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ONE-POT SYNTHSIS OF ALKYL INDENO[1,2-*b*]-QUINOXALIN-11-YLIDENEACETATES UNDER SOLVENT-FREE CONDITIONS

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Abstract – A series of alkyl indeno[1,2-*b*]quinoxalin-11-ylideneacetates (**3a-f**) were prepared using the simple one-pot reactions involving triphenylphosphine, alkyl bromoacetate, ninhydrin, 1,2-phenylenediamines and NaOAc under solvent free-condition.

Recently, multicomponent condensation reactions have become one of the most powerful methods in the synthesis of small molecule libraries, since products are formed from the single step composed of several condensation reactions with simultaneity and the molecular diversity required as such in combinatorial libraries can be achieved only if one component is revised.[1]

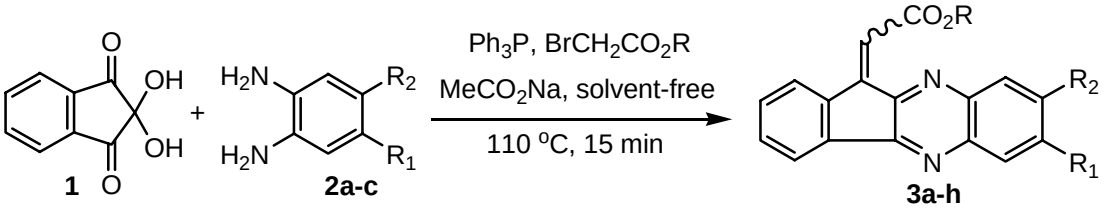
On the other hand, there is an increasing interest in the use of environmentally feasible reagents particularly in solvent-free conditions. Prevention of organic solvents during reactions in organic synthesis leads to a clean, efficient, and economical technology; not only with the increment of safety, the simpleness of work up, and the reduction of cost, but also increased amounts of reactants can be achieved in the same equipment without huge modifications. Reactivity and sometimes selectivity may be enhanced without dilution.[2]

Quinoxaline derivatives are notified as an important class of nitrogen-containing heterocycles and they constitute useful intermediates in organic synthesis.[3] They have been important for their applications in dye stuffs,[4] pharmaceuticals[5] and also in the utility as building blocks in the synthesis of organic semiconductors.[6]

Due to these significances and in continuation of our general interest in multicomponent reactions[7] and as a part of our ongoing research programs in the area of reactions involving quinoxaline derivatives,[8] we herein

report the facile and three-component synthesis of some alkyl indeno[1,2-*b*]quinoxalin-11-ylideneacetates (**3a-f**) under solvent-free conditions (Scheme 1).

Scheme 1. Preparation of alkyl Indeno[1,2-*b*]quinoxalin-11-ylideneacetates (**3a-f**)



Typical experimental procedure: to a mixture of triphenylphosphine (3 mmol), methyl bromoacetate (3 mmol) and sodium acetate (3 mmol) in minimum amount of acetonitrile, ninhydrin **(1)**, (3 mmol) and 1,2-phenylenediamine (**2**), (3 mmol) were added and the mixture was stood to evaporate acetonitrile at room temperature. The mixture was then heated in an oil bath at 110 ^{o}C for 15 min and then cooled to room temperature. Product (**3a**) was obtained after addition of water and recrystalisation of crude resulting mixture from ethanol in good yield. The results obtained are summarized in Table 1.

Our attempts to obtain crystals from products (**3**) which were suitable for X-Ray crystallography failed. On the other hand there is not meagerable NOE effect between olefinic methine protons or R groups and H-9 (Scheme 3) and consequently the stereochemistry of products (**3a-h**) was not exactly established.

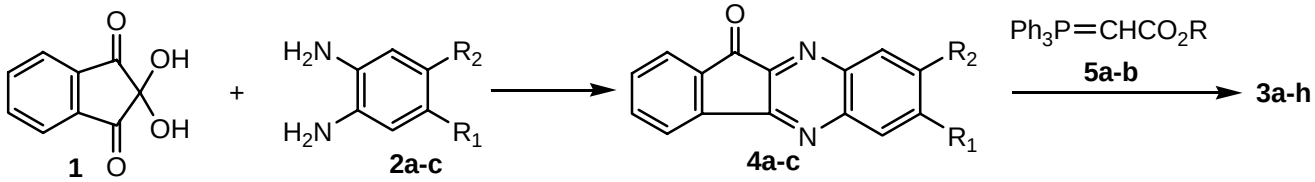
Table 1. Preparation of compounds (**3a-f**)

