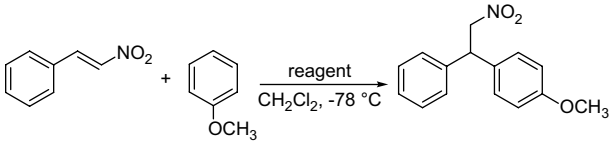
Friedel–Crafts alkylation of various arenes/heteroarenes to β-nitrostyrenes mediated by aluminum chloride is described. The interesting feature of this methodology pertain the formation of different products by tuning the reaction temperature. α-Arylated nitroalkanes were formed predominately at −78 °C, whereas α-arylated hydroximoyl chlorides were obtained at room temperature without any side products in high yields.

1. Introduction

Metal-catalyzed addition of aromatic substrates to electron deficient σ- and π-systems, commonly known as Friedel–Crafts (F–C) alkylation,[1] have long been established as a powerful strategy for C–C bond formation.[2] Originally, the F–C reaction occurs between alkyl halides and electron-rich arenes in the presence of different Lewis acids.[3] Other alkylating agents, which are widely used for alkylation of arenes are alcohols,[4] esters,[5] and alkenes.[6] Among alkenes, nitroalkenes and their F–C adducts gained importance due to their application as intermediates in pharmaceutical preparations.[7] Several methods have been reported in the literature regarding the reaction between nitroolefins and aromatic/heteroaromatic systems.[8] Nevertheless, most reports[9] in this area are still focused on relatively more reactive indole and pyrrole compounds; a few methods described the F–C reaction of benzene derivatives bearing highly electron-donating groups with nitroalkenes.[10] Hence, there is need to develop a versatile F–C reaction, which is applicable to undeveloped electron-rich arenes (benzene derivatives). $AlCl_3$ have been demonstrated as a versatile reagent for F–C reaction.[11] However, its application with β-nitrostyrene for F–C reaction has been rarely explored. Lambert et al.[12] and Hurd et al.[13] investigated the reaction of nitroalkenes with benzene in the presence of aluminum chloride to obtain α-arylated hydroximoyl chloride. However, their study was restricted to a limited number of nitroolefins with benzene.

Nitrile oxides serves as 1,3-dipoles to undergo a variety of 1,3-dipolar cycloaddition reactions with olefinic and acetylenic compounds forming isoxazolines and isoxazoles.[14] Several methods have been described in the literature for the in situ generation of nitrile oxides,[15] amongst which base-induced dehydro halogenation of hydroximoyl chlorides are the most frequently used. Usually, hydroximoyl chlorides are prepared by chlorination of aldoximes, for which a number of chlorinating reagents such as chlorine,[16] nitrosyl chloride,[17] *tert*-butyl hypochlorite,[18] *N*-chloro succinimide[19] in *N*,*N*-dimethyl formamide and HCl/*N*,*N*-dimethylformamide/oxone[20] have been employed. A literature survey revealed that very few hydroximoyl chlorides/nitrile oxides possessing α-functionalities have been reported.[21] So far, such compounds have always been obtained by multistep synthesis, involving routine reactions. Hence, hydroximoyl chlorides, which

Table 1
Arylation of β-nitrostyrene with anisole under various reaction conditions



Entry	Reagent (equiv)	Time (h)	Yield[a] (%)
1	$AlCl_3$ (1.0)	6	58
2	$AlCl_3$ (1.5)	6	71
3	$AlCl_3$ (2.0)	4	87
4	$FeCl_3$ (2.0)	12	0
5	$BF_3.OEt_2$ (2.0)	12	0
6	$SnCl_4$ (2.0)	12	0
7	$ZrCl_4$ (2.0)	12	0

[a] Isolated yield.

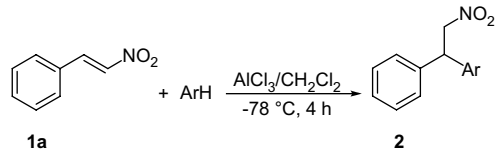
* Corresponding author.
E-mail address: cheyaocf@ntnu.edu.tw (C.-F. Yao).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.01.075

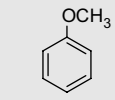
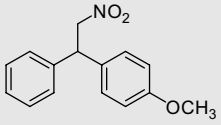
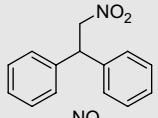
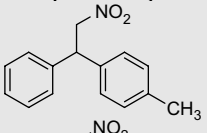
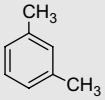
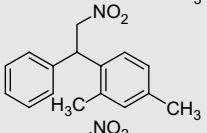
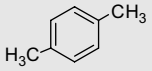
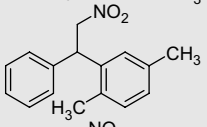
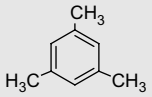
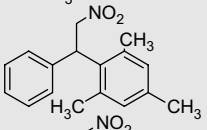
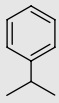
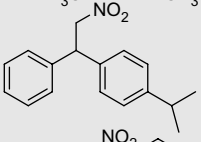
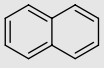
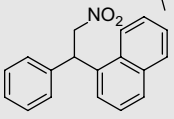
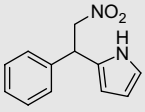
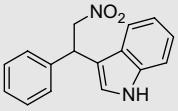
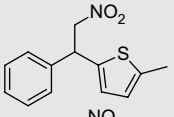
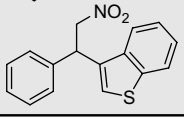
are precursors of nitrile oxides, have generated considerable interest in organic synthesis.

2,2-Diphenethylamine and their derivatives possess biological importance due to their ability to suppress adrenal steroid biosynthesis in humans.[7a,b] Bridges et al. reported the synthesis of 2,2-diphenethylamines by the multistep synthesis starting from an aromatic aldehyde.[7c] Usually 2,2-diphenethylamines were prepared by reduction of the nitro moiety in 1,1-diphenyl-2-nitroethane.[7d] Hence, 1,1-diphenyl-2-nitroethane is the important building blocks for the synthesis of biologically important amines. Earlier, α-arylated nitroalkanes were prepared by the 1,4-addition of various organometallic reagents to nitroolefins.[22] Recently, Umera et al. utilized a mixture of salts ($PdCl_2$/LiCl and $BiCl_3$) for the α-arylation of β-nitrostyrenes. However, they were not able to control the formation of homocoupled biaryl product along with the desired adduct.[23] In continuation of our research work on nitroolefins,[24] we have developed a newer route for the synthesis of α-arylated nitroalkanes and α-arylated hydroximoyl chlorides from conjugated nitroalkenes mediated by $AlCl_3$.

Table 2
$AlCl_3$-induced arylation of β-nitrostyrene with various arenes and heteroarenes



1a **2**

Entry	Arene	Product		Yield[a] (%)
1			**2a**	87
2			**2b**	76
3			**2c**	71
4			**2d**	70
5			**2e**	50
6			**2f**	45
7			**2g**	89
8			**2h**	78[b]
9			**2i**	86
10			**2j**	67
11			**2k**	80
12			**2l**	28

[a] Isolated yield.
[b] α and β isomers were obtained.

