Heteroatom Chemistry
Volume 16, Number 7, 2005

One-Pot Three Components Synthesis of Alkyl Indeno [1,2-*b*]-quinoxalin-11-ylideneacetates in Water and Under Solvent-Free Conditions

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Received 17 January 2005; revised 25 April 2005

ABSTRACT: *We introduced a very simple, one-pot three component procedure for preparation of alkyl indeno[1,2-b]quinoxalin-11-ylideneacetates* **4** *from reaction of ninhydrin* **1**, *phenylenediamines* **2**, *(alkoxycarbonylmethyl)triphenylphosphonium bromides* **3**, *and sodium acetate in water and under solvent-free conditions.* © 2005 Wiley Periodicals, Inc. Heteroatom Chem 16:549–552, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20136

INTRODUCTION

Water has all factors of an ideal solvent, so in synthetic organic chemistry water has been widely used in recent years [1,2]. Moreover, because of high heat capacity, water provides the best surroundings for product scale up. Unfortunately ylides are often unstable in water and only a few reports exist on the Wittig reaction in water or aqueous media and they excluded only stable ylides [3].

On the other hand, there is an increasing interest in the use of environmentally feasible reagents particularly in solvent-free conditions. Prevention of organic solvents during reactions in organic synthesis leads to a clean, efficient, and economical technology; not only with the increment of safety, the simpleness of work up, and the reduction of cost, but also increased amount of reactants can be achieved in the same equipment without huge modifications. Reactivity and sometimes selectivity may be enhanced without dilution [4].

Quinoxaline derivatives are notified as an important class of nitrogen-containing heterocycles, and they constitute useful intermediates in organic synthesis [5]. They have been important for their applications in dye stuffs [6], pharmaceuticals [7], and also in the utility as building blocks in the synthesis of organic semiconductors [8].

Due to these significance and as a part of our ongoing research programs in the area of reactions involving quinoxaline derivatives [9], we herein report the simple and highly efficient method for synthesis of some alkyl indeno[1,2-*b*]quinoxalin-11-ylideneacetates in water as eco-compatible solvent and under solvent-free conditions (Scheme 1).

RESULTS AND DISCUSSION

The reaction for synthesis of **4** is shown in Scheme 1. As a typical procedure for method A: To a 1:1 mixture of ninhydrin **1** and phenylenediamine **2** in water, 1.5 equivalents of (alkoxycarbonylmethyl)triphenylphosphonium bromides **3** and sodium acetate were added and the reaction mixture was allowed to stirred at room temperature for an appropriate time (see Table 1). The pure products

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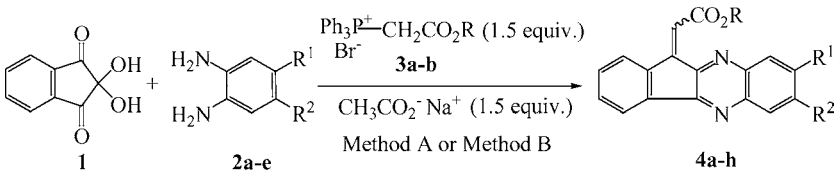


SCHEME 1

4 were afforded, in good to excellent yields, with recrystallization from ethanol (for entry **a–f**) or DMSO (for entry **g–h**). The results obtained are summarized in Table 1.

It is well known that quinoxaline **5** was formed from the condensation of ninhydrin **1** with 1,2-phenylenediamine **2** [10], and ylide **6** was produced from the reaction of (alkoxycarbonylmethyl)triphenylphosphonium bromides **3** with sodium acetate as a base [11]. The ylide **6** subsequently underwent the Wittig reaction with quinoxaline **5** to produce new adduct **4** (Scheme 2).

