

## Unexpected synthesis of indolo[1,2-*c*]quinazolines by a sequential Ugi 4CC–Staudinger–aza–Wittig–nucleophilic addition reaction†

Ping He, Yi-Bo Nie, Jing Wu and Ming-Wu Ding\*

Received 9th October 2010, Accepted 16th November 2010

DOI: 10.1039/c0ob00855a

A new sequential Ugi–Staudinger–aza–Wittig–nucleophilic addition reaction was developed to construct indolo[1,2-*c*]quinazoline derivatives, starting from the easily accessible 2-azidobenzaldehyde, carboxylic acid, 2-acylaniline and isocyanide. It is noteworthy that this is the first report of the cyclization of the Ugi adduct to give a dihydroindole ring system with two quaternary carbon centers, *via* the nucleophilic addition reaction of the methine group to the carbonyl group.

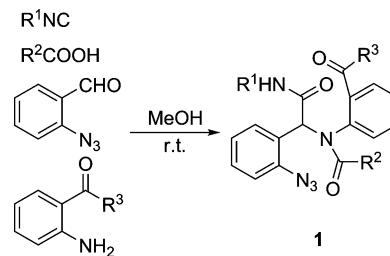
### Introduction

The Ugi reaction is a powerful and atom-economical way to construct complex structures from the four readily accessible component starting materials isonitrile, amine, aldehyde and carboxylic acid.<sup>1</sup> The sequence of Ugi isocyanide multicomponent reaction, followed by post-condensation transformations, constitutes an extremely powerful synthetic tool for the preparation of structurally diverse complex molecules, especially heterocyclic compounds.

The aza–Wittig reactions of iminophosphoranes have received increased attention in view of their utility in the synthesis of N-heterocycles.<sup>2</sup> Recently the sequence of Ugi and Passerini reaction, followed by post-condensation Staudinger and aza–Wittig reaction, has been utilized in synthesis of a series of biologically useful heterocycles.<sup>3–10</sup> For example, 2-azidobenzoic acid or other azido acids were successfully used in an Ugi 4CC–Staudinger–aza–Wittig sequence to generate heterocycles such as dibenzo[*b,f*]-1,5-diazocine-6(5*H*)-ones,<sup>3</sup> 1,4-benzodiazepine-5-ones<sup>4</sup> and 5-oxo-1,4-diazepines<sup>5</sup> by García-Valverde and Torroba. 2-Azidobenzaldehyde or α-azido aldehydes were also utilized in sequential Passerini 3CC or Ugi 4CC–Staudinger–aza–Wittig reaction in synthesis of 4*H*-3,1-benzoxazine,<sup>6</sup> 3,4-dihydroquinazolines<sup>7</sup> and oxazolines<sup>8</sup> by Basso and by us. Continuing our interest in the synthesis of various heterocycles *via* aza–Wittig reaction,<sup>11</sup> we wish to report herein an unexpected synthesis of previously unreported indolo[1,2-*c*]quinazolines by a sequential Ugi 4CC–Staudinger–aza–Wittig–nucleophilic addition reaction.

### Results and discussion

Initially, the Ugi reactions of 2-azidobenzaldehyde, carboxylic acid, 2-acylaniline with isocyanide were carried out smoothly in methanol at room temperature (Scheme 1). In many cases the reaction products precipitate during the reaction and the azides **1** were obtained after recrystallization (Table 1). As indicated in Table 1, most of the Ugi reaction products **1** were obtained in satisfactory yields; relatively lower yields were observed when *ortho*-substituted benzoic acids were used (**1d**, **1e**, **1o**), which is probably due to the steric hindrance of the *ortho*-substituent.



Scheme 1 Synthesis of azides **1** by Ugi reaction.

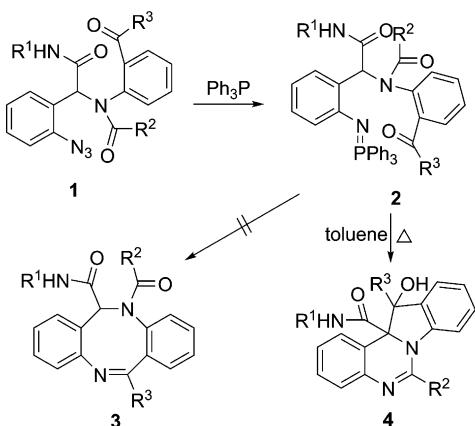
The reactions of azides **1** with triphenylphosphine were examined in toluene at room temperature for 2 h, followed by heating at reflux for 6–24 h. Nitrogen evolution *via* the Staudinger reaction had ceased during the first 2 h. To our surprise, the final products indolo[1,2-*c*]quinazolines **4** were obtained directly from the reaction mixture (Scheme 2). The results are listed in Table 2. As indicated in Table 2, the required heating time is related to the R<sup>2</sup> substituent: a shorter time (6–8 h) is needed when R<sup>2</sup> is an alkyl group (compounds **4i**, **4j**, **4k** and **4p**) whereas a longer time (10–24 h) is required when R<sup>2</sup> is an aromatic group. The structure of the indolo[1,2-*c*]quinazolines **4** was confirmed by their spectral data. Furthermore a single crystal of **4e** was obtained from a CH<sub>2</sub>Cl<sub>2</sub> solution of **4e**. X-Ray structural analysis verified the proposed structure and showed the intramolecular hydrogen

Key Laboratory of Pesticide & Chemical Biology of Ministry of Education, Central China Normal University, Wuhan, 430079, P. R. China. E-mail: mwding@mail.ccnu.edu.cn; Fax: (+86)-27-67862041; Tel: (+86)-27-67867958

† Electronic supplementary information (ESI) available: NMR spectra of **1a–r** and **4a–r**. CCDC reference numbers 784275 (**4e**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0ob00855a

**Table 1** Preparation of azides **1** via Ugi 4CC reaction

	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Reaction time (h)	Yield (%) <sup>a</sup>
<b>1a</b>	n-Bu	Ph	Me	20	85
<b>1b</b>	n-Bu	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	Me	20	91
<b>1c</b>	n-Bu	4-CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub>	Me	20	83
<b>1d</b>	n-Bu	2-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	Me	24	60
<b>1e</b>	n-Bu	2-Cl-C <sub>6</sub> H <sub>4</sub>	Me	24	58
<b>1f</b>	n-Bu	4-Cl-C <sub>6</sub> H <sub>4</sub>	Me	20	90
<b>1g</b>	n-Bu	3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	20	92
<b>1h</b>	n-Bu	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	20	85
<b>1i</b>	n-Bu	PhCH <sub>2</sub> CH <sub>2</sub>	Me	16	90
<b>1j</b>	n-Bu	CH <sub>3</sub> CH <sub>2</sub>	Me	16	84
<b>1k</b>	n-Bu	2,4-2Cl-C <sub>6</sub> H <sub>3</sub> OCH <sub>2</sub>	Me	16	88
<b>1l</b>	t-Bu	Ph	Me	20	78
<b>1m</b>	t-Bu	3,5-2CH <sub>3</sub> -C <sub>6</sub> H <sub>3</sub>	Me	20	80
<b>1n</b>	t-Bu	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	20	85
<b>1o</b>	t-Bu	2-Cl-C <sub>6</sub> H <sub>4</sub>	Me	24	55
<b>1p</b>	t-Bu	PhCH <sub>2</sub> CH <sub>2</sub>	Me	16	70
<b>1q</b>	c-C <sub>6</sub> H <sub>11</sub>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	Et	20	80
<b>1r</b>	c-C <sub>6</sub> H <sub>11</sub>	Ph	Et	20	85

<sup>a</sup> Isolated yields based on 2-azidobenzaldehyde.**Scheme 2** Synthesis of indolo[1,2-c]quinazolines **4** by a tandem Staudinger–aza-Wittig–nucleophilic addition reaction.

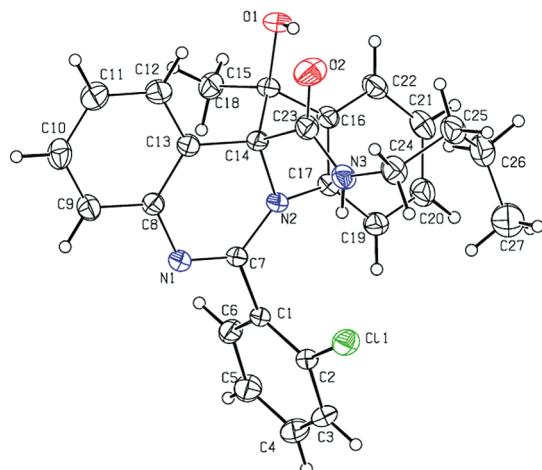
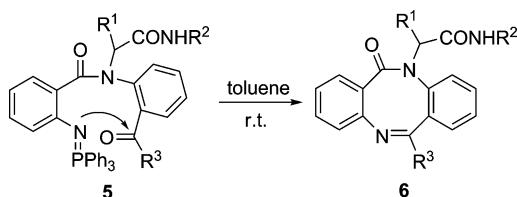
bond formation between the hydroxy hydrogen (O1H) and the amido oxygen (O2) (Fig. 1).

Intramolecular aza-Wittig reaction between an iminophosphorane and a ketone carbonyl group generally takes place easily to form five to seven or even eight membered heterocycles.<sup>12</sup> For example, the cyclization of iminophosphorane **5** gave dibenzo[b,f][1,5]diazocine **6** in good yield in toluene at room temperature (Scheme 3).<sup>3</sup> The initial purpose of this research was to prepare the eight membered benzodiazocine **3** by intramolecular aza-Wittig reaction of **2** between the iminophosphorane group and the ketone carbonyl (R<sup>3</sup>CO) (Scheme 2). But under our experimental conditions, no benzodiazocine **3** was detected and indolo[1,2-c]quinazoline **4** was obtained instead. This is probably due to the restricted conformation of the iminophosphorane **2** that could be entropically unfavorable for the cyclization between the iminophosphorane moiety and the ketone carbonyl group.

