Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 64 (2008) 2225–2232
www.elsevier.com/locate/tet

Synthesis of pseudopeptidic [(5*H*)-6-oxodibenzo[*b*,*f*][1,5]diazocine-5-yl]arylglycinamides by an Ugi 4CC/Staudinger/aza-Wittig sequence

Nazaret Corres [a], Jacinto J. Delgado [b], María García-Valverde [a,*], Stefano Marcaccini [c], Teresa Rodríguez [a], Josefa Rojo [a], Tomás Torroba [a,*]

[a] *Departamento de Química, Facultad de Ciencias, Universidad de Burgos, Pza. Misael Bañuelos s/n, 09001-Burgos, Spain*
[b] *SCAI, Centro de I+D+i, Universidad de Burgos, Plaza Misael Bañuelos s/n, 09001 Burgos, Spain*
[c] *Dipartimento di Chimica Organica 'Ugo Schiff', Università degli Studi di Firenze, 50019 Sesto Fiorentino (FI), Italy*

Received 12 November 2007; received in revised form 5 December 2007; accepted 7 December 2007
Available online 15 December 2007

Abstract

Sequential Ugi reaction between *p*-substituted benzaldehydes, 2-acetyl or 2-benzoylanilines, cyclohexyl or benzyl isocyanides, and 2-azidobenzoic acid, followed by a Staudinger/aza-Wittig cyclization in the presence of triphenylphosphine afforded pseudopeptidic [(5*H*)-6-oxodibenzo[*b*,*f*][1,5]diazocine-5-yl]arylglycinamides.

Keywords: Isocyanide; Ugi reaction; Staudinger/aza-Wittig; Diazocine

1. Introduction

The dibenzo[*b*,*f*][1,5]diazocine nucleus is a privileged structure found in the Tröger's base[1] and its analogs,[2] that are mainly intended for supramolecular chemistry. Other derivatives are much more scarce, with the exception of the dibenzo[*b*,*f*][1,5]diazocine-6,12-diones (dianthranilides), easily accessible from anthranilic acids.[3] Such dilactams have been of interest as chemosensitizers and reversal agents in multidrug resistance,[4] and in conformational studies.[3b,d,e] Polycyclic benzodiazocines of natural origin are potent inhibitors of protein kinase C and cyclic nucleotide-dependent protein kinases, used in experimental pharmacology,[5] and simple benzodiazocines have been used as homologues of benzodiazepine drugs.[6] Because of its structural similarity with diazepam and oxazepam, dibenzo[*b*,*f*][1,5]diazocine-6(5*H*)-one derivatives have attracted some interest for long time, but the lack of a secure method for their synthesis has stopped any further practical development.[7] We have recently shown that the sequences of classical Ugi or Passerini isocyanide multicomponent reactions, followed by post-condensation transformations, constitute extremely powerful synthetic tools for the preparation of structurally diverse complex molecules, among them are heterocyclic compounds with elaborate substitution patterns, constrained peptides, peptide mimetics, and pseudopeptides.[8] As a new contribution of this methodology, we want to report in this paper a new synthesis of pseudopeptidic [(5*H*)-6-oxo-dibenzo[*b*,*f*][1,5]diazocine-5-yl]arylglycinamides by the Ugi reaction between *p*-substituted benzaldehydes, 2-acetyl or 2-benzoylanilines, cyclohexyl or benzyl isocyanides, and 2-azidobenzoic acid, followed by a Staudinger/aza-Wittig cyclization of the Ugi products in the presence of triphenylphosphine.

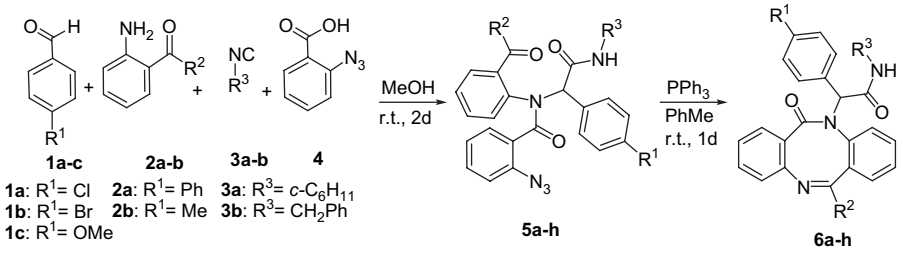
2. Results and discussion

A mixture of *p*-substituted benzaldehyde **1a**–**c** (1 equiv), 2-benzoyl- or 2-acetylaniline **2a**,**b** (1 equiv), cyclohexyl or benzyl isocyanide[9] **3a**,**b** (1 equiv), and 2-azidobenzoic acid[10] **4** (1 equiv) was stirred in methanol at room temperature for

* Corresponding authors. Tel.: +34 947258088; fax: +34 947258831.
E-mail addresses: magaval@ubu.es (M. García-Valverde), ttorroba@ubu.es (T. Torroba).

0040-4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.12.028

two days until solid **5a–h** precipitated.[11] Filtration and recrystallization of the solid afforded *N*-cyclohexyl (or benzyl) 2-[*N*-(2-benzoyl(or acetyl)phenyl)-*N*-(2-azidobenzoyl)amino]-2-arylacetamides **5a–h** in good yields (48–89%) (Scheme 1 and Table 1), which were subsequently stirred in dry toluene with triphenylphosphine (1.5 equiv) for one day to get *N*-cyclohexyl (or benzyl) 2-aryl-2-{12-phenyl(or methyl)-(5*H*)-6-oxodibenzo[*b*,*f*][1,5]diazocine-5-yl}acetamides **6a–h** in good yields (54–93%) (Scheme 1 and Table 1).



Scheme 1. Dibenzo[*b*,*f*][1,5]diazocine-5-yl arylglycinamides by the Ugi 4CC/Staudinger/aza-Wittig sequence.

The recrystallized products **5a–h** and **6a–h** were characterized by the usual spectroscopic and analytical techniques. COSY, NOESY, EXSY, DEPT, HMBC, and HMQC experiments of selected examples permitted to assign all NMR signals.

^{1}H and ^{13}C NMR spectra of **5a–h** were complicated by the presence of diastereotopic protons, coming from the restricted rotation of the tertiary amide bond in every racemic mixture, and the axial chirality due to the hindered anilide, giving rise to the presence of atropisomers. Assuming the general rule that groups cis to oxygen are shifted downfield,[12] we assigned the *E* geometry to the downfield signals and the *Z* geometry to the upfield signals, from which the *Z*/*E* ratio was obtained (Table 1). The rather complicated spectra were much simplified at increasingly high temperatures, in which signals coalesced to finally show a single racemic structure for each product, such as **5a** shown in Figure 1.

The *Z*/*E* ratio depended on the benzoyl or acetyl substituent, being inverted by the presence of one or the other group, and depended strongly on the solvent polarity. For example, **5h** showed a *Z*/*E* ratio of 20:80 in $CDCl_3$ and 93:7 in CD_3OD, therefore the presence of H-bonds may account for the results. Single crystal X-ray diffraction of one of the samples, **5d**, confirmed the expected structure. The unit cell consisted of a racemic mixture of two enantiomeric *E*-rotamers associated by two H-bonds [H(1A)···O(1): 2.59 Å, N(1)–H(1A)···O(1): 162.8°]. One enantiomer is shown in Figure 2. The racemic unit cell, showing the H-bonds that supports the packing, is shown in Figure 3.

