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# Facile And Clean Synthesis Of Disubstituted-1,2-Dihydroisoqunoline Derivatives Via Three-Component Reaction Without Catalyst At Room Temperature

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**Abstract:** One-pot and efficient approach to the synthesis of dialkyl 2-[1 [(alkoxycarbonyl)anilino]-2(1H)-isoquinolinyl]-2-butenedioates and dialkyl 2-[1 [(alkyl)amino]-2(1H)- isoquinolinyl]-2-butenedioates is described. This method involves the reaction of isoquinoline, dialkyl acetylenedicarboxylate and *N*-phenyl carbamates in $CH_2Cl_2$, without using of catalyst at room temperature. The mild reaction conditions and high yields of the products are advantages of this method.
**Keywords:** 1,2-Dihydroisoquinoline, activated acetylenic compound, urethane.

## Introduction:

Multi component reactions (MCRs) are defined as one-pot reactions in which at least three function groups are joined through covalent bonds. These reactions have gained more use in synthesis organic chemistry[1,2,3]. The isoquinoline skeleton is found in a large number of naturally occurring and synthesis biologically active heterocyclic compounds[4]. in particular 1,2-dihydroisoquinoline derivatives act as delivery systems that transport drugs through the otherwise highly impermeable blood-brain barrier[5]. These compounds also exhibit sedative[6], antidepressant[7], antitumor and antimicrobial activities[8]. Usually, the addition of nucleophiles devoid of an acidic hydrogen atom leads to a 1:1 zwitterionic intermediate that can undergo further transformations culminating in a stabilized product[9]. A facile and efficient method for synthesis of dialkyl-2-[1-[(alkoxycarbonyl) aniline]-2(1H)-isoquinolinyl-2-butendioate derivatives using reaction of dialkyl acetylendi carboxylates, *N*-phenyl carbamates and isoquinoline in $CH_2Cl_2$ is described. We present herein our result of a new discovery involving synthesis of disubstituted-1,2-dihydroisoqunoline derivatives, using commercially available starting materials in high yields.

## Experimental

### *General*

Isoquinoline, Urethanes, dialkyl acetylene dicarboxylate, cychlohexanol, 1-propanol, 2-propanol and solvents purchased from Fluka, Merck and Aldrich and used without further purification. IR spectra were recorded using a Bruker FT-IR spectro photometr. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker DRX-500 and 400 spectrometer for the sample as indicated with tetramethylsilan as an internal reference.

**General procedure for the synthesis of Disubstituted-1,2- dihydroisoqunoline derivatives [4a-4f]:** Isoquinoline (2mmol) was added to a solution of dialkyl acetylenedicarboxylate (2mmol) and the Urethan (2mmol) in $CH_2Cl_2$ (10mL) at room temperature. Then, reaction mixture stirred for 8 hour. The progress of reaction was followed with thin-layer chromatography (TLC) using silica gel SILG/UV 254 and 365 plates. After completion, the solvent was removed under reduced pressure, and the residue was purified by column chromatography ($SiO_2$; *n*-hexane/AcOEt 5:1) to afford the pure products.

**General procedure for the synthesis of Disubstituted-1,2- dihydroisoqunoline derivatives [6g-6l]:** Isoquinoline (2mmol) was added to a solution of DMAD (2mmol) and the amides (2mmol) in $CH_2Cl_2$ (10mL) at room temperature. Then, reaction mixture stirred for 8 hour. The progress of reaction was followed with thin-layer chromatography (TLC) using silica gel SILG/UV 254 and 365 plates. After completion, the solvent was removed under reduced pressure, and the residue was purified by column chromatography ($SiO_2$; *n*-hexane/AcOEt 4:1) to afford the pure products.