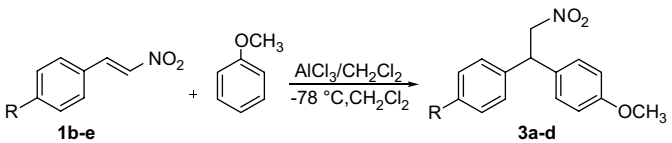
2. Results and discussion

As $FeCl_3$ [25] and $AlCl_3$[11] are well known reagents for F–C alkylation reactions. We investigated the reaction between β-nitrostyrene and anisole with 1 equiv of $FeCl_3$ in CH_2Cl_2. Unfortunately, we were not able to isolate any of the corresponding alkylated products. Secondly, we tested the efficacy of $AlCl_3$–CH_2Cl_2 system in our alkylation reaction. We were pleased to find α-arylated hydroximoyl chloride **4a** in quantitative yield. Further, we investigated the fate of the reaction at low temperatures. Conducting the reaction at 0 °C, α-arylated hydroximoyl chloride **4a** (74%) along with α-arylated nitroalkane (1-methoxy-4-(2-nitro-1-phenylethyl)benzene) **2a** (21%) was isolated. Further, upon decreasing the temperature to −78 °C, we found exclusively α-arylated nitroalkane (1-methoxy-4-(2-nitro-1-phenylethyl)benzene) **2a** without any additional products.

With this encouraging result in hand, we carried out the optimization studies at −78 °C varying the amount of $AlCl_3$. With 1 equiv of $AlCl_3$ afforded the product **2a** in 58% yield, after 6 h (entry 1, Table 1). By means of 1.5 equiv of aluminum chloride, though product yields were improved to 71%, the reaction time is almost same as that of 1 equiv. On the other hand, using 2 equiv of $AlCl_3$ as a reagent afforded the product in 87% yield in 4 h (entry 3). Various other potential Lewis acids such as $FeCl_3$, $BF_3{\cdot}OEt_2$, $SnCl_4$, and $ZrCl_4$ were tested, the starting material was recovered without any desired product. According to Table 1, the best yield of the α-arylated products was obtained with $AlCl_3$ (2 equiv) in dichloromethane at −78 °C. Similarly, this $AlCl_3$–CH_2Cl_2 system also holds good for the synthesis of α-arylated hydroximoyl chloride at room temperature.

When 1.0 equiv of β-nitrostyrene **1a** was reacted with 1.25 equiv of arene in the presence of 2 equiv of $AlCl_3$ using dry

Table 3
$AlCl_3$-mediated alkylation of anisole with nitroolefins



1b-e **3a-d**

Entry	R		Time (h)		Yield[a] (%)
1	Cl	(**1b**)	4	**3a**	77
2	NO_2	(**1c**)	2	**3b**	90
3	Me	(**1d**)	7	**3c**	69
4	OMe	(**1e**)	12[b]	**3d**	NR

[a] Isolated yield.
[b] The reaction was prolonged for 24 h.

dichloromethane as solvent at −78 °C afforded α-arylated nitroalkanes **2** exclusively in moderate to good yields in 4 h.

To further explore the scope and limitations of this methodology, we tested various arenes under optimized conditions (Table 2). As can be seen from Table 2, the arylation of β-nitrostyrene proceeds well with various aryl and heteroaryl reactants. Excellent yields were obtained with activated arenes such as anisole (entry 1). Other than benzene, various methyl-substituted benzenes showed high reactivities, including those with two or more methyl groups equipped on the benzene ring (entries 3–7). The selectivity of the arylation was controlled by both electronic and steric factors of the reactant. For example, with toluene as the substrate, alkylation on the arene occurred exclusively at *para* position with high efficiency (entry 3, Table 2).

With polysubstituted substrate, such as mesitylene, the arylation proceeded with lower yields, which may arise from the severe steric hindrance of the methyl groups (entry 6). $AlCl_3$-induced arylation of β-nitrostyrenes were found to be successful with heteroarenes, e.g., pyrrole, indole, 2-methylthiophene, and benzothiophene (entries 9–12) in good yields. The reaction failed with the acid sensitive heteroarene substrates furan and 2-methoxyfuran. Obviously, the results shown provide an efficient route for the synthesis of functionalized arenes with further elaboration of the nitro moiety.

So as to utilize this effective protocol, we examined the arylation reaction of structurally different β-nitrostyrenes with anisole. The reaction time varied according to the nature of the substituent on β-nitrostyrene. For example, the substrate containing an electron-withdrawing group (Cl) in 4-chloro-(β-nitrostyrene) (**1b**), was arylated to give the product (**3a**) in 4 h. Similarly, with 4-nitro-(β-nitrostyrene) (**1c**) containing strong electron-withdrawing group (NO_2), the reaction furnished the product (**3b**) relatively in short time 2 h and high yield. This may be attributed to the presence of electron-withdrawing groups (Cl and NO_2), which decrease the electron density on the phenyl ring, thereby generating an electron deficient center at the benzylic sp^3 carbon of the β-nitrostyrene. This species undergoes an electrophilic attack on the electron-rich arene to give the corresponding α-arylated product. However, β-nitrostyrene bearing electron-donating group (Me) such as 4-methyl-(β-nitrostyrene) (**1d**) took longer time (7 h), whereas starting material was recovered in case of 1-methoxy-4-(2-nitrovinyl) benzene (**1e**). The results are summarized in Table 3.

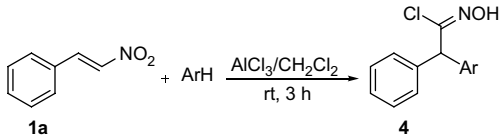
Taking cues from our optimization studies, further we extended the scope of our methodology toward the synthesis of α-arylated hydroximoyl chloride.

One equivalent of β-nitrostyrene **1a** reacted with 1.25 equiv of arenes/heteroarenes in the presence of 2 equiv of $AlCl_3$ using dichloromethane as solvent at room temperature afforded α-arylated hydroximoyl chlorides **4** without any additional products. Apart from unactivated arene benzene, the reaction also proceeds smoothly with activated arenes such as anisole, toluene, *m*, *p*-xylene, mesitylene, and cumene (entries1–7, Table 4). The reaction of β-nitrostyrene with toluene gave predominately the *para* substituted product in excellent yield. The arylation reaction adducts of β-nitrostyrene and heteroarenes e.g., thiophene, indole, and benzothiophene (entries 8–10, Table 4) were also obtained successfully in good yields.