All products **4a–e** are new compounds, and they were characterized unambiguously by their elemental analysis and spectroscopic data (see Experimental section). However, our attempts to obtain crystals from products **4** which were suitable for X-ray crystallography failed. On the other hand, there is no measurable NOE effect between olefinic methine protons or R groups and H-9 (Scheme 3) and consequently the stereochemistry of products **4** around the alkene double bond was not exactly established.

Based on theoretical calculations [12] and coupling constants (J), we concluded that protons H-6 and H-9 are located at $\delta = 7.8$–8.2 and 8.1–8.6 ppm, respectively. For compound **4c**, singlet at $\delta = 7.83$ was correlated to H-6, and a doublet with $J = 8.4$ Hz at $\delta = 7.90$ was correlated to H-9. Similar trends were found from the ^{1}H NMR spectrum of **4d**, and we assumed that in **4c–d** methyl groups are located at C-7 position (Scheme 3). Conversely, for compound **4g**, H-6 and H-7 were resonated as doublets with $J = 8.5$ Hz at $\delta = 8.03$ and 8.24 respectively, whereas singlets at 8.24 was correlated to H-9. Similar trends were found from the ^{1}H NMR spectrum of **4h**, and we conclude that nitro group in **4g** and carboxylic substituent in **4h** are located at C-8 position (Scheme 3). However, the obtained regioselectivity is apparently in agreement with the electron-donating character of methyl group and electron-withdrawing nature of nitro and carboxylic groups.

TABLE 1 Reaction Time and Yields of Synthesized Compounds

	R	R_1	R_2	*Time (h)*[a]	*Yield (%)*[b]	*Yield (%)*[c]
4a	Me	H	H	1.5	75	70
4b	Et	H	H	1.5	70	77
4c	Me	Me	H	1.5	80	76
4d	Et	Me	H	1.5	82	89
4e	Me	Me	Me	2	70	80
4f	Et	Me	Me	2	77	75
4g	Me	H	NO_2	1	95	93
4h	Me	H	CO_2H	1	90	94

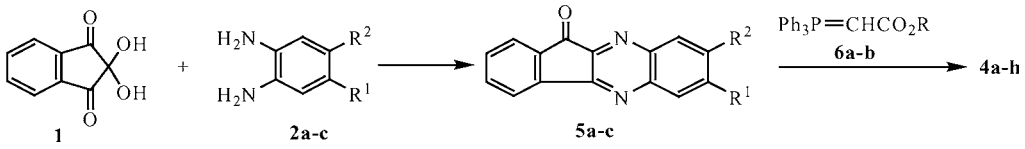
[a]Reaction times for method A.
[b]Yields are referred to isolated yields from method A.
[c]Yields are referred to isolated yields from method B.

As an alternative procedure, we decided to repeat all reactions under solvent-free conditions and surprisingly target quinoxaline **4** was simply obtained in good to excellent yields (Scheme 1, method B). We observed when a finely homogenized mixture of ninhydrin **1**, phenylenediamine **2**, (alkoxycarbonylmethyl)triphenylphosphonium bromides **3** (1.5 equivalents), and sodium acetate (1.5 equivalents) was heated for 10 min, reactions were completed and pure products **4** were afforded, in good to excellent yields, by addition of water to reaction mixture and recrystallization of crude products from ethanol (for entry **a–f**) or DMSO (for entry **g–h**). The obtained results are summarized in Table 1 (column 7).

In summary, we have described a very simple, efficient, and three components procedure for preparation of alkyl indeno[1,2-*b*]-quinoxalin-11-ylideneacetates in water as eco-compatible solvent and solvent-free conditions. The studies carried out allow us to obtain entitled compounds in good to excellent yields, using ordinary temperature. Besides, reaction times are dramatically low.

