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Lewis Acid and/or Lewis Base catalyzed [3+2] cycloaddition reaction: Synthesis of pyrazoles and pyrazolines

Palakodety Radha Krishna* and E. Raja Sekhar

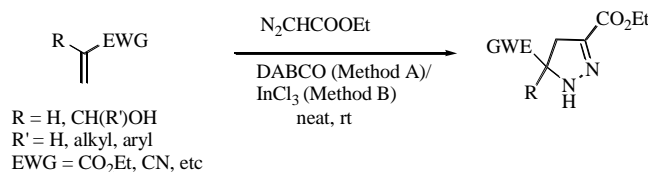
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Abstract: A facile, 1,3-dipolar cycloaddition of ethyl diazoacetate (EDA) with various activated olefins including Baylis-Hillman adducts, activated and simple alkynes to afford 3,5-disubstituted pyrazolines and pyrazoles respectively in moderate to good yields, in high regioselective manner in the presence of Indium chloride and/or DABCO is reported. All the reactions were carried out under no strong bases/acids, solvent free conditions and at ambient temperature to afford the heterocyclic compounds.

Keywords: Ethyl diazoacetate, DABCO, Indium trichloride, activated olefins, Baylis-Hillman adducts, pyrazolines, pyrazoles.

Formation of heterocycles or carbocyclic five membered ring systems continue to be attractive for the synthesis of a variety of bioactive compounds.¹ The most accessible route is either a) cyclization, which proceeds stepwise through one or more intermediates involving the expulsion of a small molecule such as an alcohol or water or b) cycloaddition, which proceed via no distinct intermediate but the bond formation may be asynchronous. Alternatively, [3+2] cycloaddition reaction strategy to form five membered ring systems through the reaction partners of 1,3-dipoles and dipolarophiles is an attractive protocol. According to FMO theory, the reaction to take place is a certain similarity of the interacting HOMO and LUMO orbitals depending on the relative orbital energies of both the dipolarophile and dipole. Electron withdrawing groups on the dipolarophile normally favor an interaction of the LUMO of the dipolarophile (electron poor olefin/alkyne) with HOMO of the dipole that leads to the formation of the new bonds, whereas electron donating groups on the dipolarophile normally favor the inverse of this reaction.² In continuation of our efforts in the development of various aspects of Baylis-Hillman reaction,³ and utility of the adducts thereof in the organic synthesis,⁴ herein we report the use of Baylis-Hillman adducts for C-N bond formation⁵ to result in the heterocyclic ring formation affording corresponding pyrazolines (Scheme 1).

Scheme 1. Cycloaddition between various olefins and ethyl diazoacetate.



Pyrazoles⁶ and pyrazolines⁷ derivatives are widely useful in agrochemistry as insecticides and in pharmaceuticals for varied applications. In general pyrazolines has been synthesized⁸ by cycloaddition of nitrile imines,⁹ 1,2-disubstituted (-COOR) alkene,¹⁰

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azides.¹¹ Interestingly, it may be noted that Baylis-Hillman adducts were less studied as substrates in cycloaddition reactions.¹² Towards this endeavor, here in, we report our results on the cycloaddition of various types of Baylis-Hillman adducts as dipolarophiles with Ethyl diazoacetate (dipole) including simple acrylates to afford corresponding pyrazolines, as well as the synthesis pyrazoles from activated and simple alkynes as dipolarophiles.

The initial [3+2] cycloaddition reaction was conducted between ethyl acrylate **1** and ethyl diazoacetate (EDA) to afford **1a** as the product. During the study, we found that DABCO/ InCl_3 effectively catalyzes pyrazoline formation from simple Michael acceptor/electron poor olefin (ethyl acrylate) and EDA in 97 and 80% yield respectively in 2 h at ambient temperature. For this protocol various solvents were examined and the maximum yield was obtained under neat conditions in shorter time scales. Subsequent to these preliminary investigations, the effects of different Lewis acids/and bases for the [3+2] cycloaddition reaction were examined (entries 1-11, Table 1).