**Dimethyl 2-[1-[(propoxycarbonyl)anilino]-2(1H)-isoquinolinyl]-2-butenedioates [4a]:** Yellow oil, IR (KBr) 3421, 3055, 2985, 2362, 1734, 1651, 1562, 1420, 1265, 1025, 900, $cm^{-1}$ $^1H$ NMR (400 MHz, $CDCl_3$) δ1.00 (t, $^3J_{HH}$ = 7.1, $CH_3$), 1.73 (m, $^3J_{HH}$ = 7.2, $CH_2$), 3.70 (s, $OCH_3$), 3.83 (s, $OCH_3$), 4.16 (t, $^3J_{HH}$ =7.0, $CH_2$), 6.80 (s, CH), 7.08 (d, $^3J_{HH}$ = 7.3, CH), 7.09 (d, $^3J_{HH}$ = 7.3, CH), 7.32–7.50 (m, 10CH). $^{13}C$ NMR: (100 MHz, $CDCl_3$) δ11.0, 23.0, 51.5, 52.0, 67.6, 68.2, 93.6, 106.5, 118.6, 123.3, 123.7, 128.8, 129.1, 129.3, 132.4, 136.3, 138.1, 140.5, 154.8, 163.8, 167.8; CHN Analyses: Elem. Anal. Calcd for $C_{25}H_{26}N_2O_6$: C, 66.65; H, 5.82; N, 6.22; O, 21.31. Found: C, 66.70; H, 5.58; N, 6.42; (E/MS) 450($M^+$).

**Diethyl2-[1-[(propoxycarbonyl)anilino]-2(1H)-isoquinolinyl]-2-butenedioates [4b]:** Yellow oil, $^1H$ NMR (400 MHz, $CDCl_3$) δ1.02 (t, $^3J_{HH}$ = 7.2, $CH_3$), 1.22 (t, $^3J_{HH}$ = 7.1, $CH_3$), 1.24 (t, $^3J_{HH}$ = 7.1, $CH_3$), 1.74 (m, $^3J_{HH}$ = 7.0, $CH_3$), 4.15 (q, $^3J_{HH}$ = 7.1, $CH_2$), 4.16 (q, $^3J_{HH}$ = 7.2, $CH_2$), 4.21 (t, $^3J_{HH}$ = 7.0, $CH_2$), 6.81 (s, CH), 7.07 (d, $^3J_{HH}$ = 7.3, CH), 7.09 (d, $^3J_{HH}$ = 7.4, CH), 7.10–7.80 (m, 10CH). $^{13}C$ NMR: (100 MHz, $CDCl_3$) δ10.14, 14.0, 14.1, 22.3, 61.1, 62.3, 66.8, 68.3, 93.8, 105.1, 118.6, 123.3, 124.0, 128.5 (2CH), 128.9 (2CH), 129.0, 132.5, 136.3, 138.0, 138.1, 154.8, 163.8, 167.8. CHN Analyses: Elem. Anal. Calcd for $C_{27}H_{30}N_2O_6$: C, 67.77; H, 6.32; N, 5.85; O, 20.06. Found: C, 67.70; H, 6.39; N, 5.71; (E/MS) 478($M^+$).

**Dimethyl2-[1-[(isopropoxycarbonyl)anilino]-2(1H)-isoquinolinyl]-2-butenedioates [4c]:** Yellow oil, IR (KBr): 3421, 3055, 2985, 2362, 1734, 1651, 1562, 1420, 1265, 1025, 900, 741 $cm^{-1}$. $^1H$ NMR (400 MHZ, $CDCl_3$) δ1.23 (d, $^3J_{HH}$ = 6.2, $CH_3$), 1.30 (d, $^3J_{HH}$ = 6.2, $CH_3$), 3.70 (s, $OCH_3$), 3.83 (s, $OCH_3$), 5.03 (heptet, $^3J_{HH}$ = 6.2, CH), 6.80 (s, CH), 7.08 (d, $^3J_{HH}$ = 7.3, CH), 7.09 (d, $^3J_{HH}$ = 7.3, CH), 7.32–7.54 (m, 10CH). $^{13}C$ NMR: (100 MHz, $CDCl_3$) δ21.8, 52.0, 53.1, 68.2, 70.6, 94.0, 107.1, 118.5, 123.5, 128.8 (2CH), 129.1 (2CH), 129.2, 132.5, 136.1, 138.2, 139.1, 153.2, 164.2, 167.8. CHN Analyses: Elem. Anal. Calcd for $C_{25}H_{26}N_2O_6$: C, 66.65; H, 5.82; N, 6.22; O, 21.31. Found: C, 66.51; H, 5.92; N, 6.28; (E/MS) 450($M^+$).