EXPERIMENTAL

Melting points were measured on a Electrothermal 9100 apparatus and are uncorrected. IR spectra were measured on a Bomen FT-IR-MB 100 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a



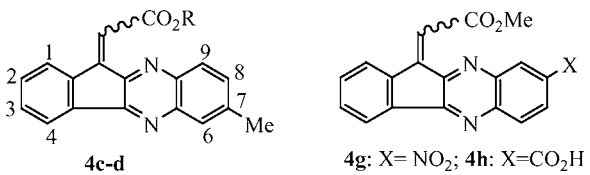
SCHEME 2

Bruker DRX-500 Avance spectrometer at 500.1 and 125.8 MHz using TMS as an internal standard. MS spectra were recorded on a Shimadzu QP 1100 EX mass spectrometer. Elemental analysis for C, H, and N was performed using a Heraus CHN rapid analyzer. All chemicals were obtained from Merck or Fluka, and used without further purification.

*Synthesis of 2 Indeno[1,2-b]quinoxalin-11-ylideneacetate (**4a**) as General Procedure*

Method A. To a magnetically stirred suspension of ninhydrin **1** (0.18 g, 1.0 mmol), 1,2-phenylenediamine **2a** (0.11 g, 1.0 mmol) and sodium acetate (0.12 g, 1.5 mmol) in water (40 mL), (methoxycarbonylmethyl)triphenylphosphonium bromide **3a** (0.12 g, 1.5 mmol) was added, and the reaction mixture was stirred at room temperature for 1.5 h. After filtration, crude product was recrystallized from ethanol to give the pure compound **4a** as yellow solid. Yield 75%, mp 170°C. IR (KBr) υ: 1715, 1201, 1175 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.93 (s, 3H, OCH_3), 7.42 (s, 1H, $=CHCO_2Me$), 7.59 (br, 2H, H_7, and H_8), 7.68–7.75 (br, 2H, H_2, and H_3), 8.08–8.12 (br, 2H, H_6, and H_9), 8.16 (d, 1H, $J = 6.5$ Hz, H_4), 9.01 (d, 1H, $J = 6.5$ Hz, H_1). ^{13}C NMR ($CDCl_3$) δ: 52.10, 116.90, 122.12, 129.23, 129.34, 129.40, 129.94, 130.23, 131.78, 132.00, 137.25, 138.38, 141.88, 142.80, 143.26, 153.23, 153.40, 165.50. MS *m/z* (%): 288(71), 273(12), 257(48), 230(100). Anal calcd for $C_{18}H_{12}N_2O_2$ (288): C, 74.99; H, 4.20; N, 9.72. Found: C, 74.91; H, 4.00; N, 9.56.

Method B. To a mixture of ninhydrin **1** (0.18 g, 1.0 mmol) and 1,2-phenylenediamine **2a** (0.11 g, 1.0 mmol) in minimum amount of acetonitrile, (methoxycarbonylmethyl)triphenylphosphonium bromide **3a** (0.12 g, 1.5 mmol) and sodium acetate (0.12 g, 1.5 mmol) were added and the mixture was stood to evaporate acetonitrile at room temperature (rt). The mixture was then heated in an oil bath at 110°C for 15 min and then cooled to rt. Water was added, reaction mixture was filtered, and then product **4a** was obtained by recrystallization of crude adduct from ethanol. Yield 70%, mp 170°C.



SCHEME 3

*Ethyl Indeno[1,2-b]quinoxalin-11-ylideneacetate (**4b**)*

Yellow crystals; mp 178°C, IR (KBr) υ: 1705, 1257, 1176 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.42 (t, 3H, $J =$ 7.1 Hz, CH_3), 4.39 (q, 2H, $J = 7.1$ Hz, OCH_2Me), 7.48 (s, 1H, $=CHCO_2Et$), 7.61–7.65 (br, 2H, H_7, and H_8), 7.72–7.78 (br, 2H, H_2, and H_3), 8.11–8.17 (br, 2H, H_6, and H_9), 8.22 (d, 1H, $J = 7.0$ Hz, H_4), 9.05 (d, 1H, $J = 7.0$ Hz, H_1). ^{13}C NMR ($CDCl_3$) δ: 14.32, 61.18, 118.57, 127.89, 128.45, 128.60, 129.42, 129.90, 130.00, 131.15, 132.22, 132.31, 132.90, 141.87, 142.22, 143.00, 154.86, 154.57, 165.83. MS *m/z* (%): 302(48), 257(43), 230(100). Anal calcd for $C_{19}H_{14}N_2O_2$ (302.33): C, 75.48; H, 4.67; N, 9.27. Found: C, 75.42; H, 4.64; N, 9.19.

