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A diastereoselective synthesis of pseudopeptidic hydantoins by an Ugi/cyclization/ Ugi sequence

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ABSTRACT

A diastereoselective synthesis of helix-forming pseudopeptidic hydantoins by an Ugi 4CC/cyclization/ reduction/Ugi 4CC sequence of reactions, giving mainly the L-adduct when benzoic acids were used, is described.

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1. Introduction

Hydantoins (imidazolidine-2,4-diones) constitute a very old class of cyclic ureides of α -amino acids,¹ largely used as anticonvulsant drugs (i.e., phenytoin and its derivatives),² also present in a plethora of other commercial pharmaceutical products.³ Furthermore, hydantoins are privileged scaffolds in the structure of several new leads for current pharmacological developments such as small-molecule inhibitors of cell division,⁴ a model for the discovery of the PDE5 inhibitor tadalafil,⁵ nonsteroidal androgen receptor antagonists or agonists,⁶ and are present in some important pharmacologically active naturally occurring hydantoin alkaloids⁷ or their synthetic precursors.⁸ The conformational rigidity of the hydantoin scaffold in aminoacid derivatives⁹ and, very specially, in peptidomimetics¹⁰ is crucial for their biological stability and activity, often mimicking the appropriate conformation of the natural polypeptide whose biological action is sought. Therefore the synthesis of hydantoins is a very active research field,¹¹ even if the preparative methods for pseudopeptide hydantoins are still uncommon. We have previously developed some synthetic methods for the preparation of pseudopeptidic benzodiazepines, diazepines, diazocines, and triazinylalaninamides,¹² as well as monocyclic hydantoins,¹³ via Ugi four-component condensations followed by cyclization reactions.¹⁴ We reasoned that a sequential combination

of Ugi/cyclization/Ugi reactions could easily give rise to peptidehydantoin chivmeras belonging to a new class of drug-like peptidomimetics. Not only the design demonstrated to be successful but, as a bonus of the sequence, the second Ugi reaction showed an unexpected diastereoselectivity, giving mainly the L-adduct when benzoic acids were used. Diastereoselective Ugi reactions are scarce,¹⁵ therefore in this paper we want to report our results in the diastereoselective synthesis of pseudopeptidic hydantoins by a sequence of Ugi/cyclization/reduction/Ugi reactions.

2. Results and discussion

We selected the readily available *m*- and *p*-nitrobenzaldehydes as starting materials for the first Ugi reaction because the nitro group could activate the carbonyl moiety and because the nitro group could serve as a masked amino group for a further Ugi reaction. Therefore, a mixture of nitrobenzaldehydes **1a,b** (1 equiv) and anilines **2a**-e (1 equiv) was stirred in methanol at room temperature for 10 min, then isocyanides **3a,b** (1 equiv) and trichloroacetic acid **4** (1 equiv) were added consecutively to the imine solution, and the mixture was stirred in methanol at room temperature for one day until solid **5a**-**f** precipitated.¹⁶ Filtration and recrystallization of the solid afforded 2-[*N*-aryl-*N*-(trichloroacetyl) amino]-2-arylacetamide derivatives **5a**-**f** in fair yields (44–88%) (Scheme 1), that were subsequently stirred in methanol with 1 M sodium ethoxide (1 equiv) for 5 min, chilled, and the precipitate filtered off to get 3-alkyl-1,5-diarylimidazolidin-2,4-dione





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Table 3 ^a Relative configuration I:u

Scheme 1. Synthesis of hydantoin pseudopeptides 10a-u.

derivatives 6a-f in fair yields (66-95%). Nitro groups in 6a-f were reduced to the amino derivatives **7a**–**f** by iron powder in acetic acid at 60 °C for 30 min. Aqueous work-up, extraction with chloroform, and recrystallization gave 3-alkyl-1,5-diarylimidazolidin-2,4-dione derivatives 7a-f in fair yields (48-94%). Finally, a mixture of aldehydes **8a**–**d** (1 equiv) and hydantoin aniline **7a**–**f** (1 equiv) was refluxed in methanol for 30 min, then isocyanides **3a,b** (1 equiv) and carboxylic acid 9a-g(1 equiv) were added consecutively to the imine solution, and the mixture was refluxed in methanol until all reagents dissolved, then the mixture was maintained at room temperature for 1 day without stirring until solid 10a-u precipitated. Filtration and recrystallization of the solid afforded hydantoin pseudopeptides 10a-f, from 7a,b, and 10g-u, from 7c-f, in fair yields (44-88%) (Scheme 1). The recrystallized products **10a–u** were characterized by the usual spectroscopic and analytical techniques. DEPT experiments of selected examples permitted to assign all NMR signals. Products 10a-u were obtained in most cases as uneven mixtures of diastereoisomers, the relation of them was calculated on the basis of NMR spectra in CDCl₃ taken from the reaction product previously to and after recrystallization, to guarantee that no enrichment in the diastereomeric mixture happened during recrystallization. The best diastereoselection was achieved by using benzoic acids, suggesting that the planar aromatic nucleus had a strong influence on the mechanism. A plausible