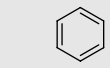
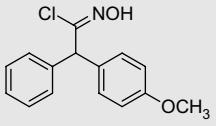
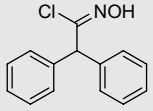
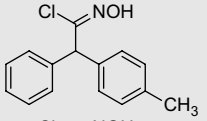
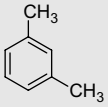
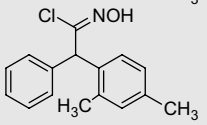
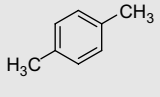
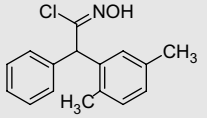
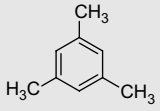
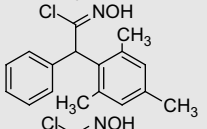
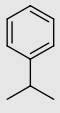
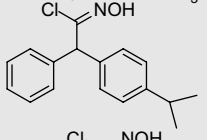
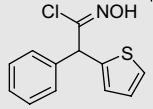
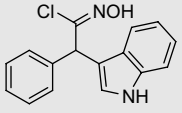
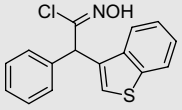
The mechanism probably involves the complexation of $AlCl_3$ with β-nitrostyrene **1a**, to generate a carbocationic center at benzylic carbon of the activated β-nitrostyrene (**A**). Electrophilic attack of this reactive species on the arene generates the σ-complex (**B**), which upon protonation affords the intermediate (**C**). Elimination of $AlCl_2$ gives the *aci*-nitro compound (**D**), which at low temperature (−78 °C) rearranges to give the corresponding nitroalkane **2a**.

At room temperature the formation of hydroximoyl chloride can be explained in two plausible pathways starting from the intermediate (**C**). **Path A** describes the formation of *aci*-nitro compound (**D**), which further undergoes intramolecular oxidation and reduction leading to form (**E**). The reaction of aluminum chloride with (**E**) gives the hydroximoyl chloride.[13] **Path B** can be explained by the formation of α-arylated nitroso derivative (**G**), which upon chloride transfer gives the intermediate (**F**), further tautomerizes to form hydroximoyl chloride **4a**.

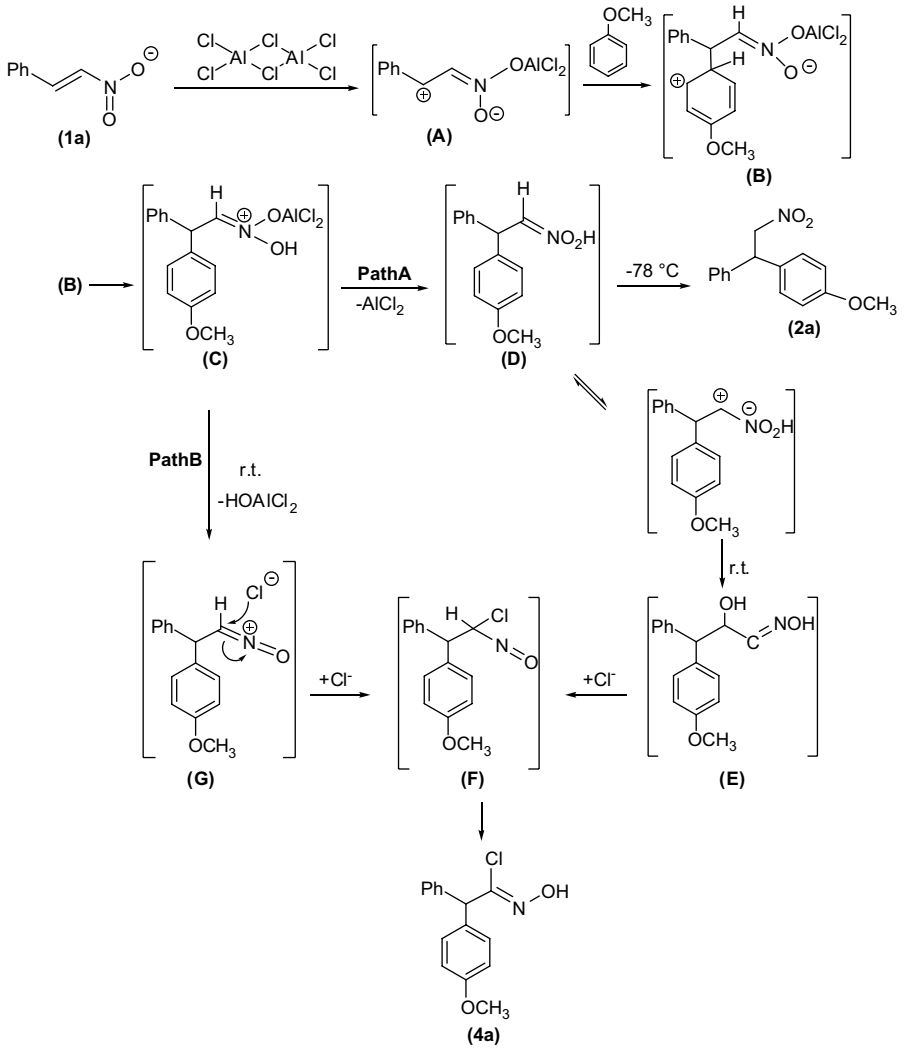
Table 4
Synthesis of α-arylated hydroximoyl chlorides mediated by $AlCl_3$



1a **4**

Entry	Arene	Product		Yield[a] (%)
1			**4a**	93
2			**4b**	90
3			**4c**	99
4			**4d**	95
5			**4e**	95
6			**4f**	88
7			**4g**	97
8			**4h**	62
9			**4i**	43
10			**4j**	59

[a] Isolated yield.



3. Conclusion

In summary, we have developed a new and efficient $AlCl_3$-mediated arylation reaction of β-nitrostyrenes with various arenes/heteroarenes under mild conditions. This procedure provides a simple route toward the synthesis of α-arylated nitroalkanes at −78 °C and α-arylated hydroximoyl chlorides at room temperature employing the same reagent in moderate to good yields. The use of readily available or cheap starting materials, inexpensive reagents and wide range of arenes make this protocol an alternative to the present existing methods.

4. Experimental

4.1. General

All the reactions were performed in oven (130 °C) dried glassware under an inert atmosphere of argon unless otherwise specified. Solvents for extraction and chromatography were distilled before use. Anhydrous solvents were obtained by following the standard procedure. All the chemicals used in this study were of commercial grade and used after distillation. Analytical thin layer chromatography was performed with E. Merck silica gel 60 F_{254} aluminum plates. All purifications were carried out by flash chromatography using 230–400 mesh silica gel. $AlCl_3$ was purchased from the Acros Organics Co. Melting points were determined with a microscope hot-stage apparatus and uncorrected. ^1H and ^{13}C NMR were recorded with Varian Gemini-200 or Bruker Avance EX 400 FT NMR. Chemical shifts were reported in parts per million (δ) using TMS as internal standard, and coupling constants were expressed in hertz. MS or HRMS were measured using a JEOL JMS-D300 or JEOL JMS-HX 110 spectrometer.