Table 1
Ugi products **5a–h** and dibenzodiazocines **6a–h**

R^1	R^2	R^3	**5** (%)	*Z*/*E*	**6** (%)
Cl	Ph	*c*-C_6H_{11}	**5a** (62)	74:26	**6a** (81)
Br	Ph	*c*-C_6H_{11}	**5b** (55)	74:26	**6b** (57)
OMe	Ph	*c*-C_6H_{11}	**5c** (89)	75:25	**6c** (75)
Br	Ph	CH_2Ph	**5d** (48)	75:25	**6d** (54)
Cl	Me	*c*-C_6H_{11}	**5e** (70)	20:80	**6e** (93)
Br	Me	*c*-C_6H_{11}	**5f** (60)	20:80	**6f** (57)
OMe	Me	*c*-C_6H_{11}	**5g** (68)	18:82	**6g** (81)
Br	Me	CH_2Ph	**5h** (61)	20:80	**6h** (68)

Although we employed reaction conditions that were selective for the cyclization of the intermediate iminophosphorane with the ketone group,[13] the formation of the diazocine ring was undoubtedly probed from the EI HRMS patterns of **6a–h**, as, for example, detection of *m*/*z* peak 235.087 corresponding to the ring fragment ($C_{15}H_{11}N_2O^{+\bullet}$, calcd *m*/*z* 235.087) in **6h**.

^{1}H and ^{13}C NMR spectra of **6a–h** were much complicated by the presence of four diastereoisomers coming from the planar chiral ring[3b] and the restricted rotation of the arylglycine group bonded to the amide ring nitrogen. At higher temperatures the signals coalesced. Thus, at 80 °C, the ^{1}H NMR

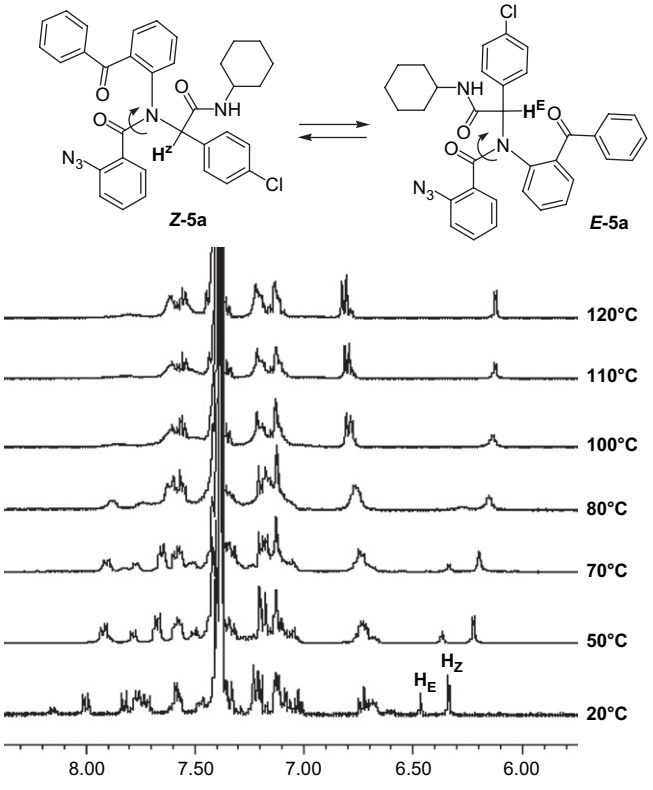


Figure 1. Selected region of ^{1}H NMR spectra of **5a** in deuterated chlorobenzene at different temperatures.

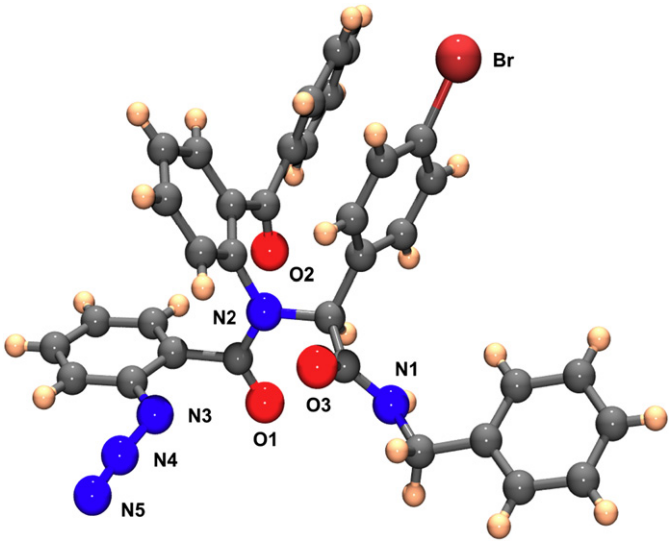


Figure 2. Single crystal X-ray diffraction structure of **5d**.

spectrum of **3a** showed only large signals corresponding to two rotamers (Fig. 4).

A similar transition of signals was obtained by changing the polarity of the solvent. Thus, ^{1}H NMR spectrum of **6f** in $CDCl_3$ showed four signals for the cyclohexyl methyne proton next to the NH group, but in CD_3OD it showed only two large signals, therefore the presence of H-bonds in $CDCl_3$, which are broken in CD_3OD, may be the cause of the latter behavior (Fig. 5).

3. Conclusion

In summary, we have described the synthesis of new *N*-cyclohexyl (or benzyl) 2-aryl-2-{12-phenyl(or methyl)-(5*H*)-6-oxodibenzo[*b*,*f*][1,5]diazocine-5-yl}acetamides by means of a sequence of Ugi four component condensation followed by a Staudinger/aza-Wittig cyclization of the intermediate Ugi products to give the final products. The reaction employs all commercial or easily available starting materials, performed under very simple experimental conditions and does not require chromatographic work-up, but only recrystallization of the products, therefore being appropriate for combinatorial schemes.

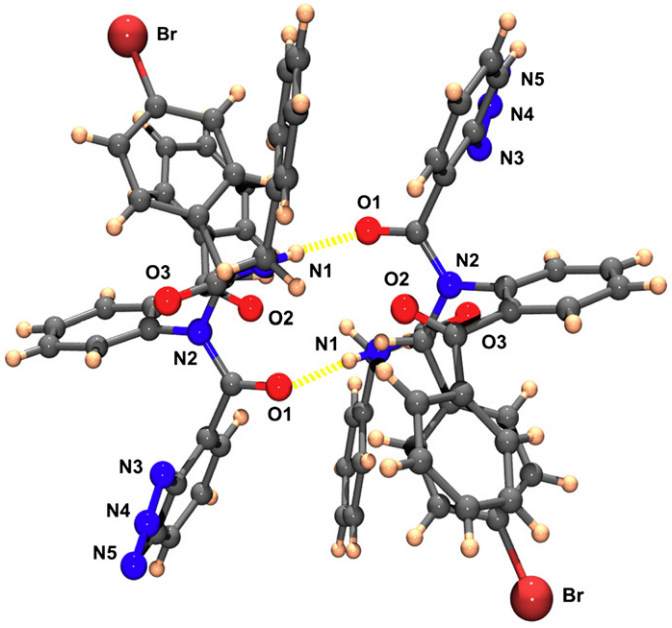


Figure 3. Crystal packing of **5d** unit cell showing a racemic mixture of two enantiomeric *E*-rotamers associated by two H-bonds.

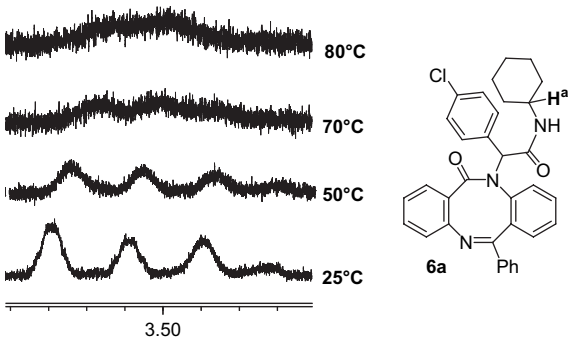


Figure 4. H^a region of the ^{1}H NMR spectra of **6a** in deuterated chlorobenzene at different temperatures.

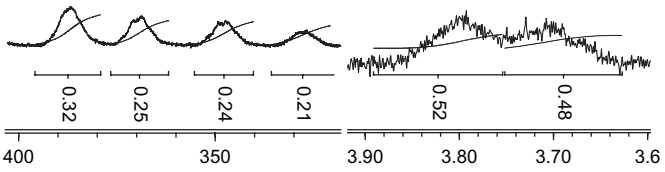


Figure 5. Cyclohexyl methyne region of the ^{1}H NMR spectra of **6f** in $CDCl_3$ (left) and CD_3OD (right).

