1,3-DIPOLAR CYCLOADDITION OF ARYLNITRILE OXIDS WITH ETHYL 1-ALLYL-2-BENZYL-3-OXO-2,3-DIHYDRO-1H-ISOINDOLE-1-CARBOXYLATES

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Résumé : L'utilisation de la réaction de cycloaddition dipolaire-1,3 permet la formation d'hétérocycles hautement fonctionnalisés. Dans ce cadre, nous nous sommes intéressés à synthétiser des nouveaux hétérocycles de type isoxazoline en partant des 1-allyl-2-benzyl-3-oxo-2, 3-dihydro-1H-isoindole-1-carboxylate d'éthyle **5** et des arylnitrile oxydes **6** en utilisant la réaction de cycloaddition dipolaire-1,3 dont l'étude a montré qu'elle est régiosélective et chémioselective. La structure des cycloadduits est déterminée par spectroscopie RMN ^{1}H et ^{13}C.

Abstract: Synthesis of a series of cyclic fused-isoxazolines has been accomplished by regioselective and chemioselective 1,3-dipolar cycloaddition of ethyl 1-allyl-2-benzyl-3-oxo-2, 3-dihydro-1H-isoindole-1-carboxylates **5** to arylnitrile oxides **6**. The structure of the cycloadducts was elucidated by ^{1}H and ^{13}C NMR spectroscopy. The regioselectivity observed is in accordance with the one normally found in nitrile oxide cycloaddition with terminal alkenes.

1. Introduction

Research on the synthesis of the heterocyclic compounds is very widespread in the field of organic chemistry, actually it requires a particular synthetic planning that because the heterocyclic compounds are often synthetic showpieces of targets of biological interest. The 1,3-dipolar cycloaddition constitutes a versatile synthetic methodology for the construction of five-membered ring heterocycles [1].

The intermolecular 1,3-dipolar cycloaddition reaction of arylnitrile oxides with various alkenes represents an efficient and convergent method for the construction of isoxazoline rings [2,3]. It is pertinent to note that isoxazolines exhibit biological activities such as anti-VIH [4-6], antiviral [7], antibacterial [8], and are also useful intermediates for the synthesis of a wide variety of bioactive natural product [9]. Furthermore, isoindolinone derivatives have attracted much attention from the scientific community, because of their importance as key intermediates in organic synthesis [10] and their profound physiological and chemotherapeutic activities [11]. For example, indoprofen is anti-inflammatory [12], AKS 186 was found to inhibit vasoconstriction induced by thromboxane A2 analog [13], and thiazoloisoindolone is a non-nucleosidic HIV-reverse transcriptase inhibitor [14].

The above importance of isoindolinone, and heterocyclic compounds led us to investigate the synthesis of novel heterocyclic compounds via arylnitrile oxides **6** cycloaddition to ethyl 1-allyl-2-benzyl-3-oxo-2, 3-dihydro-1H-isoindole-1-carboxylates **5.**

We have investigated the cycloaddition of **5** to **6** furnishing two diastereoisomers pure of the isoxazoline type. It is pertinent to note that the present work is the first report on the arylnitrile oxides cycloaddition with **5**.

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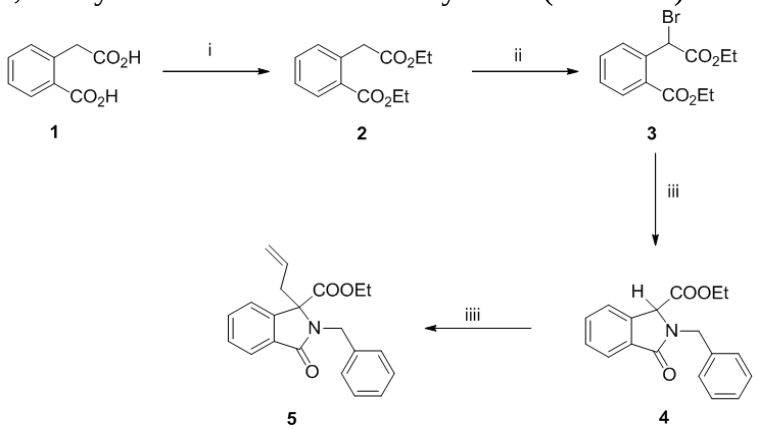
2. Results and discussion

