Short communication

Three-component Synthesis of Novel Highly Functionalized 2,6-dihydropyrimido[2,1-a]isoindole Derivatives

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Abstract

Three-component reaction of dialkyl acetylenedicarboxylates, isocyanides and 1,3- diimino isoindoline affords highly functionalized 2,6-dihydropyrimido[2,1-a]isoindole derivatives in good yields under catalyst free and mild reaction conditions.

Keywords: Alkyl isocyanides, dialkyl acetylenedicarboxylates, 1,3-diimino isoindoline, 2,6-dihydropyrimido[2,1-a]isoindole derivatives, three-component reaction.

1. Introduction

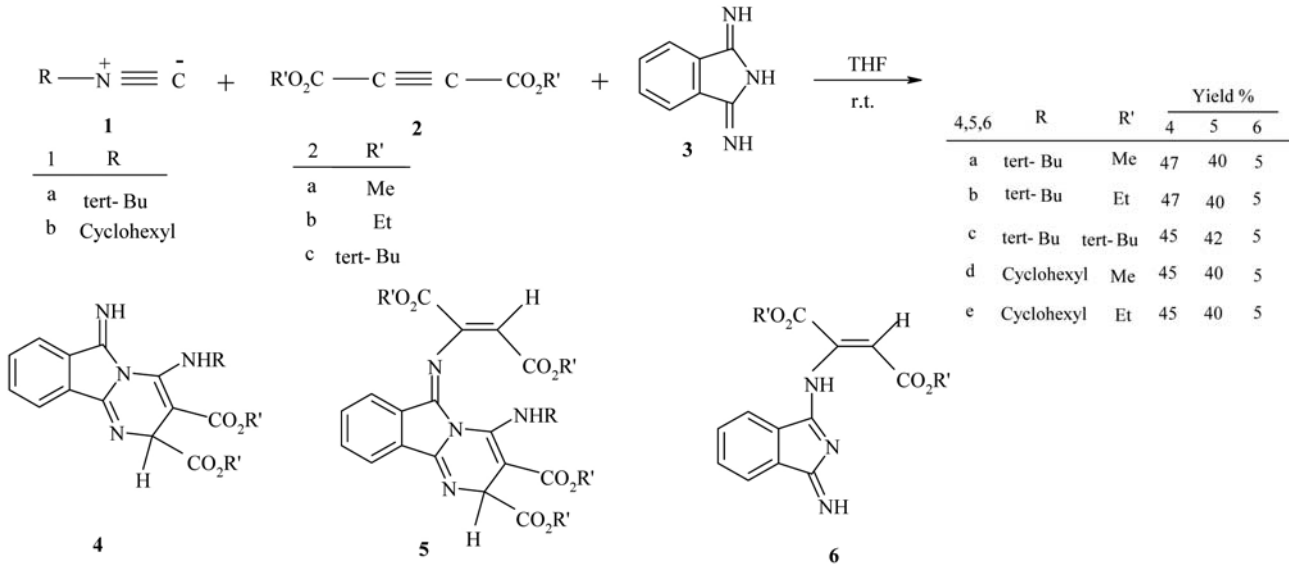
Multi-component (MCR) reactions play an important role in the synthesis of various N-containing heterocyclic compounds,[1,2] and become a widespread area of research in organic, combinatorial, and medicinal chemistry.[3] The MCR strategy offers significant advantages over the conventional linear-type synthesis due to its flexibility, convergence, atom efficient nature and the fast assembly of poly-substituted systems without isolation of unstable intermediates.[1, 4]