Table 1: Optimization of reaction conditions for cycloaddition reaction between ethyl acrylate **1** and ethyl diazoacetate

Entry	Lewis Acid/Lewis Base	Solvent	Time [h]	Product (%) ^{ab}
1	DABCO	THF	24	0
2	DABCO	DCM	24	25
3	DABCO	DMF	10	82
4	DABCO	Dioxane:H ₂ O	6	90
5 ^c	DABCO	neat	2	97
6	DBU	neat	2	0
7	Urotropine	neat	4	89
8	NMM	neat	5	83
9	$\text{BF}_3 \cdot \text{OEt}_2$	neat	4	45
10	FeCl_3	neat	5	61
11 ^c	InCl_3	neat	2	80
12	no catalyst	neat	24	0

^a Determined by ¹H NMR of pure compound. ^b Isolated yields after column chromatography

^c The best yield under these conditions.

Among the various Lewis bases that were examined, DABCO (Table 1, entry 1), provided the desired product (**1a**, Table 2) in the best yield under solvent free conditions (neat) when compared to NMM (Table 1, entry 4) and Urotropine (Table 1, entry 3). Surprisingly DBU (table 1, entry 2) did not catalyze the [3+2] cycloaddition reaction. However, Indium chloride (Table 1, entry 7), among the Lewis acids catalyzed the reaction to afford the desired product **1a** in best yield under solvent free conditions when compared to other Lewis acids such as $\text{BF}_3 \cdot \text{OEt}_2$ and FeCl_3 (entries 5-6, Table 1).

Amongst the two DABCO and InCl₃, the reaction was more facile with DABCO to afford products in good yields and in shorter time. As illustrated (entries 5-7, Table 1) the product yield increased with decreasing acidity of the Lewis acids.

Table 2. Cycloaddition between electron poor olefins and ethyldiazoacetate under methods A/B

Entry	Dipolarophile	Product ^a	Method ^b	Time [h]	Yield (%) ^c
1			A	2	97
			B	4	80
2			A	6	52
			B	10	46
3 ^d			A	4	69
			B	8	56
4 ^d			A	5	58
			B	7	49

^a All the products were characterized their spectral data.

^b **Method A:** Olefin (1.0 eq.), EDA (1.0 eq.), DABCO (0.1 eq.) were stirred at ambient temperature for specified hours to afford the products after purification; **Method B:** Olefin (1.0 eq.), EDA (1.0 eq.), InCl₃ (0.1 eq.) were stirred at ambient temperature until the completion of the reaction.

^c Isolated yields.

^d For these substrates, olefin and EDA were taken in 2:1 ratio with the catalyst (0.1 eq.).

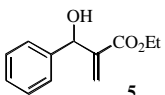
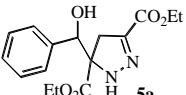
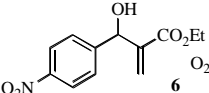
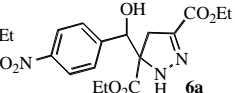
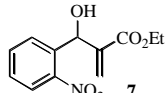
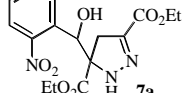
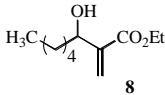
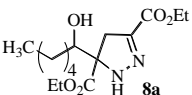
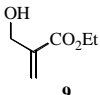
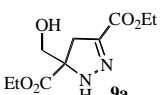
Pyrazoline **1a** was characterized through its spectral data. For instance, its ¹H NMR spectrum revealed characteristic H-5 at δ 4.40 (dd, $J = 6.0, 12.8$ Hz) and H-4 at δ 3.30 (ddd, $J = 1.5, 5.8, 18.8$ Hz) and δ 3.17 (dd, $J = 12.6, 18.8$ Hz). IR spectrum displayed the characteristic 1571 cm^{-1} for C-N stretching frequencies, apart from frequencies due to the other functional groups present.

Later, we applied this cycloaddition reaction under both Method A and Method B conditions to several simple electron poor olefins such as acrylonitrile **2** (entry 2, Table 2), *N,N*-dibenzyl acrylamide **3** (entry 3, Table 2), and 4-acryloylmorpholine **4** (entry 4, Table 2) with EDA to afford the corresponding pyrazolines (**2a-4a**) in good yields (Table 2).

The scope of the cycloaddition was further investigated with Baylis-Hillman adducts and EDA (Table 3). For instance, adduct **5** (Table 3, entry 1) underwent cycloaddition with EDA in the presence of DABCO (method A) as well as with InCl₃ (method B) to afford

corresponding pyrazoline **5a** in 75 and 60% yields respectively under solvent free conditions (neat). Later other adducts, such as the one containing an electron withdrawing group (*p*-NO₂ group) on the benzene ring (entry 2, Table 3), yielded the desired product **6a** in excellent yield (95 %) while the adduct possessing the *o*-NO₂ group (entry 3, Table 3) led to comparatively less yield of the corresponding product **7a** (86 %) under similar reaction conditions. Adduct **8** possessing a long carbon chain (entry 4, Table 3) and a simple adduct **9** with least number of carbon atoms (entry 5, Table 3) also provided the corresponding pyrazolines **8a** and **9a** in good yields. All the products were identified by their spectral data (Please see reference section).