4.2. General procedure for the arylation of β-nitrosytrenes with arenes mediated by aluminum chloride

In a 25 mL round bottom flask were first added β-nitrosytrene (1 mmol), dry dichloromethane (4 mL) and anhydrous aluminum chloride (2 mmol). The mixture was thoroughly degassed using vacuum and nitrogen was purged in cycles. The reaction mixture was stirred at −78 °C, to this suspension, arene (1.25 mmol) was added via a syringe. After completion of the reaction as indicated by TLC, the reaction mixture was quenched with an ice cold saturated sodium chloride solution and extracted with dichloromethane (3×25 mL). The combined organic layer was dried over anhydrous magnesium sulfate and evaporated under reduced pressure to obtain the crude mixture. The crude mixture was purified by flash chromatography (ethyl acetate–hexane 1:20) to afford the desired pure product.

*4.2.1. 1-Methoxy-4-(2-nitro-1-phenylethyl)benzene (**2a**)*

Colorless oil (87% yield) ^1H NMR ($CDCl_3$) δ 7.33–7.20 (m, 5H), 7.13 (d, J=8.72 Hz, 2H), 6.84 (d, J=8.72 Hz, 2H), 4.95–4.82 (m, 2H), 3.74

(s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 139.5, 131.2, 128.9, 128.7, 127.5, 127.4, 114.3, 79.4, 55.2, 48.2. MS *m*/*z* (relative intensity) 257 (M^+, 11), 210 (100), 197 (51), 166 (46), 135 (22), 61 (29). HRMS calcd for $C_{15}H_{15}NO_3$ (M^+) 257.1052, found 257.1055.

*4.2.2. 1,1-Diphenyl-2-nitroethane (**2b**)*[7c]

Colorless oil (76% yield) ^{1}H NMR ($CDCl_3$) δ 7.34–7.30 (m, 5H), 7.26–7.22 (m, 5H), 4.98 (d, *J*=8.72 Hz, 2H), 4.92–4.88 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 139.1, 128.9, 127.5, 127.4, 79.0, 48.8.

*4.2.3. 1-Methyl-4-(2-nitro-1-phenylethyl)benzene (**2c**)*

Colorless oil (71%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.22 (m, 5H), 7.12 (s, 4H), 4.97–4.84 (m, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 137.3, 136.2, 129.7, 129.0, 127.6, 127.5, 79.4, 48.6, 21.0; MS *m*/*z* (relative intensity) 241 (M^+, 1), 194 (100), 179 (52), 165 (24), 103 (11), 91 (10); HRMS calcd for $C_{15}H_{15}NO_2$ (M^+) 241.1103, found 241.1109.

*4.2.4. 2,4-Dimethyl-1-(2-nitro-1-phenylethyl)benzene (**2d**)*

Colorless oil (70% yield) ^{1}H NMR ($CDCl_3$) δ 7.33–7.01 (m, 8H), 5.08 (t, *J*=8.04 Hz, 1H), 5.00–4.89 (m, 2H), 2.30 (s, 3H), 2.29 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 139.0, 137.1, 136.3, 134.1, 132.1, 128.9, 127.9, 127.4, 127.0, 125.8, 79.3, 44.7, 20.9, 19.5. MS *m*/*z* (relative intensity) 255 (M^+, 11), 209 (82), 193 (100), 178 (37), 105 (33), 77 (32). HRMS calcd for $C_{16}H_{17}NO_2$ (M^+) 255.1259, found 255.1261.

*4.2.5. 1,4-Dimethyl-2-(2-nitro-1-phenylethyl)benzene (**2e**)*

Colorless oil (50% yield) ^{1}H NMR ($CDCl_3$) δ 7.32–6.98 (m, 8H), 5.08 (dd, *J*=8.64, 7.40 Hz, 1H), 4.97 (dd, *J*=12.80, 7.40 Hz, 1H), 4.91 (dd, *J*=12.80, 8.64 Hz, 1H), 2.32 (s, 3H), 2.26 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 138.9, 136.9, 135.8, 133.3, 131.1, 128.9, 128.1, 127.9, 127.4, 126.6, 79.2, 44.9, 21.2, 19.1. MS *m*/*z* (relative intensity) 255 (M^+, 17), 210 (95), 193 (100), 178 (31), 165 (24), 103 (14). HRMS calcd for $C_{16}H_{17}NO_2$ (M^+) 255.1259, found 255.1260.

*4.2.6. 1,3,5-Trimethyl-2-(2-nitro-1-phenylethyl)benzene (**2f**)*

Colorless oil (45% yield) ^{1}H NMR ($CDCl_3$) δ 7.30–7.20 (m, 3H), 7.05 (d, *J*=7.28 Hz, 2H), 6.86 (s, 2H), 5.52 (dd, *J*=8.00, 6.80 Hz, 1H), 5.33 (dd, *J*=12.84, 8.00 Hz, 1H), 4.89 (dd, *J*=12.84, 6.80 Hz, 1H), 2.26 (s, 3H), 2.20 (s, 6H). ^{13}C NMR ($CDCl_3$) δ 139.6, 137.2, 137.0, 133.4, 130.4, 128.8, 126.7, 126.4, 77.8, 42.1, 21.0, 20.8. MS *m*/*z* (relative intensity) 269 (M^+, 18), 223 (37), 207 (100), 192 (33), 135 (47), 91 (21). HRMS calcd for $C_{17}H_{19}NO_2$ (M^+) 269.1410, found 269.1416.

*4.2.7. 1-Isopropyl-4-(2-nitro-1-phenylethyl)benzene (**2g**)*

Colorless oil (89% yield) ^{1}H NMR ($CDCl_3$) δ 7.33–7.23 (m, 5H), 7.18–7.13 (m, 5H), 4.97 (d, *J*=8.8 Hz, 2H), 4.89–4.85 (m, 1H), 2.88–2.84 (m, 1H), 1.22 (s, 3H), 1.20 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 148.1, 139.4, 136.4, 128.9, 127.6, 127.5, 127.4, 127.2, 126.9, 79.2, 48.6, 33.6, 23.8. MS *m*/*z* (relative intensity) 269 (M^+, 5), 206 (100), 177 (62), 165 (57), 118 (32), 102 (27), 91 (32), 77 (13). HRMS calcd for $C_{17}H_{19}NO_2$ (M^+) 269.1410, found 269.1403.

*4.2.8. 1-(2-Nitro-1-phenylehtyl)naphthalene (**2h**)*

Colorless oil (78% yield) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89–7.87 (m, 1H), 7.84–7.72 (m, 4H), 7.54–7.45 (m, 6H), 7.37–7.26 (m, 13H), 5.79 (t, *J*=8 Hz, 1H), 5.16–5.04 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 138.9, 136.6, 134.6, 134.1, 133.3, 132.6, 131.1, 129.1, 129.0, 128.9, 128.4, 127.9, 127.8, 127.7, 127.6, 126.7, 126.4, 126.2, 126.0, 125.9, 125.8, 125.2, 124.2, 123.0, 79.1, 79.0, 48.9, 44.6. MS *m*/*z* (relative intensity) 277 (M^+, 51), 229 (100), 216 (80), 214 (50), 203 (22), 190 (5), 152 (89), 114 (14), 101 (11). HRMS calcd for $C_{18}H_{15}NO_2$ (M^+) 277.1097, found 277.1099.