4. Experimental

*4.1. Synthesis of N-cyclohexyl (or benzyl) 2-[N-(2-benzoyl(or acetyl)phenyl)-N-(2-azidobenzoyl)amino]-2-arylacetamides **5a–h***

A mixture of 2-azidobenzoic acid **4** (163 mg, 1 mmol) and the corresponding *p*-substituted benzaldehyde **1a–c** (1 mmol), aniline **2a**,**b** (1 mmol), and isocyanide **3a**,**b** (1 mmol) was stirred in methanol (20 mL) at room temperature for two days until a solid precipitated (addition of diisopropylether was sometimes necessary). Filtration and recrystallization from the appropriate solvent afforded acetamides **5a–h**.

*4.1.1. N-Cyclohexyl 2-[N-(2-benzoylphenyl)-N-(2-azidobenzoyl)amino]-2-(4-chlorophenyl)acetamide **5a***

Yellow crystals (367 mg, 62%), mp 163–165 °C (isopropylether–isopropanol). IR (KBr, cm^{-1}): 3333 (NH), 3024 (C_{Ar}–H), 2132 (N_3), 1678 (C=O), 1664 (C=O), 1635 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64–7.44 (m, 2.26H, 2H$_{Ar}$+0.26H NH, rot. A), 7.35–7.01 (m, 13H$_{Ar}$), 6.73–6.63 (m, 2.74H, 2H$_{Ar}$+0.74H NH, rot. B), 6.01 (s, 0.26H, rot. A), 5.90 (s, 0.74H, rot. B), 3.93–3.83 (m, 0.74H, rot. B), 3.57–2.66 (m,

0.26H, rot. A), 2.08–0.83 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2 (C_q), 168.5 (C_q, rot. A), 168.0 (C_q, rot. B), 139.7 (C_q), 136.8 (C_q), 134.4 (C_q), 133.3 (CH_{Ar}), 32.8 (CH_{Ar}), 132.5 (CH_{Ar}), 131.4 (CH_{Ar}), 131.3 (CH_{Ar}), 130.8 (CH_{Ar}), 130.5 (CH_{Ar}), 130.4 (CH_{Ar}), 129.9 (CH_{Ar}), 128.6 (CH_{Ar}), 128.4 (CH_{Ar}), 128.3 (CH_{Ar}), 127.2 (CH_{Ar}, rot. B), 127.0 (CH_{Ar}, rot. A), 124.4 (CH_{Ar}), 118.9 (CH_{Ar}, rot. B), 118.5 (CH_{Ar}, rot. A), 68.4 (CH, rot. B), 66.8 (CH, rot. A), 49.1 (CH, rot. A), 48.6 (CH, rot. B), 33.2 (CH_2), 33.0 (CH_2), 25.9 (CH_2), 25.1 (CH_2). MS (EI) *m/z* 563 (M^+-N_2, 11.8), 437 (100), 320 (47), 271 (73). Anal. Calcd for $C_{34}H_{30}ClN_5O_3$: C, 68.97; H, 5.11; N, 11.83. Found: C, 69.06; H, 5.19; N, 11.67.

4.1.2. *N*-Cyclohexyl 2-[*N*-(2-benzoylphenyl)-*N*-(2-azidobenzoyl)amino]-2-(4-bromophenyl)acetamide **5b**

Yellow crystals (350 mg, 55%), mp 170–172 °C (isopropyl ether–isopropanol). IR (KBr, cm^{-1}): 3329 (NH), 2126 (N_3), 1644 (C=O), 1653 (C=O), 1661 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.51 (m, 2.74H, $2H_{Ar}$+0.74NH, rot. A), 7.43–7.00 (m, $13H_{Ar}$), 6.77–6.59 (m, 2.26H, $2H_{Ar}$+0.26NH, rot. B), 5.99 (s, 0.26H, rot. B), 5.87 (s, 0.74H, rot. A), 3.81–3.75 (m, 0.26H, rot. B), 3.69–3.63 (m, 0.74H, rot. A), 2.13–1.10 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.0 (C_q), 194.0 (C_q), 168.2 (C_q), 139.5 (C_q), 136.5 (C_q), 133.5 (C_q), 133.2 (C_q), 133.0 (CH_{Ar}), 132.2 (CH_{Ar}), 131.3 (CH_{Ar}), 131.1 (CH_{Ar}), 130.9 (CH_{Ar}), 130.6 (CH_{Ar}), 130.3 (CH_{Ar}), 130.2 (CH_{Ar}), 129.6 (CH_{Ar}), 128.0 (CH_{Ar}), 127.0 (CH_{Ar}), 124.2 (CH_{Ar}), 118.3 (Cq), 68.2 (CH, rot B), 66.6 (CH, rot. A), 48.8 (CH, rot. A), 48.4 (CH, rot. B), 33.0 (CH_2), 32.8 (CH_2), 25.6 (CH_2), 24.8 (CH_2). MS (EI) *m/z* 609 (M^++2–N_2, 5.9), 607 (M^+-N_2, 5.5), 483 (78), 363 (47), 271 (100). Anal. Calcd for $C_{34}H_{30}BrN_5O_3$: C, 64.15; H, 4.75; N, 11.00. Found: C, 63.98; H, 4.87; N, 10.88.

4.1.3. *N*-Cyclohexyl 2-[*N*-(2-benzoylphenyl)-*N*-(2-azidobenzoyl)amino]-2-(4-methoxyphenyl)acetamide **5c**

Yellow crystals (523 mg, 89%), mp 166–168 °C (isopropyl ether–isopropanol). IR (KBr, cm^{-1}): 3336 (NH), 2129 (N_3), 1634 (C=O), 1660 (C=O), 1672 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.68 (m, 1.75H, $1H_{Ar}$+0.75NH, rot. B), 7.57–6.93 (m, $12H_{Ar}$), 6.76–6.45 (m, 4.25H, $4H_{Ar}$+0.25NH, rot. A), 5.94 (s, 0.25H, rot. A), 5.89 (s, 0.75H, rot. B), 3.91–3.83 (m, 0.25H, rot. A), 3.74–3.60 (m, 0.75H, rot. B), 3.60 (s, 0.75H, rot. A), 3.07 (s, 2.25H, rot. B), 2.05–1.10 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8 (C_q), 169.0 (C_q), 159.2 (C_q), 139.5 (C_q), 136.7 (C_q), 133.4 (C_q), 132.7 (CH_{Ar}), 132.5 (CH_{Ar}), 132.4 (CH_{Ar}), 131.5 (Cq), 131.0 (CH_{Ar}), 130.8 (CH_{Ar}), 130.6 (CH_{Ar}), 130.2 (CH_{Ar}), 130.1 (CH_{Ar}), 129.6 (CH_{Ar}), 129.4 (CH_{Ar}), 128.0 (CH_{Ar}), 127.8 (CH_{Ar}), 126.6 (CH_{Ar}), 124.0 (CH_{Ar}), 118.2 (CH_{Ar}), 113.6 (CH_{Ar}, rot. B), 113.2 (CH_{Ar}, rot. A), 68.5 (CH, rot. B), 66.3 (CH, rot. A), 55.1 (CH_3, rot. B), 55.0 (CH_3, rot. A), 48.7 (CH, rot. A), 48.2 (CH, rot. B), 33.0 (CH_2), 32.8 (CH_2), 25.6 (CH_2), 24.8 (CH_2). MS (EI) *m/z* 559 (M^+-N_2, 1.6), 432 (47), 271 (100). Anal. Calcd for $C_{35}H_{33}N_5O_4$: C, 71.53; H, 5.66; N, 11.92. Found: C, 71.45; H, 5.81; N, 11.82.