Table 3. Cycloaddition between various Baylis-Hillman adducts (dipolarophile) and ethyldiazoacetate under methods A/B

Entry	Dipolarophile	Product ^a	Method ^b	Time [h]	Yield (%) ^c
1			A	6	75
			B	8	60
2			A	2	95
			B	5	78
3			A	2	86
			B	5	66
4			A	3	85
			B	7	61
5			A	4	82
			B	7	71

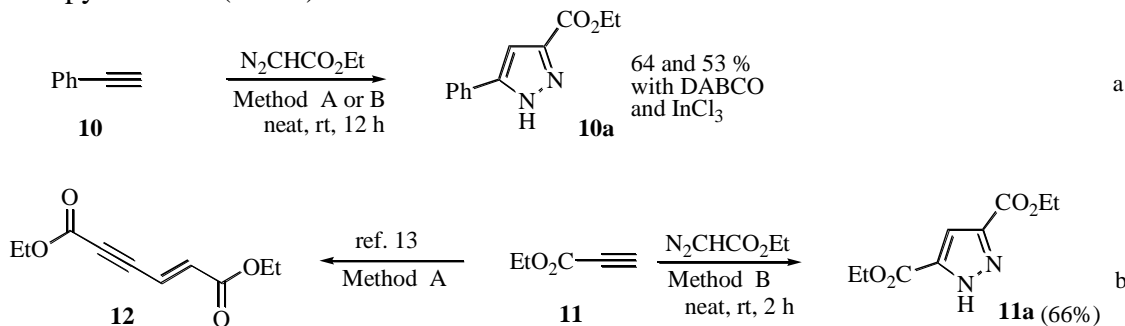
^a All the products were characterized their spectral data.

^b **Method A:** Olefin (1.0 eq.), EDA (1.0 eq.), DABCO (0.1 eq.) were stirred at ambient temperature for specified hours to afford the products after purification; **Method B:** Olefin (1.0 eq.), EDA (1.0 eq.), InCl₃ (0.1 eq.) were stirred at ambient temperature until the completion of the reaction.

^c Isolated yields.

Interestingly, when [3+2] cycloaddition reaction was performed on a simple alkyne such as phenylacetylene **10** and electron poor alkyne such as ethyl propiolate **11** gave the corresponding pyrazoles **10a** and **11a** in good yields. The earlier reported method did not give the products under the Lewis acid in under aqueous conditions.¹³ Herein, while **10** gave **10a** under both the reaction conditions (Method A and B, Scheme 2, route a) in comparable yields, **11** gave the desired product **11a** (Scheme 2, route b), under Method B conditions alone. Thus, with DABCO (Method A) a facile self coupling led to the undesired diethyl-2*E*-en-4-yn-1,6-dioate¹⁴ as the only product (Scheme 2, route b). But the same reaction in the presence of Lewis acid (InCl₃), cycloaddition product was obtained exclusively (Scheme 2, route b). Both **10a** and **11a** were characterized by their spectral data. For instance, ¹H NMR spectrum of **10a** and **11a** revealed the lone aromatic proton at δ 7.08 and at δ 7.27 respectively. The spectral data of **10a** and **11a** matched

with reported values.^{6,14} Thus, this result conclusively proves the regioselectivity of [3+2] cycloaddition reaction. The same analogy was extending to assign the regioselectivity of all the pyrazolines (**1a-9a**) as well.



Scheme 2. Reaction of phenylacetylene and ethylpropiolate with ethyldiazoacetate under method A and/or B conditions.

Thus, while the Lewis acid catalyzed cycloaddition followed the standard reaction pathway of activating dipolarophile¹⁵ by lowering the energy of the LUMO that consequently acts with HOMO of dipole in affording the products, Lewis base promoted activation presumably may have taken the course of forming the Huisgen zwitterions upon addition on the ethyl acrylate or EDA which subsequently reacts with its counterpart to result in products.