3	R	R_1	R_2	Yield %[a]
a	Me	H	H	75
b	Et	H	H	70
c	Me	Me	H	80
d	Et	Me	H	82
e	Me	Me	Me	70
f	Et	Me	Me	77
g	Me	H	NO_2	95
h	Me	H	CO_2H	90

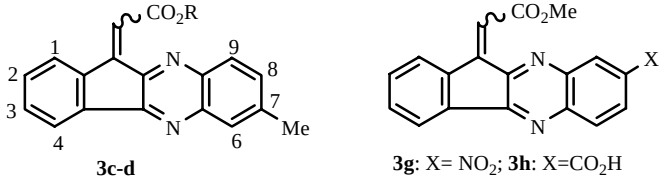
[a] Yields are referred to isolated yields.

Presumably quinoxaline (**4**) was formed from the condensation of ninhydrin (**1**) with 1,2-phenylenediamine (**2**),[9] and ylide (**5**) was produced from the reaction of triphenylphosphine with ethyl bromoacetate in the presence of sodium acetate as a base.[10] The ylide (**5**) subsequently underwent Wittig reaction with quinoxaline (**4**) to produce new adduct (**3**) (Scheme 2). All products (**3a-f**) are characterized by their physical properties and spectroscopic data.

Scheme 2. Reaction pathway for preparation of **3**



There is no sufficient evidence in the assignment of the aromatic protons in the ^{1}H NMR spectra of **3,** but based on theoretical calculations,[11] and coupling constants (*J*) we concluded that protons H-6 and H-9 were located at δ=7.9-8.1 and 8.9-9.1 ppm, respectively. For compound (**3c**) singlet at δ=7.83 was correlated to H-6, and a doublet with *J*=6.9 Hz at δ= 8.99 was correlated to H-9. Similar trends were found from the ^{1}H NMR spectra of **3d**, and we assumed that in **3c-d** methyl groups are located at C-7 position (Scheme 3). Conversely, for compounds (**3g)** and **(3h)** H-9 was resonated as singlets at δ = 8.65 and δ = 8.89 respectively, and we conclude that nitro group in **3g** and carboxylic substituent in **3h** are located at C-8 position (Scheme 3). However the obtained regioselectivity is apparently in agreement with the electron-donating characteristic of methyl group and electron-withdrawing nature of nitro and carboxylic substituents.



Scheme 3

In conclusion, we succeeded in a novel one-pot and efficient procedure for preparation of alkyl indeno[1,2-*b*]quinoxalin-11-ylideneacetates **(3a-f)** from the simplest starting materials. Based on our procedure, omission in the preparation and purification steps of phosphonium salts and ndeno[1,2-*b*]quinoxalin-11-ones (**3**) and prevention of organic solvents during the reactions would lead to a clean, efficient, simple and economical methodology.

EXPERIMENTAL

Melting points were measured on the Electrothermal 9100 apparatus and are uncorrected. IR spectra were measured on a Bomen FT-IR-MB 100 spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured with a 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 were performed using a Heraus CHN rapid analyzer. All chemicals were obtained from Merck or Fluka, and used without further purification.

Preparation of methyl indeno[1,2-*b*]quinoxalin-11-ylideneacetate (3a) as general procedure for synthesis of 3a-f. To a mixture of triphenylphosphine (262 mg, 3 mmol), methyl bromoacetate (277 mg, 3 mmol) and sodium acetate (246 mg, 3 mmol) in minimum amount of acetonitrile, ninhydrin (534 mg, 3 mmol) and 1,2-phenylenediamine (324 mg, 3 mmol) were added and the mixture was stood to evaporate acetonitrile at 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 **(3a)** was obtained by recrystalisation of crude adduct from ethanol. Yellow solid, mp 170 °C. IR (KBr) (υ_{max}/cm^{-1}): 1715, 1201, 1175. ^{1}H NMR ($CDCl_3$) δ_H: 3.93 (s, 3H, OCH_3), 7.42 (s, 1H, =$CHCO_2Me$), 7.57-9.02 (8H, arom). ^{13}C NMR ($CDCl_3$) δ_C: 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(M^+, 71), 273(12), 257(48), 230(100). *Anal.* Calcd for $C_{18}H_{12}N_2O_2$: C, 74.99; H, 4.20; N, 9.72. Found: C, 74.91; H, 4.00; N, 9.56.