Pyrimidines and fused pyrimidines are important classes of heterocyclic compounds exhibiting a broad spectrum of biological activities.[5–8] Among them, pyrimido indoles and pyrimido isoindoles are well known for their potential biological and pharmalogical activities, [9,10] such as analgesic, anti-allergy, bactericide, infective, antihypertensive, anti-inflammatory, antitumor, anti-HIV activities as well as their synthetic applications.[11,12] In recent years, the synthesis and synthetic applications of the pyrimidine derivatives have been widely investigated.[13–16] In spite of developments in the chemistry of fused pyrimidines, little attention has been paid to the synthesis of pyrimido[2,1-a]isoindoles.[17] The development of a new and effective synthetic method for preparation of heterocyclic compounds containing pyrimidine ring fragments is therefore, an interesting challenge. Due to the biological activity of fused pyrimidines, and our interest in the synthesis of heterocyclic compounds, [18–22] herein, we report a simple and efficient method for the preparation of novel 2,6-dihydropyrimido[2,1-a]isoindole derivatives.

2. Results and Discussion

Alkyl isocyanides (**1**), dialkyl acetylenedicarboxylates (**2**) and 1,3-diimino isoindoline (**3**) undergo a smooth 1:1:1 or 1: 2:1 additional reaction in THF at room temperature, to produce 2,6- dihydro[2,1-a]isoindole derivatives (**4**) and (**5**) in good yields along with N-vinyl isoindoles (**6**) as by-product (Scheme 1).

The structures of the compounds **4a-e** and **5a-e** were deduced from their IR and high-field ^{1}H and ^{13}C NMR spectra. The mass spectra of **4a** and **5a** display the molecular ion (M^+) peak at 370 and 512 m/z, respectively, which are consistent with a 1:1:1 or 1:2:1 adduct of *tert*-butyl isocyanide, dimethyl acetylene dicarboxylate, and 1,3-diimino isoindoline. The ^{1}H NMR spectrum of **4a** exhibits four sharp lines arising from tert-butyl (δ = 1.57 ppm), two methoxy (δ = 3.68 and 3.78 ppm) and methine (δ =5.86 ppm) protons which are readily recognized. Furthermore, two broad singlets were observed for the two NH groups, along with characteristic multiplet signals for the aromatic protons. Upon the addition of a drop of D_2O to the NMR tube containing $CDCl_3$ solution of **4a** the latter signal disappeared. Additionally, the proton decoupled ^{13}C NMR spectrum of **4a** shows 17 distinct resonances in agreement