**Diethyl 2-[1-[(isopropoxycarbonyl)anilino]-2(1H)-isoquinolinyl]-2-butenedioates [4d]***:* Yellow oil, $^1H$ NMR (400 MHz, $CDCl_3$) δ1.22 (t, $^3J_{HH}$ = 6.2, $CH_3$), 1.24 (t, $^3J_{HH}$ = 6.2, $CH_3$), 1.30 (d, $^3J_{HH}$ = 6.5, $CH_3$), 1.34 (d, $^3J_{HH}$ = 6.2, $CH_3$), 4.13 (q, $^3J_{HH}$ = 7.1, $CH_2$), 4.26 (q, $^3J_{HH}$ = 7.1, $CH_2$), 4.18 (heptet, $^3J_{HH}$ = 6.2, CH), 6.80 (s, CH), 7.07 (d, $^3J_{HH}$ = 7.3, CH), 7.09 (d, $^3J_{HH}$ = 7.3, CH), 7.20–7.42 (m, 10CH). $^{13}C$ NMR: (100 MHz, $CDCl_3$) δ14.0, 14.1, 21.8 (2Me), 60.6, 61.1, 67.7, 70.60, 94.1, 106.2, 118.5, 123.2, 124.0, 128.5 (2CH), 129.0 (2CH), 129.2, 132.4, 138.1, 140.5, 140.6, 153.2, 164.2, 167.8. CHN Analyses: Elem. Anal. Calcd for $C_{27}H_{30}N_2O_6$: C, 67.77; H, 6.32; N, 5.85; O, 20.06. Found: C, 67.89; H, 6.38; N, 5.61; (E/MS) 478($M^+$).

**Dimethyl2-[1-[(cyclohexyloxycarbonyl)anilino]-2(1H)-isoquinolinyl] 2butenedioates [4e]:** Yellow oil, $^1H$ NMR (400 MHz, $CDCl_3$) δ1.60-1.65 (m, $CH_2$), 1.72-1.80 (m, $2CH_2$), 1.94-2.00 (m, $2CH_2$), 3.70 (s, $OCH_3$), 3.83 (s, $OCH_3$), 4.80 (m, CH), 6.80 (s, CH), 7.06 (d, $^3J_{HH}$ = 7.3, CH), 7.08 (d, $^3J_{HH}$ = 7.4, CH), 7.06–7.52 (m, 10CH). $^{13}C$ NMR: (100 MHz, $CDCl_3$) δ23.4 ($2CH_2$), 25.4, 32.0 ($2CH_2$), 52.0, 53.1, 73.7, 75.3, 94.1, 107.3, 118.5, 123.2, 124.2, 128.5 (2CH), 129.0 (2CH), 129.1, 132.4, 136.3, 138.5, 139.2, 153.1, 164.2, 166.7. CHN Analyses: Elem. Anal. Calcd for $C_{28}H_{30}N_2O_6$: C, 68.56; H, 6.16; N, 5.71; O, 19.57. Found: C, 68.40; H, 6.30; N, 5.82; (E/MS) 490($M^+$).

**Diethyl2-[1-[(cyclohexyloxycarbonyl)anilino]-2(1H)-isoquinolinyl]-2-butenedioates [6f]:** Yellow oil, $^1H$ NMR (400 MHz, $CDCl_3$) δ1.31 (t, $^3J_{HH}$ = 6.3, $CH_3$), 1.41 (t, $^3J_{HH}$ = 6.3, $CH_3$), 1.60-1.65 (m, $CH_2$), 1.72-1.80 (m, $2CH_2$), 1.94-2.00 (m, $2CH_2$), 4.11 (q, $^3J_{HH}$ = 7.1, $CH_2$), 4.22 (q, $^3J_{HH}$ = 7.1, $CH_2$), 4.77-4.80 (m, CH), 6.80 (s, CH), 7.07 (d, $^3J_{HH}$ = 7.3, CH), 7.09 (d, $^3J_{HH}$ = 7.3, CH), 7.14–7.65 (m, 10CH). $^{13}C$ NMR: (100 MHZ, $CDCl_3$) δ23.5, 25.6, 52.1, 53.3, 73.3, 75.2, 94.2, 107.3, 118.5, 123.5, 124.2, 128.6, 129, 129.1, 132.4, 136.5, 138.6, 139.2, 155.1, 163.2, 166.5; CHN Analyses: Elem. Anal. Calcd for