*4.2.9. 2-(2-Nitro-1-phenylethyl)-1H-pyrrole (**2i**)*

Black solid (86% yield) Mp 73 °C. ^{1}H NMR ($CDCl_3$) δ 7.84 (br s, 1H), 7.38–7.29 (m, 3H), 7.26–7.23 (m, 2H), 6.69–6.68 (m, 1H), 6.18–6.16 (m, 1H), 6.0 (s, 1H), 5.01–4.96 (m, 1H), 4.90 (t, *J*=7.48 Hz, 1H), 4.83–4.78 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 137.9, 129.1, 128.8, 128.0, 127.8, 118.1, 108.5, 105.7, 79.10, 42.8. MS *m*/*z* (relative intensity) 216 (M^+, 15), 169 (100), 154 (32), 92 (8). HRMS calcd for $C_{12}H_{12}N_2O_2$ (M^+) 216.0893, found 216.0886.

*4.2.10. 3-(2-Nitro-1-phenylehtyl)-1H-indole (**2j**)*

Colorless oil (67% yield) ^{1}H NMR ($CDCl_3$) δ 7.93 (s, 1H), 7.40 (d, *J*=8.00 Hz, 1H), 7.27–7.10 (m, 8H), 6.82 (d, *J*=2.36 Hz, 1H), 5.12 (dd, *J*=8.36, 7.68 Hz, 1H), 4.95 (dd, *J*=12.52, 7.68 Hz, 1H), 4.84 (dd, *J*=12.52, 8.36 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 139.1, 136.3, 128.7, 127.6, 127.4, 125.9, 122.3, 121.5, 119.7, 118.7, 113.9, 111.4, 79.3, 41.3. MS *m*/*z* (relative intensity) 266 (M^+, 8), 219 (100), 204 (44), 178 (19), 115 (11), 108 (17). HRMS calcd for $C_{16}H_{14}N_2O_2$ (M^+) 266.1055, found 266.1051.

*4.2.11. 2-Methyl-5-(2-nitro-1-phenylethyl)thiophene (**2k**)*

Colorless oil (80% yield) ^{1}H NMR ($CDCl_3$) δ 7.38–7.34 (m, 2H), 7.31–7.26 (m, 3H), 6.69–6.68 (m, 1H), 6.59–6.58 (m, 1H), 5.04–5.02 (m, 1H), 4.98–4.87 (m, 2H), 2.41 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 140.0, 139.9, 139.0, 129.1, 128.0, 127.6, 125.1, 125.0, 79.9, 44.9, 15.3. MS *m*/*z* (relative intensity) 247 (M^+, 7), 211 (34), 199 (100), 184 (75), 153 (15), 102 (10), 76 (8). HRMS calcd for $C_{13}H_{13}NO_2S$ (M^+) 247.0662, found 247.0673.

*4.2.12. 3-(2-Nitro-1-phenylethyl)benzo[b]thiophene (**2l**)*

Colorless oil (28% yield) ^{1}H NMR ($CDCl_3$) δ 7.86–7.84 (m, 1H), 7.66–7.64 (m, 1H), 7.35–7.25 (m, 8H), 5.28 (dd, *J*=8.24, 7.60 Hz, 1H), 5.10 (dd, *J*=12.84, 7.60 Hz, 1H), 4.96 (dd, *J*=12.84, 8.24 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 140.6, 137.8, 137.6, 133.5, 129.2, 128.0, 127.8, 124.8, 124.4, 122.9, 122.6, 121.8, 79.0, 43.5. MS *m*/*z* (relative intensity) 283 (M^+, 40), 226 (100), 221 (37), 204 (29), 115 (17), 61 (35). HRMS calcd for $C_{16}H_{13}NO_2S$ (M^+) 283.0667, found 283.0668.

*4.2.13. 1-Chloro-4-(1-(4-methoxyphenyl)-2-nitroethyl) benzene (**3a**)*

Colorless oil (77% yield) ^{1}H NMR ($CDCl_3$) δ 7.32–7.29 (m, 2H), 7.17–7.11 (m, 4H), 6.87–6.85 (m, 2H), 4.93–4.90 (m, 2H), 4.86–4.81 (m, 1H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 159.3, 138.3, 133.6, 130.9, 129.4, 129.1, 128.8, 114.7, 79.4, 55.5, 47.8. MS *m*/*z* (relative intensity) 291 (M^+, 11), 244 (100), 230 (28), 178 (15), 166 (25), 152 (19), 139 (6), 76 (4). HRMS calcd for $C_{15}H_{14}ClNO_3$ (M^+) 291.0657, found 291.0665.

*4.2.14. 1-Methoxy-4-(2-nitro-1-(4-nitrophenyl)ethyl)benzene (**3b**)*

Colorless oil (90% yield) ^{1}H NMR ($CDCl_3$) δ 8.20 (d, *J*=8.76 Hz, 2H), 7.43 (d, *J*=8.72 Hz, 2H), 7.13 (d, *J*=8.68 Hz, 2H), 6.89 (d, *J*=8.72 Hz), 5.02–5.01 (m, 2H), 4.99–4.95 (m, 1H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 159.6, 147.1, 147.0, 129.8, 128.9, 128.7, 124.4, 114.9, 78.86, 55.5, 48.1. MS *m*/*z* (relative intensity) 302 (M^+, 17), 254 (100), 241 (38), 191 (12), 132 (20), 115 (16), 77 (6). HRMS calcd for $C_{15}H_{14}N_2O_5$ (M^+) 302.0903, found 302.0909.

*4.2.15. 1-Methoxy-4-(2-nitro-1-p-tolylethyl)benzene (**3c**)*

Colorless oil (69% yield). ^{1}H NMR ($CDCl_3$) δ 7.15–7.09 (m, 5H), 6.85–6.81 (m, 3H), 4.93 (d, *J*=8.4 Hz, 2H), 4.83 (t, *J*=8.2 Hz, 1H), 3.76 (s, 3H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 159.2, 137.5, 136.8, 131.8, 129.9, 128.9, 127.7, 114, 79.9, 55.5, 48.2, 21.3. MS *m*/*z* (relative intensity) 271 (M^+, 13), 223 (100), 210 (45), 208 (17), 166 (12), 115 (6), 105 (3). HRMS calcd for $C_{16}H_{17}NO_3$ (M^+) 271.1203, found 271.1218.

4.3. General procedure for the synthesis of α-arylated hydroximoyl chloride

The 25 mL round bottom flask was cooled to 0 °C containing β-nitrostyrene (1 mmol) and anhydrous aluminum chloride (2 mmol)

in 4 mL of dry dichloromethane. To this stirred suspension 1.25 mmol of arene was added via a syringe, all the additions were carried out at 0 °C. After complete addition, the ice bath was removed and stirring was continued at room temperature for 3 h. After completion of the reaction as indicated by TLC, the reaction mixture was quenched with an ice cold saturated sodium chloride solution and extracted with dichloromethane (3×25 mL). The organic fraction was dried over anhydrous magnesium sulfate and evaporated to give the crude product, which was purified by flash chromatography using ethyl acetate and hexane to obtain the corresponding hydroximoyl chloride.