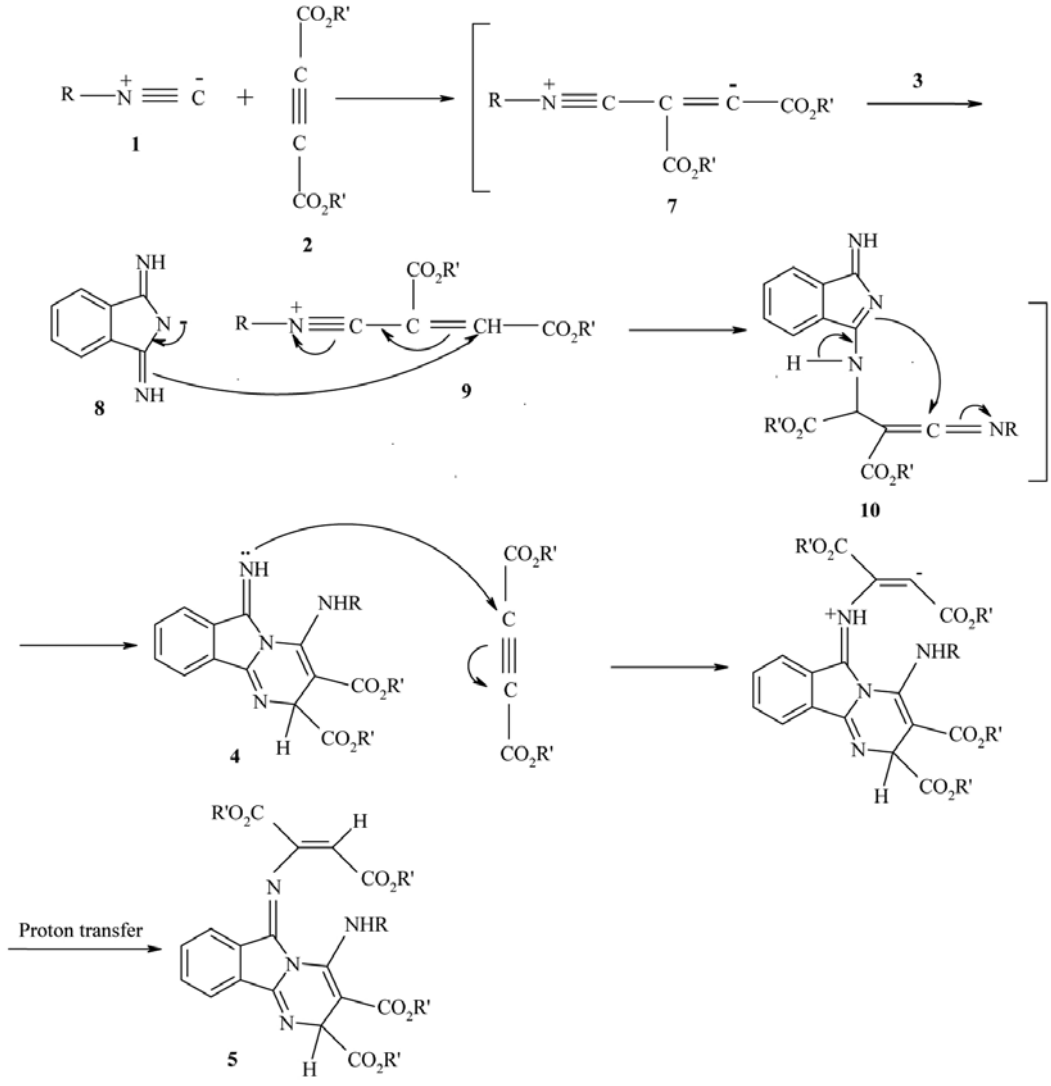


1	R
a	tert- Bu
b	Cyclohexyl

2	R'
a	Me
b	Et
c	tert- Bu

4,5,6	R	R'	Yield % 4	5	6
a	tert- Bu	Me	47	40	5
b	tert- Bu	Et	47	40	5
c	tert- Bu	tert- Bu	45	42	5
d	Cyclohexyl	Me	45	40	5
e	Cyclohexyl	Et	45	40	5

Scheme 1



Scheme 2

with the proposed structure. The partial assignment of these resonances is provided in the experimental section. The ^{1}H NMR spectrum of the compound **5a** is similar to that of **4a**, except that one of the NH groups, which was replaced by a N-vinyl group that exhibits three singlets for two methoxy groups and a vinylic (δ =5.79 ppm) proton.

The ^{1}H and ^{13}C NMR spectra of compounds **4b-e** and **5b-e** are similar to those of **4a** and **5a**, respectively, except for the alkylamino and ester moieties, which exhibit their characteristic signals with appropriate chemical shifts (see experimental section).

Although we have not established the mechanism of the reaction between isocyanides and acetylenic esters in the presence of compound **3** in an experimental manner, a plausible mechanism is proposed in Scheme 2. Based on the well stablished chemistry of isocyanides, it is reasonable to assume that the functionalized 2,6- dihydropyrimido[2,1-a]isoindoles **4** apparently resulted from the initial additions of the isocyanide to the acetylenic ester and subsequent protonation of the 1:1 adduct **7** by compound **3**, followed by the conjugate addition of the anion of the NH-acid **8** on the positively charged ion **9** to form ketenimine **10**. The ketenimine intermediate **10** can be cyclized *via* an intramolecular attack of the NH-acid on the Csp of the ketenimine under the reaction conditions employed to produce the fused ring system **4**. The reaction of the product **4** with another molecule of acetylenic ester generates the highly functionalized *N*-vinyl derivatives of **5**.

3. Experimental

Dialkyl acetylene dicarboxylates, *tert*-butyl isocyanide, cyclohexyl isocyanide and 1,3-diimino isoindoline were obtained from Fluka (Buchs, Switzerland) and were used without further purification. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. ^{1}H, ^{13}C NMR spectra was measured with Bruker DRX-400 Advance spectrometers. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a FT-IR BRUKER VECTOR 22 spectrometer.