mechanism should consist on the attack of the isocyanide on the protonated imine through a seven-centered transition state, stabilized by $\pi-\pi$ stacking of the aromatic rings, by the opposite side to the bulk hydantoin moiety with *lk*-selectivity (Scheme 2). When there is no $\pi-\pi$ stacking, the classic mechanism should apply,^{15f} therefore losing most of the diastereoselectivity.



Scheme 2. A mechanism for hydantoin pseudopeptide **10k**. Inset: X-ray diffraction structure of **10k** (only the *S/S* enantiomer).

The *lk*-selectivity is in agreement with the structure observed by single crystal X-ray diffraction of the main diastereoisomer of **10k** (Scheme 2). The relative configuration of the main diastereoisomer for similar hydantoins **10d**,**h**,**n**,**p**,**s** (obtained from aromatic acids **9b**,**f**,**g**) was assigned as L on the basis of ¹H NMR spectra (6.4–5.0 ppm region, Table 1).

The molecules pack helicoidally in the solid state, and the helix structure is supported by two different hydrogen bonds, one of them between the **O1** of one molecule and the proton of an OH group from an isopropanol solvent molecule, and the other one between the oxygen of the same OH group and the proton from a N4-H group of a nearby molecule, therefore forming enantiomeric helixes, one of them (from the R/R enantiomer) is shown in Fig. 1. In addition to the helix-forming behavior, these compounds show a certain drug-conforming behavior, with positive druglikeness scores by the OSIRIS Property Explorer,17 for some of these structures (such as 10d or 10h) although other characteristics (such as c log P and therefore their suspected solubilities) should be improved for satisfactory drug-scores. But because of the easy manipulation of the final structures and the high diversity achieved from very few simple starting materials, this method can be a useful tool for the design of libraries of new drug-like compounds.

Table 1

H NMR signals for some hydantoins in the 6.4-5.0 ppm region

	,	11 8
10	δ ¹ H NMR (ppm) diast.1	δ ¹ H NMR (ppm) <i>diast.2</i>
d	6.05 (s, 1H, CH)	
	5.53 (d, J=8.1 Hz, 0.92H, NH)	5.57 (d, J=8.1 Hz, 0.08H, NH)
	5.11 (s, 1H, CH)	
h	6.19 (s, 0.93H, CH),	6.13 (s, 0.07H, CH),
	5.42 (d, J=7.8 Hz, 0.93H, NH)	5.58 (d, J=8.2 Hz, 0.07H, NH)
	5.10 (s, 1H, CH)	
k	6.11 (s, 0.93H, CH),	6.07 (s, 0.07H, CH),
	5.55 (d, <i>J</i> =8.1 Hz, 0.93H, NH)	5.71 (d, J=8.5 Hz, 0.07H, NH)
	5.09 (s, 0.93H, CH)	5.07 (s, 0.07H, CH)
n	6.05 (s, 1H, CH)	
	5.53 (d, J=8.1 Hz, 0.92H, NH)	5.57 (d, J=8.1 Hz, 0.08H, NH)
	5.11 (s, 1H, CH)	
р	6.28–6.20 (m, 1.96H, H _{Ar} +0.96H, CH)	6.13 (s, 0.04H, CH),
	5.59 (d, <i>J</i> =7.9 Hz, 1H, NH)	
	5.28 (s, 1H, CH)	
S	6.18 (s, 0.86H, CH)	6.13 (s, 0.14H, CH)
	5.50 (d, J=8.3 Hz, 0.86H, NH)	5.66 (d, J=8.1 Hz, 0.14H, NH)
	5.15 (s, 1H, CH)	



Fig. 1. Crystal packing of **10k** in a helix fashion (only the helix from the *R*/*R* enantiomer is shown). (a) A view along the vertical axis. (b) An orthogonal view of the same helix showing (in yellow dotted lines) the hydrogen bonds.