The dipolarophiles: ethyl 1-allyl-2-benzyl-3-oxo-2, 3-dihydro-1H-isoindole-1-carboxylates **5** was obtained by a literature procedure [15,16]. They were synthesized in high yield 90%. We started our synthesis from diethylhomophthalate **2** readily available in quantitative yield, through the esterification of commercially available homophthalic acid **1**, as previously described by M .M Rammah *et all* [16]. The conversion of **2** into the corresponding diethyl *α*-bromohomophthalate **3** was accomplished under standard conditions by treatment with *N*-bromosuccinimide and a catalytic amount of AIBN. Condensation of bromine **3** with two equivalent of the required benzylamines in acetonitrile at room temperature for 8 h afforded the desired bicyclic lactams **4** in high yield 90%. Treatment of lactams **4** with K_2CO_3 to effect enolate formation followed by alkylation with allyl bromide, afforded ethyl 1-allyl-2-benzyl-3-oxo-2, 3-dihydro-1H-isoindole-1-carboxylates **5** (Scheme 1).

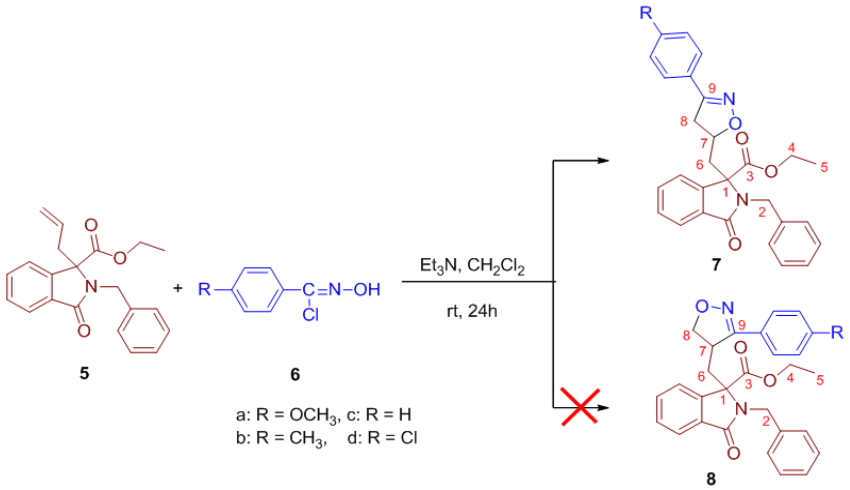


Scheme 1. Reagents and conditions: (i) HCl, EtOH, 0 °C, 4 h then reflux, 4 h; (ii) NBS, AIBN, CCl_4, reflux, 12 h; (iii) benzylamines,CH_3CN, rt, 8 h; (iiii) K_2CO_3, Allyl bromide, CH_3CN, reflux, 12h, 90 %

The arylnitrile oxides used as dipole were generated *in situ* by dehydrogenation of the corresponding arylhydroxamoyl chloride **6** with triethylamine following a known procedure [17].