$C_{30}H_{34}N_2O_6$: C, 69.48; H, 6.61; N, 5.40; O, 18.51. Found: C, 69.38; H, 6.88; N, 5.30; (E/MS) 518($M^+$).

**Dimethyl-2-(1-formamidoisoquinolin-2(1H)-yl)but-2-enedioate [6g]**: mp 161–162 °C.. IR (KBr) $cm^{-1}$: 1717, 1712, 1639. $^1H$ NMR (500 MHz, $CDCl_3$,) δd = 3.66 and 3.92 (2s, 6H, $2OCH_3$), 5.71 (s, 1H CH), 5.97 (d, 1H, $^3J$ = 7.7, CH), 6.34 (d, 1H, $^3J$ = 7.7, CH), 6.52 (d, 1H, $^3J$ = 9.7, NH), 6.93 (d, 1H, $^3J$ = 9.7, CH), 7.11 (d, 1H, $^3J$ = 7.5, CH), 7.23 (t, 1H, $^3J$ = 7.0, CH), 7.29 (t, 1H, $^3J$ = 7.5, CH), 7.32 (d, 1H, $^3J$=7.2, CH), 7.97 (s, 1H, CH). $^{13}C$ NMR (125 MHz, $CDCl_3$) δ51.5, 53.5, 58.8, 94.6, 108.1, 124.7, 124.9, 126.8, 128.0, 128.5, 128.6, 129.3, 148.5, 158.8, 165.0, 167.1; CHN Analyses: Anal. Calc. for $C_{16}H_{16}N_2O_5$: C, 60.76; H, 5.10; N, 8.86%. Found C, 60.72; H, 5.13; N, 8.77%; (E/MS): m/z: 316 ($M^+$).

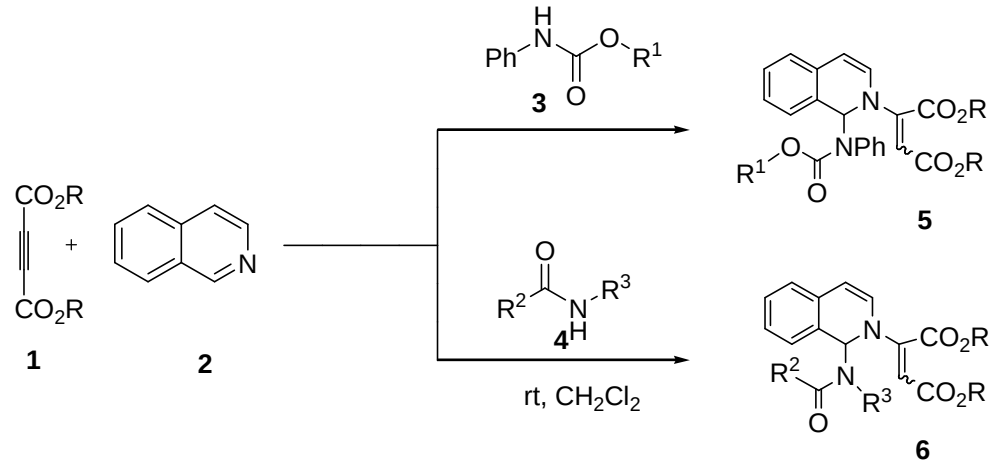
**Dimethyl-2-(1-(2-chloroacetamido)isoquinolin-2(1H)-yl)but-2-enedioate [6h]:** mp 162–163 °C. IR (KBr): 1733, 1697, 1633 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$) δd = 3.69 and 3.96 (2s, 6H, $2OCH_3$), 4.01 (2H, AB system, $J_{AB}$ = 15.4, CH2), 5.69 (s, 1H, CH), 6.05 (d, 1H, $^3J$ = 7.6, CH), 6.39 (d, 1H, $^3J$ = 7.6, CH), 6.89 (d, 1H, $^3J$ = 9.6, NH), 7.17 (d, 1H, $^3J$ = 7.5, CH), 7.26 (t, 2H, $^3J$ = 7.0, 2CH), 7.34 (d, 2H, $^3J$ = 7.6, 2CH). $^{13}C$ NMR (125 MHz, $CDCl_3$) δ51.5, 53.5, 60.8, 94.7, 108.5, 124.7, 125.1, 126.7, 128.01, 128.2, 128.5, 129.5, 149.0, 164.1, 164.9, 167.0; CHN Analyses: Anal. Calc. for $C_{17}H_{17}ClN_2O_5$: C, 55.97; H, 4.70; N, 7.68. Found: C, 55.86; H, 4.35; N, 7.62; (E/MS): m/z: 364 ($M^+$).