3. Conclusion

In summary, we have described a diastereoselective synthesis of helix-forming pseudopeptidic hydantoins by an Ugi 4CC/cyclization/reduction/Ugi 4CC sequence of reactions, giving mainly the Ladduct when benzoic acids were used. The reactions employ all commercial or easily available starting materials, and are performed under very simple experimental conditions and work-up, without the use of column chromatography, which makes it useful for new drug design.

4. Experimental section

4.1. General

Melting points are not corrected. Infrared spectra were registered in potassium bromide tablets. ¹H and ¹³C NMR spectra were recorded in DMSO- d_6 , CDCl₃, CD₃CN, or CD₃OD, with instruments operating at 300 and 75 MHz, respectively, or at 400 and 100 MHz, respectively. Chemical shifts are reported in parts per million with respect to residual solvent protons, coupling constants ($J_{x-x'}$) are reported in hertz. Low resolution mass spectra and HRMS were recorded in the positive ion mode by electronic impact at 70 eV. All solvents were previously dried according to standard procedures. Analytical TLC was performed on silica gel 60 F₂₅₄ plates. Flash column chromatography was carried out on silica gel (0.040–0.063 mm).

4.2. General procedure for the synthesis of hydantoins 10a-u

A solution of isocyanides **3a,b** (2.5 mmol) in methanol (5 mL) and trichloroacetic acid 4 (0.4 g, 2.5 mmol) were successively added to a previously stirred (10 min, room temperature) mixture of nitrophenylaldehydes **1a**,**b** (2.5 mmol) and arylamines **2a**–**e** (2.5 mmol) in methanol (30 mL) and the mixture was stirred at room temperature for 24 h. Then the mixture was chilled, filtered, and the precipitate was recrystallized from the appropriate solvent to give 2-N-trichloroacetylaminoacetamides 5a-f. Then a solution of 1 M sodium ethoxide (2.8 mmol) was slowly added to a solution of the corresponding 2-N-trichloroacetylaminoacetamides 5a-f (2.5 mmol) in methanol (15 mL). The mixture was stirred for 5 min, chilled, and the precipitate was collected and recrystallized from the appropriate solvent to obtain nitrophenylhydantoins **6a-f**. Then the corresponding nitrophenylhydantoins 6a-g (2.5 mmol) were dissolved in acetic acid (20 ml) at 70 °C, then the solution was warmed to 50 $^{\circ}$ C and iron powder (2 g) was added. When the reaction temperature arose to 60 °C. the mixture was stirred for additional 30 min. Then the mixture was cooled to -10 °C and chloroform (100 mL) and water (600 mL) was poured over it. The mixture was filtered through a pad of Celite, and the organic and aqueous layers were separated. The aqueous layer was extracted with chloroform. The combined organic layers were washed with sodium hydrogencarbonate aqueous solution, dried with anhydrous sodium sulfate, and the solvent was eliminated under reduced pressure. The residue was recrystallized from the appropriate solvent to get aminophenylhydantoins 7a-f. Then the corresponding aminophenylhydantoins 7a-f(2.5 mmol) and aldehydes 8a-d(2.5 mmol)were dissolved in the minimum amount of methanol and the solution was refluxed for 30 min. Then isocyanides **3a,b** (2.5 mmol) and acids **9a**-**f** (2.5 mmol) were added consecutively. The mixture was refluxed until all reagents were dissolved and then refrigerated slowly to room temperature without stirring until the precipitation of a solid. The precipitate was filtered and recrystallized from the appropriate solvent to give hydantoins **10a–u**.

X-ray diffraction: A single crystal of 10k was coated in highvacuum grease and mounted on a glass fiber. X-ray measurements were made using a diffractometer with Mo Ka radiation $(\lambda = 0.71073 \text{ Å})$.¹⁸ Intensities were integrated¹⁹ from several series of exposures, each exposure covering 0.3° in ω , and the total data set being a hemisphere/sphere. Absorption corrections were applied, based on multiple and symmetry-equivalent measurements.²⁰ The structure was solved by direct methods and refined by least squares on weighted F^2 values for all reflections.²¹ All non-hydrogen atoms were assigned anisotropic displacement parameters and refined without positional constraints. Hydrogen atoms H(100), were located in the electron density difference map, assigned isotropic displacement parameters and refined without positional constraints. All other hydrogen atoms were constrained to ideal geometries and refined with fixed isotropic displacement parameters. Refinement proceeded smoothly to give the residuals. Complex neutral-atom scattering factors were used.²²