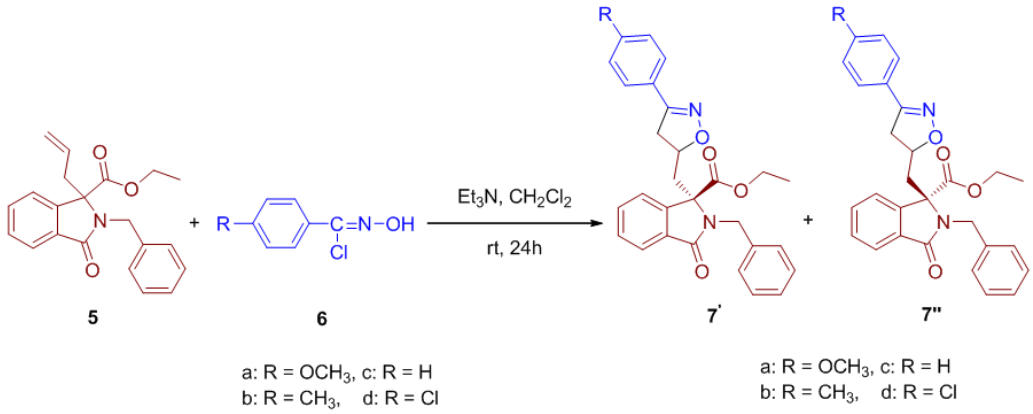
When equimolar amounts of ethyl 1-allyl-2-benzyl-3-oxo-2, 3-dihydro-1H-isoindole-1-carboxylates **5** was reacted with the arylnitrile oxides in dichloromethane at room temperature for 24h. Theoretically, the reaction afforded two regioisomerics of isoxazoline compound **7** and **8**, but spectroscopic analysis of cycloadducts revealed the presence of single regioisomeric **7** (Schema 2). The observed regiochemistry was confirmed by ^{13}C NMR chemical shift of the carbons atom **C7** which resonate around 75 – 76 ppm and **C8** which resonate around 40 – 41 ppm. In the case of the presence of the inverse regioisomeric **8** the chemical shift values of the carbons atom **C7** and **C8** should be close to 35 ppm and 72 ppm respectively [18].

The regioselectivity observed is in accordance with the one normally found in nitrile oxides cycloaddition with terminal alkenes [19].



Scheme 2.

Also, after purification of the reaction mixture with column chromatographic separation on silica gel using dichloromethane-acetone (98% - 2%) and spectroscopic analysis of purified products revealed the presence of two pur distereoisomerism **7'** and **7"** (Schema 3) in 17-54% total yield (table 1).



Scheme 2: 1,3-dipolar cycloaddition reaction.

Table 1: Yield, diasteriotopic excess of isoxazolines

Product	R	Total yield (%)	Yield of Diastereomer 1 (%)	Yield of Diastereomer 2 (%)	d.e
7a	OCH_3	54	50	50	1 : 1
7b	CH_3	26	49	51	1 : 1
7c	H	20	48	52	1 : 1
7d	Cl	17	49	51	1 : 1

The observed two diastereoisomers were confirmed through analytical and spectroscopic data (IR, ^{1}H, ^{13}C and 2D NMR spectroscopic technique XHcor). For example, the IR absorptions of two compounds **7'c** and **7"c** at $\nu_{(C=N)}$ = 1635 cm^{-1} indicated the existence of the isoxazoline C=N group. The two spectra **NMR ^{1}H** of two diastereoisomers of **7c** showed a multiplet in the range between 3.70 ppm - 3.97 ppm for CH stereogenic centre (**H_7**). The two spectra **NMR ^{13}C** of two diastereoisomers of **7c** exhibited a signal at 76.43 ppm and 76.47 ppm corresponding to **C_7**, signal to 40.65 ppm and 40.83 ppm relative to **C_8** and signal at 156.50 ppm and 156.40 ppm corresponding to **C_9** (Figure 1).