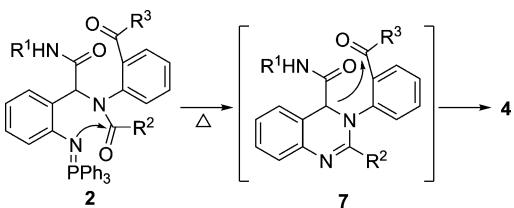
A possible mechanism for the tandem formation of indolo[1,2-c]quinazolines **4** is proposed (Scheme 4). It presumably involves the formation of quinazoline intermediate **7** through the intramolecular aza-Wittig reaction of **2** between its iminophosphorane moiety and the amide group. Further intramolecular nucleophilic attack

**Table 2** Preparation of indolo[1,2-c]quinazolines **4** by tandem Staudinger–aza-Wittig–nucleophilic addition

	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Reaction time (h)	Yield (%) <sup>a</sup>
<b>4a</b>	n-Bu	Ph	Me	12	80
<b>4b</b>	n-Bu	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	Me	16	72
<b>4c</b>	n-Bu	4-CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub>	Me	16	70
<b>4d</b>	n-Bu	2-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	Me	16	74
<b>4e</b>	n-Bu	2-Cl-C <sub>6</sub> H <sub>4</sub>	Me	16	75
<b>4f</b>	n-Bu	4-Cl-C <sub>6</sub> H <sub>4</sub>	Me	16	84
<b>4g</b>	n-Bu	3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	10	86
<b>4h</b>	n-Bu	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	10	86
<b>4i</b>	n-Bu	PhCH <sub>2</sub> CH <sub>2</sub>	Me	6	90
<b>4j</b>	n-Bu	CH <sub>3</sub> CH <sub>2</sub>	Me	6	92
<b>4k</b>	n-Bu	2,4-2Cl-C <sub>6</sub> H <sub>3</sub> OCH <sub>2</sub>	Me	6	88
<b>4l</b>	t-Bu	Ph	Me	16	70
<b>4m</b>	t-Bu	3,5-2CH <sub>3</sub> -C <sub>6</sub> H <sub>3</sub>	Me	20	67
<b>4n</b>	t-Bu	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	16	80
<b>4o</b>	t-Bu	2-Cl-C <sub>6</sub> H <sub>4</sub>	Me	20	65
<b>4p</b>	t-Bu	PhCH <sub>2</sub> CH <sub>2</sub>	Me	8	82
<b>4q</b>	c-C <sub>6</sub> H <sub>11</sub>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	Et	24	65
<b>4r</b>	c-C <sub>6</sub> H <sub>11</sub>	Ph	Et	24	70

<sup>a</sup> Isolated yields based on azide **1**.**Fig. 1** X-Ray crystal structure of compound **4e** (drawn at the 50% thermal ellipsoid level. The 2-chlorophenyl group is disordered. Only one is shown for clarity).**Scheme 3** Literature synthesis of dibenzo[b,f][1,5]diazocine **6** through intramolecular aza-Wittig reaction.

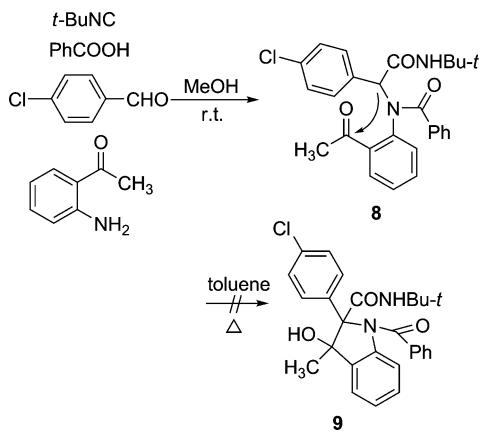
of the methine group to the carbonyl group takes place to give the indolo[1,2-c]quinazoline **4**. Although amide carbonyls are typically inert toward aza-Wittig reactions due to their low electrophilicity,<sup>13</sup> there are some examples of intramolecular aza-Wittig reactions involving “activated” amide carbonyl groups (*i.e.* imide or sulfonyl amide groups).<sup>14</sup> Consequently, it is understandable that cyclization of iminophosphorane **2** will produce quinazoline intermediate **7** *via* intramolecular aza-Wittig



**Scheme 4** A possible mechanism for this tandem cyclization.

reaction involving amide, which is substituted with an electron-withdrawing *N*-acylphenyl group.

Reports of the cyclization of the Ugi adduct through the methine group are rare. To the best of our knowledge, there is no report of the cyclization of the Ugi adduct to give a dihydroindole ring system with a quaternary carbon center, *via* the nucleophilic addition reaction of the methine group to the carbonyl group. In order to verify whether the process is general to other Ugi adducts, we prepared compound **8** by the four-component Ugi reaction of *tert*-butyl isonitrile, benzoic acid, 4-chlorophenylaldehyde and 2-acetyl aniline. Further heating of the compound **8** in toluene did not provide the dihydroindole **9** (Scheme 5). It is conceivable that only in the case of the quinazoline intermediate **7** can the intramolecular addition reaction of the methine group to the carbonyl group take place to give indolo[1,2-*c*]quinazolines **4**.



**Scheme 5** Attempted synthesis of the indole derivative *via* direct nucleophilic addition reaction.

## Conclusions

In conclusion, we have developed a new sequential Ugi–Staudinger–aza–Wittig–nucleophilic addition reaction process that allows the facile synthesis of indolo[1,2-*c*]quinazoline derivatives, starting from easily accessible materials. More importantly, this is the first report of the cyclization of the Ugi adduct to give a dihydroindole ring system with two quaternary carbon centers, *via* the nucleophilic addition reaction of the methine group to the carbonyl group.

## Experimental

### General

All reactions were performed in round-bottomed flasks under an atmosphere of air. Unless otherwise noted, materials were

purchased from commercial suppliers and used without further purification. Dichloromethane was used after distillation from CaH<sub>2</sub>. Toluene was distilled from CaH<sub>2</sub>, and stored over 4 Å molecular sieves. Column chromatography purifications were performed under “flash” conditions using 400–630 mesh silica gel. Analytical thin-layer chromatography (TLC) was carried out on silica gel 60 F<sub>254</sub> plates, which were visualized by exposure to ultraviolet light. Melting points were uncorrected. MS were measured on Finnigan Trace MS spectrometer or determined using API 2000 liquid chromatography-tandem mass spectrometer. IR were recorded on a PE-983 infrared spectrometer as KBr pellets with absorption in cm<sup>-1</sup>. NMR were recorded in CDCl<sub>3</sub> on a Varian Mercury 400 or 600 spectrometer and resonances relative to TMS. Data are reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. <sup>13</sup>C NMR spectra were recorded on Varian Mercury 400/600 (100/150 MHz) with complete proton decoupling spectrophotometers (CDCl<sub>3</sub>; 77.0 ppm). Elemental analyses were taken on a Vario EL III elemental analysis instrument. The X-ray diffraction data were collected on a Bruker SMART AXS CCD diffract meter, Mo-K $\alpha$ ,  $2\theta = 1.86\text{--}27.50^\circ$ .

**General procedure for preparation of azide **1**.** *o*-Azidobenzaldehyde (1 equiv), carboxylic acid (1 equiv), and isocyanide (1 equiv) were added sequentially to a solution of amine (1 equiv) in methanol (1 M) at room temperature. The reaction mixture was stirred at ambient temperature for 16 to 24 h until the solid precipitated completely, and the solvent was evaporated. The crude reaction mixture was purified by recrystallization.

**N-((Butylcarbamoyl)(2-azidophenyl)methyl)-N-(2-acetylphenyl)benzamide (**1a**).** White crystals; mp 170–171 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 7.57–6.98 (m, 14H, Ar–H and CONH), 6.36 (s, 0.4H, 0.4COCH), 6.08 (s, 0.6H, 0.6COCH), 3.39–3.29 (m, 1.2H, 0.6NCH<sub>2</sub>), 3.09 (s, 0.8H, 0.4NCH<sub>2</sub>), 2.10 (s, 2H, 0.67COCH<sub>3</sub>), 2.06 (s, 1H, 0.33COCH<sub>3</sub>), 1.55–0.83 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 201.1, 199.2, 167.5, 166.1, 139.8, 139.7, 138.5, 134.7, 132.2, 132.0, 131.5, 129.8, 129.4, 128.7, 128.5, 128.3, 127.7, 127.3, 127.2, 127.1, 126.2, 124.6, 62.0, 61.8, 42.0, 41.4, 36.4, 35.3, 28.6, 27.9, 20.9, 15.0, 14.0; IR (v, KBr): 3335, 3061, 2958, 2931, 2870, 2133, 1687, 1673, 1637, 1597 cm<sup>-1</sup>; MS: *m/z* (%) = 427 (8) [M<sup>+</sup> – N<sub>3</sub>], 327 (100), 119 (49), 77 (61); C<sub>27</sub>H<sub>27</sub>N<sub>5</sub>O<sub>3</sub> (469.5): calcd. C 69.07, H 5.80, N 14.92; found C 69.33, H 5.89, N 14.76%.

**N-((Butylcarbamoyl)(2-azidophenyl)methyl)-N-(2-acetylphenyl)-4-methylbenzamide (**1b**).** White crystals; mp 203–204 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 7.55–6.91 (m, 13H, Ar–H and CONH), 6.37 (s, 0.4H, 0.4COCH), 6.03 (s, 0.6H, 0.6COCH), 3.37–3.29 (m, 1.2H, 0.6NCH<sub>2</sub>), 3.06–3.05 (m, 0.8H, 0.4NCH<sub>2</sub>), 2.23 (d, *J* = 12.0 Hz, 3H, Ar–CH<sub>3</sub>), 2.07 (d, *J* = 7.8 Hz, 3H, COCH<sub>3</sub>), 1.55–0.82 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 201.1, 199.6, 170.3, 168.5, 167.8, 140.3, 139.9, 139.5, 138.8, 138.7, 136.6, 132.7, 132.5, 132.3, 132.2, 132.0, 131.1, 130.8, 129.5, 129.4, 129.3, 129.2, 129.0, 128.9, 128.8, 128.7, 128.3, 128.2, 127.6, 127.3, 124.6, 124.5, 118.0, 117.7, 62.6, 62.0, 39.6, 39.2, 31.3, 31.0, 28.7, 28.6, 21.2, 20.0, 13.7, 13.6; IR (v, KBr): 3330, 3053, 2958, 2871, 2460, 2144, 1687, 1635 cm<sup>-1</sup>; MS: *m/z* (%) = 441 (4)

$[M^+ - N_3]$ , 341 (100), 119 (85), 77 (73);  $C_{28}H_{29}N_5O_3$  (483.5): calcd. C 69.55, H 6.04, N 14.48; found C 69.39, H 5.89, N 14.71%.