4.2.1. N-Cyclohexyl-2-[N-phenyl-N-(trichloroacetyl)amino]-2-(p-nitrophenyl)acetamide **5a**. White solid (0.72 g, 72%). Mp 245–247 °C $\begin{array}{l} (\text{EtOH/DMF}). \text{ IR } (\text{KBr, cm}^{-1}) \ 3272, \ 3069, \ 1651, \ 1606, \ 1557, \ 1375, \ 705. \\ ^{1}\text{H } \text{ NMR } (400 \ \text{MHz, } \text{CDCl}_3) \ \delta \ 8.06-8.02 \ (m, \ 2\text{H}, \ \text{H}_{\text{Ar}}), \ 7.91-7.69 \ (m, \ 1\text{H}, \ \text{H}_{\text{Ar}}), \ 7.37-7.33 \ (m, \ 2\text{H}, \ \text{H}_{\text{Ar}}), \ 7.24-7.20 \ (m, \ 2\text{H}, \ \text{H}_{\text{Ar}}), \ 7.15-6.97 \ (m, \ 1\text{H}, \ \text{H}_{\text{Ar}}), \ 6.86-6.70 \ (m, \ 1\text{H}, \ \text{H}_{\text{Ar}}), \ 5.90 \ (s, \ 1\text{H}, \ \text{CH}), \ 5.63 \ (d, \ J=7.9 \ \text{Hz}, \ 1\text{H}, \ \text{NH}), \ 3.89-3.80 \ (m, \ 1\text{H}, \ \text{CH}_{\text{ar}}), \ 5.90 \ (s, \ 1\text{H}, \ \text{CH}), \ 5.63 \ (d, \ J=7.9 \ \text{Hz}, \ 1\text{H}, \ \text{NH}), \ 3.89-3.80 \ (m, \ 1\text{H}, \ \text{CH}_{\text{ar}}), \ 1.25-0.98 \ (m, \ 3\text{H}), \ 1.32 \ \text{NMR} \ (100 \ \text{MHz}, \ \text{CDCl}_3) \ \delta \ 166.3 \ (\text{Cq}), \ 161.2 \ (\text{Cq}), \ 147.9 \ (\text{Cq}) \ 140.3 \ (\text{Cq}), \ 137.8 \ (\text{Cq}), \ 132.3 \ (\text{CH}_{\text{Ar}}), \ 123.2 \ (\text{C$

4.2.2. *N*-*Cyclohexyl*-2-[*N*-(*p*-methylphenyl)-*N*-(*trichloroacetyl*) amino]-2-(*p*-nitrophenyl)acetamide **5b**. White solid (0.82 g, 80%). Mp 117–120 °C (EtOH/DMF). IR (KBr, cm⁻¹): 3306, 3050, 1651, 1604, 1519, 1345, 703. ¹H NMR (200 MHz, DMSO-*d*₆) δ 8.16 (d, *J*=7.6 Hz, 1H, NH), 7.99 (d, *J*=8.5 Hz, 2H, H_{Ar}), 7.77 (m, 1H, H_{Ar}), 7.37 (d, *J*=8.5 Hz, 2H, H_{Ar}), 7.08–6.71 (m, 3H, H_{Ar}), 6.05 (s, 1H, CH), 3.66–3.50 (m, 1H, CH cyclohexyl), 2.14 (s, 3H, CH₃), 2.14–1.46 (m, 5H), 1.33–0.91 (m, 5H). ¹³C NMR (50 MHz, DMSO-*d*₆) δ 166.4 (Cq), 159.4 (Cq), 146.8 (Cq) 141.5 (Cq), 137.9 (Cq), 134.5 (Cq), 132.4 (CH_{Ar}), 131.8 (CH_{Ar}), 127.8 (CH_{Ar}), 122.6 (CH_{Ar}), 92.8 (Cq), 67.0 (CH), 48.0 (CH), 31.9 (CH₂), 25.0 (CH₂), 24.4 (CH₂), 24.2 (CH₂), 20.4 (CH₃). MS (EI) *m/z* (relative intensity) 515 (M⁺+4, 8), 513 (M⁺+2, 24) 511 (M⁺, 30), 369 (50), 353 (100). HRMS (EI) *m/z* calcd for C₂₃H₂₄Cl₃N₃O₄ [M⁺] 511.0832, found 511.0841.