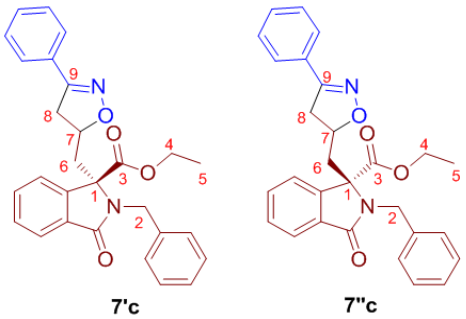


Figure 1

The study of the diastereotopic excess show that we have 50%, 50% from both diastereoisomers **7'** and **7"** (table 1). The predominant of **7** and **7'** during the reaction shows that the cycloaddition steps is on the one hand: regioselective, the oxygen of the nitrile oxide adding over

the α-carbone of the C=C bond of **5**. On other hand is chemoselective, because the addition was proceeds as on only C=C and not on C=O of **5**. This attribution is corroborated by the detection of two $\nu_{(C=O)}$ vibration around 1730 cm^{-1} and 1700 cm^{-1} in the IR spectrum.

3. Conclusion

The present work describes the 1,3-dipolar cycloaddition of arylnitrile oxides to the 1-allyl-2-benzyl-3-oxo-2, 3-dihydro-1H-isoindole-1-ethyl carboxylate affording novel isoxazolines. The 1,3-dipolar cycloaddition reaction occurs chemoselectively and regioselectively to provide two pure diasteromers pure.

4. Experimental

4.1. General methods

Melting points were taken using open capillary tubes and are uncorrected. ^{1}H, ^{13}C, and two-dimensional NMR spectra were recorded on a Bruker 300 MHz instrument in CDCl3 using TMS as an internal standard. Chemical shifts are given in parts per million (δ-scale) and the coupling constants are given in Hertz. Elementary analysis (C, H, N) are realised by Leco Elemental CHN 900. apparatus

4.2. Alkylation with allyl bromide

To a mixture of **4** (5.76 mmol), potassium carbonate (0.95 g, 6.91 mmol), and 30 mL of acetonitrile were added allyl bromide (6.91mmol). The reaction mixture was refluxed over-night. The cooled resulting suspension was filtered off. The filtrate was concentrated in vaccuo, diluted with water, and extracted with dichloromethane (3×30 mL). The organic phase was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (dichloromethane/acetone 90/10) to give **5**.

*4.2.1. Ethyl 1-allyl-2-benzyl-3-oxo-2, 3-dihydro-1H-isoindole-1-carboxylate***s 5**

Yellow liquid; yield: 90%; **NMR ^{1}H (300 MHz, $CDCl_3$, 25 °C)** δ 0.84 (t, J =7.0 Hz, 3H), 2.93 (dd, J = 15.6, J = 6.3Hz, 1H), 3.09 (dd, J = 15.6 Hz, J = 6.3 Hz, 1H), 3.61 (dq, J = 15.6 Hz, J = 7.2 Hz, 1H), 3.83 (dq, J = 15.6 Hz, J = 7.2 Hz, 1H), 4.75 (d, J = 15.5 Hz, 1H), 4.68-4.90 (m, 4H), 7.15-7.51 (m, 8H), 7.81 (d, J = 8.6 Hz, 1H); **NMR ^{13}C (75 MHz, $CDCl_3$, 25 °C)** δ 13.97 (CH_3), 37.37 (CH_2), 45.08 (CH_2), 62.39 (CH_2), 71.57 (Cq), 120.46 (CH_2), 122.031 (CH), 124.34 (CH), 127.89 (CH), 128.73 (CH), 129.41 (CH), 129.44 (CH), 130.35 (CH),132.09 (Cq), 132.44 (CH), 137.45 (Cq), 144.21 (Cq), 169.79 (CO), 170.55 (CO). Anal . Calcd for $C_{21}H_{21}NO_3$ (335.15): C, 75.20; H, 6.31; N, 4.18. Found: C, 75.30; H, 6.22; N, 4.25.