**N-((Butylcarbamoyl)(2-azidophenyl)methyl)-N-(2-acetylphenyl)-4-methoxybenzamide (1c).** White crystals; mp 153–154 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm): 7.55–7.00 (m, 11H, Ar–H and CONH), 6.63 (t,  $J$  = 9.6 Hz, 2H, 2Ar–H), 6.38 (s, 0.4H, 0.4COCH), 6.00 (s, 0.6H, 0.6COCH), 3.72 (d,  $J$  = 10.8 Hz, 3H, Ar–OCH<sub>3</sub>), 3.38–3.29 (m, 1.2H, 0.6NCH<sub>2</sub>), 3.05 (s, 0.8H, 0.4NCH<sub>2</sub>), 2.10 (s, 3H, COCH<sub>3</sub>), 1.55–0.81 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm): 201.1, 199.6, 169.6, 168.3, 167.6, 160.6, 160.3, 139.4, 138.5, 138.4, 136.3, 134.9, 132.4, 132.0, 131.8, 130.9, 130.6, 130.5, 130.4, 129.2, 129.0, 128.8, 128.6, 127.5, 127.4, 127.1, 127.0, 126.9, 126.4, 124.4, 124.2, 117.8, 117.5, 112.7, 112.6, 62.5, 62.1, 54.9, 54.8, 39.3, 38.9, 31.0, 30.8, 28.5, 19.8, 19.7, 13.5, 13.4, 13.3; IR (v, KBr): 3332, 3072, 3005, 2959, 2934, 2871, 2838, 2134, 1688, 1637, 1609 cm<sup>-1</sup>; MS:  $m/z$  (%) = 462 (11) [ $M^+ - N_3$ ], 362 (100), 139 (45), 119 (23), 77 (78);  $C_{27}H_{26}ClN_5O_3$  (503.9): calcd. C 64.35, H 5.20, N 13.90; found C 64.23, H 5.04, N 13.61%.

**N-((Butylcarbamoyl)(2-azidophenyl)methyl)-N-(2-acetylphenyl)-2-methylbenzamide (1d).** White crystals; mp 200–201 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm): 7.52–6.77 (m, 13H, Ar–H and CONH), 6.34 (s, 0.4H, 0.4COCH), 6.00 (s, 0.6H, 0.6COCH), 3.36–3.31 (m, 1.2H, 0.6NCH<sub>2</sub>), 3.18–3.17 (m, 0.8H, 0.4NCH<sub>2</sub>), 2.45 (s, 2H, 0.67COCH<sub>3</sub>), 2.39 (s, 1H, 0.33COCH<sub>3</sub>), 2.14 (s, 1H, 0.33Ar–CH<sub>3</sub>), 2.05 (s, 2H, 0.67Ar–CH<sub>3</sub>), 1.55–0.80 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm): 200.8, 198.9, 170.5, 168.7, 168.3, 139.4, 139.0, 138.8, 136.4, 135.4, 135.0, 132.2, 132.0, 131.8, 131.3, 130.7, 130.5, 130.3, 129.6, 129.5, 129.3, 129.2, 129.0, 128.8, 128.6, 127.7, 127.6, 127.3, 127.0, 126.7, 126.4, 124.5, 124.3, 117.9, 117.8, 62.0, 60.1, 39.6, 39.2, 31.3, 31.1, 28.7, 28.6, 28.5, 19.9, 19.7, 19.5, 13.7, 13.6; IR (v, KBr): 3326, 3071, 2954, 2932, 2870, 2104, 1682, 1635 cm<sup>-1</sup>; MS:  $m/z$  (%) = 441 (3) [ $M^+ - N_3$ ], 331 (100), 119 (43), 77 (59).  $C_{28}H_{29}N_5O_3$  (483.6): calcd. C 69.55, H 6.04, N 14.48; found C 69.29, H 6.11, N 14.53%.

**N-((Butylcarbamoyl)(2-azidophenyl)methyl)-N-(2-acetylphenyl)-2-chlorobenzamide (1e).** White crystals; mp 206–207 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm): 7.60–6.90 (m, 13H, Ar–H and CONH), 6.39 (s, 0.3H, 0.3COCH), 6.24 (s, 0.7H, 0.7COCH), 3.47 (s, 0.2H, 0.07COCH<sub>3</sub>), 3.40–3.22 (m, 2H, NCH<sub>2</sub>), 2.44 (s, 0.8H, 0.27COCH<sub>3</sub>), 2.08 (s, 2H, 0.66COCH<sub>3</sub>), 1.59–0.90 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm): 198.6, 168.4, 168.3, 139.4, 137.8, 136.2, 135.0, 133.1, 132.5, 132.3, 131.7, 130.8, 130.0, 129.9, 129.8, 129.6, 129.5, 129.2, 129.1, 128.6, 128.2, 127.7, 126.1, 125.5, 124.2, 117.8, 58.8, 39.7, 31.4, 29.2, 28.8, 20.1, 13.8, 13.7; IR (v, KBr): 3334, 3053, 2960, 2933, 2871, 2104, 1684, 1642 cm<sup>-1</sup>; MS:  $m/z$  (%) = 462 (30) [ $M^+ - N_3$ ], 362 (100), 119 (39), 77 (90);  $C_{27}H_{26}ClN_5O_3$  (503.9): calcd. C 64.35, H 5.20, N 13.90; found C 64.59, H 5.01, N 13.97%.

**N-((Butylcarbamoyl)(2-azidophenyl)methyl)-N-(2-acetylphenyl)-4-chlorobenzamide (1f).** White crystals; mp 218–219 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm): 7.60–7.02 (m, 11H, 11Ar–H), 6.93 (d,  $J$  = 7.2 Hz, 1H, Ar–H), 6.63 (s, 1H, CONH), 6.29 (s, 0.4H, 0.4COCH), 6.18 (s, 0.6H, 0.6COCH), 3.35–3.28 (m, 1H, 0.5NCH<sub>2</sub>), 3.16–3.11 (m, 1H, 0.5NCH<sub>2</sub>), 2.21 (s, 1H, 0.33COCH<sub>3</sub>), 2.09 (s, 2H, 0.67COCH<sub>3</sub>), 1.52–0.84 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm): 200.5, 198.8, 168.9, 167.7, 139.1, 132.6, 132.1, 131.6, 130.4, 130.0, 129.9, 129.8, 129.6,

129.5, 129.2, 127.9, 127.8, 124.7, 124.4, 118.0, 117.9, 62.1, 60.6, 39.7, 39.4, 31.4, 28.8, 28.7, 20.0, 13.8, 13.7, 13.6; IR (v, KBr): 3332, 3065, 2954, 2930, 2869, 2134, 1689, 1675, 1637 cm<sup>-1</sup>; MS:  $m/z$  (%) = 462 (11) [ $M^+ - N_3$ ], 362 (100), 139 (45), 119 (23), 77 (78);  $C_{27}H_{26}ClN_5O_3$  (503.9): calcd. C 64.35, H 5.20, N 13.90; found C 64.23, H 5.04, N 13.61%.

**N-((Butylcarbamoyl)(2-azidophenyl)methyl)-N-(2-acetylphenyl)-3-nitrobenzamide (1g).** White crystals; mp 164–165 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm): 8.25–7.06 (m, 11.4H, 11.4Ar–H), 6.89 (s, 0.6H, 0.6CONH), 6.80 (s, 0.4H, 0.4CONH), 6.38 (s, 0.6H, 0.6COCH), 6.28 (s, 0.4H, 0.4COCH), 6.19 (s, 0.6H, 0.6Ar–H), 3.32–3.19 (m, 2H, NCH<sub>2</sub>), 2.32 (s, 1H, 0.33COCH<sub>3</sub>), 2.07 (s, 2H, 0.67COCH<sub>3</sub>), 1.50–0.88 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm): 197.8, 168.8, 168.4, 146.7, 139.1, 138.0, 137.4, 137.3, 135.5, 133.9, 133.6, 132.2, 131.9, 129.8, 129.1, 128.2, 128.1, 124.5, 123.4, 123.2, 117.8, 117.7, 59.0, 39.2, 39.0, 31.1, 30.9, 28.4, 28.3, 28.2, 19.6, 13.3; IR (v, KBr): 3332, 3073, 2960, 2932, 2862, 2129, 1694, 1678, 1636 cm<sup>-1</sup>; MS:  $m/z$  (%) = 472 (44) [ $M^+ - N_3$ ], 372 (100), 122 (87), 119 (73), 77 (50);  $C_{27}H_{26}N_6O_5$  (514.5): calcd. C 63.03, H 5.09, N 16.33; found C 63.12, H 5.22, N 16.14%.

**N-((Butylcarbamoyl)(2-azidophenyl)methyl)-N-(2-acetylphenyl)-4-nitrobenzamide (1h).** White crystals; mp 199–200 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm): 7.98–6.71 (m, 12H, 12Ar–H), 6.71 (s, 0.3H, 0.3CONH), 6.40 (s, 0.7H, 0.7COCH), 6.24 (s, 0.3H, 0.3COCH), 6.00 (s, 0.7H, 0.7CONH), 3.32–3.20 (m, 2H, NCH<sub>2</sub>), 2.32 (s, 1H, 0.33COCH<sub>3</sub>), 2.03 (s, 2H, 0.67COCH<sub>3</sub>), 1.49–0.87 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm): 199.8, 198.0, 169.4, 169.2, 169.1, 167.5, 147.5, 142.8, 139.4, 137.5, 135.8, 134.1, 132.6, 132.2, 131.9, 130.9, 130.2, 130.0, 129.6, 129.4, 129.3, 129.1, 128.4, 128.3, 124.8, 124.6, 124.3, 122.6, 118.0, 117.9, 61.0, 59.0, 56.1, 39.6, 39.4, 31.3, 28.6, 19.9, 13.6; IR (v, KBr): 3333, 3071, 2952, 2868, 2437, 2131, 1691, 1679, 1640 cm<sup>-1</sup>; MS:  $m/z$  (%) = 472 (6) [ $M^+ - N_3$ ], 372 (66), 122 (37), 119 (100), 77 (39);  $C_{27}H_{26}N_6O_5$  (514.5): calcd. C 63.03, H 5.09, N 16.33; found C 63.28, H 5.24, N 16.19%.