4.2.3. *N*-Benzyl-2-[*N*-(4-methylphenyl)-*N*-(trichloroacetyl)amino]-2-(*m*-nitrophenyl)acetamide **5c**. White solid (0.80 g, 77%). Mp 151–154 °C (*i*-PrOH). IR (KBr, cm⁻¹) 3276, 3030, 1733, 1673, 1528, 1350, 696. ¹H NMR (200 MHz, DMSO- d_6) δ 8.80 (t, *J*=5.5 Hz, 1H, H_{Ar}), 8.64–6.61 (m, 13H, 12H_{Ar}+NH), 6.16 (s, 1H, CH), 4.48–4.24 (m, 2H, CH₂ benz), 2.11 (s, 3H, CH₃). ¹³C NMR (50 MHz, DMSO- d_6) δ 167.9 (Cq), 159.5 (Cq), 146.9 (Cq), 138.8 (Cq), 138.1 (Cq), 137.4 (CH_{Ar}), 135.7 (Cq), 134.5 (Cq), 132.6 (CH_{Ar}), 129.3 (CH_{Ar}), 128.1 (CH_{Ar}), 127.9 (CH_{Ar}), 127.0 (CH_{Ar}), 126.7 (CH_{Ar}), 125.3 (CH_{Ar}), 123.1 (CH_{Ar}), 92.9 (Cq), 67.1 (CH), 42.3 (CH₂), 20.5 (CH₃). MS (EI) *m/z* (relative intensity) 523 (M⁺+4, 15), 521 (M⁺+2, 45), 519 (M⁺, 47), 471 (30), 418 (50), 373 (100). HRMS (EI) *m/z* calcd for C₂₄H₂₀Cl₃N₃O₄ [M⁺] 519.0519, found 519.0510.

4.2.4. N-Benzyl-2-[N-(p-fluorophenyl)-N-(trichloroacetyl)amino]-2-(m-nitrophenyl)acetamide **5d**. White solid (0.90 g, 86%). Mp 91–93 °C (EtOH). IR (KBr, cm⁻¹) 3293, 3030, 1680, 1600, 1537, 1504, 1348, 1215, 727. ¹H NMR (400 MHz, CDCl₃) δ 7.99–7.95 (m, 2H, H_{Ar}), 7.93 (br s, 1H, H_{Ar}), 7.41–7.39 (m, 1H, H_{Ar}), 7.31 (t, *J*=7.9 Hz, 1H, NH), 7.25–7.14 (m, 5H, H_{Ar}), 6.95 (br s, 1H, H_{Ar}), 6.65–6.62 (m, 3H, H_{Ar}), 6.11 (s, 1H, CH), 4.41 (d, *J*=5.8 Hz, 2H, CH₂ benz). ¹³C NMR (100 MHz, CDCl₃) δ 167.8 (Cq), 162.2 (d, ¹*J*=251.3 Hz, Cq), 161.1 (Cq), 147.7 (Cq), 137.4 (Cq), 136.5 (CH_{Ar}), 135.3 (d, ³*J*=8.1 Hz, CH_{Ar}), 134.7 (d, ³*J*=8.1 Hz, CH_{Ar}), 127.5 (CH_{Ar}), 127.4 (CH_{Ar}), 125.6 (CH_{Ar}), 123.9 (CH_{Ar}), 115.2 (d, ²*J*=23.8 Hz, CH_{Ar}), 114.7 (d, ²*J*=24.5 Hz, CH_{Ar}), 92.5 (Cq), 67.9 (CH), 43.7 (CH₂). ¹⁹F NMR (100 MHz, CDCl₃) δ –110.7. MS (EI) *m/z* (relative intensity) 527 (M⁺+4, 30), 525 (M⁺+2, 95), 523 (M⁺, 100), 512 (55), 367 (35), 284 (65), 247 (30). HRMS (EI) *m/z* calcd for C₂₃H₁₇Cl₃FN₃O₄ [M⁺] 523.0269, found 523.0258.

4.2.5. *N*-Benzyl-2-[*N*-(3-trifluoromethylphenyl)-*N*-(trichloroacetyl) amine]-2-(m-nitrophenyl)acetamide **5e**. White solid (0.50 g, 44%). Mp 163–166 °C (*i*-PrOH). IR (KBr, cm⁻¹), 3281, 3031, 1679, 1613, 1569, 1351, 711. ¹H NMR (400 MHz, CDCl₃) δ 8.33–7.87 (m, 3H, H_{Ar}), 7.43–7.18 (m, 9H, H_{Ar}), 6.96–6.78 (m, 1H, H_{Ar}), 6.41 (t, *J*=5.1 Hz, 1H, NH), 6.15 (s, 1H, CH), 4.51–4.39 (m, 2H, CH₂ benz). ¹³C NMR (100 MHz, CDCl₃) δ 167.5 (Cq), 161.0 (Cq), 147.9 (Cq), 137.6 (Cq), 137.3 (Cq), 136.4 (CH_{Ar}), 134.4 (Cq), 130.1 (CH_{Ar}), 129.6 (CH_{Ar}), 128.7