4.3. Cycloaddition of 4-chlorobenzohydroximoyl chloride with 1-allyl-2-benzyl-3-oxo-2, 3-dihydro-1H-isoindole-1-ethyl carboxylate 5

General procedure.: 1-Allyl-2-benzyl-3-oxo-2,3-dihydro-1H-isoindole-1-ethyl carboxylates **5** (1.79 mmol) was dissolved in dichloromethane (7.8 mL). To this solution, para-benzohydroximoyl (1.79 mmol) was added and the mixture was stirred at room temperature. Triethylamine (0.54 mL) was added dropwise to the above mixture and stirring continued for 24 h. The reaction mixture was diluted with water, and extracted with dichloromethane. The organic phase was dried over $MgSO_4$ and evaporated under reduced pressure. The residue subjected to column chromatography on silica gel (dichloromethane/ acetone, 98:2).

4.3.1. Ethyl 2-benzyl-1-[(4,5-dihydro-3-(methoxyphenyl)isoxazole-5-yl) methyl]-3-oxo-2,3dihydro-1H-isoindole-1-carboxylate (7a); Total yield = 54%.

Diastereomer 1: (White solid, yield: 50 %, mp: 151°C); **IR (KBr, cm^{-1})** $\nu_{(C=N)}$ = 1630, $\nu_{(C=O)}$ = 1732, 1693; **NMR ^{1}H (300 MHz, $CDCl_3$, 25°C)** δ 1.10 (t, J = 7.2 Hz, 3H), 2.16-2.37 (m, 3H), 3.02 (dd, J =15.6 Hz, J = 8.1 Hz, 1H), 3.71-3 .75 (m, 1H), 3.79 (s, 3H), 4.02 (q, J = 7.2 Hz, 2H), 4.20 (d, J = 15.3 Hz, 1H), 5.30 (d, J = 15.3 Hz, 1H), 6.81-7.92 (aromatiques protons); **NMR ^{13}C (75MHz, $CDCl_3$, 25 °C)** δ 13.91 (CH_3), 38.48 (CH_2), 40.56 CH_2), 45.07 (CH_2), 55.35 (CH_3), 62.61 (CH_2), 71.67 (Cq), 75.78 (CH), 114.04 ($2CH_2$), 121.80 (Cq), 123.41 (CH), 123.92 (CH), 127.78 (CH), 128.03 (2CH), 128.87 (2CH), 129.22 (CH), 129.46 (2CH), 131.07 (Cq), 132.22 (CH), 138.07 (Cq), 142.83 (Cq), 155.76 (Cq), 160.98 (Cq), 169.90 (CO), 170.05 (CO). Anal . Calcd for $C_{29}H_{28}N_2O_5$ (484.20): C, 71.88; H, 5.82; N, 5.78. Found: C, 71.67; H, 5.75; N, 5.60.

Diastereomer 2 : (White solid, yield: 50 %, mp: 151°C**)**; **IR (KBr, cm^{-1})** $\nu_{(C=N)}$ =1632, $\nu_{(C=O)}$ = 1730, 1695; **NMR ^{1}H (300 MHz, CDCl$_3$, 25°C)** δ 0.83 (t, *J* = 7.2 Hz, 3H), 2.56-2.79 (m, 3H), 3.05 (dd, *J* = 15.3 Hz, *J* = 6.6 Hz, 1H), 3.42 (dq, *J* = 15.6 Hz, *J* = 7.2 Hz, 1H), 3.74 (dq, *J* = 15.6 Hz, *J* = 7.2 Hz, 1H), 3.80 (s, 3H), 3.94-4.00 (m, 1H), 4.58 (d, *J* = 15.3 Hz, 1H), 5.18 (d, *J* = 15.3 Hz, 1H), 6.83-7.97 (aromatic protons); **NMR ^{13}C (75MHz, CDCl$_3$, 25°C)** δ 13.81 (CH_3) 38.45 (CH_2), 41.54 (CH_2), 45.37 (CH_2), 55.73 (CH_3), 62.49 (CH_2), 71.08 (Cq), 76.58(CH), 114.46 (2CH), 121.93 (Cq), 122.14 (CH), 124.86 (CH), 127.93 (CH), 128.44 (2CH), 128.81 (2CH), 129.42 (CH), 129.91 (2CH), 132.26 (Cq), 132.50 (CH), 137.23 (Cq), 144.68 (Cq), 156.41 (Cq), 161.42 (Cq) 169.32 (CO), 170.28 (CO). Anal . Calcd for $C_{29}H_{28}N_2O_5$ (484.20): C, 71.88; H, 5.82; N, 5.78. Found: C, 71.67; H, 5.76; N, 5.61.