4.1.4. *N*-Benzyl 2-[*N*-(2-benzoylphenyl)-*N*-(2-azidobenzoyl)amino]-2-(4-bromophenyl)acetamide **5d**

Yellow crystals (310 mg, 48%), mp 172–174 °C (isopropanol–DMF). IR (KBr, cm^{-1}): 3356 (NH), 2125 (N_3), 1691 (C=O), 1653 (C=O), 1635 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (t, J=5.5 Hz, 0.25NH, rot. B), 7.70–6.89 (m, $20H_{Ar}$), 6.73–6.60 (m, 2.75H, $2H_{Ar}$+0.75NH, rot. A), 6.07 (s, 0.25H, rot. B), 6.06 (s, 0.75H, rot. A), 4.60 (dd, J=4.2, 13.6 Hz, 0.75H, rot. A), 4.56 (dd, J=4.2, 13.6 Hz, 0.75H, rot A), 4.39 (dd, J=5.5, 14.6 Hz, 0.25H, rot. B), 4.29 (dd, J=5.5, 14.6 Hz, 0.25H, rot. B). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3 (C_q, rot. B), 194.2 (C_q, rot. A), 169.6 (C_q, rot. A), 168.6 (C_q, rot. B), 168.4 (C_q, rot. B), 168.1 (C_q, rot. A), 140.0 (C_q, rot. B), 139.7 (C_q, rot. A), 138.4 (C_q, rot. A), 138.2 (C_q, rot. B), 137.2 (C_q), 136.7 (C_q), 135.1 (C_q), 133.3 (CH_{Ar}), 132.6 (CH_{Ar}), 131.6 (CH_{Ar}), 131.5 (CH_{Ar}), 131.4 (CH_{Ar}), 130.9 (CH_{Ar}, rot. B), 130.8 (CH_{Ar}, rot. A), 130.5 (CH_{Ar}, rot. B), 130.4 (CH_{Ar}, rot. A), 130.0 (CH_{Ar}, rot. B), 129.8 (CH_{Ar}, rot. A), 128.8 (CH_{Ar}, rot. A), 128.6 (CH_{Ar}, rot. B), 128.3 (CH_{Ar}), 128.0 (CH_{Ar}), 127.5 (CH_{Ar}), 127.3 (CH_{Ar}), 124.5 (CH_{Ar}, rot. B), 124.3 (CH_{Ar}, rot. A), 122.9 (Cq, rot. A), 122.4 (Cq, rot. B), 118.4 (CH_{Ar}, rot. B), 118.4 (CH_{Ar}, rot. A), 68.2 (CH, rot. B), 66.8 (CH, rot. A), 44.3 (CH_2, rot. A), 44.1 (CH_2, rot. B). MS (EI) *m/z* 617 (M^++2–N_2, 5.9), 615 (M^+-N_2, 5.5), 483 (100), 364 (75), 271 (28). Anal. Calcd for $C_{35}H_{26}BrN_5O_3$: C, 65.22; H, 4.07; N, 10.87. Found: C, 65.10; H, 4.19; N, 10.74. *Crystal data for compound* **5d**: $C_{35}H_{26}BrN_5O_3$, MW=644.52, triclinic, *P*-1, a=11.489(3) Å, b=11.599(3) Å, c=12.230(3) Å, α=74.893(5)°, β=77.874(5)°, γ=89.569(5)°; V=1536.5(7) Å^3, Z=2, D_{calcd}=1.393 g cm^{-1}, μ(Mo Kα)=1.382 mm^{-1}. Yellow prism (0.50×0.50×0.25) mm^3. 14,829 measured reflections, 5360 independent (R_{int}=0.0467), 3099 observed ($I>2\sigma(I)$). R_1=0.0512, wR_2=0.1421 (all data). CCDC 667058 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Center, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 (1223) 336033; email: deposit@ccdc.cam.ac.uk.

4.1.5. *N*-Cyclohexyl 2-[*N*-(2-acetylphenyl)-*N*-(2-azidobenzoyl)amino]-2-(4-chlorophenyl)acetamide **5e**

Yellow crystals (371 mg, 70%), mp 155–157 °C (isopropyl ether–isopropanol). IR (KBr, cm^{-1}): 3348 (NH), 2130 (N_3), 1684 (C=O), 1670 (C=O), 1652 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.00 (m, 10.2H, $10H_{Ar}$+0.2NH, rot. B), 6.96–6.78 (m, 2.8H, $2H_{Ar}$+0.8NH, rot. A), 6.04 (s, 0.8H, rot. A), 6.01 (s, 0.2H, rot. B), 3.93–3.84 (m, 0.8H, rot. A), 3.69–3.60 (m, 0.2H, rot. B), 2.26 (s, 0.6H, rot. B), 2.06 (s, 2.4H, rot. A), 1.96–1.10 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5 (C_q, rot. A), 168.7 (C_q, rot. B), 168.6 (C_q, rot. A), 168.5 (C_q, rot. A), 167.5 (C_q, rot. B), 138.0 (C_q, rot. B), 137.7 (C_q, rot. A), 136.7 (C_q, rot. B), 136.4 (C_q, rot. A), 136.1 (C_q, rot. B), 135.5 (C_q, rot. A), 134.4 (C_q, rot. A), 134.1 (C_q, rot. B), 133.0 (CH_{Ar}), 132.5 (CH_{Ar}), 132.2 (CH_{Ar}), 131.1 (CH_{Ar}, rot. A), 130.9 (CH_{Ar}, rot. B), 130.7 (CH_{Ar}), 129.9 (CH_{Ar}), 128.8 (C_q), 128.6 (CH_{Ar}, rot. A), 128.5

(CH_{Ar}, rot. B), 128.1 (CH_{Ar}), 124.7 (CH_{Ar}), 118.3 (CH_{Ar}, rot. B), 118.0 (CH_{Ar}, rot. A), 66.6 (CH, rot. B), 65.2 (CH, rot. A), 49.0 (CH, rot. A), 48.6 (CH, rot. B), 33.4 (CH_2), 33.1 (CH_2), 29.3 (CH_3, rot. B), 29.0 (CH_3, rot. A), 25.8 (CH_2), 25.2 (CH_2), 25.1(CH_2). MS (EI) *m/z* 501 (M^+-N_2, 3.1), 375 (100), 258 (80), 209 (28). Anal. Calcd for $C_{29}H_{28}ClN_5O_3$: C, 65.72; H, 5.32; N, 13.21. Found: C, 65.61; H, 5.39; N, 13.11.

4.1.6. N-Cyclohexyl 2-[N-(2-acetylphenyl)-N-(2-azidobenzoyl)amino]-2-(4-bromophenyl)acetamide ***5f***

Colorless crystals (345 mg, 60%), mp 152–154 °C (isopropyl ether–isopropanol). IR (KBr, cm^{-1}): 3334 (NH), 2125 (N_3), 1656 (C=O), 1654 (C=O), 1620 (C=O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.68–7.64 (m, 1.2H, $1H_{Ar}$+0.2NH, rot. B), 7.44–6.86 (m, $11H_{Ar}$), 6.81 (d, *J*=8.1 Hz, 0.8H, rot. A), 6.04 (s, 0.8H, rot. A), 6.02 (s, 0.2H, rot. B), 3.96–3.84 (m, 0.8H, rot. A), 3.71–3.60 (m, 0.2H, rot. B), 2.27 (s, 0.6H, rot. B), 2.07 (s, 2.4H, rot. A), 2.10–1.15 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.2 (C_q, rot. B), 199.2 (C_q, rot. A), 168.4 (C_q, rot. B), 168.3 (C_q, rot. A), 168.2 (C_q, rot. A), 167.1 (C_q, rot. B), 167.9 (C_q), 137.5 (C_q), 136.2 (C_q), 135.3 (C_q), 133.1 (CH_{Ar}), 132.7 (CH_{Ar}), 132.2 (CH_{Ar}), 132.0 (CH_{Ar}), 131.3 (CH_{Ar}), 131.2 (CH_{Ar}), 130.9 (CH_{Ar}), 130.4 (CH_{Ar}), 129.6 (CH_{Ar}), 128.7 (CH_{Ar}), 128.4 (CH_{Ar}), 124.4 (CH_{Ar}), 122.5 (CH_{Ar}), 118.1 (C_q, rot. B), 117.8 (C_q, rot. A), 66.4 (CH, rot. B), 65.1 (CH, rot. A), 48.8 (CH, rot. A), 48.4 (CH, rot. B), 33.1 (CH_2), 32.8 (CH_2, rot. B), 29.1 (CH_3, rot. B), 28.8 (CH_3, rot. A), 25.6 (CH_2), 24.9 (CH_2), 24.8 (CH_2). MS (EI) *m/z* 547 (M^++2−N_2, 7.8), 545 (M^+-N_2, 7.5), 421 (78), 302 (35), 209 (100). Anal. Calcd for $C_{29}H_{28}BrN_5O_3$: C, 60.63; H, 4.91; N, 12.19. Found: C, 60.69; H, 5.08; N, 12.05.