*Methyl (7-Methylindeno[1,2-b]quinoxalin-11-ylidene)acetate (**4c**)*

Yellow powder; mp 168°C. IR (KBr) υ: 1713, 1207, 1171 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.56 (s, 3H, CH_3), 3.91 (s, 3H, OCH_3), 7.34 (s, 1H, $=CHCO_2Me$), 7.47 (d, 1H, $J = 8.4$ Hz, H_8), 7.52–7.57 (br, 2H, H_2, and H_3), 7.83 (s, 1H, H_6), 7.90 (d, 1H, $J = 8.4$ Hz, H_9), 8.09 (d, 1H, $J = 6.8$ Hz, H_4), 8.97 (d, 1H, $J = 6.9$ Hz, H_1). ^{13}C NMR ($CDCl_3$) δ: 21.83, 52.04, 116.42, 121.98, 128.45, 129.24, 129.43, 131.37, 131.60, 131.88, 137.16, 138.43, 140.27, 140.92, 142.98, 143.23, 152.33, 153.32, 166.56. MS *m/z* (%): 302 (38), 271(38), 244(84), 43(100). Anal calcd for $C_{19}H_{14}N_2O_2$ (302.33): C, 75.48; H, 4.67; N, 9.27. Found: C, 75.43; H, 4.58; N, 8.95.

*Ethyl (7-Methylindeno[1,2-b]quinoxalin-11-ylidene)acetate (**4d**)*

Yellow powder; mp 172°C, IR (KBr) υ: 1703, 1205, 1177 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.41 (t, 3H, $J =$

7.1 Hz, OCH_2CH_3), 2.56 (s, 3H, CH_3), 4.37 (q, 2H, $J = 7.1$ Hz, OCH_2Me), 7.35 (s, 1H, $=CHCO_2Et$), 7.48 (d, 1H, $J = 8.4$ Hz, H_8), 7.53–7.58 (br, 2H, H_2 and H_3), 7.84 (s, 1H, H_6), 7.91 (d, 1H, $J = 8.4$ Hz, H_9), 8.11 (d, 1H, $J = 6.6$ Hz, H_4), 8.99 (d, 1H, $J = 6.8$ Hz, H_1). ^{13}C NMR ($CDCl_3$) δ: 14.30, 21.83, 60.97, 117.05, 121.98, 128.49, 129.27, 129.42, 131.36, 131.59, 131.80, 137.24, 138.39, 140.29, 140.88, 142.68, 143.21, 152.41, 153.31, 166.12. MS *m/z* (%): 316 (9), 271(5), 243(40), 69(99), 41(100). Anal calcd for $C_{20}H_{16}N_2O_2$ (316.35): C, 75.93; H, 5.10; N, 8.86. Found: C, 75.88; H, 5.00; N, 8.82.