4.3.2. Ethyl 2-benzyl-1-[(4,5-dihydro-3-p-tolyl isoxazole-5-yl) méthyl]-3-oxo-2,3dihydro-1H- isoindole-1-carboxylate (**7b**) ; *Total yield = 26 %*

Diastereomer 1: (white solid, yield=49%, mp: 154°C); **IR (KBr, cm^{-1})** $\nu_{(C=N)}$ = 1634, $\nu_{(C=O)}$ = 1726, 1701; **NMR ^{1}H (300 MHz, CDCl$_3$, 25°C)** δ 1.03 (t, *J* = 6.9, 3H), 2.11-2.31 (m, 3H), 2.26 (s, 3H), 2.95 (dd, *J* = 15.6 Hz, *J* = 8.1Hz, 1H), 3.61-3.71 (m, 1H), 3.95 (q, *J* = 6.9 Hz, 2H), 4.12 (d, *J* = 15.6 Hz, 1H), 5.25 (d, *J* = 15.6 Hz, 1H), 7.03-7.85 (aromatic protons); **NMR ^{13}C (75 MHz, CDCl$_3$, 25°C)** δ 14.26 (CH_3), 21.81 (CH_3), 38.85 (CH_2), 40.78 (CH_2), 45.42 (CH_2), 62.85 (CH_2), 72.08 (Cq), 76.24 (CH), 123.75 (CH), 124.28 (CH), 126.5O (Cq), 126.79 (CH), 128.15 (2CH), 129.22 (2CH), 129.57 (2CH), 129.70 (2CH), 129.82 (CH), 131.42 (Cq), 132.57 (CH), 138.42 (Cq), 140.65 (Cq), 143.16 (Cq), 156.48 (Cq), 170.24 (CO), 170.41 (CO). Anal . Calcd for $C_{29}H_{28}N_2O_4$ (468.20): C, 74.34; H, 6.02; N, 5.98. Found: C, 74.45; H, 5.96; N, 5.94.

Diastereomer 2: (white solid; yield = 51%, mp: 154°C); **IR (KBr, cm^{-1})** $\nu_{(C=N)}$ = 1690, $\nu_{(C=O)}$ = 1728, 1703; **NMR ^{1}H (300 MHz, CDCl$_3$, 25°C)** δ 1.10 (t, *J* = 7.2 Hz, 3H), 2.27 (s, 3H), 2.59-2.74 (m, 3H), 2.96 (dd, *J* = 15.3 Hz, *J* = 6.6 Hz, 1H), 3.35 (dq, *J* = 18 Hz, *J* = 7.2 Hz, 1H), 3.67 (dq, *J* = 18 Hz, *J* = 7.2 Hz, 1H), 2.92 (m, 1H), 4.50 (d, *J* = 15.6 Hz, 1H), 5.10 (d, *J* = 15.6 Hz, 1H), 7.06-7.90 (aromatic protons); **NMR ^{13}C (75 MHz, CDCl$_3$, 25°C)** δ 13.81 (CH_3), 21.84 (CH_3), 38.49 (CH_2), 41.43 (CH_2), 45.37 (CH_2), 62.50 (CH_2), 70.07 (Cq), 76.69 (CH), 121.92 (CH), 124.88 (CH), 126.77 (Cq), 126.85 (CH), 127.93 (CH), 128.81 (2CH), 129.42 (2CH), 129.77 (2CH), 129.92 (2CH), 132.26 (Cq), 132.50 (CH), 137.23 (Cq), 140.79 (Cq), 144.05 (Cq), 156.78 (Cq), 169.32 (CO), 170.28 (CO). Anal . Calcd for $C_{29}H_{28}N_2O_4$ (468.20): C, 74.34; H, 6.02; N, 5.98. Found: C, 74.43; H, 5.97; N, 5.94.