4.3.1. *N-hydroxy-2-(4-methoxyphenyl)-2-phenyl acetimidoyl chloride (**4a**)*

Colorless solid (93% yield). Mp 163 °C. ^{1}H NMR ($CDCl_3$) δ 7.65 (s, 1H), 7.34–7.15 (m, 8H), 6.87 (d, J=6.72 Hz, 2H), 5.21 (s, 1H), 3.81 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 158.87, 143.58, 138.80, 130.51, 130.11, 128.88, 128.55, 127.40, 113.97, 57.55, 55.24. MS m/z (relative intensity) 277 ($(M+2)^+$, 4), 275 (11), 258 (4), 239 (5), 223 (11), 209 (100), 194 (26), 178 (14), 165 (47), 153 (17), 139 (7), 115 (5), 102 (3), 91 (10), 77 (6), 51 (2). HRMS calcd for $C_{15}H_{14}NClO_2$ (M^+) 275.0713, found 275.0709.

4.3.2. *N-Hydroxy-2,2-diphenylacetimidoylchloride (**4b**)*

Colorless solid (90% yield). Mp 110 °C. ^{1}H NMR ($CDCl_3$) δ 7.70 (s, 1H), 7.36–7.30 (m, 5H), 7.29–7.24 (m, 5H), 5.25 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 143.4, 138.5, 129.0, 128.6, 127.6, 58.4. MS m/z (relative intensity) 245 (M^+, 100), 229 (39), 193 (37), 178 (89), 166 (70), 125 (35), 89 (12), 82 (16). HRMS calcd for $C_{14}H_{12}ClNO$ (M^+) 245.0602, found 245.0595.

4.3.3. *N-Hydroxy-2-phenyl-2-p-tolylacetimidoyl chloride (**4c**)*

Colorless solid (99% yield). Mp 125 °C. ^{1}H NMR ($CDCl_3$) δ 8.27 (s, 1H), 7.33–7.09 (m, 9H), 5.18 (s, 1H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 143.4, 138.6, 137.2, 135.4, 129.3, 128.9, 128.8, 128.6, 127.4, 58.0, 21.0. MS m/z (relative intensity) 261 ($(M+2)^+$, 12), 259 (M^+, 34), 242 (19), 224 (9), 207 (21), 193 (100), 178 (59), 165 (34), 139 (11), 125 (8), 115 (24), 102 (4), 89 (9), 65 (3), 57 (3). HRMS calcd for $C_{15}H_{14}ClNO$ (M^+) 259.0764, found 259.0768.

4.3.4. *2-(2,4-Dimethylphenyl)-N-hydroxy-2-phenyl acetimidoyl chloride (**4d**)*

Colorless solid (95% yield). Mp 152 °C. ^{1}H NMR ($CDCl_3$) δ 7.35-7.00 (m, 7H), 6.89 (s, 1H), 5.31 (s, 1H), 2.29 (s, 3H), 2.22 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 143.23, 137.96, 136.66, 135.57, 133.34, 130.61, 129.16, 129.12, 128.56, 128.29, 127.39, 55.55, 21.15, 19.14. MS m/z (relative intensity) 273 (M^+, 8), 256 (8), 238 (60), 220 (19), 208 (21), 207 (100), 192 (41), 165 (28), 152 (7), 129 (33), 115 (36), 91 (10), 77 (8), 57 (6). HRMS calcd for $C_{16}H_{16}ClNO$ (M^+) 273.0920, found 273.0921.

4.3.5. *2-(2,5-Dimethylphenyl)-N-hydroxy-2-phenyl acetimidoyl chloride (**4e**)*

Colorless solid (95% yield). Mp 130 °C. ^{1}H NMR ($CDCl_3$) δ 7.70 (s, 1H), 7.39–6.96 (m, 8H), 5.30 (s, 1H), 2.30 (s, 3H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 143.23, 137.96, 136.66, 135.57, 133.34, 130.61, 129.16, 129.12, 128.56, 128.29, 127.39, 55.55, 21.15, 19.14. MS m/z (relative intensity) 273 (M^+, 4), 268 (10), 256 (5), 238 (100), 220 (28), 207 (94), 192 (42), 178 (34), 165 (31), 160 (17), 132 (8), 129 (41), 115 (51), 105 (19), 91 (21), 88 (29), 73 (26), 70 (60), 61 (66). HRMS calcd for $C_{16}H_{16}ClNO$ (M^+) 273.0920, found 273.0915.

4.3.6. *N-Hydroxy-2-mesityl-2-phenylacetimidoyl chloride (**4f**)*

Colorless solid (88% yield). Mp 113 °C. ^{1}H NMR ($CDCl_3$) δ 7.69 (s, 1H), 7.31–7.21 (m, 3H), 7.15 (d, J=7.15 Hz, 2H), 5.57 (s, 1H), 2.28 (s, 3H), 2.20 (s, 6H). ^{13}C NMR ($CDCl_3$) δ 143.48, 137.63, 137.19, 137.08, 131.79, 130.31, 128.95, 128.32, 127.02, 53.85, 21.17, 20.83. MS m/z (relative intensity) 287 (M^+, 1), 270 (2), 253 (6), 252 (34), 234 (5), 221 (100), 206 (24), 191 (13), 178 (9), 165 (6), 152 (2), 143 (11), 128 (5), 115 (11), 103 (1), 91 (4), 77 (2). HRMS calcd for $C_{17}H_{18}ClNO$ (M^+) 287.1077, found 287.1082.

4.3.7. *N-Hydroxy-2-(4-isopropylphenyl)-2-phenyl acetimidoyl chloride (**4g**)*

Colorless solid (97% yield). Mp 116 °C. ^{1}H NMR ($CDCl_3$) δ 7.73 (s, 1H), 7.34–7.15 (m, 10H), 5.22 (s, 1H), 2.90 (m, 1H), 1.24 (d, J=6.92 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ 148.04, 143.45, 138.69, 135.71, 129.00, 128.87, 128.53, 127.40, 126.63, 57.98, 33.68, 23.89. MS m/z (relative intensity) 289 ($(M+2)^+$, 5), 287 (M^+, 15), 268 (24), 251 (4), 228 (6), 222 (19), 221 (100), 191 (12), 178 (35), 165 (17), 152 (7), 128 (7), 115 (11), 97 (11), 91 (17), 71 (20), 57 (24). HRMS calcd for $C_{17}H_{18}ClNO$ (M^+) 287.1077, found 287.1079.