Ethyl Indeno[1,2-*b*]quinoxalin-11-ylideneacetate (3b). Yellow crystals, mp 178 °C. IR (KBr) (υ_{max}/cm^{-1}): 1705, 257, 1176. ^{1}H NMR ($CDCl_3$) δ_H: 1.42 (t, 3H, *J*= 7.1 Hz, CH_3), 4.39 (q, 2H, *J*= 7.1 Hz, OCH_3), 7.48 (s, 1H, =$CHCO_2Et$), 7.61-7.82 (br, 4H), 8.12 (d, 1H, *J*= 8.0 Hz), 8.15 (d, 1H, *J*= 8.0 Hz), 8.22 (d, 1H, *J*=7.0 Hz), 9.05 (d, 1H, *J*=7.01 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 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(M^+, 48), 257(43), 230(100). *Anal.* Calcd for $C_{19}H_{14}N_2O_2$: 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 (3c). Yellow powder. mp 168 °C. IR (KBr) (υ_{max}/cm^{-1}): 1713, 1207, 1171. ^{1}H NMR ($CDCl_3$) δ_H: 2.56 (s, 3H, CH_3), 3.92 (s, 3H, OCH_3), 7.35 (s, 1H, =$CHCO_2Me$), 7.47 (d, 1H, *J*= 8.1 Hz), 7.54 (br, 2H), 7.83 (s, 1H, H_6), 7.91 (d, 1H, *J*=8.2 Hz), 8.11 (d, 1H, *J*=6.9 Hz, H_8), 8.99 (d, 1H, *J*=6.9 Hz, H_9). ^{13}C NMR ($CDCl_3$) δ_C: 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 (M^+, 38), 271(38), 244(84), 43(100). *Anal.* Calcd for $C_{19}H_{14}N_2O_2$: 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 (3d). Yellow powder, mp 172 °C. IR (KBr) (υ_{max}/cm^{-1}): 1703, 1205, 1177. ^{1}H NMR ($CDCl_3$) δ_H: 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), 7.54 (br, 2H), 7.84 (s, 1H, H_6), 7.91 (d, 1H, *J*=8.5 Hz), 8.11 (d, 1H, *J*=6.6 Hz, H_8), 8.99 (d, 1H, *J*=6.6 Hz, H_9). ^{13}C NMR ($CDCl_3$) δ_C: 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 (M^+, 9), 271(5), 243(40), 69(99), 41(100). *Anal.* Calcd for $C_{20}H_{16}N_2O_2$: 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 (3e). Light-yellow solid, mp 172 °C. IR (KBr) (υ_{max}/cm^{-1}): 1701, 1205, 1176. ^{1}H NMR ($CDCl_3$) δ_H: 2.50 (s, 6H, $2CH_3$), 3.90 (s, 3H, OCH_3), 7.40

(s, 1H, =CHCO$_2$Me), 7.6-7.9 (br, 4H), 8.16 (d, 1H, *J*=6.1 Hz, H$_6$), 9.00 (d, 1H, *J*=6.1 Hz, H$_9$). ^{13}C NMR (CDCl$_3$) δ_C: 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 (M$^+$, 98), 301(17), 285(79), 258(100), 243(41). *Anal.* Calcd for $C_{20}H_{16}N_2O_2$: 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 (3f). Yellow powder, mp 184 ^{o}C. IR (KBr) (υ_{max}/cm^{-1}): 1703, 1203, 1176. ^{1}H NMR (CDCl$_3$) δ_H: 3.07 (br t, 3H, OCH$_2$CH$_3$), 2.48 (s, 6H, 2CH$_3$), 4.38 (br q, 2H), 7.26-7.88 (br, 5H, arom and =CHCO$_2$Et), 8.17 (s, 1H, H$_6$), 9.01 (s, 1H, H$_9$). ^{13}C NMR (CDCl$_3$) δ_C: 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(M$^+$, 55), 301(7), 286(33), 258(100). *Anal.* Cald for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.49; N, 8.48. Found: C, 76.03; H, 5.21; N, 8.27.

11-((Methoxycarbonyl)methylene)indeno[1,2-*b*]quinoxaline-8-carboxylic acid (3g). Products **3g-h** are exclusively soluble in DMSO at elevated temperatures, so we could not able to achieve their ^{13}C NMR. Yellow powder (recrystalised from DMSO), mp 280 ^{o}C (decomp). IR (KBr) (υ_{max}/cm^{-1}): 3430, 2990, 1712, 1698. ^{1}H NMR (DMSO-*d*$_6$, 80 ^{o}C) δ_H: 3.89 (s, 3H, OCH$_3$), 7.31 (s, 1H, =CHCO$_2$Me), 7.76-8.27 (br, 5H), 8.62 (s, 1H, arom), 8.89 (s, 1H, arom), 12.50 (br s, 1H, CO$_2$H). MS (m/z, %): 332 (M$^+$, 45), 301(100), 257(70). *Anal.* Calcd for $C_{19}H_{12}N_2O_4$: C, 68.67; H, 3.64; N, 8.43; O, 19.26. Found: C, 68.61; H, 3.60; N, 19.17.