4.3.3. Ethyl 2-benzyl-1-[(4,5-dihydro-3-phenyl isoxazole-5-yl) méthyl]-3-oxo-2,3dihydro-1H- isoindole-1-carboxylate (**7c**)**,** *Total yield* = 20 %

Diastereomer 1: (white solid, yield=48 %, mp: 174°C); **IR (KBr, cm^{-1})** $\nu_{(C=N)}$ = 1635, $\nu_{(C=O)}$ = 1731, 1697; **NMR ^{1}H (300 MHz, CDCl$_3$, 25°C)** δ 1.10 (t, *J* = 7.2 Hz, 3H), 2.19-2.40 (m, 3H), 3.03 (dd, *J* = 15.6 HZ, *J* = 8.1 Hz, 1H), 3.70-3.82 (m, 1H), 4.03 (q, *J* = 7.2 Hz, 2H), 4.20 (d, *J* = 15.3 Hz, 1H), 5.34 (d, *J* = 15.3 Hz, 1H), 7.26-7.93 (aromatic protons); **NMR ^{13}C (75 MHz, CDCl$_3$, 25°C)** δ 14.27 (CH_3), 38.90 (CH_2), 40.65 (CH_2), 45.42 (CH_2), 62.88 (CH_2), 72.01 (Cq), 76.43 (CH), 123.75 (CH), 124.28 (CH), 126.84 (CH), 128.17 (2CH), 129.01 (2CH), 129.25 (2CH), 129.58 (2CH), 129.85 (CH), 130.42 (2CH), 131.44 (Cq), 132.59 (CH), 138.44 (Cq), 143.15 (Cq), 156.50 (Cq), 170.23 (CO), 170.38 (CO). Anal . Calcd for $C_{28}H_{26}N_2O_4$ (454.19): C, 73.99; H, 5.77; N, 6.16. Found: C, 73.94; H, 5.72; N, 6.06.

Diastereomer 2: (white solid, yield=52 %, mp: 174°C); **IR (KBr, cm^{-1})** $\nu_{(C=N)}$ = 1635, $\nu_{(C=O)}$ = 1730, 1700; **NMR ^{1}H (300 MHz, CDCl$_3$, 25°C)** δ 0.83 (t, *J* = 7.2 Hz, 3H), 2.59-2.82 (m, 3H), 3.05 (dd, *J* = 15.3 Hz, *J* = 6.6 Hz, 1H), 3.43 (dq, *J* = 15.5 Hz, *J* = 7.2 Hz, 1H), 3.74 (dq, *J* = 15.5 Hz, *J* = 7.2 Hz, 1H), 3.97-4.04 (m, 1H), 4.60 (d, *J* = 15.6 Hz, 1H), 5.18 (d, *J* = 15.6 Hz, 1H),7.30-8.05 (aromatic protons); **NMR ^{13}C (75 MHz, CDCl$_3$, 25°C)** δ 13.40 (CH_3), 38.07 (CH_2), 40.88 (CH_2), 44.96 (CH_2), 62.10 (CH_2), 69.65 (Cq), 76.47 (CH), 121.51 (CH), 124.46 (CH), 126.48 (CH), 127.53 (CH), 128.40 (CH), 128.66 (2CH), 129.00 (2CH), 129.17 (2CH), 129.85 (CH), 130.12 (2CH), 131.83 (Cq), 132.12 (CH), 136.79 (Cq), 143.59 (Cq),156.40 (Cq), 168.90 (CO), 169.83 (CO). Anal . Calcd for $C_{28}H_{26}N_2O_4$ (454.19): C, 73.99; H, 5.77; N, 6.16. Found: C, 73.96; H, 5.73; N, 6.06.