In conclusion, a simple, general one-pot protocol for the synthesis of heterocyclic 3,5-disubstituted pyrazolines and pyrazoles was developed from different type of electron poor olefins/alkyne including Baylis-Hillman adducts and EDA under mild conditions in good to excellent yields. Alkynes also provided the desired products. On the other hand, variety of Lewis bases such as Urotropine, NMM, DBU and Lewis acids like $BF_3 \cdot OEt_2$, $FeCl_3$ apart from DABCO and $InCl_3$ were also screened during the standardization of cycloaddition reaction.

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References

1. Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products (Eds: A. Padwa, W. H. Pearson), Wiley, Hoboken, 2003.
2. Huisgen, R.; Grashey, R.; Sauer, J. In: Chemistry of alkenes, Interscience, New York, **1964**, 806.
3. a) Radha Krishna, P.; Kannan, V.; Ilangoan, A.; Sharma, G. V. M. *Tetrahedron: Asymm.* **2001**, *12*, 829-837; b) Radha Krishna, P.; Raja Sekhar, E.; Kannan, V. *Tetrahedron Lett.* **2003**, *44*, 4973-4975; c) Radha Krishna, P.; Kannan, V.; Sharma, G. V. M. *Synth. Commun.* **2004**, *34*, 55-64; d) Radha Krishna, P.;

- Manjuvani, A.; Kannan, V.; Sharma, G. V. M. *Tetrahedron Lett.* **2004**, *45*, 1183-1185; e) Radha Krishna, P.; Raja Sekhar, E.; Kannan, V. *Synthesis* **2004**, 857-860; f) Radha Krishna, P.; Kannan, V.; Narasimha Reddy, P. V. *Adv. Synth. Cat.* **2004**, *346*, 603-606.
4. a) Radha Krishna, P.; Kannan, V.; Sharma, G. V. M. *Synth. Commun.* **2004**, *34*, 55. b) Radha Krishna, P.; Narsingam, M.; Kannan, V. *Tetrahedron Lett.* **2004**, *45*, 4773-4775. c) Radha Krishna, P.; Narsingam, M.; Srinivas Reddy, P.; Srinivasulu, G.; Kunwar, A. C. *Tetrahedron Lett.* **2005**, *46*, 8885. d) Radha Krishna, P.; Narsingam, M. *J. Comb. Chem.* **2007**, *9*, 62.
 5. Nair, V.; Menon, R. S.; Sreekanth, A. R.; Abhilash, N.; Biju, A. T. *Acc. Chem. Res.* **2006**, *39*, 520 – 530.
 6. See synthesis and biological activity of pyrazoles: Qi, X.; Ready, J. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 3242-3244 and references cited therein.
 7. See for information of Pyrazolines: Lévai, A. *Chemistry of Heterocyclic Compounds*, **1997**, *33*, 647-659.
 8. (a) Eleguero, J. in *Comprehensive Heterocyclic Chemistry*, Vol. 5 (Eds.: A. R. Katritzky, C. W. Rees, K. T. Potts), Pergamon, Oxford, **1984**, p. 167; (b) Eleguero, J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R.; Rees, C. W.; Scriven, E. F., Eds.; Pergamon Press: Oxford, **1996**; Vol. 3, pp. 1-75.
 9. Kanemasa, S.; Kobayashi, S. *Bull. Chem. Soc. Jpn.*, **1993**, *66*, 2685-2693.
 10. Yamauchi, M.; Yajima, M. *Chem. Pharm. Bull.* **2001**, *49*, 1638-1639.
 11. Yadav, J. S.; Subba Reddy, B. V.; Geetha, V. *Synlett* **2002**, 513-515.
 12. Basavaiah, D.; Jaganmohan Rao, A.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811-891.
 13. Jiang, N.; Li, C. –J. *Chem. Commun.* **2004**, 394-395.
 14. Ramachandran, P. V.; Rudd, M. T.; Reddy, M. V. R. *Tetrahedron Lett.* **2005**, *46*, 2547.
 15. Gothelf, K. V.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 863.
 16. **General experimental procedure: Method A:** Activated olefin, ethyl acrylate **1** (0.1 g, 1 mmol), ethyl diazoacetate (57 mg, 0.5 mmol) and DABCO (11 mg, 0.1 mmol) were placed in a dry round bottom flask and the reaction mixture was allowed to stir for 2 h under neat at ambient temperature until the completion of reaction (tlc) and the reaction mixture was absorbed directly and purified by column chromatography (Silica gel, 60-120 mesh, EtOAc:hexane, 2:8) to afford pure **1a** in 97% yield. **Method B:** A mixture of activated olefin, ethyl acrylate **1** (0.1g, 1 mmol), ethyl diazoacetate (57 mg, 0.5 mmol) and InCl₃ (22 mg, 0.1 mmol) were placed and stirred under neat at ambient temperature for 4 h following absorption of reaction mixture, purified by column chromatography to afford **1a** in 80% yield.
 17. **Spectral data for selected compounds: 1a.** Yellow oil; ¹H NMR (200 MHz, CDCl₃): δ = 6.72 (br s, 1H, NH), 4.40 (dd, 1H, *J* = 6.0, 12.8 Hz, H-5), 4.34-4.15 (m, 4H, 2 x -OCH₂), 3.30 (ddd, 1H, *J* = 1.5, 5.8, 18.8 Hz, H-4), 3.17 (dd, 1H, *J* = 12.6, 18.8 Hz, H-4'), 1.50-1.20 (m, 6H, 2 x CH₃); ¹³C NMR (75 MHz, CDCl₃): δ 171.5, 142.6, 111.2, 61.9, 61.4 (2C), 34.6, 14.1 (2C); IR (neat): 3356, 2984, 1734, 1571, 1250 cm⁻¹; ES-MS: *m/z* = 214 (M⁺); Anal. calcd. for C₉H₁₄N₂O₄: C, 50.46; H, 6.59%; found C, 50.41; H, 6.62%. **3a.** Syrup; ¹H NMR (200 MHz, CDCl₃): δ =