General procedure for the synthesis of 2,6-dihydropyrimido[2,1-a]isoindole derivatives (4a) and (5a)

To a magnetically stirred solution of 0.28 g of dialkyl acetylenedicarboxylate (2 mmol) and 0.29 g of 1,3-diimino isoindoline (2 mmol) in 10 mL THF was added dropwise a solution of 0.166 g of alkyl isocyanide (2 mmol) in 2 mL THF at room temperature over 10 min. The reaction mixture was stirred for 48 h. The solvent was then removed under reduced pressure and the desired compounds were separated from the resultant residue by silica gel column chromatography (Merck 230–400 mesh) using n-hexane: ethyl acetate mixture as an eluant.

Dimethyl 4-(tert-butylamino)-6-imino-2,6-dihydropyrimido[2,1-a]isoindole-2,3-dicarboxylate (4a): Orange powder, m.p. 120–122 °C, yield 47%, IR (KBr) (ν_{max}, cm^{-1}): 3330–3530 (NH), 1620–1750 (C=O); MS, m/z (%): 370 (M$^+$, 3), 353 (18), 311 (100), 255) 92), 223 (39), 57 (14); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ_H 1.57 [9H, s, $C(CH_3)_3$], 3.68 and 3.78 (6H, 2s, 2 OCH_3), 5.86 (1H, s, NCH), 7.69–8.01 (4H, m, 4 CH, Ar), 8.73 and 9.23 (2H, 2br s, 2 NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ_C 30.92 (C (CH_3)$_3$), 50.69 and 50.85 (2 OCH_3), 52.53 (NCMe$_3$), 52.82 (NCH), 72.46 (N-C=*C*), 121.78, 123.16, 132.18 and 132.82 (4 CH, Ar),131.32 and 133.11 (2 C, Ar), 155.95 (C=NH), 158.68 (N-C=N), 158.83 (N-C-NH), 168.88 and 171.28(2 C=O).

Diethyl 4-(tert-butylamino)-6-imino-2,6-dihydropyrimido[2,1-a]isoindole-2,3-dicarboxylate (4b): Orange powder, m.p. 123–125 °C, yield 47%, IR (KBr) (ν_{max}, cm^{-1}): 3300–3500 (NH), 1620–1730 (C=O); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ_H 1.24 and 1.35 (6H, 2t, $^3J_{HH}$=7.2 Hz, 2 CH_3), 1.57 [9H, s, $C(CH_3)_3$], 4.08–4.32 (4H, m, 2 OCH_2), 5.84 (1H, s, NCH), 7.67–8.00 (4H, m, 4 CH, Ar),8.65 and 9.32 (2H, 2br s, 2 NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ_C 14.08 and 14.73 (2 CH_3), 30.94 (C(CH$_3$)$_3$), 51.00 (NCMe$_3$), 52.74 (NCH), 59.15 and 61.39 (2 OCH_2), 72.62 (N-C=*C*), 121.72, 123.13, 132.12 and 132.72 (4 CH, Ar), 131.86 and 133.15 (2 C, Ar), 155.86 (C=NH), 158.60 (N-C=N), 158.75 (N-C-NH), 168.58 and 170.95 (2 C=O).