**N-((Butylcarbamoyl)(2-azidophenyl)methyl)-N-(2-acetylphenyl)-3-phenylpropanamide (1i).** White crystals; mp 135–136 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm): 7.65–6.76 (m, 12.7H, 12.7Ar–H), 6.58 (s, 0.3H, 0.3CONH), 6.49 (d,  $J$  = 7.8 Hz, 0.3H, 0.3Ar–H), 6.42 (s, 0.7H, 0.7COCH), 6.16 (s, 0.3H, 0.3COCH), 6.00 (s, 0.7H, 0.7CONH), 3.24–2.94 (m, 4H, NCH<sub>2</sub>+CH<sub>2</sub>), 2.68 (s, 1H, 0.33COCH<sub>3</sub>), 2.53–2.25 (m, 2H, CH<sub>2</sub>), 2.00 (s, 2H, 0.67COCH<sub>3</sub>), 1.50–0.88 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm): 199.9, 197.7, 173.4, 173.1, 169.4, 168.1, 141.0, 139.0, 137.1, 136.7, 133.0, 131.9, 129.6, 128.0, 127.8, 125.5, 125.4, 124.6, 123.8, 117.6, 57.1, 39.1, 37.0, 31.0, 30.9, 30.8, 28.9, 28.4, 19.6, 13.4; IR (v, KBr): 3608, 3505, 3299, 3073, 3025, 2959, 2931, 2872, 2129, 2100, 1737, 1691, 1643 cm<sup>-1</sup>; MS:  $m/z$  (%) = 455 (13) [ $M^+ - N_3$ ], 355 (100), 119 (80), 77 (67);  $C_{27}H_{31}N_5O_3$  (497.6): calcd. C 70.00, H 6.28, N 14.07; found C 70.21, H 6.45, N 14.12%.

**N-((Butylcarbamoyl)(2-azidophenyl)methyl)-N-(2-acetylphenyl)propionamide (1j).** White crystals; mp 179–180 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm): 7.82–6.76 (m, 8H, 8Ar–H), 6.56 (s, 0.3H, 0.3CONH), 6.41 (s, 0.7H, 0.7COCH), 6.12 (s, 0.3H, 0.3COCH), 5.94 (s, 0.7H, 0.7CONH), 3.26–3.16 (m, 2H, NCH<sub>2</sub>), 2.49 (s, 1H, 0.33COCH<sub>3</sub>), 2.19–1.99 (m, 4H, 0.67COCH<sub>3</sub>+CH<sub>2</sub>),

1.47–0.86 (m, 10H,  $\text{CH}_2\text{CH}_2\text{CH}_3+\text{CH}_3$ );  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 200.1, 197.8, 175.2, 174.8, 169.7, 168.4, 139.3, 137.6, 137.3, 133.2, 132.6, 132.1, 132.0, 131.7, 131.6, 129.8, 129.6, 128.9, 128.8, 128.4, 128.2, 124.7, 124.3, 123.9, 117.8, 117.6, 58.7, 57.0, 39.3, 39.2, 31.2, 28.7, 28.6, 28.5, 19.9, 19.8, 13.6, 13.5, 9.0, 8.9; IR ( $\nu$ , KBr): 3327, 3105, 2959, 2930, 2873, 2130, 1688, 1671, 1641  $\text{cm}^{-1}$ ; MS:  $m/z$  (%) = 379 (21) [ $\text{M}^+ - \text{N}_3$ ], 279 (100), 119 (56), 77 (93);  $\text{C}_{23}\text{H}_{27}\text{N}_5\text{O}_3$  (421.5): calcd. C 65.54, H 6.46, N 16.62; found C 65.61, H 6.29, N 16.92%.

***N*-(2-Acetylphenyl)-*N*-(1-(2-azidophenyl)-2-(butylamino)-2-oxoethyl)-2-(4-dichlorophenoxy)acetamide (1k).** White crystals; mp 166–167  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.98–7.96 (m, 1H, 1Ar–H), 7.68–6.67 (m, 11H, 11Ar–H), 6.44 (s, 0.7H, 0.7COCH), 6.38 (s, 0.3H, 0.3CONH), 6.23 (s, 0.3H, 0.3COCH), 5.93 (s, 0.7H, 0.7CONH), 4.60–4.34 (m, 2H, COCH<sub>2</sub>), 3.22–3.18 (m, 2H, NCH<sub>2</sub>), 2.57 (s, 1H, 0.33COCH<sub>3</sub>), 1.97 (s, 2H, 0.67COCH<sub>3</sub>), 1.48–0.85 (m, 7H,  $\text{CH}_2\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 200.3, 198.1, 169.1, 167.9, 152.6, 139.2, 137.9, 134.4, 133.7, 132.3, 129.9, 129.0, 128.7, 127.2, 125.1, 124.1, 123.9, 122.5, 117.8, 114.6, 67.2, 57.3, 56.9, 39.3, 31.0, 28.4, 28.3, 19.7, 13.5, 13.4; IR ( $\nu$ , KBr): 3343, 3069, 2961, 2933, 2871, 2133, 1695, 1664  $\text{cm}^{-1}$ ; MS:  $m/z$  (%) = 526 (36) [ $\text{M}^+ - \text{N}_3$ ], 426 (100), 264 (69), 119 (87), 77 (63);  $\text{C}_{28}\text{H}_{27}\text{Cl}_2\text{N}_5\text{O}_4$  (568.5): calcd. C 59.16, H 4.79, N 12.32; found C 59.01, H 4.74, N 12.54%.

***N*-((tert-Butylcarbamoyl)(2-azidophenyl)methyl)-*N*-(2-acetylphenyl)benzamide (1l).** White crystals; mp 170–171  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.58–6.97 (m, 14H, Ar–H and CONH), 6.37 (s, 0.53H, 0.53COCH), 5.96 (s, 0.47H, 0.47COCH), 2.12 (s, 1.4H, 0.47COCH<sub>3</sub>), 2.02 (s, 1.6H, 0.53COCH<sub>3</sub>), 1.41 (s, 4H, 1.3CH<sub>3</sub>), 1.01 (s, 5H, 1.7CH<sub>3</sub>);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 201.2, 199.0, 169.6, 166.0, 139.5, 138.5, 136.7, 134.9, 132.2, 132.0, 131.8, 130.0, 129.4, 129.2, 127.6, 127.5, 127.4, 124.6, 124.5, 118.1, 117.7, 63.5, 61.5, 51.3, 50.7, 28.7, 28.5, 27.9, 27.8; IR ( $\nu$ , KBr): 3335, 2971, 2925, 2130, 2099, 1699, 1668, 1655  $\text{cm}^{-1}$ ; MS:  $m/z$  (%) = 427 (6) [ $\text{M}^+ - \text{N}_3$ ], 326 (100), 238 (60), 119 (45), 77 (86);  $\text{C}_{27}\text{H}_{27}\text{N}_5\text{O}_3$  (469.5): calcd. C 69.07, H 5.80, N 14.92; found C 69.33, H 5.68, N 14.95%.

***N*-((tert-Butylcarbamoyl)(2-azidophenyl)methyl)-*N*-(2-acetylphenyl)-3,5-dimethylbenzamide (1m).** White crystals; mp 152–153  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.65–6.81 (m, 12H, Ar–H and CONH), 6.35 (s, 0.53H, 0.53COCH), 5.91 (s, 0.47H, 0.47COCH), 2.31 (s, 1.4H, 0.47COCH<sub>3</sub>), 2.13 (s, 6H, 2CH<sub>3</sub>), 2.01 (s, 1.6H, 0.53COCH<sub>3</sub>), 1.43 (s, 3H, 1CH<sub>3</sub>), 1.32 (s, 1H, 0.3CH<sub>3</sub>), 0.97 (s, 5H, 1.7CH<sub>3</sub>);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 201.1, 169.8, 166.1, 139.8, 139.7, 138.5, 137.2, 137.0, 134.7, 132.2, 132.0, 131.5, 131.0, 129.8, 129.4, 128.7, 128.5, 128.3, 127.7, 127.5, 127.4, 127.3, 127.2, 127.1, 127.0, 126.3, 126.2, 124.6, 118.2, 63.6, 61.8, 51.3, 50.7, 28.7, 28.6, 28.5, 27.9, 27.8, 20.9; IR ( $\nu$ , KBr): 3338, 2964, 2918, 2125, 1703, 1670, 1652  $\text{cm}^{-1}$ ; MS:  $m/z$  (%) = 455 (11) [ $\text{M}^+ - \text{N}_3$ ], 355 (100), 133 (40), 119 (75), 57 (46);  $\text{C}_{29}\text{H}_{31}\text{N}_5\text{O}_3$  (497.6): calcd. C 70.00, H 6.28, N 14.07; found C 69.74, H 6.09, N 14.25%.

***N*-((tert-Butylcarbamoyl)(2-azidophenyl)methyl)-*N*-(2-acetylphenyl)-4-nitrobenzamide (1n).** White crystals; mp 180–181  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.89–6.87 (m, 12H, 12Ar–H), 6.62 (s, 0.33H, 0.33COCH), 6.27 (s, 0.67H, 0.67CONH), 6.22 (s, 0.33H, 0.33CONH), 5.93 (s, 0.67H, 0.67COCH), 2.28 (s, 1H,

0.33COCH<sub>3</sub>), 2.09 (s, 2H, 0.67CH<sub>3</sub>), 1.37 (s, 6H, 2CH<sub>3</sub>), 1.19 (s, 3H, 1CH<sub>3</sub>);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 200.0, 197.9, 169.0, 168.7, 167.9, 166.1, 147.4, 142.8, 139.1, 137.5, 135.4, 133.8, 132.3, 132.1, 130.0, 129.6, 129.5, 129.4, 129.1, 129.0, 128.2, 126.7, 124.8, 124.7, 124.3, 122.5, 122.3, 117.9, 62.1, 59.4, 51.5, 51.0, 28.7, 28.6, 28.5, 28.4, 28.0; IR ( $\nu$ , KBr): 3353, 2969, 2929, 2837, 2747, 2637, 2545, 2127, 1682, 1640  $\text{cm}^{-1}$ ; MS:  $m/z$  (%) = 472 (17) [ $\text{M}^+ - \text{N}_3$ ], 372 (100), 150 (38), 119 (83);  $\text{C}_{27}\text{H}_{26}\text{N}_6\text{O}_5$  (514.5): calcd. C 63.03, H 5.09, N 16.33; found C 63.11, H 5.24, N 16.59%.

***N*-((tert-Butylcarbamoyl)(2-azidophenyl)methyl)-*N*-(2-acetylphenyl)-2-chlorobenzamide (1o).** White crystals; mp 151–152  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.46–6.94 (m, 13H, Ar–H and CONH), 6.27 (s, 0.33H, 0.33COCH), 6.10 (s, 0.67H, 0.67COCH), 2.38 (s, 1H, 0.33COCH<sub>3</sub>), 2.16 (s, 2H, 0.67CH<sub>3</sub>), 1.45 (s, 6H, 2CH<sub>3</sub>), 1.26 (s, 3H, 1CH<sub>3</sub>);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 198.7, 168.1, 167.0, 139.0, 138.7, 137.9, 134.6, 132.4, 131.8, 130.7, 129.8, 129.7, 129.5, 129.1, 128.6, 126.0, 124.1, 117.6, 59.5, 51.3, 28.6, 28.5, 28.2, 27.4; IR ( $\nu$ , KBr): 3347, 3063, 2968, 2928, 2125, 1689, 1641  $\text{cm}^{-1}$ ; MS:  $m/z$  (%) = 463 (8) [ $\text{M}^+ - \text{N}_3$ ], 362 (100), 119 (67), 77 (49);  $\text{C}_{27}\text{H}_{26}\text{ClN}_5\text{O}_3$  (504.0): calcd. C 64.35, H 5.20, N 13.90; found C 64.51, H 5.06, N 14.10%.