4.1.7. N-Cyclohexyl 2-[N-(2-acetylphenyl)-N-(2-azidobenzoyl)amino]-2-(4-methoxyphenyl)acetamide ***5g***

Colorless crystals (358 mg, 68%), mp 147–149 °C (isopropyl ether–isopropanol). IR (KBr, cm^{-1}): 3335 (NH), 2126 (N_3), 1642 (C=O), 1668 (C=O), 1692 (C=O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J*=1.1, 7.9 Hz, 1H, $0.82H_{Ar}$+0.18NH, rot. B), 7.40–6.50 (m, 12H, $11.18H_{Ar}$+0.82H NH, rot. A), 6.07 (s, 0.82H, rot. A), 5.92 (s, 0.18H, rot. B), 3.96–3.80 (m, 0.82H, rot. A), 3.78–3.65 (m, 0.18H, rot. B), 3.74 (s, 0.54H, rot. B), 3.69 (s, 2.46H, rot. A), 2.28 (s, 0.54H, rot. B), 2.02 (s, 2.46H, rot. A), 2.09–1.00 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1 (C_q, rot. B), 198.1 (C_q, rot. A), 169.0 (C_q, rot. A), 168.5 (C_q, rot. B), 168.3 (C_q, rot. A), 168.0 (C_q, rot. B), 159.3 (C_q), 137.5 (C_q), 136.2 (C_q), 135.7 (C_q), 132.7 (CH_{Ar}), 132.4 (CH_{Ar}), 131.7 (CH_{Ar}), 131.1 (C_q), 130.2 (CH_{Ar}), 129.3 (CH_{Ar}), 129.0 (CH_{Ar}), 128.6 (CH_{Ar}), 128.1 (CH_{Ar}), 125.5 (CH_{Ar}), 124.3 (CH_{Ar}), 118.0 (CH_{Ar}, rot. B), 117.4 (CH_{Ar}, rot. A), 113.6 (CH_{Ar}, rot. B), 113.1 (CH_{Ar}, rot. A), 64.8 (CH), 55.2 (CH_3, rot. B), 55.1 (CH_3, rot. A), 48.7 (CH, rot. A), 48.2 (CH, rot. B), 33.1 (CH_2), 32.8 (CH_2), 29.2 (CH_3, rot. B), 28.7 (CH_3, rot. A), 25.6 (CH_2), 25.9 (CH_2), 24.8 (CH_2). MS (EI) *m/z* 497 (M^+-N_2, 14), 371 (100), 209 (89). Anal. Calcd for $C_{30}H_{31}N_5O_4$: C, 68.55; H, 5.94; N, 13.32. Found: C, 68.66; H, 6.13; N, 13.20.

4.1.8. N-Benzyl 2-[N-(2-acetylphenyl)-N-(2-azidobenzoyl)amino]-2-(4-bromophenyl)acetamide ***5h***

Light red crystals (355 mg, 61%), mp 143–145 °C (isopropanol–DMF). IR (KBr, cm^{-1}): 3360 (NH), 2132 (N_3), 1697 (C=O), 1673 (C=O), 1639 (C=O). ^1H NMR (400 MHz, CD_3OD) δ 7.85 (dd, *J*=1.2, 7.9 Hz, 1H), 7.50 (dd, *J*=1.5, 7.9 Hz, 1H), 7.40–6.88 (m, 11H, $10H_{Ar}$+1NH), 6.14 (s, 0.07H, rot. B), 6.05 (s, 0.93H, rot. A), 4.51 (d, *J*=15.2 Hz, 0.93H, rot. A), 4.44 (d, *J*=15.2 Hz, 0.93H, rot. A), 4.40–4.35 (m, 0.14H, rot. B), 2.28 (s, 0.21H, rot. B), 2.18 (s, 2.79H, rot. A). ^{13}C NMR (100 MHz, CD_3OD) δ 200.7 (C_q), 172.2 (C_q), 170.4 (C_q), 139.7 (C_q), 138.4 (C_q), 138.1 (C_q), 136.6 (C_q), 134.8 (CH_{Ar}), 134.3 (CH_{Ar}), 133.9 (C_q), 133.4 (CH_{Ar}), 132.6 (CH_{Ar}), 132.1 (CH_{Ar}), 131.9 (CH_{Ar}), 131.3 (CH_{Ar}), 129.9 (CH_{Ar}), 129.5 (CH_{Ar}), 129.3 (CH_{Ar}), 128.4 (CH_{Ar}), 128.1 (CH_{Ar}), 125.4 (CH_{Ar}), 123.8 (Cq), 119.1 (CH_{Ar}), 66.6 (CH), 44.3 (CH_2), 29.2 (CH_3). MS (EI) *m/z* 555 (M^++2−N_2, 4), 553 (M^+-N_2, 4), 421 (41), 302 (28), 209 (100). Anal. Calcd for $C_{30}H_{24}BrN_5O_3$: C, 61.86; H, 4.15; N, 12.02. Found: C, 62.01; H, 4.19; N, 11.87.

4.2. Synthesis of N-cyclohexyl (or benzyl) 2-aryl-2-{12-phenyl(or methyl)-(5H)-6-oxodibenzo[b,f][1,5]diazocine-5-yl}acetamides ***6a–h***

A mixture of acetamides **5a–h** (1 mmol) in dry toluene (15 mL) was treated with triphenylphosphine (393 mg, 1.5 mmol) in dry toluene (5 mL). The mixture was stirred for one day. Then the solvent was evaporated and the residue was treated with hexane. The solid obtained was recrystallized from the appropriate solvent yielding the corresponding dibenzodiazocinones **6a–h**.

4.2.1. N-Cyclohexyl 2-(4-chlorophenyl)-2-{12-phenyl-(5H)-6-oxodibenzo[b,f][1,5]diazocine-5-yl}acetamide ***6a***

Colorless crystals (444 mg, 81%), mp 136–138 °C (hexane–ethyl acetate). IR (KBr, cm^{-1}): 3420 (NH), 1660 (C=O), 1652 (C=O), 1633 (C=N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.70 (br s, 0.25H, NH, isom. C), 8.29 (d, *J*=7.95 Hz, 0.30H, NH, isom. B), 8.03 (d, *J*=7.45 Hz, $0.38H_{Ar}$, isom. A), 7.85 (br s, 0.38H, NH, isom. A), 7.74–6.32 (m, 16H, $15.68H_{Ar}$+0.32H CH, isom. C+D), 6.10 (s, 0.30H, CH, isom. B), 6.05–5.85 (m, 1H, H_{Ar}), 5.08 (s, 0.38H, CH, isom. A), 3.91–3.84 (m, 0.38H, $CH_{cyclohexyl}$, isom. A), 3.70–3.65 (m, 0.30H, $CH_{cyclohexyl}$, isom. B), 3.51–3.45 (m, 0.25H, $CH_{cyclohexyl}$, isom. C), 3.22 (br s, 0.07H, $CH_{cyclohexyl}$, isom. D), 2.09–0.65 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.7, 196.4, 172.2, 169.2, 168.8, 167.9, 148.8, 148.1, 143.2, 140.7, 137.2, 135.6, 134.8, 133.2, 133.1, 133.0, 132.9, 132.8, 132.3, 132.1, 131.9, 131.7, 131.5, 131.3, 131.1, 130.8, 130.5, 129.3, 129.0, 128.9, 128.8, 128.3, 128.2, 128.1, 128.1, 128.0, 125.8, 125.5, 121.6, 121.4, 117.0, 116.9, 116.6, 70.1, 68.4, 67.8, 48.9, 48.7, 48.4, 41.6, 36.3, 33.4, 33.2, 33.1, 33.0, 32.7, 32.7, 32.6, 29.3, 26.0, 25.9, 25.9, 25.5, 25.4, 25.3, 25.2, 22.8, 20.7, 19.7, 19.0. MS (EI) *m/z* 547 (M^+, 2), 422 (21), 277 (100), 201 (20). HRMS (EI) calcd for $C_{34}H_{30}ClN_3O_2$