**Dimethyl-2-(1-benzamidoisoquinolin-2(1H)-yl)but-2-enedioate [6i]**: 153–154 °C. IR (KBr): 1728, 1704, 1642 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$) δd = 3.72, 4.00 (2s, 6H, $2OCH_3$), 5.90 (s, 1H, CH), 6.08 (d, 1H, $^3J$ = 7.7, CH), 6.49 (dd, 1H, J = 7.7, 4J = 1.1, CH), 6.92 (d, 1H, $^3J$ = 9.6, NH), 7.19 (d, 1H, $^3J$ = 5.3, CH), 7.29 (t, 1H, $^3J$ = 7.5, CH), 7.35 (t, 1H, $^3J$ = 7.5, CH), 7.42–7.43 (m, 2H, 2CH), 7.50 (d, 1H, $^3J$ = 7.8, CH), 7.51 (t, 1H, $^3J$ = 7.7, CH), 7.72 (d, 1H, $^3J$ = 8.5, CH), 7.73 (d, 1H, $^3J$ = 8.5, CH), 7.86 (d, 1H, $^3J$ = 9.6, CH). $^{13}C$ NMR (125 MHz, CDCl3) δ51.8, 53.9, 61.3, 94.7, 108.6, 125.3, 127.3, 127.7, 128.3, 128.9, 129.0, 129.5, 129.6, 132.5, 133.6, 149.3, 165.6, 165.9, 167.7; CHN Analyses: Anal. Calc. for $C_{22}H_{20}N_2O_5$: C, 67.34; H, 5.14; N, 7.14%. Found: C, 67.32; H, 5.15; N, 7.20%. EIMS: m/z (%) = 392 (M+, 2), 169 (24), 69 (100), 59 (60), 43 (30).

**Dimethyl-2-(1-(N-methylpropionamido) isoquinolin-2(1H)-yl)but-2-enedioate [6j]:** mp 175–177 °C IR (KBr): 1720, 1701, 1644 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δd = 3.63 and 3.90 (2s, 6H, $2OCH_3$), 5.74 (s, 1H, CH), 5.89 (d, 1H, $^3J$ = 7.7, CH), 6.32 (d, 1H, $^3J$ = 7.6, CH), 7.05 (d, 1H, $^3J$ = 7.3, CH), 7.11 (d, 1H, $^3J$ = 9.2, CH), 7.19–7.25 (m, 3H, 3CH), 7.40 (d, 1H, $^3J$ = 7.2, CH), 7.67 (d, 1H, $^3J$ = 9.2, NH), 8.0 (d, 1H, $^3J$ = 7.9, CH), 8.46 (d, 1H, $^3J$ = 5, CH), 8.66 (s, 1H, CH). $^{13}C$ NMR (125 MHz, $CDCl_3$) δ51.4, 53.5, 60.9, 94.5, 108.2, 123.4, 124.9, 125.0, 126.8 127.9, 128.6, 128.7, 129.1, 129.3, 135.6, 148.0, 148.7, 152.4, 163.6, 165.0, 167.0; CHN Analyses: Anal. Calc. for $C_{21}H_{19}N_3O_5$: C, 64.12; H, 4.87; N, 10.68%. Found: C, 64.10; H, 4.85; N, 10.70. (E/MS), m/z: 393 ($M^+$).