***N*-((tert-Butylcarbamoyl)(2-azidophenyl)methyl)-*N*-(2-acetylphenyl)-3-phenylpropanamide (1p).** White crystals; mp 126–127  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.64–6.48 (m, 13H, 13Ar–H), 6.38 (s, 0.33H, 0.33COCH), 6.32 (s, 0.67H, 0.67COCH), 6.06 (s, 0.33H, 0.33CONH), 5.92 (s, 0.67H, 0.67CONH), 3.05–2.94 (m, 2H, CH<sub>2</sub>), 2.52 (s, 1H, 0.33COCH<sub>3</sub>), 2.50–2.28 (m, 2H, CH<sub>2</sub>), 2.00 (s, 2H, 0.67CH<sub>3</sub>), 1.33 (s, 9H, 3CH<sub>3</sub>);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 197.9, 173.2, 168.7, 167.4, 141.4, 139.3, 137.4, 137.2, 133.0, 132.7, 132.3, 128.3, 128.1, 125.7, 124.0, 117.8, 57.2, 51.3, 51.1, 37.3, 31.1, 28.6, 28.5, 28.3; IR ( $\nu$ , KBr): 3366, 3068, 2973, 2916, 2126, 1687, 1655  $\text{cm}^{-1}$ ; MS:  $m/z$  (%) = 455 (10) [ $\text{M}^+ - \text{N}_3$ ], 355 (100), 119 (48), 77 (87);  $\text{C}_{29}\text{H}_{31}\text{N}_5\text{O}_3$  (497.6): calcd. C 70.00, H 6.28, N 14.07; found C 69.72, H 6.43, N 14.12%.

***N*-((2-Azidophenyl)-2-(cyclohexylamino)-2-oxoethyl)-4-methyl-*N*-(2-propionylphenyl)benzamide (1q).** White crystals; mp 197–198  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.52–6.90 (m, 13H, Ar–H and CONH), 6.36 (s, 0.5H, 0.5COCH), 5.90 (s, 0.5H, 0.5COCH), 3.85–3.83 (m, 0.5H, 0.5NCH), 3.56–3.54 (m, 0.5H, 0.5NCH), 2.68–2.62 (m, 0.5H, 0.25COCH<sub>2</sub>), 2.46–2.43 (m, 0.5H, 0.25COCH<sub>2</sub>), 2.39 (s, 3H, Ar–CH<sub>3</sub>), 2.22–0.64 (m, 14H, 5.5CH<sub>2</sub>+CH<sub>3</sub>);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 203.7, 202.1, 170.0, 167.3, 166.5, 138.8, 138.7, 135.1, 132.1, 132.0, 131.8, 130.0, 129.5, 129.4, 129.1, 128.8, 128.5, 128.4, 128.2, 127.5, 127.4, 124.5, 124.4, 118.0, 117.5, 63.0, 61.6, 61.5, 48.6, 48.0, 33.5, 33.4, 32.7, 32.6, 32.5, 25.5, 24.7, 24.6, 24.5, 7.6; IR ( $\nu$ , KBr): 3326, 3056, 2928, 2848, 2134, 1696, 1678, 1645  $\text{cm}^{-1}$ ; MS:  $m/z$  (%) = 481 (15) [ $\text{M}^+ - \text{N}_3$ ], 355 (100), 266 (60), 77 (89);  $\text{C}_{31}\text{H}_{33}\text{N}_5\text{O}_3$  (523.6): calcd. C 71.11, H 6.35; N 13.37; found C 71.17, H 6.19, N 13.51%.

***N*-((2-Azidophenyl)-2-(cyclohexylamino)-2-oxoethyl)-*N*-(2-propionylphenyl)benzamide (1r).** White crystals; mp 199–200  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.53–6.99 (m, 14H, Ar–H and CONH), 6.34 (s, 0.5H, 0.5COCH), 5.96 (s, 0.5H, 0.5COCH), 3.85–3.84 (m, 0.5H, 0.5NCH), 3.58–3.56 (m, 0.5H, 0.5NCH), 2.67–2.63 (m, 0.5H, 0.25COCH<sub>2</sub>), 2.40–2.31 (m, 0.5H, 0.25COCH<sub>2</sub>), 2.07–0.69 (m, 14H, 5.5CH<sub>2</sub>+CH<sub>3</sub>); IR ( $\nu$ , KBr): 3329, 2930, 2844, 2130, 1692, 1688, 1641  $\text{cm}^{-1}$ ;  $^{13}\text{C}$  NMR

(150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 203.8, 202.3, 170.1, 169.9, 167.2, 166.5, 140.4, 139.7, 139.4, 138.7, 138.6, 136.8, 132.8, 132.1, 131.8, 129.0, 128.6, 128.4, 128.3, 128.1, 127.8, 127.3, 127.2, 124.5, 124.4, 118.0, 117.5, 63.0, 61.9, 50.0, 48.6, 48.5, 48.0, 33.5, 33.4, 32.7, 32.6, 32.5, 25.5, 25.3, 24.7, 24.6, 21.2, 7.6, 7.5; MS:  $m/z$  (%) = 467 (8) [ $\text{M}^+ - \text{N}_3$ ], 341 (100), 252 (45), 77 (58);  $\text{C}_{30}\text{H}_{31}\text{N}_5\text{O}_3$  (509.6): calcd. C 70.71; H 6.13; N 13.74; found C 70.94, H 6.37, N 13.60%.

**General procedure for preparation of indolo[1,2-*c*]quinazoline 4.** Triphenylphosphine (1 equiv) was added to a solution of azide 1 in dry toluene under stirring. After stirring for about 2 h, iminophosphorane 2 was formed which was monitored by TLC. Then the solution was heated to reflux for 6–24 h without isolation. After the reaction was completed, the solvent was evaporated and the residue was purified by column chromatography.

**N-Butyl-12,12a-dihydro-12-hydroxy-12-methyl-6-phenylindolo[1,2-*c*]quinazoline-12a-carboxamide (4a).** White crystals; mp 211–212 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.66–7.21 (m, 10H, 10Ar–H), 7.02 (t,  $J$  = 7.2 Hz, 1H, Ar–H), 6.82 (t,  $J$  = 7.2 Hz, 1H, Ar–H), 6.28 (s, 1H, OH), 6.04 (s, 1H, CONH), 5.77 (d,  $J$  = 8.0 Hz, 1H, Ar–H), 3.26–3.21 (m, 1H, 0.5NCH<sub>2</sub>), 3.12–3.06 (m, 1H, 0.5NCH<sub>2</sub>), 1.44 (s, 3H, CH<sub>3</sub>), 1.32–1.28 (m, 2H, CH<sub>2</sub>), 1.08–1.06 (m, 2H, CH<sub>2</sub>), 0.75 (t,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): v = 172.9, 152.7, 141.0, 139.7, 137.4, 135.6, 130.2, 129.8, 128.9, 127.9, 127.9, 126.2, 126.1, 125.8, 125.0, 122.6, 121.4, 115.5, 84.3, 73.5, 39.4, 31.1, 26.9, 19.5, 13.4; IR (v, KBr): 3199, 2973, 2952, 2930, 1631 cm<sup>-1</sup>; LC/MS:  $m/z$  425.7 [M]<sup>+</sup>;  $\text{C}_{27}\text{H}_{27}\text{N}_3\text{O}_2$  (425.5): calcd. C 76.21, H 6.40, N 9.87; found C 76.05, H 6.23, N 9.60%.

**N-Butyl-12,12a-dihydro-12-hydroxy-12-methyl-6-p-tolylindolo[1,2-*c*]quinazoline-12a-carboxamide (4b).** White crystals; mp 203–204 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.64 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 7.39–7.20 (m, 8H, Ar–H), 7.02 (t,  $J$  = 7.2 Hz, 1H, Ar–H), 6.84 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 6.27 (s, 1H, CONH), 6.03 (s, 1H, OH), 5.86 (d,  $J$  = 8.4 Hz, 1H, Ar–H), 3.24–3.21 (m, 1H, 0.5NCH<sub>2</sub>), 3.09–3.06 (m, 1H, 0.5NCH<sub>2</sub>), 2.45 (s, 3H, CH<sub>3</sub>), 1.43 (s, 3H, CH<sub>3</sub>), 1.30–1.27 (m, 2H, CH<sub>2</sub>), 1.09–1.05 (m, 2H, CH<sub>2</sub>), 0.75 (t,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 172.7, 152.8, 141.1, 140.3, 139.7, 137.2, 132.7, 129.7, 129.4, 127.8, 126.0, 125.8, 125.7, 124.8, 122.5, 121.5, 115.4, 84.2, 73.4, 39.3, 31.0, 27.0, 21.4, 19.4, 13.4; IR (v, KBr): 3165, 2954, 2928, 1629 cm<sup>-1</sup>; LC/MS:  $m/z$  439.6 [M]<sup>+</sup>;  $\text{C}_{27}\text{H}_{27}\text{N}_3\text{O}_2$  (439.5): calcd. C 76.51, H 6.65, N 9.56; found C 76.75, H 6.41, N 9.70%.

**N-Butyl-12,12a-dihydro-12-hydroxy-6-(4-methoxyphenyl)-12-methylindolo[1,2-*c*]quinazoline-12a-carboxamide (4c).** Yellow crystals; mp 208–209 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.62 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 7.47–6.99 (m, 9H, Ar–H), 6.86 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 6.20 (s, 1H, CONH), 5.92 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 5.85 (s, 1H, OH), 3.88 (s, 3H, OCH<sub>3</sub>), 3.23–3.20 (m, 1H, 0.5NCH<sub>2</sub>), 3.10–3.08 (m, 1H, 0.5NCH<sub>2</sub>), 1.42 (s, 3H, CH<sub>3</sub>), 1.30–1.28 (m, 2H, CH<sub>2</sub>), 1.10–1.07 (m, 2H, CH<sub>2</sub>), 0.76 (t,  $J$  = 7.8 Hz, 3H, CH<sub>3</sub>);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 172.7, 161.1, 152.6, 141.4, 139.9, 137.2, 129.9, 129.8, 129.7, 128.0, 128.0, 126.0, 125.8, 124.7, 122.6, 121.8, 115.3, 114.2, 84.3, 73.5, 55.4, 39.4, 31.1, 27.3, 19.5, 13.5; IR (v, KBr): 3166, 2955, 2928, 2869, 1633 cm<sup>-1</sup>; LC/MS:  $m/z$  455.7 [M]<sup>+</sup>;  $\text{C}_{28}\text{H}_{29}\text{N}_3\text{O}_3$  (455.5): calcd. C 73.82, H 6.42, N 9.22; found C 73.55, H 6.62, N 9.30%.