547.2027, found 547.2031. Anal. Calcd for $C_{34}H_{30}ClN_3O_2$: C, 74.51; H, 5.52; N, 7.67. Found: C, 74.42; H, 5.58; N, 7.56.

4.2.2. *N*-Cyclohexyl 2-(4-bromophenyl)-2-{12-phenyl-(5H)-6-oxodibenzo[b,f][1,5]diazocine-5-yl}acetamide **6b**

Yellow crystals (338 mg, 57%), mp 137–139 °C (hexane–ethyl acetate). IR (KBr, cm^{-1}): 3432 (NH), 1660 (C=O), 1652 (C=O), 1634 (C=N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.68 (br s, 0.26H, NH, isom. C), 8.24 (d, J=7.8 Hz, 0.31H, NH, isom. B), 7.85 (br s, 0.41H, NH, isom. A), 8.04–5.85 (m, 17.69H, 17H_{Ar}+0.69H CH, isom. A, C, D), 5.06 (s, 0.31H, CH, isom. B), 3.91–3.84 (m, 0.41$H_{cyclohexyl}$, isom. A), 3.68–3.63 (m, 0.31$H_{cyclohexyl}$, isom. B), 3.51–3.43 (m, 0.26$H_{cyclohexyl}$, isom. C), 3.21 (br s, 0.02$H_{cyclohexyl}$, isom. D), 2.03–0.85 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.6, 196.3, 174.5, 173.2, 172.2, 169.0, 168.7, 167.8, 148.2, 148.1, 140.8, 137.2, 136.0, 135.3, 134.8, 133.2, 133.0, 132.9, 132.9, 132.8, 132.6, 132.4, 132.3, 132.1, 131.6, 131.5, 131.2, 131.1, 131.0, 131.0, 130.9, 130.8, 130.5, 130.4, 130.2, 130.0, 129.8, 129.5, 129.3, 129.0, 128.9, 128.8, 128.6, 128.3, 128.2, 127.9, 125.8, 125.5, 121.8, 121.5, 117.0, 70.1, 68.4, 67.8, 48.9, 48.7, 48.4, 33.3, 33.1, 33.1, 32.7, 32.7, 32.5, 31.8, 29.3, 26.0, 25.9, 25.4, 25.3, 25.2, 22.9, 22.8. MS (EI) m/z 593 (M^++2, 3), 591 (M^+, 3), 467 (43), 277 (100), 201 (25), 119 (53). HRMS (EI) calcd for $C_{34}H_{30}BrN_3O_2$ 591.1521, found 591.1531. Anal. Calcd for $C_{34}H_{30}BrN_3O_2$: C, 68.92; H, 5.10; N, 7.09. Found: C, 69.07; H, 5.24; N, 6.88.

4.2.3. *N*-Cyclohexyl 2-(4-methoxyphenyl)-2-{12-phenyl-(5H)-6-oxodibenzo[b,f][1,5]diazocine-5-yl}acetamide **6c**

Colorless crystals (408 mg, 75%), mp 143–145 °C (hexane–ethyl acetate). IR (KBr, cm^{-1}): 3429 (NH), 1674 (C=O), 1665 (C=O), 1632 (C=N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J=7.2 Hz, 0.32H, NH, isom. C), 8.45 (d, J=8.4 Hz, 0.32H, NH, isom. B), 7.87 (br s, 0.32H, NH, isom. A), 8.03–5.87 (m, 17.68H, 17H_{Ar}+0.68H CH, isom. A, C, D), 5.17 (s, 0.32H, CH, isom. B), 3.67 (br s, 0.32H, $CH_{cyclohexyl}$, isom. A), 3.79 (br s, 0.32H, $CH_{cyclohexyl}$, isom. B), 3.69, 3.63, 3.58, 3.56 (s, 3H, CH_3, isom. A, B, C, D), 3.50 (br s, 0.32H, $CH_{cyclohexyl}$, isom. C), 3.24 (br s, 0.04H, $CH_{cyclohexyl}$, isom. D), 2.08–0.82 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 173.5, 173.4, 172.3, 170.1, 170.0, 159.0, 158.9, 147.9, 147.8, 142.9, 137.5, 137.4, 133.8, 133.3, 133.1, 133.0, 132.9, 132.8, 132.5, 132.2, 132.1, 132.0, 131.9, 131.8, 131.6, 131.5, 131.4, 131.3, 131.2, 131.0, 130.8, 130.4, 130.3, 130.2, 129.8, 129.5, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.3, 128.1, 127.9, 125.7, 125.2, 124.9, 121.6, 117.0, 116.9, 113.5, 113.4, 69.1, 69.1, 67.9, 55.3, 48.7, 48.6, 48.3, 33.3, 33.1, 32.9, 32.8, 32.7, 26.0, 25.5, 25.3, 25.2, 25.2. MS (EI) m/z 543 (M^+, 1.1), 417 (91), 277 (100). Anal. Calcd for $C_{35}H_{33}N_3O_3$: C, 77.32; H, 6.12; N, 7.73. Found: C, 77.46; H, 6.24; N, 7.61.

4.2.4. *N*-Benzyl 2-(4-bromophenyl)-2-{12-phenyl-(5H)-6-oxodibenzo[b,f][1,5]diazocine-5-yl}acetamide **6d**

Yellow crystals (324 mg, 54%), mp 197–199 °C (ethyl acetate–DMF). IR (KBr, cm^{-1}): 3440 (NH), 1671 (C=O), 1662 (C=O), 1633 (C=N). ^1H NMR (400 MHz, $CDCl_3$) δ 10.21 (br s, 0.15H, NH, isom. D), 8.69 (t, J=5.1 Hz, 0.24H, NH, isom. C), 8.32 (br s, 0.28H, NH, isom. B), 8.01–5.86 (m, 23.05H, 22H_{Ar}+0.33NH, isom. A+0.72H CH, isom. A, C, D), 5.50 (s, 0.28H, CH, isom. B), 4.60–4.10 (m, 1.70H, CH_2, isom. A, B, C), 3.32–3.23 (m, 0.30H, CH_2, isom. D). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 169.9, 169.5, 142.4, 139.2, 139.0, 138.8, 138.7, 137.2, 137.1, 133.1, 133.0, 132.9, 132.3, 132.2, 132.0, 131.7, 131.5, 131.3, 131.1, 131.0, 130.8, 130.6, 130.4, 130.1, 129.8, 129.3, 129.0, 128.9, 128.8, 128.5, 128.3, 128.1, 128.0, 127.9, 127.0, 126.9, 125.9, 125.6, 125.3, 121.9, 117.1, 116.9, 116.7, 69.2, 68.4, 67.3, 43.9. MS (EI) m/z 601 (M^++2, 79), 599 (M^+, 73), 469 (44), 364 (77), 362 (75), 209 (69), 91 (100). HRMS (EI) calcd for $C_{35}H_{26}BrN_3O_2$ 599.1208, found 599.1129. Anal. Calcd for $C_{35}H_{26}BrN_3O_2$: C, 70.00; H, 4.36; N, 7.00. Found: C, 70.11; H, 4.44; N, 6.87.