Di(tert-butyl) 4-(tert-butylamino)-6-imino-2,6 dihydropyrimido[2,1a]isoindole-2,3-dicarboxylate (4c): Orange powder, m.p. 137–140 °C, yield 45%, IR (KBr) (ν_{max}, cm^{-1}): 3330–3520 (NH), 1620–1730 (C=O); MS, m/z (%): 454(M$^+$, 5), 353 (44), 297 (100), 241) 61), 57 (36); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ_H 1.42, 1.56 and 1.57 (27H, 3s, 3C(CH_3)$_3$), 5.58 (1H, s, NCH), 7.65–7.98 (4H, m, 4 CH, Ar), 8.56 and 9.17 (2H, 2br s, 2 NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ_C 28.06, 28.78 and 31.04 (3C(CH_3)$_3$), 50.77 (NCMe$_3$), 52.53 (NCH), 74.56 (N-C=*C*), 79.01 and 81.97 (2 OCMe$_3$), 121.79, 122.96, 131.92 and 132.50 (4 CH, Ar), 130.85 and 133.30 (2 C, Ar), 150.40 (C=NH), 156.11 (N-C=N), 158.44 (N-C-NH), 168.30 and 170.09 (2 C=O).

Dimethyl 4-(cyclohexylamino)-6-imino-2,6-dihydropyrimido[2,1a]isoindole-2,3-dicarboxylate (4d): Orange powder, m.p. 176–180 °C, yield 45%, IR (KBr) (ν_{max}, cm^{-1}): 3350–3520 (NH), 1600–1730 (C=O); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ_H 1.26–2.08 [10H, m, CH(CH_2)$_5$], 3.68 and 3.78 (6H, 2s, 2 OCH_3), 4.27–4.34 (1H, m, NHC*H*), 5.89 (1H, s, NCH), 7.68–8.04 (4H, m, 4 CH, Ar), 8.56 and 9.07 (2H, 2 br s, 2 NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ_C 24.71, 24.79, 25.70, 33.73 and 34.24 (5 CH_2), 49.50 (NHCH), 50.63 and 50.87 (2 OCH_3), 52.52 (NCH), 71.82 (N-C=*C*), 121. 69, 123.34, 132.11

and 132.82 (4 CH, Ar), 131.34 and 133.02 (2 C, Ar), 157.14 (C=NH), 157.36 (N-C=N), 158.81 (N-C-NH), 168.76 and 171.30 (2 C=O).

Diethyl 4-(cyclohexylamino)-6-imino-2,6-dihydropyrimido[2,1-a]isoindole-2,3-dicarboxylate (4e): Orange powder, m.p. 152–155 °C, yield 45%, IR (KBr) (ν_{max}, cm^{-1}): 3330–3530 (NH), 1600–1720 (C=O); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ_H 1.23 and 1.35 (6H, 2t, $^3J_{HH}$=7.2 Hz, 2 CH_3), 1.26–2.07 [10H, m, CH(CH_2)$_5$], 4.13 (2H, q, $^3J_{HH}$=7.2 Hz, OCH_2), 4.17–4.23 (1H, m, NHC*H*), 4.24–4.32 (2H, m, OCH_2), 5.82 (1H, s, NCH), 7.69–8.03 (4H, m, 4 CH, Ar), 8.52 and 9.08 (2H, 2 br s, 2 NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ_C 14.08 and 14.72 (2 CH_3), 24.74, 24.82, 25.68, 33.74 and 34.27 (5 CH_2), 49.45 (NHCH), 51.04 (NCH), 59.09 and 61.37 (2 OCH_2), 71.99 (N-C=*C*), 121.64, 123.31, 132.05 and 132.73 (4 CH, Ar), 131.51 and 133.07 (2 C, Ar), 157.04 (C=NH), 157.27 (N-C=N), 158.82 (N-C-NH), 168.47 and 170.99 (2 C=O).