4.3.8. *N-Hydroxy-2-phenyl-2-(thiophen-2-yl)acetimidoyl chloride (**4h**)*

Colorless solid (62% yield). Mp 123 °C. ^{1}H NMR ($CDCl_3$) δ 8.26 (s, 1H), 7.29–7.39 (m, 5H), 7.28–7.25 (m, 1H), 6.99–6.96 (m, 1H), 6.93–6.92 (m, 1H), 5.45 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 142.72, 141.14, 138.25, 128.70, 128.53, 127.95, 127.04, 126.71, 125.60, 53.42. MS m/z (relative intensity) 253 ($(M+2)^+$, 10), 251 (M^+, 27), 236 (4), 234 (10), 207 (6), 199 (17), 185 (100), 184 (63), 173 (34), 171 (20), 152 (14), 141 (11), 115 (9), 89 (4), 77 (6), 63 (3), 51 (3). HRMS calcd for $C_{12}H_{10}ClNOS$ (M^+) 251.0172, found 251.0169.

4.3.9. *N-Hydroxy-2-(indolin-3-yl)-2-phenylacetimidoyl chloride (**4i**)*

Colorless solid (43% yield). Mp 150 °C. ^{1}H NMR ($CDCl_3$) δ 8.08 (s, 1H), 7.71 (s, 1H), 7.44–7.20 (m, 8H), 7.09 (t, J=7.92 Hz, 1H), 6.94 (d, J=2.40 Hz, 1H), 5.48 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 143.23, 138.41, 136.27, 128.69, 128.56, 127.49, 126.47, 123.69, 122.49, 119.89, 119.27, 114.18, 111.30, 50.33. MS m/z (relative intensity) 286 ($(M+2)^+$, 4), 284 (M^+, 13), 248 (11), 232 (11), 218 (100), 206 (11), 191 (28), 178 (10), 165 (4), 155 (10), 151 (4), 141 (2), 128 (4), 108 (4), 89 (4), 77 (5), 57 (3). HRMS calcd for $C_{16}H_{13}Cl\,N_2O$ (M^+) 284.0716, found 284.0715.

4.3.10. *2-(2,3-Dihydrobenzo[b]thiophen-3-yl)-N-hydroxy-2-phenylacetimidoyl chloride (**4j**)*

Colorless solid (59% yield). Mp 130 °C. ^{1}H NMR ($CDCl_3$) δ 7.87–7.84 (m, 1H), 7.73 (s, 1H), 7.61–7.59 (m, 1H), 7.39–7.31 (m, 7H), 7.12 (d, J=0.68 Hz, 1H), 5.51 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 142.09, 140.39, 137.31, 137.90, 133.36, 128.84, 127.93, 125.47, 124.63, 124.34, 122.98, 121.95, 52.76. MS m/z (relative intensity) 303 ($(M+2)^+$, 4), 301 (M^+, 77), 284 (31), 249 (46), 235 (100), 221 (62), 178 (17), 158 (6), 125 (12), 88 (9). HRMS calcd for $C_{16}H_{12}ClNOS$ (M^+) 301.0328, found 301.0323.

Acknowledgements

Financial support provided by the National Science Council of the Republic of China and National Taiwan Normal University (96TOP001) is gratefully acknowledged.

References and notes

1. Friedel, C.; Crafts, J. M. *Bull. Soc. Chim. Fr.* **1877**, *27*, 530.
2. (a) Olah, G. A.; Krishnamurti, R.; Prakash, G. K. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, Chapter 1.8, p 293; (b) Roberts, R. M.; Khalaf, A. A. *Friedel–Crafts Alkylation Chemistry*; Marcel Dekker: New York, NY, 1984; (c) *Friedel–Crafts Chemistry*; Olah, G. A., Ed.; Wiley: New York, NY, 1973; (d) *Friedel–Crafts and Related Reactions*; Olah, G. A., Ed.; Wiley-Interscience: New York, NY, 1963–65; Vols. 1–4.
3. (a) Calloway, N. O. *Chem. Rev.* **1935**, *17*, 327–392; (b) Gore, P. H. *Chem. Rev.* **1955**, *55*, 229–281; (c) Giovanni; Maggi, R. *Chem. Rev.* **2006**, *106*, 1077–1104.
4. Yamato, T.; Hideshima, C.; Surya Prakash, G. K.; Olah, G. A. *J. Org. Chem.* **1991**, *56*, 2089–2091.
5. Hwang, J. P.; Surya Prakash, G. K.; Olah, G. A. *Tetrahedron* **2000**, *56*, 7199–7203.