4.2.5. *N*-Cyclohexyl 2-(4-chlorophenyl)-2-{12-methyl-(5H)-6-oxodibenzo[b,f][1,5]diazocine-5-yl}acetamide **6e**

Colorless crystals (452 mg, 93%), mp 159–161 °C (hexane–ethyl acetate). IR (KBr, cm^{-1}): 3429 (NH), 1684 (C=O), 1629 (C=N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.90 (br s, 0.15H, NH, isom. D), 8.44 (br s, 0.24H, NH, isom. C), 8.19 (d, J=8.2 Hz, 0.27H, NH, isom. B), 7.82–6.35 (m, 13.07H, 12H_{Ar}+0.34H NH, isom. A+0.73H CH, isom. A, C, D), 5.23 (s, 0.27H, CH, isom. B), 3.93–3.86 (m, 0.34H, $CH_{cyclohexyl}$, isom. A), 3.77–3.69 (m, 0.27H, $CH_{cyclohexyl}$, isom. B), 3.55–3.45 (m, 0.24H, $CH_{cyclohexyl}$, isom. C), 3.34–3.26 (m, 0.15H, $CH_{cyclohexyl}$, isom. D), 2.73, 2.31, 2.25, 2.20 (s, 3H, CH_3, isom. A, B, C, D), 2.10–0.93 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 173.2, 168.9, 168.5, 148.2, 140.9, 138.6, 134.9, 134.7, 133.4, 133.3, 132.9, 132.8, 132.5, 132.4, 132.3, 132.1, 132.0, 131.9, 131.8, 131.5, 131.2, 131.1, 130.9, 130.2, 130.1, 129.9, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.1, 128.0, 127.9, 127.8, 127.5, 127.3, 127.1, 126.7, 126.3, 125.2, 121.9, 121.2, 119.2, 117.1, 116.4, 67.5, 48.8, 48.6, 33.3, 32.7, 29.7, 29.3, 25.9, 25.2, 25.2. MS (EI) m/z 487 (M^++2, 2.4), 485 (M^+, 6), 380 (75), 359 (56), 277 (100), 201 (23). HRMS (EI) calcd for $C_{29}H_{28}ClN_3O_2$ 485.1870, found 485.1860. Anal. Calcd for $C_{29}H_{28}ClN_3O_2$: C, 71.67; H, 5.81; N, 8.65. Found: C, 71.58; H, 5.92; N, 8.58.

4.2.6. *N*-Cyclohexyl 2-(4-bromophenyl)-2-{12-methyl-(5H)-6-oxodibenzo[b,f][1,5]diazocine-5-yl}acetamide **6f**

Colorless crystals (302 mg, 57%), mp 144–146 °C (hexane–ethyl acetate). IR (KBr, cm^{-1}): 3432 (NH), 1684 (C=O), 1633 (C=N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.90 (br s, 0.15H, NH, isom. D), 8.44 (br s, 0.23H, NH, isom. C), 8.16 (d, J=8.0 Hz, 0.29H, NH, isom. B), 7.84–5.95 (m, 13.04H, 12H_{Ar}+0.33H NH, isom. A+0.71H CH, isom. A, C, D), 5.20 (s, 0.29H, CH, isom. B), 3.92–3.85 (m, 0.33H, $CH_{cyclohexyl}$, isom. A), 3.74–3.68 (m, 0.29H, $CH_{cyclohexyl}$, isom. B), 3.53–3.45 (m, 0.23H, $CH_{cyclohexyl}$, isom. C), 3.33–3.28 (m, 0.15H, $CH_{cyclohexyl}$, isom. D), 2.74, 2.31, 2.26, 2.21 (s, 3H, CH_3, isom. A, B, C, D), 2.10–0.48 (m,

10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 173.1, 172.3, 168.8, 168.5, 148.7, 148.2, 141.0, 138.8, 137.7, 136.9, 136.4, 135.5, 135.1, 133.4, 132.9, 132.7, 132.3, 132.2, 132.1, 131.9, 131.8, 131.1, 131.0, 130.9, 130.8, 130.5, 130.2, 129.9, 129.0, 128.9, 128.8, 128.2, 128.1, 127.3, 127.1, 126.7, 126.3, 125.2, 124.4, 123.7, 122.0, 121.8, 121.7, 121.3, 119.2, 117.1, 116.4, 116.3, 69.1, 67.7, 67.6, 50.1, 49.0, 48.5, 33.3, 33.0, 32.6, 31.8, 29.7, 29.3, 28.7, 25.9, 25.3. MS (EI) *m/z* 531 (M^++2, 1.5), 529 (M^+, 1.5), 380 (100), 277 (62). Anal. Calcd for $C_{29}H_{28}BrN_3O_2$: C, 65.66; H, 5.32; N, 7.92. Found: C, 65.49; H, 5.21; N, 7.79.

4.2.7. N-Cyclohexyl 2-(4-methoxyphenyl)-2-{12-methyl-(5H)-6-oxodibenzo[b,f][1,5]diazocine-5-yl}acetamide ***6g***

Colorless crystals (390 mg, 81%), mp 155–157 °C (hexane–ethyl acetate). IR (KBr, cm^{-1}): 3431 (NH), 1683 (C=O), 1627 (C=N). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (br s, 0.15H, NH, isom. D), 8.51 (br s, 0.25H, NH, isom. C), 8.41 (d, J=8.2 Hz, 0.28H, NH, isom. B), 7.86–5.91 (m, 13.04H, $12H_{Ar}$+0.32H NH, isom. A+0.72H CH, isom. A, C, D), 5.43 (s, 0.28H, CH, isom. B), 3.95–3.50 (m, 0.85H, $CH_{cyclohexyl}$, isom. A, B, C), 3.34–3.30 (m, 0.15H, $CH_{cyclohexyl}$, isom. D), 3.75, 3.70, 3.73, and 3.65 (s, 3H, CH_3, isom. A, B, C, D), 2.74, 2.35, and 2.15 (s, 3H, CH_3, isom. A, B, C, D), 2.05–0.86 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 174.6, 173.3, 172.4, 172.4, 172.4, 170.5, 170.0, 169.9, 169.6, 169.5, 169.2, 160.0, 159.1, 159.0, 148.0, 147.9, 140.6, 140.4, 138.6, 137.6, 137.3, 137.0, 136.4, 133.7, 133.5, 133.4, 133.1, 133.0, 132.9, 132.8, 132.7, 132.5, 132.3, 132.2, 132.1, 132.0, 131.9, 131.8, 131.7, 131.5, 131.3, 130.9, 130.6, 130.5, 130.3, 130.0, 129.7, 129.0, 128.9, 128.8, 128.8, 128.7, 128.6, 128.4128.2, 128.0, 127.2 127.0, 126.9, 126.5, 126.1, 125.0, 124.3, 121.1, 117.2, 116.3, 113.9, 113.4, 113.3, 113.2, 112.9, 68.2, 68.0, 64.0, 63.9, 55.5, 55.3, 55.3, 55.2, 48.8, 48.7, 48.3, 33.4, 33.3, 33.0, 32.9, 29.9, 29.4, 29.3, 26.8, 26.0, 25.9, 25.8, 25.7, 25.6, 25.5, 25.3, 25.2, 24.9. MS (EI) *m/z* 481 (M^+, 3), 380 (40), 355 (100), 277 (70), 201 (16). HRMS (EI) calcd for $C_{30}H_{31}N_3O_3$ 481.2365, found 481.2375. Anal. Calcd for $C_{30}H_{31}N_3O_3$: C, 74.82; H, 6.49; N, 8.73. Found: C, 74.91; H, 6.57; N, 8.61.