**N-Butyl-12,12a-dihydro-12-hydroxy-12-methyl-6-*o*-tolylindolo[1,2-*c*]quinazoline-12a-carboxamide (4d).** White crystals; mp 95–96 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.71–7.65 (m, 1H, Ar–H), 7.41–7.02 (m, 9H, Ar–H), 6.80 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 6.47 (d,  $J$  = 5.4 Hz, 0.5H, 0.5OH), 6.41 (s, 0.5H, 0.5CONH), 6.30 (s, 0.5H, 0.5CONH), 6.09 (d,  $J$  = 5.4 Hz, 0.5H, 0.5OH), 3.25–3.09 (m, 2H, NCH<sub>2</sub>), 2.50 (s, 1.3H, 0.43COCH<sub>3</sub>), 2.35 (s, 2.6H, 0.57COCH<sub>3</sub>), 2.07 (s, 1.5H, 0.5CH<sub>3</sub>), 1.47–1.05 (m, 5.5H, 2CH<sub>2</sub>+0.5CH<sub>3</sub>), 0.76 (t,  $J$  = 6.6 Hz, 3H, CH<sub>3</sub>);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 173.4, 172.7, 152.4, 152.2, 140.7, 140.6, 139.6, 139.2, 137.6, 137.5, 135.5, 135.4, 135.3, 131.0, 130.3, 129.9, 129.9, 129.7, 128.9, 128.2, 128.1, 128.1, 127.9, 127.5, 126.7, 126.2, 125.7, 125.5, 125.4, 122.7, 122.4, 120.8, 120.6, 115.2, 114.6, 84.2, 84.1, 73.6, 73.2, 39.3, 39.3, 31.0, 30.9, 26.5, 22.5, 19.5, 19.4, 18.9, 13.4; IR (v, KBr): 3355, 2958, 2928, 2869, 1674, 1643, 1610 cm<sup>-1</sup>; LC/MS:  $m/z$  439.8 [M]<sup>+</sup>;  $\text{C}_{28}\text{H}_{29}\text{N}_3\text{O}_2$  (439.5): calcd. C 76.51, H 6.65, N 9.56; found C 76.75, H 6.49, N 9.80%.

**N-Butyl-6-(2-chlorophenyl)-12,12a-dihydro-12-hydroxy-12-methylindolo[1,2-*c*]quinazoline-12a-carboxamide (4e).** White crystals; mp 167–168 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.76–7.24 (m, 11H, Ar–H), 7.06 (t,  $J$  = 7.2 Hz, 1H, Ar–H), 6.87 (d,  $J$  = 7.8 Hz, 0.85H, 0.85OH), 6.42 (s, 0.15H, 0.15OH), 5.77 (d,  $J$  = 7.8 Hz, 0.85H, 0.85CONH), 5.56 (d,  $J$  = 7.8 Hz, 0.15H, 0.15CONH), 3.27–3.23 (m, 1H, 0.5NCH<sub>2</sub>), 3.06–3.03 (m, 1H, 0.5NCH<sub>2</sub>), 1.52 (s, 0.5H, 0.17COCH<sub>3</sub>), 1.40 (s, 2.5H, 0.83COCH<sub>3</sub>), 1.31–0.70 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 173.4, 149.6, 139.6, 139.1, 137.2, 134.5, 132.3, 131.1, 129.7, 129.4, 129.3, 128.0, 127.9, 127.8, 126.5, 125.9, 125.5, 122.8, 120.3, 115.4, 84.3, 72.6, 39.1, 30.6, 26.1, 19.1, 13.2; IR (v, KBr): 3418, 3276, 2955, 2932, 2869, 1650, 1611 cm<sup>-1</sup>; LC/MS:  $m/z$  459.8 [M]<sup>+</sup>;  $\text{C}_{27}\text{H}_{26}\text{ClN}_3\text{O}_2$  (460.0): calcd. C 70.50, H 5.70, N 9.14; found C 70.27, H 5.55, N 9.02%.

**N-Butyl-6-(4-chlorophenyl)-12,12a-dihydro-12-hydroxy-12-methylindolo[1,2-*c*]quinazoline-12a-carboxamide (4f).** White crystals; mp 213–214 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.63 (t,  $J$  = 4.2 Hz, 1H, Ar–H), 7.47–7.23 (m, 8H, Ar–H), 7.04 (t,  $J$  = 7.2 Hz, 1H, Ar–H), 6.89 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 6.17 (d,  $J$  = 4.8 Hz, 1H, CONH), 5.88 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 5.76 (d,  $J$  = 4.8 Hz, 1H, OH), 3.22–3.18 (m, 1H, 0.5NCH<sub>2</sub>), 3.11–3.06 (m, 1H, 0.5NCH<sub>2</sub>), 1.44 (s, 3H, COCH<sub>3</sub>), 1.31–0.75 (m, 7H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 172.3, 151.6, 141.0, 139.5, 137.1, 136.2, 133.9, 129.8, 129.5, 129.0, 129.0, 126.1, 126.1, 122.6, 121.6, 121.5, 115.1, 84.1, 73.7, 39.3, 31.0, 27.1, 19.4, 13.4; IR (v, KBr): 3411, 3189, 2959, 2930, 2862, 1628 cm<sup>-1</sup>; LC/MS:  $m/z$  460.2 [M]<sup>+</sup>;  $\text{C}_{27}\text{H}_{26}\text{ClN}_3\text{O}_2$  (460.0): calcd. C 70.50, H 5.70, N 9.14; found C 70.73, H 5.58, N 9.39%.

**N-Butyl-12,12a-dihydro-12-hydroxy-12-methyl-6-(3-nitrophenyl)indolo[1,2-*c*]quinazoline-12a-carboxamide (4g).** White crystals; mp 198–199 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.47 (s, 1H, Ar–H), 8.40 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 7.83–7.27 (m, 7H, Ar–H), 7.07 (t,  $J$  = 7.2 Hz, 1H, Ar–H), 6.87 (t,  $J$  = 7.2 Hz, 1H, Ar–H), 6.20 (d, 1H, CONH), 5.81 (d,  $J$  = 8.4 Hz, 1H, Ar–H), 5.72 (s, 1H, OH), 3.25–3.21 (m, 1H, 0.5NCH<sub>2</sub>), 3.14–3.09 (m, 1H, 0.5NCH<sub>2</sub>), 1.47 (s, 3H, COCH<sub>3</sub>), 1.32–1.29 (m, 2H, CH<sub>2</sub>), 1.10–1.06 (m, 2H, CH<sub>2</sub>), 0.77 (t,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 172.2, 150.4, 148.3, 140.6, 139.4, 137.4, 137.2, 130.1, 130.0, 129.9, 129.8, 129.7, 128.1, 126.3, 125.4, 125.4, 123.1, 123.0,

121.5, 115.0, 84.3, 74.7, 39.5, 31.1, 27.1, 19.5, 13.5; IR ( $\nu$ , KBr): 3402, 3163, 2961, 2929, 2871, 1633  $\text{cm}^{-1}$ ; LC/MS:  $m/z$  470.7 [M]<sup>+</sup>;  $\text{C}_{27}\text{H}_{26}\text{N}_4\text{O}_4$  (470.0): calcd. C 68.92, H 5.57, N 11.91; found C 68.63, H 5.72, N 11.96%.

**N-Butyl-12,12a-dihydro-12-hydroxy-12-methyl-6-(4-nitrophe-nyl)indolo[1,2-c]quinazoline-12a-carboxamide (4h).** Yellow crystals; mp 216–217 °C; <sup>1</sup>H NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.39–8.32 (m, 2H, Ar–H), 7.75–7.27 (m, 7H, Ar–H), 7.07 (t,  $J$  = 7.2 Hz, 1H, Ar–H), 6.88 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 6.15 (s, 1H, CONH), 5.80 (d,  $J$  = 8.4 Hz, 1H, Ar–H), 5.57 (d,  $J$  = 7.8 Hz, 1H, OH), 3.23–3.19 (m, 1H, 0.5NCH<sub>2</sub>), 3.13–3.10 (m, 1H, 0.5NCH<sub>2</sub>), 1.47 (s, 3H, COCH<sub>3</sub>), 1.31–1.28 (m, 2H, CH<sub>2</sub>), 1.09–1.07 (m, 2H, CH<sub>2</sub>), 0.77 (t,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>). <sup>13</sup>C NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 172.1, 150.6, 148.6, 141.5, 140.7, 139.3, 137.2, 130.0, 130.0, 129.6, 126.6, 126.3, 125.3, 124.5, 123.5, 122.9, 121.6, 114.8, 84.2, 74.1, 39.5, 31.0, 27.2, 19.5, 13.5; IR ( $\nu$ , KBr): 3398, 3183, 2960, 2930, 2860, 1629  $\text{cm}^{-1}$ ; LC/MS:  $m/z$  470.3 [M]<sup>+</sup>;  $\text{C}_{27}\text{H}_{26}\text{N}_4\text{O}_4$  (470.0): calcd. C 68.92, H 5.57, N 11.91; found C 68.95, H 5.33, N 11.74%.

**N-Butyl-12,12a-dihydro-12-hydroxy-12-methyl-6-phenethylin-dolo[1,2-c]quinazoline-12a-carboxamide (4i).** White crystals; mp 198–199 °C; <sup>1</sup>H NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.61 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 7.45 (d,  $J$  = 7.2 Hz, 1H, Ar–H), 7.34–7.13 (m, 11H, Ar–H), 6.89 (s, 1H, OH), 6.57 (s, 1H, CONH), 3.19–2.94 (m, 6H, NCH<sub>2</sub>+2CH<sub>2</sub>), 1.28 (s, 3H, CH<sub>3</sub>), 1.22–0.88 (m, 4H, 2CH<sub>2</sub>), 0.71 (t,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 174.2, 153.7, 140.7, 140.6, 140.1, 139.2, 129.7, 128.6, 128.5, 128.2, 126.6, 126.4, 126.1, 125.4, 125.4, 123.5, 120.3, 117.6, 84.3, 74.1, 39.2, 36.4, 32.5, 31.1, 25.3, 19.4, 13.5; IR ( $\nu$ , KBr): 3415, 3209, 3027, 2958, 2930, 2869, 1649, 1607  $\text{cm}^{-1}$ ; LC/MS:  $m/z$  453.9 [M]<sup>+</sup>;  $\text{C}_{29}\text{H}_{31}\text{N}_3\text{O}_2$  (453.6): calcd. C 76.79, H 6.89, N 9.26; found C 76.95, H 6.93, N 9.08%.