7.40-7.10 (m, 10H, Ar-H), 6.40 (br. s, 1H, NH), 4.84 (d, $J = 5.3$ Hz, 2H, $-\text{CH}_2\text{Ph}$), 4.56 (d, $J = 6.4$ Hz, 2H, $-\text{CH}_2\text{Ph}$), 4.22 (dd, 1H, $J = 5.2, 12.4$ Hz, H-5), 4.20 (q, $J = 6.7$ Hz, 2H, $-\text{OCH}_2$), 3.49-3.25 (m, 2H, CH_2), 1.29 (t, $J = 6.3$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ 162.7, 146.6, 136.3, 128.0, 127.8, 127.5, 127.0, 126.8, 61.3, 59.3, 50.2, 47.7, 37.1, 13.5; IR (neat): 3348, 2925, 1735, 1622, 1449, 1239 cm^{-1} ; ESI-MS: $m/z = 338$ ($\text{M}^+ + 1$); Anal. Calcd for $\text{C}_{20}\text{H}_{23}\text{N}_3\text{O}_2$: C, 71.19; H, 6.87%; Found: C, 71.13; H, 6.93%. **4a.** Syrup; ^1H NMR (200 MHz, CDCl_3): $\delta = 6.81$ (br s, 1H, NH), 4.51 (t, 1H, $J = 5.2$ Hz, H-5), 4.25 (q, 2H, $J = 7.4$ Hz, OCH_2), 3.70-3.54 (m, 4H, CH_2), 3.51-3.44 (m, 2H, CH_2), 3.28 (dd, 1H, $J = 12.6, 17.0$ Hz, CH_2), 3.01 (dd, 1H, $J = 5.2, 17.0$ Hz, CH_2), 1.40-1.18 (m, 3H, CH_3). ESI-MS: $m/z = 256$ [$\text{M}^+ + 1$]. Anal. Calcd for $\text{C}_{11}\text{H}_{17}\text{N}_3\text{O}_4$: C, 51.76; H, 6.71%; Found: C, 51.71; H, 6.78%. **5a.** Syrup; ^1H NMR (200MHz, CDCl_3): $\delta = 7.31$ (s, 5H, Ar-H), 6.81 (br, s, 1H, NH), 4.99 (s, 1H, $-\text{CHOH}$), 4.30 – 4.10 (m, 4H, 2 x OCH_2), 3.18 (d, $J = 2.5$ Hz, 2H, H-4), 1.40 – 1.15 (m, 6H, 2XCH_3); ^{13}C NMR (75 MHz, CDCl_3): δ 143.2, 137.3, 126.6, 127.9, 75.1, 61.8, 60.8, 35.3, 29.2, 13.7, 13.4; IR (neat): 3448, 2984, 1731, 1638, 1253 cm^{-1} ; ESI-MS: $m/z = 343$ [$\text{M}^+ + 23$]; Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_5$: C, 59.99; H, 6.29%; Found: C, 60.04; H, 6.22%. **7a.** Syrup; ^1H NMR (200 MHz, CDCl_3): $\delta = 7.92$ (d, $J = 7.8$ Hz, 2H, Ar-H), 7.61 (t, $J = 8.6$ Hz, 1H Ar-H), 7.51 (t, $J = 7.8$ Hz, 1H, Ar-H), 7.10 (s, NH), 5.81 (s, 1H, $-\text{CHOH}$), 4.19 (m, 4H, 2XCH_2), 3.10 (d, $J = 3.4$ Hz, 2H, H-4), 1.22 (m, 6H, 2XCH_3); ^{13}C NMR (75 MHz, CDCl_3): δ 172.0, 148.7, 143.7, 133.5, 130.2, 129.2, 124.3, 68.9, 62.8, 61.4, 61.3, 59.8, 14.1, 13.8; IR (neat): 3449, 2924, 1727, 1636, 1256 cm^{-1} ; ESI-MS: $m/z = 388$ [$\text{M}^+ + 23$]. Anal. Calcd for $\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_7$: C, 52.60; H, 5.24%; Found: C, 52.65; H, 5.22%. **8a.