*Methyl(7,8-Dimethylindeno[1,2-b]quinoxalin-11-ylidene)acetate (**4e**)*

Light-yellow solid; mp 172°C, IR (KBr) υ: 1701, 1205, 1176 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 2.47 (s, 6H, $2CH_3$), 3.92 (s, 3H, OCH_3), 7.38 (s, 1H, $=CHCO_2Me$), 7.55–7.58 (br, 2H, H_2, and H_3), 7.80 (s, 1H, H_6), 7.87 (s, 1H, H_9), 8.16 (d, 1H, $J = 6.1$ Hz, H_4), 9.00 (d, 1H, $J = 6.1$, H_1). ^{13}C NMR ($CDCl_3$) δ: 20.23, 20.45, 52.13, 116.54, 122.26, 128.10, 129.26, 129.25, 129.33, 131.65, 131.97, 137.11, 139.93, 140.86, 142.80, 142.90, 154.23, 154.44, 166.60. MS *m/z* (%): 316 (98), 301 (17), 285 (79), 258 (100), 243 (41). Anal Calcd for $C_{20}H_{16}N_2O_2$ (316.35): C, 75.93; H, 5.10; N, 8.86. Found: C, 75.88; H, 4.98; N, 8.79.

*Ethyl (7,8-Dimethylindeno [1,2-b]quinoxalin-11-ylidene)acetate (**4f**)*

Yellow powder; mp 184°C, IR (KBr) υ: 1703, 1203, 1176 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.41 (br, 3H, OCH_2CH_3), 2.48 (s, 6H, $2CH_3$), 4.38 (br, 2H, OCH_2Me), 7.39 (s, 1H, $=CHCO_2Et$), 7.55 (br, 2H, H_2, and H_3), 7.82 (s, 1H, H_6), 7.86 (s, 1H, H_9), 8.17 (br, 1H, H_4), 9.01 (br, 1H, H_1). ^{13}C NMR ($CDCl_3$) δ: 14.29, 20.23, 20.38, 61.00, 117.14, 122.13, 128.45, 128.54, 129.19, 129.26, 131.58, 131.88, 132.07, 132.15, 137.16, 139.87, 140.80, 142.74, 150.45, 152.48, 166.15. MS *m/z* (%): 330 (55), 301 (7), 286 (33), 258 (100). Anal Calcd for $C_{21}H_{18}N_2O_2$ (330.38): C, 76.34; H, 5.49; N, 8.48. Found: C, 76.03; H, 5.21; N, 8.27.

*Methyl (8-Nitroindeno[1,2-b]quinoxalin-11-ylidene)acetate (**4g**)*

Products **4g–h** are exclusively soluble in DMSO at elevated temperatures, and we could not able to achieve their ^{13}C NMR. Yellow powder (recrystallized from DMSO); mp 195°C, IR (KBr) υ: 1713, 1570 cm^{-1}. ^{1}H NMR (DMSO-d_6, 80°C) δ: 3.89 (s, 3H, OCH_3), 7.14 (s, 1H, $=CHCO_2Me$), 7.51 (m, 2H, H_2, and H_3), 7.91(m, 1H, H_4), 8.03 (d, 1H, $J = 8.5$ Hz, H_6), 8.24 (d, 1H, $J = 8.5$ Hz, H_7), 8.57 (s, 1H, H_9), 8.59 (br, 1H, H_1). MS *m/z* (%): 333 (5), 302 (100). Anal Calcd for $C_{18}H_{11}N_3O_4$ (333.3): C, 64.86; H, 3.33; N, 12.61. Found: C, 64.80; H, 3.29; N, 19.15.

*Methyl (8-Carboxylindeno[1,2-b]quinoxalin-11-ylidene)acetate (**4h**)*

Yellow powder (recrystallized from DMSO); mp 280°C (decomp), IR (KBr) υ: 3430, 2990, 1712, 1698 cm^{-1}. ^{1}H NMR (DMSO-d_6, 80°C) δ: 3.89 (s, 3H, OCH_3), 7.31 (s, 1H, $=CHCO_2Me$), 7.76 (br, 2H, H_2, and H_3), 8.21–8.27 (br, 3H, H_6, H_7, and H_4), 8.62 (s, 1H, H_9), 8.89 (s, 1H, H_1). MS *m/z* (%): 332 (45), 301 (100), 257 (70). Anal Calcd for $C_{19}H_{12}N_2O_4$ (332.31): C, 68.67; H, 3.64; N, 8.43. Found: C, 68.61; H, 3.60; N, 19.17.

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