Dimethyl 4-(tert-butylamino)-6-{[(E)-3-methoxy-1-(methoxycarbonyl)-3-oxo-1-propenyl]imino}-2,6-dihydropyrimido[2,1a]isoindole-2,3-dicarboxylate(5a): Red powder, m.p. 143–146 °C, yield 40%, IR (KBr) (ν_{max}, cm^{-1}): 3380–3450 (NH), 1620–1700 (C=O); MS, m/z (%): 512 (M^+, 3), 453 (70), 438 (50), 394) 100), 57 (20); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ_H 1.56 [9H, s, C(CH_3)$_3$], 3.66, 3.78, 3.79 and 3.90 (12H, 4s, 4 OCH_3), 5.51 (1H, s, NCH), 5.79 (1H, s, CH), 7.67–8.27 (4H, m, 4 CH, Ar), 9.22(1H, br s, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ_C 30.92(C(*C*H_3)$_3$), 50.75, 51.14, 51.86 and 52.53 (4 OCH_3), 52.90 (N-*C*Me_3), 53.06 (NCH), 72.81 (N-C=*C*), 104.45 (C=*C*H), 123.50, 126.33, 132.68 and 133.03 (4 CH, Ar), 128.61 and 134.21 (2 C, Ar), 151.89 (*C*=CH), 152.96 (C=NH), 155.28 (N-C=N), 158.23 (N-C-NH), 165.12, 165.67, 168.85 and 170.96 (4 C=O).

Diethyl 4-(tert-butylamino)-6-{[(E)-3-ethoxy-1-(ethoxycarbonyl)-3-oxo-1-propenyl]imino}-2,6-dihydropyrimido[2,1-a]isoindole-2,3-dicarboxylate (5b): Red powder, m.p. 136–139 °C, yield 40%, IR (KBr) (ν_{max}, cm^{-1}): 3400–3500 (NH), 1600–1730 (C=O); MS, m/z (%): 568 (M^+, 75) 495 (100), 439 (25), 57(25); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ_H 1.23, 1.32, 1.34 and 1.35 [12H, 4t, $^3J_{HH}$=7.2 Hz, 4 CH_3], 1.63 [9H, s, C(CH_3)$_3$], 4.05–4.33 (6H, m, 3 OCH_2), 4.35(2H, q, $^3J_{HH}$=7.2 Hz, OCH_2), 5.48 (1H, s, NCH), 5.79 (1H, s, CH), 7.64–8.27 (4H, m, 4 CH, Ar), 9.32 (1H, br s, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ_C 13.93, 14.08, 14.19 and 14.76 (4 CH_3), 30.94 (C(*C*H_3)$_3$), 51.27 (N*C*Me_3), 52.81 (NCH), 59.24, 60.68, 61.38 and 62.33(4 OCH_2), 73.04 (N-C=*C*), 104.59 (C=*C*H) 123.40, 126.36, 132.54 and 132.88 (4 CH, Ar), 128.61 and 134.23 (2 C, Ar),151.86 (*C*=CH), 153.06 (C=NH), 155.28 (N-C=N), 158.20 (N-C-NH), 164.68, 165.20, 168.56 and 170.62 (4 C=O).

Di(tert-butyl) 6-{[(E)-3-(tert-butoxy)-1-(tert-butoxycarbonyl)-3-oxo-1-propenyl]imino}-4-(tert-butylamino)-2,6-dihydropyrimido[2,1-a]isoindole-2,3-dicarboxylate (5c): Red powder, m.p. 169–173 °C, yield 42%, IR (KBr) (ν_{max}, cm^{-1}): 3380–3520 (NH), 1600–1750 (C=O); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ_H 1.41, 1.51, 1.52, 1.55 and 1.57 (45H, 5s, 5 C(CH_3)$_3$), 5.34 (1H, s, NCH), 5.58 (1H, s, CH), 7.61–8.24 (4H, m, 4 CH, Ar), 9.15 (1H, br s, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ_C 27.93, 28.11, 28.22, 28.77 and 31.04 (5 C(*C*H_3)$_3$), 52.17 (N*C*Me_3), 52.55 (NCH), 74.71 (N-C=*C*), 78.98, 80.65, 81.70 and 83.48 (4 O*C*Me_3), 105.88 (C=*C*H), 123.08, 126.56, 132.13 and 132.45 (4 CH, Ar), 127.36 and 134.34 (2 C, Ar), 151.86 (*C*=CH), 152.50 (C=NH), 156.40 (N-C=N), 158.10 (N-C-NH), 163.47, 164.58, 168.33 and 170.06 (4 C=O).