** Syrup; ^1H NMR (300 MHz, CDCl_3): $\delta = 6.63$ (br s, 1H, NH), 5.25 (t, $J = 7.3$ Hz, 1H, $-\text{CH-OH}$), 4.31 - 4.02 (m, 4H, 2XCH_2), 3.41 - 2.98 (m, 2H, H-4), 1.45 – 1.23 (m, 12H), 0.92 – 0.85 (br, t, 3H, CH_3); ^{13}C NMR (200MHz, CDCl_3): δ 171.1, 161.8, 138.3, 64.3, 61.5, 36.8, 34.6, 31.2, 29.0, 25.0, 22.2, 13.7; IR (neat): 3354, 2980, 2934, 2867, 1739, 1703, 1252 cm^{-1} ; ESI-MS: $m/z = 296$ ($\text{M}^+ + 23$). **9a.** Syrup; ^1H NMR (200 MHz, CDCl_3): $\delta = 4.29$ -4.14 (m, 4H, CH_2), 3.70 (dd, 2H, $J = 10.5, 26.2$ Hz, CH_2OH), 3.03 (dd, 2H, $J = 17.2, 60.8$ Hz, H-4), 1.32 (hextet, 6H, $J = 4.5, 7.5, 11.2$ Hz, 2 x CH_3). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 172.1, 161.7, 142.9, 73.8, 70.3, 65.1, 62.8, 62.2, 37.2, 14.0$. ESI-MS: 245 [$\text{M}^+ + 1$]. Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}_5$: C, 49.18; H, 6.60%; Found: 49.24; H, 6.56%. **10a.** Syrup; ^1H NMR (300 MHz, CDCl_3): $\delta = 7.76$ (d, 2H, $J = 6.79$ Hz, Ar-H), 7.43-7.30 (m, 3H, Ar-H), 7.08 (s, 1H, Ar-H), 4.37 (q, 2H, $J = 6.79$ Hz, CH_2), 1.41 (t, 3H, $J = 6.79$ Hz, CH_3). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 128.9, 128.5, 127.7, 125.7, 113.9, 105.6, 61.3, 14.2$. IR (neat): 2924, 1724, 1244 cm^{-1} . ESI-MS: 217 [$\text{M}^+ + 1$]. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_2$: C, 66.65; H, 5.59%; Found: C, 66.69; H, 5.54%. **11a.** Syrup; ^1H NMR (300 MHz, CDCl_3): $\delta = 12.9$ (br s, 1H, NH), 7.27 (s, 1H, Ar-H), 4.37 (q, 2H, $J = 6.79$ Hz, CH_2), 1.38 (t, 3H, $J = 6.79$ Hz, CH_3). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 160.3, 111.2, 61.6, 14.1$. IR (neat): 3145, 2984, 1729, 1250 cm^{-1} . ESI-MS: 213 [$\text{M}^+ + 1$]. Anal. Calcd for $\text{C}_9\text{H}_{12}\text{N}_2\text{O}_4$: C, 50.94; H, 5.70%; Found: C, 50.99; H, 5.67%.