6. (a) Olah, G. A.; DeMember, J. R. *J. Am. Chem. Soc.* **1970**, *92*, 2562–2564; (b) Olah, G. A.; Nishimura, J.; Yamada, Y. *J. Org. Chem.* **1974**, *39*, 2430–2431; (c) Yamato, T.; Hideshima, C.; Surya Prakash, G. K.; Olah, G. A. *J. Org. Chem.* **1991**, *56*, 3955–3957.
7. (a) Tinland, B. *Res. Commun. Chem. Path.* **1973**, *5*, 837–842; (b) Zuccarello, W. A.; Blank, B.; Frishmuth, G. J.; Cohen, S. R.; Scaricaciottoli, D.; Owings, F. F. *J. Med. Chem.* **1968**, *12*, 9–15 and references cited therein; (c) Bridges, A. J.; Bruns, R. F.; Ortwine, D. F.; Priebe, S. R.; Szotel, D. L.; Trivedi, B. K. *J. Med. Chem.* **1988**, *31*, 1282–1285; (d) Hass, H. B.; Neher, M. B.; Blickenstaff, R. T. *Ind. Eng. Chem.* **1951**, *43*, 2875–2878.
8. (a) Yadav, J. S.; Abraham, S.; Reddy, B. V. S.; Sabitha, G. *Synthesis* **2001**, 2165–2169; (b) Bandini, M.; Melchiorre, P.; Melloni, A.; Umani-Ronchi, A. *Synthesis* **2002**, 1110–1114; (c) Komoto, I.; Kobayashi, S. *J. Org. Chem.* **2004**, *69*, 680–688; (d) Zhan, Z.-P.; Yang, R.-F.; Lang, K. *Tetrahedron Lett.* **2005**, *46*, 3859–3862; (e) Bartoli, G.; Bosco, M.; Giuli, S.; Giuliani, A.; Lucarelli, L.; Marcantoni, E.; Sambri, L.; Torregiani, E. *J. Org. Chem.* **2005**, *70*, 1941–1944; (f) Lin, C.; Hsu, J.; Sastry, M. N. V.; Fang, H.; Tu, Z.; Liu, J.-T.; Yao, C.-F. *Tetrahedron* **2005**, *61*, 11751–11757; (g) Firouzabadi, H.; Iranpoor, N.; Nowrouzi, F. *Chem. Commun.* **2005**, 789–791; (h) Azizi, N.; Arynasab, F.; Saidi, M. R. *Org. Biomol. Chem.* **2006**, 4275–4277; (i) Ballini, R.; Clemente, R. R.; Palmieri, A.; Petrini, M. *Adv. Synth. Catal.* **2006**, *348*, 191–196; (j) Wu, P.; Wan, Y.; Cai, J. *Synlett* **2008**, 1193–1198.
9. (a) Harrington, P. E.; Kerr, M. A. *Synlett* **1996**, 1047–1048; (b) Komoto, I.; Kobayashi, S. *Org. Lett.* **2002**, *4*, 1115–1118; (c) Alam, M. M.; Varala, R.; Adapa, S. R. *Tetrahedron Lett.* **2003**, *44*, 5115–5119.
10. (a) Dessole, G.; Herrera, R. P.; Ricci, A. *Synlett* **2004**, 2374–2378; (b) Liu, T.-Y.; Cui, H.-L.; Chai, Q.; Long, J.; Li, B.-J.; Wu, Y.; Ding, L.-S.; Chen, Y.-C. *Chem. Commun.* **2007**, 2228–2230.
11. (a) Piao, C.-R.; Zhao, Y.-L.; Han, X.-D.; Liu, Q. *J. Org. Chem.* **2008**, *73*, 2264–2269; (b) Pal, M.; Dakarapu, R.; Padakanti, S. *J. Org. Chem.* **2004**, *69*, 2913–2916; (c) Koltunov, K. Y.; Walspurger, S.; Sommer, J. *Tetrahedron Lett.* **2004**, *45*, 3547–3549.
12. Lambert, A.; Rose, J. D.; Weedon, B. C. L. *J. Chem. Soc.* **1949**, 42–46.
13. Hurd, C. D.; Nilson, M. E.; Wilkholm, D. M. *J. Am. Chem. Soc.* **1950**, 4697–4699.
14. (a) Kozikowski, A. P. *Acc. Chem. Res.* **1984**, *17*, 410–416; (b) Kanemasa, S.; Tsuge, O. *Heterocycles* **1990**, *30*, 719–736; (c) Shu, C.-M.; Chung, W.-S. J. *Chin. Chem. Soc.* **2000**, *47*, 173–182; (d) Kumar, H. M. S.; Anjaneyulu, S.; Yadav, J. S. *Synth. Commun.* **1999**, *29*, 877–884.
15. (a) Mukaiyama, T.; Hoshino, T. *J. Am. Chem. Soc.* **1960**, *82*, 5339–5342; (b) Knight, J.; Parson, P. J. *J. Chem. Soc., Chem. Commun.* **1987**, 189–190; (c) Cunico, R. F.; Bedell, L. *J. Org. Chem.* **1983**, *48*, 2780–2782; (d) Curran, D. P.; Fenk, C. J. *J. Am. Chem. Soc.* **1985**, *107*, 6023–6028; (e) Nishiyama, H.; Arai, H.; Okhi, T.; Itoh, K. *J. Am. Chem. Soc.* **1985**, *107*, 5310–5312; (f) Bellandi, C.; De Amici, M.; De Micheli, C. *Heterocycles* **1984**, *22*, 2187–2190; (g) Ackrell, J.; Altaf-ur-ur-Rahman, M.; Boulton, A. J.; Brown, R. C. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1587–1594; (h) Chapman, J. A.; Crosby, J. A.; Cummings, C. A.; Rennie, R. A. C.; Paton, R. M. *J. Chem. Soc., Chem. Commun.* **1976**, 240–241; (i) Whitney, R. A.; Nicholas, E. S. *Tetrahedron Lett.* **1981**, *23*, 3371–3374; (j) Curran, D. P.; Fenk, C. J. *Tetrahedron Lett.* **1986**, *27*, 4865–4868.
16. Chiang, Y. H. *J. Org. Chem.* **1971**, *36*, 2146–2155.
17. Rheinboldt, H. *Liebigs Ann. Chem.* **1927**, *451*, 161–178.
18. Peake, C. J.; Strickland, J. H. *Synth. Commun.* **1986**, *16*, 763–765.
19. Liu, K. C.; Shelton, B. R.; Howe, R. K. *J. Org. Chem.* **1980**, *45*, 3916–3918.
20. Kim, J. N.; Ryu, E. K. *J. Org. Chem.* **1992**, *57*, 6649–6650.
21. (a) Wade, P. A.; Hinney, H. R. *J. Am. Chem. Soc.* **1979**, *101*, 1319–1320; (b) Tsuge, O.; Kanemasa, S.; Suga, H. *Chem. Lett.* **1986**, 183–186; (c) Kanemasa, S.; Norisue, Y.; Suga, H.; Tsuge, O. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3973–3982; (d) Leslie-Smith, M. G.; Paton, R. M.; Webb, N. *Tetrahedron Lett.* **1994**, *35*, 9251–9254; (e) Kozikowski, A. P.; Ghosh, A. K. *J. Org. Chem.* **1985**, *50*, 778–785; (f) Kozikowski, A. P.; Ghosh, A. K. *Tetrahedron Lett.* **1983**, *24*, 2623–2626; (g) Kanemasa, S.; Nakagawa, N.; Suga, H.; Tsuge, O. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 171–179; (h) Kumaran, G.; Kulkarni, G. H. *J. Org. Chem.* **1997**, *62*, 1516–1520.
22. (a) Noland, W. E.; Christensen, G. M.; Sauer, G. L.; Dutton, G. G. S. *J. Am. Chem. Soc.* **1955**, *77*, 456–457; (b) Bridges, A. J.; Bruns, R. F.; Ortwine, D. F.; Priede, S. R.; Szotek, D. L.; Trivedi, B. K. *J. Med. Chem.* **1988**, *31*, 1282–1285.
23. Ohe, T.; Uemura, S. *Tetrahedron lett.* **2002**, *43*, 1269–1271.
24. (a) Liu, J.-Y.; Liu, J.-T.; Yao, C.-F. *Tetrahedron Lett.* **2001**, *42*, 3613–3615; (b) Yao, C.-F.; Chu, C.-M.; Liu, J.-T. *J. Org. Chem.* **1998**, *63*, 719–722; (c) Yao, C.-F.; Chen, W.-W.; Lin, Y.-M. *Tetrahedron Lett.* **1996**, *37*, 6339–6342; (d) Yao, C.-F.; Kao, K.-H.; Liu, J.-T.; Chu, C.-M.; Wang, Y.; Chen, W.-C.; Lin, Y.-M.; Lin, W.-W.; Yan, M.-C.; Liu, J.-Y.; Chuang, M.-C.; Shiue, J.-L. *Tetrahedron* **1998**, *54*, 791–822; (e) Liu, J.-T.; Lin, W.-W.; Jang, J.-J.; Liu, J.-Y.; Yan, M.-C.; Hung, C.; Kao, K.-H.; Wang, Y.; Yao, C.-F. *Tetrahedron* **1999**, *55*, 7115–7128.
25. (a) Jana, U.; Maiti, S.; Biswas, S. *Tetrahedron Lett.* **2007**, *48*, 7160–7163; (b) Wanga, B.-Q.; Xianga, S.-K.; Suna, Z.-P.; Guanb, B.-T.; Hua, P.; Zhaoa, K.-Q.; Shib, Z.-J. *Tetrahedron Lett.* **2008**, *49*, 4310–4312.