**N-Butyl-6-ethyl-12,12a-dihydro-12-hydroxy-12-methylindolo[1,2-c]quinazoline-12a-carboxamide (4j).** Yellow crystals; mp 163–164 °C; <sup>1</sup>H NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.61 (d,  $J$  = 7.2 Hz, 1H, Ar–H), 7.45 (d,  $J$  = 7.2 Hz, 1H, Ar–H), 7.33–7.14 (m, 6H, Ar–H), 6.99 (s, 1H, OH), 6.98 (s, 1H, CONH), 3.24–3.20 (m, 1H, NCH), 3.02–2.98 (m, 1H, NCH), 2.64–2.61 (m, 2H, CH<sub>2</sub>), 1.28 (s, 3H, CH<sub>3</sub>), 1.26–1.21 (m, 5H, CH<sub>2</sub>+CH<sub>3</sub>), 1.04–0.96 (m, 2H, CH<sub>2</sub>), 0.74 (t,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 174.5, 156.0, 140.4, 140.0, 139.9, 129.4, 128.1, 126.5, 125.9, 125.2, 124.8, 123.2, 120.3, 117.4, 84.3, 73.9, 39.1, 31.0, 27.9, 25.1, 19.4, 13.4, 11.0; IR ( $\nu$ , KBr): 3411, 3237, 2960, 2932, 2871, 1638, 1607  $\text{cm}^{-1}$ ; MS ( $m/z$ , %): 377 (11), [M]<sup>+</sup>, 277 (100), 262 (17);  $\text{C}_{23}\text{H}_{27}\text{N}_3\text{O}_2$  (377.5): calcd. C 73.18, H 7.21, N 11.13; found C 73.02, H 7.02, N 11.35%.

**6-((2,4-Dichlorophenoxy)methyl)-N-butyl-12,12a-dihydro-12-hydroxy-12-methylindolo[1,2-c]quinazoline-12a-carboxamide (4k).** Yellow crystals; mp 163–164 °C; <sup>1</sup>H NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.78 (d,  $J$  = 7.2 Hz, 2H, Ar–H), 7.55 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 7.36–7.21 (m, 7H, Ar–H), 6.88 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 5.88 (s, 1H, CONH), 5.55 (s, 1H, OH), 4.82 (s, 1H, 0.5OCH<sub>2</sub>), 3.11 (s, 0.9H, 0.45OCH<sub>2</sub>), 3.00–2.97 (m, 1H, 0.5NCH), 2.78–2.74 (m, 1H, 0.5NCH), 2.39 (s, 0.1H, 0.05OCH<sub>2</sub>), 1.90 (s, 0.3H, 0.1CH<sub>3</sub>), 1.51 (s, 2.7H, 0.9CH<sub>3</sub>), 0.89–0.86 (m, 4H, 2CH<sub>2</sub>), 0.61 (t,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 168.7, 152.2, 147.4, 138.3, 135.3, 131.7, 129.7, 129.3, 129.0, 128.2, 127.8, 127.4, 127.2, 125.6, 125.5, 124.0, 123.8, 121.3, 118.0, 112.3, 85.0, 71.6,

59.3, 39.3, 30.6, 24.8, 19.5, 13.3; IR ( $\nu$ , KBr): 3312, 3205, 3071, 2964, 2935, 2872, 1648, 1623  $\text{cm}^{-1}$ ; MS ( $m/z$ , %): 523 (2), [M]<sup>+</sup>, 423 (100), 262 (14), 245 (100), 219 (51);  $\text{C}_{28}\text{H}_{27}\text{Cl}_2\text{N}_3\text{O}_3$  (524.4): calcd. C 64.13, H 5.19, N 8.01; found C 64.35, H 5.02, N 8.30%.

**N-tert-Butyl-12,12a-dihydro-12-hydroxy-12-methyl-6-phenyl-indolo[1,2-c]quinazoline-12a-carboxamide (4l).** Yellow crystals; mp 236–237 °C; <sup>1</sup>H NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.65–7.23 (m, 10H, Ar–H), 7.01 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 6.83 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 6.09 (s, 1H, CONH), 5.86 (s, 1H, OH), 5.77 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 1.44 (s, 3H, CH<sub>3</sub>), 1.17 (s, 9H, 3CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 172.1, 152.6, 141.1, 139.8, 137.3, 135.6, 130.2, 129.7, 128.9, 127.9, 126.1, 126.0, 125.7, 124.8, 122.5, 121.8, 115.0, 84.3, 73.5, 52.0, 28.2, 27.2; IR ( $\nu$ , KBr): 3422, 3289, 3057, 2978, 2927, 1656, 1611  $\text{cm}^{-1}$ ; LC/MS:  $m/z$  425.9 [M]<sup>+</sup>;  $\text{C}_{27}\text{H}_{27}\text{N}_3\text{O}_2$  (425.5): calcd. C 76.21, H 6.40, N 9.87; found C 76.03, H 6.63, N 9.95%.

**N-tert-Butyl-12,12a-dihydro-12-hydroxy-12-methyl-6-(3,5-dimethylphenyl)indolo[1,2-c]quinazoline-12a-carboxamide (4m).** White crystals; mp 229–230 °C; <sup>1</sup>H NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.65 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 7.36 (d,  $J$  = 7.8 Hz, 3H, Ar–H), 7.27–7.01 (m, 5H, Ar–H), 6.86 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 6.13 (s, 1H, CONH), 6.00 (s, 1H, OH), 5.83 (d,  $J$  = 8.4 Hz, 1H, 1Ar–H), 2.36 (s, 6H, CH<sub>3</sub>), 1.42 (s, 3H, CH<sub>3</sub>), 1.17 (s, 9H, 3CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 172.2, 152.8, 141.0, 139.7, 138.6, 137.3, 135.5, 131.7, 129.6, 127.9, 126.0, 125.8, 125.7, 125.3, 124.7, 122.4, 121.7, 115.1, 84.2, 73.2, 52.0, 28.1, 27.2, 21.2; IR ( $\nu$ , KBr): 3318, 2967, 2754, 1674, 1609  $\text{cm}^{-1}$ ; LC/MS:  $m/z$  453.8 [M]<sup>+</sup>;  $\text{C}_{29}\text{H}_{31}\text{N}_3\text{O}_2$  (453.6): calcd. C 76.79, H 6.89, N 9.26; found C 76.93, H 6.94, N 9.08%.

**N-tert-Butyl-12,12a-dihydro-12-hydroxy-12-methyl-6-(4-nitro-phenyl)indolo[1,2-c]quinazoline-12a-carboxamide (4n).** White crystals; mp 206–207 °C; <sup>1</sup>H NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.37 (d,  $J$  = 7.8 Hz, 2H, Ar–H), 7.77 (d,  $J$  = 8.4 Hz, 2H, Ar–H), 7.64 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 7.43–7.28 (m, 4H, Ar–H), 7.06 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 6.88 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 5.89 (s, 1H, CONH), 5.78 (d,  $J$  = 8.4 Hz, 1H, Ar–H), 5.30 (s, 1H, OH), 1.47 (s, 3H, CH<sub>3</sub>), 1.17 (s, 9H, 3CH<sub>3</sub>); <sup>13</sup>C NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 171.3, 150.6, 148.8, 141.7, 141.0, 139.5, 137.3, 130.1, 129.6, 128.2, 126.7, 126.5, 125.9, 125.1, 124.2, 123.0, 122.1, 114.3, 84.4, 74.2, 52.2, 28.3, 28.2; IR ( $\nu$ , KBr): 3551, 3412, 3112, 2976, 1669, 1600  $\text{cm}^{-1}$ ; LC/MS:  $m/z$  470.9 [M]<sup>+</sup>;  $\text{C}_{27}\text{H}_{26}\text{N}_4\text{O}_4$  (470.5): calcd. C 68.92, H 5.57, N 11.91; found C 68.67, H 5.83, N 12.12%.

**N-tert-Butyl-6-(2-chlorophenyl)-12,12a-dihydro-12-hydroxy-12-methylindolo[1,2-c]quinazoline-12a-carboxamide (4o).** White crystals; mp 195–196 °C; <sup>1</sup>H NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.73 (d,  $J$  = 7.8 Hz, 1H, Ar–H), 7.59–7.02 (m, 10.8H, 9Ar–H+0.9OH+0.9CONH), 6.87 (t,  $J$  = 7.8 Hz, 1H, Ar–H), 6.53 (s, 0.1H, 0.1OH), 6.33 (s, 0.1H, 0.1CONH), 5.84 (d,  $J$  = 8.4 Hz, 0.9H, 0.9Ar–H), 5.55 (d,  $J$  = 7.8 Hz, 0.1H, 0.1Ar–H), 1.37 (s, 3H, CH<sub>3</sub>), 1.14 (s, 9H, 3CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 173.4, 150.3, 139.7, 137.7, 134.7, 132.7, 131.2, 129.8, 129.5, 129.3, 128.1, 127.9, 126.8, 126.2, 126.1, 126.0, 125.4, 122.9, 120.4, 116.1, 84.7, 72.9, 52.3, 28.1, 26.1; IR ( $\nu$ , KBr): 3390, 3273, 2972, 1654, 1616  $\text{cm}^{-1}$ ; LC/MS:  $m/z$  460.2 [M]<sup>+</sup>;  $\text{C}_{27}\text{H}_{26}\text{ClN}_3\text{O}_2$  (460.0): calcd. C 70.50, H 5.70, N 9.14; found C 70.37, H 5.46, N 9.42%.