4.2.8. N-Benzyl 2-(4-bromophenyl)-2-{12-methyl-(5H)-6-oxodibenzo[b,f][1,5]diazocine-5-yl}acetamide ***6h***

Colorless crystals (366 mg, 68%), mp 167–169 °C (ethyl acetate–DMF). IR (KBr, cm^{-1}): 3432 (NH), 1691 (C=O), 1666 (C=O), 1626 (C=N). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (br s, 0.34H, NH, isom. D), 8.68 (br s, 0.15H, NH, isom. C), 8.22 (br s, 0.16NH, isom. B), 7.69–6.05 (m, 18.19H, $17H_{Ar}$+0.35NH, isom. A+0.84H CH, isom. A, C, D), 5.76 (s, 0.16H, CH, isom. B), 4.50–4.02 (m, 1.32H, CH_2, isom. A, B, C), 3.20 (dd, J=14.8, 5.1 Hz, 0.68H, CH_2, isom. D), 2.21, 2.18, 2.13 (s, 3H, CH_3, isom. A, B, C, D). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 170.1, 147.6, 139.1, 139.0, 137.7, 137.1, 133.2, 133.1, 133.0, 132.9, 132.8, 132.4, 132.3, 132.1, 131.0, 130.9, 130.6, 130.2, 129.7, 129.6, 129.4, 129.2, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.2, 127.9, 127.8, 127.0, 123.1, 122.3, 122.0, 119.6, 116.5, 67.6, 67.3, 67.3, 43.8, 43.5, 43.4, 29.5, 29.2, 29.1, 28.8. MS (EI) *m/z* 539 (M^++2, 3), 537 (M^+, 3), 405 (23), 277 (100), 201 (16). HRMS (EI) calcd for $C_{30}H_{24}BrN_3O_2$ 537.1052, found 537.1028. Anal. Calcd for $C_{30}H_{24}BrN_3O_2$: C, 66.92; H, 4.49; N, 7.80. Found: C, 66.99; H, 4.53; N, 7.69.

Acknowledgements

We gratefully acknowledge financial support from the Dirección General de Investigación of Spain (Project ref. CTQ2006-15456-C04-04BQU) and Junta de Castilla y León, Consejería de Educación y Cultura, y Fondo Social Europeo (Project ref. BU013A06).

Supplementary data

^{1}H NMR and ^{13}C NMR of compounds **5a–h** and **6a–h**. COSY, NOESY, EXSY, DEPT, HMBC, and HMQC experiments of selected examples of **5a–h** and **6a–h**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.12.028.

References and notes

1. Recent examples: (a) Didier, D.; Sergeyev, S. *Eur. J. Org. Chem.* **2007**, 3905–3910; (b) Yuan, C.-X.; Tao, X.-T.; Ren, Y.; Li, Y.; Yang, J.-X.; Yu, W.-T.; Wang, L.; Jiang, M.-H. *J. Phys. Chem. C* **2007**, *111*, 12811–12816.
2. A recent example: Leganza, A.; Bezze, C.; Zonta, C.; Fabris, F.; De Lucchi, O.; Linden, A. *Eur. J. Org. Chem.* **2006**, 2987–2990.
3. See for example: (a) Acs, P.; Müller, E.; Rangits, G.; Lorand, T.; Kollar, L. *Tetrahedron* **2006**, *62*, 12051–12056; (b) Olszewska, T.; Gdaniec, M.; Połonski, T. *J. Org. Chem.* **2004**, *69*, 1248–1255; (c) Hassner, A.; Sun, B.; Gellermann, G.; Meir, S. *Tetrahedron Lett.* **2004**, *45*, 1377–1379; (d) Hoorfar, A.; Ollis, W. D.; Price, J. A.; Stephanatou, J. S.; Stoddart, J. F. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1649–1699; (e) Edge, S. J.; Ollis, W. D.; Stephanatou, J. S.; Stoddart, J. F. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1701–1714. Dilactams from Ugi reactions: (f) Ebert, B. M.; Ugi, I. K. *Tetrahedron* **1998**, *54*, 11887–11898. Polycyclic dilactams: (g) Eguchi, S.; Matsuehita, Y.; Takeuchi, H. *J. Org. Chem.* **1992**, *57*, 697–6979.
4. Nonnenmacher, E.; Brouant, P.; Mrozek, A.; Karolak-Wojciechowska, J.; Barbe, J. *J. Mol. Struct.* **2000**, *522*, 263–269.
5. See for example: (a) Nakayama, T.; Harada, N.; Asano, M.; Nomura, N.; Saito, T.; Mishima, A.; Okajima, K. *J. Pharmacol. Exp. Ther.* **2007**, *322*, 582–590; (b) Culmsee, C.; Gerling, N.; Landshamer, S.; Rickerts, B.; Duchstein, H. J.; Umezawa, K.; Klumpp, S.; Krieglstein, J. *Mol. Pharmacol.* **2005**, *68*, 1006–1017; (c) Mixcoatl-Zecuatl, T.; Flores-Murrieta, F. J.; Granados-Soto, V. *Eur. J. Pharmacol.* **2006**, *531*, 87–95.
6. Yoshida, H.; Shirakawa, E.; Honda, Y.; Hiyama, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 3247–3249 and references therein.
7. (a) Topliss, J. G.; Shapiro, E. P.; Taber, R. I. *J. Med. Chem.* **1967**, *10*, 642–646; (b) Pessoa-Mahana, H.; Martínez-Aránguiz, K. G.; Araya-Maturana, R.; Pessoa-Mahana, C. D. *Synth. Commun.* **2005**, *35*, 1493–1500; (c) Ege, G.; Beisiegel, E.; Arnold, P. *Chem. Ber.* **1972**, *105*, 2898–2912. See also: (d) Sigaut, F.; Didierdefresse, B.; Lévy, J. *Tetrahedron* **2000**, *56*, 9641–9646.
8. (a) Marcaccini, S.; Torroba, T. *Multicomponent Reactions*; Zhu, J., Bienaymé, H., Eds.; Wiley-VCH: Weinheim, Germany, 2005; Chapter 2, pp 33–75; (b) Ignacio, J. M.; Macho, S.; Marcaccini, S.; Pepino, R.; Torroba, T. *Synlett* **2005**, 3051–3054; (c) Sañudo, M.; Marcaccini, S.; Basurto, S.; Torroba, T. *J. Org. Chem.* **2006**, *71*, 4578–4584.
9. (a) Gokel, W.; Widera, R. P.; Weber, W. P. *Org. Synth. Coll. Vol.* **1988**, *6*, 232; (b) Gokel, W.; Widera, R. P.; Weber, W. P. *Org. Synth.* **1976**, *55*, 96;

(c) Alternative procedure: Ugi, I.; Meyr, R.; Lipinski, M.; Bodesheim, F.; Rosendahl, F. *Org. Synth. Coll. Vol.* **1973**, *5*, 300; (d) Ugi, I.; Meyr, R.; Lipinski, M.; Bodesheim, F.; Rosendahl, F. *Org. Synth.* **1961**, *41*, 13.

10. (a) Budruev, A. V.; Karyakina, L. N.; Levina, O. P.; Oleinik, A. V. *Russ. J. Coord. Chem.* **2005**, *31*, 181–184; (b) Lamara, K.; Smalley, R. K. *Tetrahedron* **1991**, *47*, 2277–2290.
11. Extended experimental details about the Ugi reaction, in: Marcaccini, S.; Torroba, T. *Nature Prot.* **2007**, *2*, 632–639.
12. Ahmed, A.; Bragg, R. A.; Clayden, J.; Lai, L. W.; McCarthy, C.; Pink, J. H.; Westlund, N.; Yasin, S. A. *Tetrahedron* **1998**, *54*, 13277–13294.
13. Reviews: (a) Palacios, F.; Alonso, C.; Aparicio, D.; Rubiales, G.; de los Santos, J. M. *Tetrahedron* **2007**, *63*, 523–575; (b) Bräse, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 5188–5240. A benzodiazocine via Staudinger/aza-Wittig ring closing: (c) O'Neil, I. A.; Murray, C. L.; Potter, A. J.; Kalindjian, S. B. *Tetrahedron Lett.* **1997**, *38*, 3609–3610.