**Dimethyl-2-(1-(N phenylacetamido) isoquinolin-2(1H)-yl)but-2-enedioate [6k]:** mp 135–137 °C. IR (KBr): 1739, 1700, 1638 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$) δd = 1.14 (t, 3H, $^3J$ = 7.5, $CH_3$), 2.26 (2H, $ABX_3$ system, mAB = 78, $J_{AB}$ = 16.0, $J_{AX}$ = $J_{BX}$ = 7.5, $CH_2$), 2.62 (s, 3H, $CH_3$), 3.65 and 3.95 (2s, 6H, $2OCH_3$), 5.50 (s, 1H, CH), 5.78 (d, 1H, $^3J$ = 7.8, CH), 6.40 (d, 1H, $^3J$ = 7.8, CH), 7.05 (d, 1H, $^3J$ = 7.5, CH), 7.19 (t, 1H, $^3J$ = 7.3, CH), 7.26 (t, 1H, $^3J$ = 7.3, CH), 7.36 (d, 1H, $^3J$ = 7.5, CH), 7.63 (s, 1H, CH). $^{13}C$ NMR (125 MHz, $CDCl_3$) δ9.1, 26.6, 28.9, 51.4, 53.4, 63.3, 94.0, 106.1, 124.4, 126.4, 127.3, 127.9, 128.0, 129.0, 129.8, 148.8, 165.3, 167.4, 173.0; CHN Analyses: Anal. Calc. for $C_{19}H_{22}N_2O_5$: C, 63.68; H, 6.19; N, 7.82%. Found: C, 62.93; H, 6.2; N, 7.80; E/MS: m/z (%) = 358 ($M^+$).

**Dimethyl-2-[1-[(3-pyridyl)isoquinolin-2(1H)-yl)but-2-enedioate [6l]**: mp 188–189 °C. IR (KBr): 1739, 1700, 1638 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$) δ1.68 (s, 3H, $CH_3$), 3.69 and 3.95 (2s, 6H, $2OCH_3$), 5.20 (d, 1H, $^3J$ = 7.7, CH), 5.69 (s, 1H, CH), 5.82 (d, 1H, $^3J$ = 7.7, CH), 6.00 (d, 1H, $^3J$ = 7.5, CH), 6.85 (dd, 1H, $^3J$ = 8.0, 4J = 3.4, CH), 6.98 (t, 1H, $^3J$ = 7.3, CH), 7.15 (d, 1H, $^3J$ = 7.0, CH), 7.25–7.34 (m, 4H, 4CH), 7.55 (dd, 1H, $^3J$ = 8.0, $^4J$ = 3.4, CH), 7.81 (s, 1H, CH) ppm. $^{13}C$ NMR (125 MHz, $CDCl_3$) δ22.2, 51.4, 53.4, 64.1, 93.5, 106.5, 124.4, 125.6, 127.1, 127.7, 128.3, 128.7, 128.9, 129.1, 129.2, 129.6, 130.0, 130.1, 137.6, 149.2, 165.1, 167.4, 169.4. CHN Analyses: Anal. Calc. for $C_{23}H_{22}N_2O_5$: C, 67.97; H, 5.46; N, 6.89. Found: C, 67.89; H, 5.43; N, 6.91.