Methyl (8-Nitroindeno[1,2-*b*]quinoxalin-11-ylidene)acetate (3h). Yellow powder (recrystalised from DMSO), mp 195 ^{o}C. IR (KBr) (υ_{max}/cm^{-1}): 1713, 1570. ^{1}H NMR (DMSO-*d*$_6$, 80 ^{o}C) δ_H: 3.89 (s, 3H, OCH$_3$), 7.14 (s, 1H, =CHCO$_2$Me), 7.54 (m, 2H, arom), 7.96(m, 1H, arom), 8.10 (d, 1H, arom), 8.29 (d, 1H, arom), 8.58 (m, 1H, arom), 8.65 (s, 1H, arom). MS (m/z, %): 333 (M$^+$, 35), 302(100). *Anal.* Calcd for $C_{19}H_{12}N_2O_4$: C, 64.86; H, 3.33; N, 12.61; O, 19.20. Found: C, 64.80; H, 3.29; N, 19.15.

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REFERENCES

1. A. Domling and I. Ugi, *Angew. Chem., Int. Ed*., 2000, **39**, 3168.; I. Ugi, *J. Prakt. Chem*., 1997, **339**, 499; D. Lee, J. K. Sello, and S. L. Schriber, *Org. Lett*., 2000, **2**, 709.
2. K. Tanaka and F. Toda, *Chem. Rev*., 2000, **100**, 1025; P. Lidstrom, J. Tierney, B. Wathey, and J. Westman, *Tetrahedron*, 2001, **57**, 9225.
3. T. Hartman and L. Witte, *Chemistry, Biology and Chemoecology of the Pyrrolizidine Alkaloides, in Alkaloids Chemical and Biological Perspective*, Vol. **9**, ed. by K. Pelletier, Pergamon Press, 1995; J.

R. Liddel, *Nat. Prod. Rep*., 1996, **13**, 187; G. Broggin and G. Zecchi, *Synthesis*, 1999, 905; G. Subramaniyan and R. Raghunathan, *Tetrahedron*, 2001, **57**, 2909.

4. E. D. Brock, D. M. Lewis, T. I. Yousaf, and H. H. Harper, (The Procter & Gamble Company, USA) WO, 1999, 995-1688.
5. A. Gazit, H. APP, G. McMahon, J. Chen, A. Levitzki, and F. D. Bohmer, *J. Med. Chem*., 1996, **39**, 2170; U. Sehlstedt, P. Aich, J. Bergman, H. Vallberg, B. Norden, and A. Graslund, *J. Mol. Biol*., 1998, **31**, 278.
6. S. Dailey, J. W. Feast, R. J. Peace, I. C. Sage, S. Till, and E. L. Wood, *J. Mater. Chem*., 2001, **11**, 2238; D. O. Brien, M. S. Weaver, D. G. Lidzey, and D. C. Bradley, *Appl. Phys. Lett*., 1996, **69**, 881.
7. J. Azizian, A. R. Karimi, and A. A. Mohammadi, *Synth. Commun*., 2003, **33**, 383; J. Azizian, M. R. Mohammadizadeh, M. Javadi, A. A. Mohammadi, and A. R. Karimi, *J. Chem. Res*., 2004, 125; J. Azizian, A. R. Karimi, A. A. Mohammadi, and M. R. Mohammadizadeh, *Molecular Diversity*, 2003, **6**, 223; J. Azizian, A. A. Mohammadi, and A. R. Karimi, *Synth. Commun*., 2003, **33**, 415.
8. J. Azizian, A. R. Karimi, A. A. Mohammadi, and M. R. Mohammadizadeh, *Synthesis*, in press; J. Azizian, A. R. Karimi, A. A. Mohammadi, and M. R. Mohammadizadeh, *Heterocycles*, in press.
9. B. D. Pearson, R. A. Mitsch, and N. H. Cromwell, *J. Org. Chem.*, 1962, **27**, 1674.
10. Y.-S. Hon and C.-F. Lee, *Tetrahedron*, 2000, **56**, 7893.
11. H. Friebolin, *Basic One and Two Dimensional NMR Spectroscopy*, 2nd ed., Transl. by J. Becconsall, Wiley-VCH Verlag GmbH, 1993, p. 139.