**N-tert-Butyl-12,12a-dihydro-12-hydroxy-12-methyl-6-phenethylindolo[1,2-c]quinazoline-12a-carboxamide (4p).** White crystals; mp 201–202 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ (ppm): 7.63 (d, *J* = 7.8 Hz, 1H, Ar–H), 7.45 (d, *J* = 7.2 Hz, 1H, Ar–H), 7.34–7.15 (m, 11H, Ar–H), 6.85 (s, 1H, OH), 6.30 (s, 1H, CONH), 3.13–2.99 (m, 4H, 2CH<sub>2</sub>), 1.28 (s, 3H, CH<sub>3</sub>), 1.09 (s, 9H, 3CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm): 173.7, 153.6, 140.6, 140.4, 139.1, 139.1, 129.5, 128.6, 128.3, 128.2, 126.4, 126.3, 126.0, 125.3, 125.2, 123.4, 120.4, 117.3, 84.3, 73.9, 51.9, 36.6, 32.5, 28.1, 25.4; IR (*v*, KBr): 3255, 3030, 2968, 1640, 1607 cm<sup>-1</sup>; LC/MS: *m/z* 453.8 [M]<sup>+</sup>; C<sub>29</sub>H<sub>31</sub>N<sub>3</sub>O<sub>2</sub> (453.6): calcd. C 76.79, H 6.89, N 9.26; found C 76.53, H 6.93, N 9.53%.

**N-Cyclohexyl-12-ethyl-12-hydroxy-6-(p-tolyl)-12,12a-dihydro-indolo[1,2-c]quinazoline-12a-carboxamide (4q).** White crystals; mp 199–200 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ (ppm): 7.66–7.18 (m, 9H, Ar–H), 7.02 (t, *J* = 7.2 Hz, 1H, Ar–H), 6.86 (t, *J* = 7.2 Hz, 1H, Ar–H), 6.39 (s, 1H, OH), 6.28 (d, *J* = 7.8 Hz, 1H, CONH), 5.85 (d, *J* = 8.4 Hz, 1H, Ar–H), 3.64–3.61 (m, 1H, NCH), 2.45 (s, 3H, CH<sub>3</sub>), 1.82–0.95 (m, 10H, 5CH<sub>2</sub>), 0.73 (t, *J* = 7.2 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ (ppm): 172.6, 152.6, 140.9, 140.4, 140.0, 135.0, 132.8, 129.6, 129.5, 127.8, 127.6, 125.9, 125.7, 124.6, 124.3, 120.9, 115.8, 86.0, 73.4, 48.2, 32.2, 31.9, 31.1, 25.1, 24.0, 21.5, 7.1, 7.0; IR (*v*, KBr): 3434, 3318, 2969, 2925, 2852, 1648, 1612 cm<sup>-1</sup>; MS: *m/z* (%) = 479 (14) [M]<sup>+</sup>, 252 (100), 227 (52), 192 (39), 77 (70); C<sub>31</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub> (479.6): calcd. C 77.63; H 6.94; N 8.76; found C 77.51, H 6.76, N 8.90%.

**N-Cyclohexyl-12-ethyl-12-hydroxy-6-phenyl-12,12a-dihydro-indolo[1,2-c]quinazoline-12a-carboxamide (4r).** White crystals; mp 178–179 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ (ppm): 7.67–7.19 (m, 10H, Ar–H), 7.02 (t, *J* = 7.2 Hz, 1H, Ar–H), 6.83 (t, *J* = 7.8 Hz, 1H, Ar–H), 6.40 (s, 1H, OH), 6.29 (d, *J* = 7.8 Hz, 1H, CONH), 5.77 (d, *J* = 7.8 Hz, 1H, Ar–H), 3.66–3.63 (m, 1H, NCH), 1.84–0.95 (m, 10H, 5CH<sub>2</sub>), 0.75 (t, *J* = 7.2 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ (ppm): 172.5, 152.5, 140.7, 140.2, 135.6, 135.0, 129.9, 129.7, 128.8, 127.7, 127.6, 126.0, 125.7, 125.6, 124.7, 124.3, 120.8, 115.8, 115.7, 86.0, 73.4, 48.2, 32.5, 32.1, 31.8, 31.0, 24.5, 24.4, 24.3, 24.1, 23.9, 7.18, 6.81; IR (*v*, KBr): 3435, 3310, 2965, 2927, 2859, 1651, 1617 cm<sup>-1</sup>; LC/MS: *m/z* 465 [M]<sup>+</sup>; C<sub>30</sub>H<sub>31</sub>N<sub>3</sub>O<sub>2</sub> (465.6): calcd. C 77.39; H 6.71; N 9.03; found C 77.22, H 6.93, N 9.10%.

## Acknowledgements

We gratefully acknowledge financial support of this work by the National Natural Science Foundation of China (No. 21032001 and 20772041), the PCSIRT (No. IRT0953) and the Doctor Independent Foundation of Central China Normal University (No. 2009011).

## Notes and references

- For recent examples of the Ugi reaction see: (a) A. Dömling, *Chem. Rev.*, 2006, **106**, 17; (b) J. Isaacson and Y. Kobayashi, *Angew. Chem., Int. Ed.*, 2009, **48**, 1845; (c) S. Marcaccini and T. Torroba, in *Multicomponent Reactions* (ed. J.-P. Zhu, H. Bienaymé), Wiley-VCH, Weinheim, 2005, pp. 33–75; (d) A. Domling, B. Beck, U. Eichelberger, S. Sakamuri, S. Menon, Q.-Z. Chen, Y. Lu and L. A. Wessjohann, *Angew. Chem., Int. Ed.*, 2006, **45**, 7235; (e) M. J. Thompson and B. Chen, *J. Org. Chem.*, 2009, **74**, 7084; (f) B. B. Touré and D. G. Hall, *Chem. Rev.*, 2009, **109**, 4439; (g) W. Erb, L. Neuville and J.-P. Zhu, *J. Org. Chem.*, 2009, **74**, 3109; (h) D. G. Rivera and L. A. Wessjohann, *J. Am. Chem. Soc.*, 2009, **131**, 3721; (i) D. Coffinier, L. El Kaim and L. Grimaud, *Org. Lett.*, 2009, **11**, 995; (j) L. A. Wessjohann, D. G. Rivera and O. E. Vercillo, *Chem. Rev.*, 2009, **109**, 796.
- For recent examples of the aza-Wittig reaction see: (a) J. Y. Lu, M. Riedrich, M. Mikyna and H.-D. Arndt, *Angew. Chem., Int. Ed.*, 2009, **48**, 8137; (b) M. Riedrich, S. Harkal and H.-D. Arndt, *Angew. Chem., Int. Ed.*, 2007, **46**, 2701; (c) D. Lertpibulpanya, S. P. Marsden, I. Rodriguez-Garcia and C. A. Kilner, *Angew. Chem., Int. Ed.*, 2006, **45**, 5000; (d) F. Palacios, C. Alonso, D. Aparicio, G. Rubiales and J. M. delos Santos, *Tetrahedron*, 2007, **63**, 523; (e) S. P. Marsden, A. E. McGonagle and B. McKeever-Abbas, *Org. Lett.*, 2008, **10**, 2589; (f) M. A. Arnold, S. G. Duron and D. Y. Gin, *J. Am. Chem. Soc.*, 2005, **127**, 6924.
- N. Corres, J. J. Delgado, M. García-Valverde, S. Marcaccini, T. Rodríguez, J. Rojo and T. Torroba, *Tetrahedron*, 2008, **64**, 2225.
- M. Sañudo, M. García-Valverde, S. Marcaccini, J. J. Delgado, J. Rojo and T. Torroba, *J. Org. Chem.*, 2009, **74**, 2189.
- P. Lecinska, N. Corres, D. Moreno, M. García-Valverde, S. Marcaccini and T. Torroba, *Tetrahedron*, 2010, **66**, 6783.
- P. He, J. Wu, Y. B. Nie and M. W. Ding, *Tetrahedron*, 2009, **65**, 8563.
- P. He, J. Wu, Y. B. Nie and M. W. Ding, *Eur. J. Org. Chem.*, 2010, 1088.
- F. De Moliner, S. Crosignani, L. Banfi, R. Riva and A. Basso, *J. Comb. Chem.*, 2010, **12**, 613.
- A. Ramazani and A. Rezaei, *Org. Lett.*, 2010, **12**, 2852.
- (a) L. Banfi, A. Basso, G. Guanti, S. Merlo, C. Repetto and R. Riva, *Tetrahedron*, 2008, **64**, 1114; (b) K. M. Bonger, T. Wennekes, S. V. P. de Lavori, D. Esposito, R. J. B. H. N. van den Berg, R. E. J. N. Litjens, G. A. van der Marel and H. S. Overkleft, *QSAR Comb. Sci.*, 2006, **25**, 491; (c) M. S. M. Timmer, M. D. P. Risseeuw, M. Verdoes, D. V. Filippov, J. R. Plaisier, G. A. van der Marel, H. S. Overkleft and J. H. van Boom, *Tetrahedron: Asymmetry*, 2005, **16**, 177.
- (a) N. Y. Huang, M. G. Liu and M. W. Ding, *J. Org. Chem.*, 2009, **74**, 6874; (b) N. Y. Huang, Y. J. Liang, M. W. Ding, L. W. Fu and H. W. He, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 831; (c) N. Y. Huang, Y. B. Nie and M. W. Ding, *Synlett*, 2009, 611; (d) W. J. Li, S. Liu, P. He and M. W. Ding, *Tetrahedron*, 2010, **66**, 8151; (e) M. G. Liu, Y. G. Hu and M. W. Ding, *Tetrahedron*, 2008, **64**, 9052.
- For construction of eight-membered ring systems through intramolecular aza-Wittig reaction see: (a) I. A. O’Neil, C. L. Murray, A. J. Potter and S. B. Kalindjian, *Tetrahedron Lett.*, 1997, **38**, 3609; (b) H. Fuwa, Y. Okamura, Y. Morohashi, T. Tomita, T. Iwatsubo, T. Kan, T. Fukuyama and H. Natsugari, *Tetrahedron Lett.*, 2004, **45**, 2323 and ref. 3.
- N. Kumagai, S. Matsunaga and M. Shibasaki, *Angew. Chem., Int. Ed.*, 2004, **43**, 478.
- (a) P. Loos, M. Riedrich and H.-D. Arndt, *Chem. Commun.*, 2009, 1900; (b) H. Takeuchi, S. Hagiwara and S. Eguchi, *Tetrahedron*, 1989, **45**, 6375; (c) T. Okawa, T. Sugimori, S. Eguchi and A. Kakehi, *Heterocycles*, 1998, **47**, 375; (d) S. Eguchi, Y. Matsushita and H. Takeuchi, *J. Org. Chem.*, 1992, **57**, 6975; (e) S. Eguchi, T. Suzuki, T. Okawa, Y. Matsushita, E. Yashima and Y. Okamoto, *J. Org. Chem.*, 1996, **61**, 7316.