Dimethyl 4-(cyclohexylamino)-6-{[(E)-3-methoxy-1-(methoxycarbonyl)-3-oxo-1-propenyl]imino}-2,6-dihydropyrimido[2,1-a]isoindole-2,3-dicarboxylate(5d): Red powder, m.p. 127–130 °C, yield 40%, IR (KBr) (ν_{max}, cm^{-1}): 3320–3520 (NH),1600–1720 (C=O); MS, m/z (%): 538 (M^+, 57), 479(100), 305(13), 252 (10); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ_H 1.62–2.06 [10H, m, CH(CH_2)$_5$], 3.65, 3.78, 3.79 and 3.90 [12H, 4s, 4 OCH_3], 4.24–4.31 (1H, m, NHC*H*), 5.50 (1H, s, NCH), 5.78 (1H, s, CH), 7.65–8.25 (4H, m, 4 CH, Ar), 9.06 (1H, br d, $^3J_{HH}$=8 Hz, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ_C 24.68, 24.77, 25.63,, 33.68 and 34.26 (5 CH_2), 49.59 (NHCH), 50.70, 51.19, 51.86 and 52.51 (4 OCH_3), 53.07 (NCH), 72.14 (N-C=*C*), 104.45 (C=*C*H), 123.68, 126.29, 132.64 and 133.05 (4 CH, Ar), 128.61 and 134.13 (2 C, Ar), 151.78 (*C*=CH), 152.91(C=NH), 156.40 (N-C=N), 156.90 (N-C-NH), 165.13, 165.67, 168.72 and 170.98 (4 C=O).

Diethyl 4-(cyclohexylamino)-6-{[(E)-3-ethoxy-1-(ethoxycarbonyl)-3-oxo-1-propenyl]imino}-2,6-dihydropyrimido[2,1-a]isoindole-2,3-dicarboxylate (5e): Red powder, m.p. 125–128 °C, yield 40%, IR (KBr) (ν_{max}, cm^{-1}): 3300–3530 (NH), 1600–1780 (C=O); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ_H 1.22 [3H, t, $^3J_{HH}$ = 7.2 Hz, CH_3], 1.27–1.37 (9H, 3t, $^3J_{HH}$ = 7.2 Hz, 3 CH_3), 1.38–2.07 [10H, m, CH(CH_2)$_5$], 4.06–4.33 (4H, m, 2 OCH_2), 4.24 and 4.33 (4H, 2q, $^3J_{HH}$=7.2 Hz 2 OCH_2) 4.67 (1H, m, NHC*H*), 5.48 (1H, s, NCH), 5.78 (1H, s, CH), 7.64–8.27 (4H, m, 4 CH, Ar), 9.07 (1H, br d, $^3J_{HH}$ = 8 Hz NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ_C 13.93, 14.09, 14.19 and 14.76 (4 CH_3), 24.72, 24.80, 25.66, 33.69 and 34.31 (5 CH_2), 49.57 (NHCH), 51.32 (NCH), 59.18, 60.68, 61.37 and 62.34 (4 OCH_2), 72.38 (N-C=*C*), 104.61 (C=*C*H),123.58, 126.33, 132.50 and 132.90 (4 CH, Ar),130.28 and 134.15 (2 C, Ar), 151.76 (*C*=CH), 153.00 (C=NH), 156.41 (N-C=N), 156.87 (N-C-NH), 164.69, 165.20, 168.43 and 170.65 (4 C=O).

Dimethyl (E)-2-[(3-imino-2,3-dihydro-1H-isoindol-1-yliden)amino]-2-butenedioate (6a): Yellow powder, m.p. 165–166 °C, yield 5%, IR (KBr) (ν_{max}, cm^{-1}): 3500–3650 (NH), 1620–1730 (C=O); ^{1}H NMR (400.13 MHz, DMSO–d_6): δ_H 3.64 and 3.74 (6H, 2s, 2 OCH_3), 5.85 (1H, s, CH), 7.60 (2H, m, 2 CH, Ar), 7.72 and 7.91 (2H, 2m, 2 CH, Ar), 9.11 (2H, br s, 2 NH); ^{13}C NMR (100.61 MHz, DMSO–d_6): δ_C 51.71 and 52.52 (2 OCH_3), 109.39 (C=*C*H), 121.88, 122.28, 131.38 and 132.09(4 CH, Ar), 135.45 and 139.92 (2 C, Ar), 155.24 (*C*=CH), 166.30 and 166.98 (2 C=N), 170.01 and 172.77 (2 C=O).