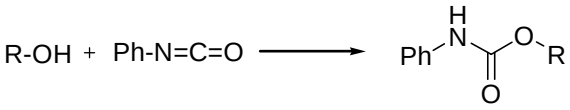



**Scheme 1. Preparation of disubstituted-1,2- dihydroisoqunoline**

**General method for the preparation of derivatives of Urethanes:**

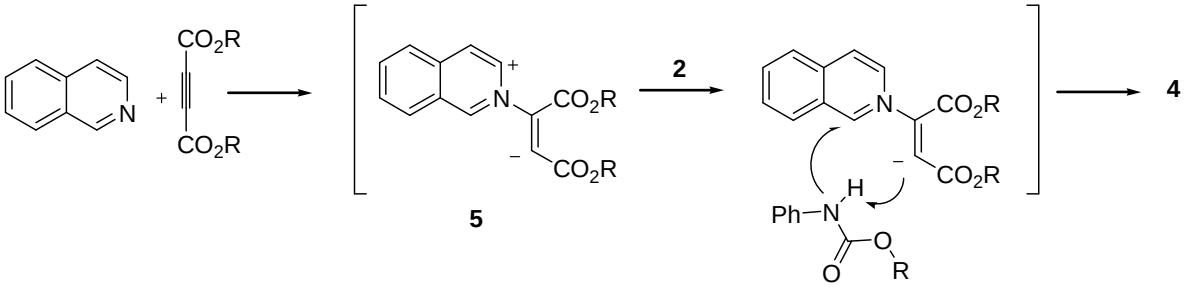
Alcohol (1mL) and phenyl isocyanat (1mL) were heated and reacted for 5 min at 50-70 $^{o}$C. The mixture cooled to obtain a pure product precipitate. The precipitate dissolved in tetrachloride carbon (5mL) at room temperature and then, the precipitate collected and dried.

**Structure assignments of new compounds:** Mechanistically, it is conceivable that the reaction involves initial formation of a 1:1 zwitterionic intermediate[10,11,12,13] **5** between isoquinoline and Dialkyl acetylene dicarboxylate.This intermediate is protonated by urethane **3** and then attacked by the conjugate base of the amide to produce **4** (scheme 3).

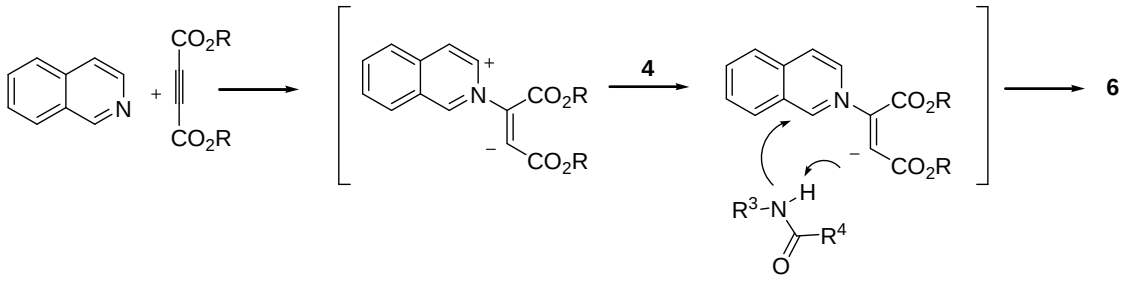



**R= 1-Propanol**
**Isopropanol**
**Cyclohexanol**

**Scheme 2. Formation of *Urethanes***



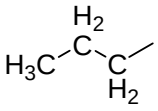
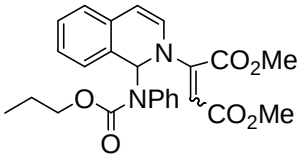
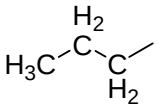
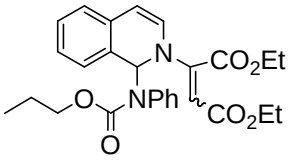
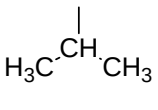
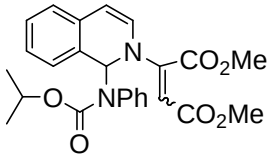
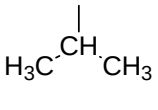
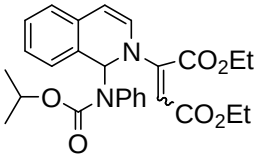
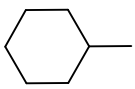
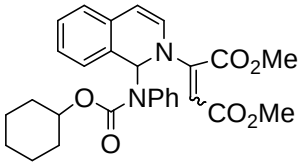
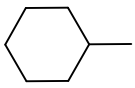
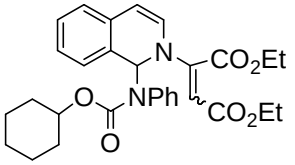
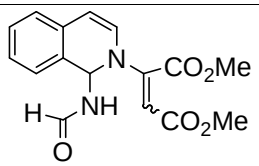
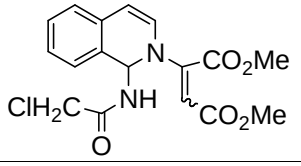