4.3.4. Ethyl 2-benzyl-1-[(3-(chlorophenyl)-4,5-dihydro isoxazole-5-yl) methyl]-3-oxo-2,3dihydro-1H-isoindole-1-carboxylate (**7d**)**,** *Total yield* = 17 %

Diastereomer 1: (White solid, yield = 49 %, mp : 122°C); **IR (KBr, cm^{-1})** $\nu_{(C=N)}$ = 1628, $\nu_{(C=O)}$ = 1725, 1698; **NMR ^{1}H (300 MHz, CDCl$_3$, 25°C)** δ 1.11 (t, *J* = 7.2 Hz, 3H), 2.15-2.38 (m, 3H), 3.08 (dd, *J* = 15.6Hz, *J* = 8.1 HZ, 1H), 3.71-3.80 (m, 1H), 4.04 (q, *J* = 7.2 Hz, 2H), 4.15 (d, *J* = 15.6 Hz, 1H), 4.32 (d, *J* =

15.6 Hz, 1H), 7.26-7.93 (aromatic protons); **NMR ^{13}C (75 MHz, $CDCl_3$, 25°C)** δ 14.27 (CH_3), 38.82 (CH_2), 40.43 (CH_2), 45.45 (CH_2), 62.92 (CH_2), 71.97 (Cq), 76.75 (CH), 123.66 (CH), 124.33 (CH), 128.05 (CH), 128.08 (Cq), 128.17 (2CH), 129.26 (2CH), 129.28 (2CH), 129.61 (2CH), 129.89 (CH), 131.41 (Cq), 132.61 (CH), 136.34 (Cq), 138.43 (Cq), 143.08 (Cq), 155.60 (Cq), 170.22 (CO), 170.35 (CO). Anal . Calcd for $C_{28}H_{25}ClN_2O_4$ (488.15): C, 68.78; H, 5.15; Cl, 7.25; N, 5.73. Found: C, 68.60; H, 6.05; N, 5.55.

Diastereomer 2: (White solid, yield= 51%, mp : 122°C); **IR** (KBr, cm^{-1}) $\nu_{(C=N)}$ = 1632, $\nu_{(C=O)}$ = 1727, 1701; **NMR ^{1}H (300 MHz, $CDCl_3$, 25°C)** δ 0.75 (t, *J* = 7.2 Hz, 3H), 2.48-2.94 (m, 3H), 2.97 (dd, *J* = 15.3 Hz, *J* = 6.6 Hz, 1H), 3.35 (dq, *J* = 15.4 Hz, *J* = 7.2 Hz, 1H), 3.65 (dq, *J* = 15.4 Hz, *J* = 7.2 Hz, 1H), 3.93 (m, 1H), 4.50 (d, *J* = 15.6 Hz, 1H), 5.07 (d, *J* = 15.6 Hz, 1H); **NMR ^{13}C (75 MHz, $CDCl_3$, 25°C)** δ 12.39 (CH_3), 36.99 (CH_2), 39.67 (CH_2), 43.94 (CH_2), 61.12 (CH_2), 68.61 (Cq), 75.61 (CH), 12O.46 (CH), 123.48 (CH), 126.55 (CH), 126.68 (CH),126.92 (Cq), 127.40 (2CH), 127.92 (2CH), 127.99 (2CH), 128.56 (2CH), 130.80 (Cq), 131.13 (CH), 135.01 (Cq), 135.73 (Cq), 142.50 (Cq), 154.48 (Cq), 167.85 (CO), 168.78 (CO). Anal . Calcd for $C_{28}H_{25}ClN_2O_4$ (488.15): C, 68.78; H, 5.15; Cl, 7.25; N, 5.73. Found: C, 68.69; H, 6.04; N, 5.56.

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