Diethyl (E)-2-[(3-imino-2,3-dihydro-1H-isoindol-1-yliden)amino]-2-butenedioate (6b): Yellow powder, m.p. 134–135 °C, yield 5%, IR (KBr) (ν_{max}, cm^{-1}): 3320–3520 (NH), 1600–1730 (C=O); Ms, m/z (%): 315(M^+, 75), 270 (33), 243 (91), 196 (50), 170 (54), 129 (100); ^{1}H NMR (400.13 MHz, DMSO–d_6): δ_H 1.20 and 1.24 (6H, 2t, $^3J_{HH}$=7.2 Hz, 2 CH_3), 4.09 and 4.20 (4H, 2q, $^3J_{HH}$=7.2 Hz, 2 OCH_2), 5.80 (1H, s, CH), 7.57–7.62 (2H, m, 2 CH, Ar), 7.69–7.92 (2H, 2m, 2CH, Ar), 9.05 and 9.17 (2H, 2s, 2 NH); ^{13}C NMR (100.61 MHz, DMSO–d_6): δ_C 14.23 and 14.60 (2 CH_3), 60.19 and 61.20 (2 OCH_2), 109.16 (C=*C*H), 121.83, 122.26, 131.34 and 132.05 (4 CH, Ar), 135.50 and 139.97 (2 C, Ar), 155.34 (*C*=CH), 165.82 and 166.39 (2 CN), 170.00 and 172.86 (2 C=O).

Di(tert-butyl)(E)-2-[(3-imino-2,3-dihydro-1H-isoindol-1-yliden)amino]-2-butenedioate (6c): Yellow powder, m.p.167–168 °C, yield 5%, IR (KBr) (ν_{max}, cm^{-1}): 3350–3520 (NH), 1620–1750 (C=O); ^{1}H NMR (400.13 MHz, DMSO–d_6): δ_H 1.44 and 1.45 (18H, 2s, 2 OC*Me*$_3$), 5.62(1H, s, CH), 7.60 (2H, m, 2 CH, Ar), 7.72 and 7.91 (2H, 2m, 2 CH, Ar), 8.92 and 9.03 (2H, 2s, 2 NH); ^{13}C NMR (100.61 MHz, DMSO–d_6): δ_C 28.11 and 28.33 (2 OC*Me*$_3$), 79.95 and 81.43 (2 O*C*Me$_3$), 109.77 (C=*C*H), 121.67, 122.19, 131.16 and 131.88 (4 CH, Ar), 135.60 and 139.98 (2 C), 154.93 (*C*=CH), 165.18 and 165.33 (2 C=N), 168.89 and 172.62 (2 C=O).

4. Conclusion

In summary, the reaction between alkyl isocyanides and dialkyl acetylene dicarboxylates in the presence of 1,3-diimino isoindoline provides a simple one-pot entry into the synthesis of polyfunctional 2,6-dihydro[2,1-a]isoindole derivatives of potential synthetic and pharmaceutical interest. The present method carries the advantage that, not only is the reaction performed under neutral condition, but also the substances can be mixed without any activation or modification. The simplicity of the present procedure makes this protocol an interesting alternative to other approaches.

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Povzetek

V prispevku je opisana priprava visoko-funkcionaliziranih 2,6-dihidropirimido [2,1-a]izoindolnih derivatov s trokomponentno reakcijo med dialkilacetilendikarboksilati, izocianidiin 1,3-diiminoizoindolini. Reakcija poteka z dobrimi izkoristki, brez katalizatorja in pri milihpogojih.