**Scheme 3. A plausible reaction mechanism**

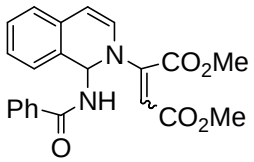
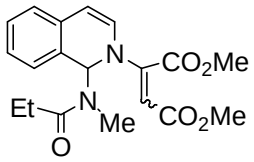
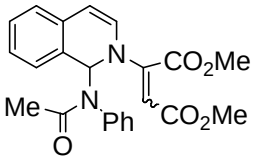
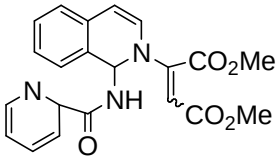



**(6g-6l)**

**Scheme 4. A plausible reaction mechanism**

**Table 1 three component reaction of isoquinoline, N-Phenylcarbamates and Dialkyl acetylenedicarboxylate**

| Entry | R | $R^1$ | $R^2$ | $R^3$ | Products | Yield % |
|---|---|---|---|---|---|---|
| A | Me |  | ---- | ---- |  | 75 |
| B | Et |  | ---- | ---- |  | 78 |
| C | Me |  | ---- | ---- |  | 80 |
| D | Et |  | ---- | ---- |  | 80 |
| E | Me |  | ---- | ---- |  | 85 |
| F | Et |  | ---- | ---- |  | 85 |
| G | Me | ---- | H | H |  | 90 |
| H | Me | ---- | $CH_2Cl$ | H |  | 92 |

| | | | | | | |
|---|---|---|---|---|---|---|
| I | Me | ---- | Ph | H |  | 95 |
| J | Me | ---- | Et | Me |  | 93 |
| K | Me | ---- | Me | Ph |  | 94 |
| L | Me | ---- | 3-pyridyl | H |  | 98 |

The reaction between isoquinoline with dimethyl acetylenedicarboxylate and heterocyclic NH compound were carried dichloromethane and finished after approximately 8 hour at room temperature. On the basis of well-established chemistry of trivalent isoquinoline nucleophile presence of heterocyclic NH compound lead to 1,2-dihydroisoquinoline yields. To explain the outcome of these reactions we postulate the reaction mechanism of these reactions is driven from the initial addition of isoquinoline to the acetylenic ester followed by the addition of the heterocyclic NH compounds. The structures of compounds confirmed by $^{1}$H NMR, $^{13}$C NMR spectrometry, IR and elemental analysis (See Experimental section). With respect to same employed conditions (effect of same solvent and temperature in our reactions) it seems that one of the important factors for assignment of the configuration (Z or E) is the structural effect of reactants. In short, we have developed a new multicomponent reaction method to access a novel class of heterocyclic derivatives. The present method not only offers the advantage of carrying out the reactions under neutral conditions but also of mixing the reactants without any pre-activation. The simplicity of this procedure makes it an interesting alternative method in comparison to other approaches.

## Conclusion

In conclusion, we have reported a new transformation involving dialkyl acetylene dicarboxylate and isoquinoline in the presence of heterocyclic NH ( e.g urethane and amide) which affords 1,2-disubstituted nitrogen-containing heterocycles. The advantage of the present procedure is that the reaction is performed under neutral conditions and without catalyst.

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