 $\begin{array}{l} ({\rm CH}_{\rm Ar}),\,127.6\,\,({\rm CH}_{\rm Ar}),\,127.5\,\,({\rm CH}_{\rm Ar}),\,125.8\,\,({\rm CH}_{\rm Ar}),\,125.6\,\,({\rm CH}_{\rm Ar}),\,124.1\,\,({\rm CH}_{\rm Ar}),\,92.4\,\,({\rm Cq}),\,67.6\,\,({\rm CH}),\,43.9\,\,({\rm CH}_2).\,\,{\rm MS}\,\,({\rm EI})\,\,m/z\,\,({\rm relative\ intensity})\,577\,\,({\rm M}^+\!+\!4,\,9),\,575\,\,({\rm M}^+\!+\!2,\,25),\,573\,\,({\rm M}^+,\,30),\,373\,\,(25),\,287\,\,(45),\,231\,\,(50),\,97\,\,(100).\,\,{\rm HRMS(EI)}\,\,m/z\,\,{\rm calcd\ for\ C_{24}H_{17}Cl_3F_3N_3O_4\,\,[{\rm M}^+]\,573.0237,\,found\,\,573.0248.\end{array}$

4.2.6. N-Benzvl-2-IN-(m-fluorophenvl)-N-(trichloroacetvl)aminol-2-(*m*-nitrophenyl)acetamide **5f**. White solid (0.92 g, 88%). Mp 168–170 °C (EtOH). IR (KBr, cm⁻¹): 3265, 3071, 1693, 1607, 1594, 1191, 714. ¹H NMR (400 MHz, CDCl₃) δ 8.06 (d, *I*=8.2 Hz, 1H, H_{Ar}), 8.02 (br s, 1H, H_{Ar}), 7.70 (br s, 1H, H_{Ar}), 7.46 (d, *J*=7.4 Hz, 1H, H_{Ar}), 7.34 (t, *J*=7.9 Hz, 1H, H_{Ar}), 7.28–7.18 (m, 5H, H_{Ar}), 7.04–6.68 (m, 2H, H_{Ar}), 6.52 (br s, 1H, H_{Ar}), 6.36 (t, *J*=5.7 Hz, 1H, NH), 6.05 (s, 1H, CH), 4.46 (d, J=5.7 Hz, 2H, CH₂ benz). ¹³C NMR (100 MHz, CDCl₃) δ 167.4 (Cq), 161.6 (d, ¹*J*=249.2 Hz, Cq), 161.0 (Cq), 147.8 (Cq), 138.7 (d, ³J=9.8 Hz, Cq), 137.3 (Cq), 136.4 (CH_{Ar}), 134.5 (Cq), 129.5 (CH_{Ar}), 128.7 (CH_{Ar}), 128.5 (d, ⁴*J*=3.0 Hz, CH_{Ar}), 127.6 (CH_{Ar}), 127.5 (CH_{Ar}), 125.6 (CH_{Ar}), 124.1 (CH_{Ar}), 120.0 (CH_{Ar}), 116.4 (d, ²J=20.7 Hz, CH_{Ar}), 92.4 (Cq), 68.3 (CH), 43.9 (CH₂). MS (EI) *m*/*z* (relative intensity) 527 (M⁺+4, 27), 525 (M⁺+2, 85), 523 (M⁺, 90), 404 (54), 314 (65), 257 (49), 205 (45), 117 (81), 91 (100). HRMS (EI) m/z calcd for C₂₃H₁₇Cl₃FN₃O₄ [M⁺] 523.0269, found 523.0258.

4.2.7. 3-Cyclohexyl-5-(*p*-nitrophenyl)-1-phenylimidazolidin-2,4dione **6a**. White solid (0.38 g, 66%). Mp 245–247 °C (EtOH/DMF). IR (KBr, cm⁻¹) 3044, 1771, 1713, 1519, 1348. ¹H NMR(200 MHz, DMSO d_6) δ 8.19 (d, *J*=8.3 Hz, 2H, H_{Ar}), 7.66 (d, *J*=8.1 Hz, 2H, H_{Ar}), 7.51 (d, *J*=8.3 Hz, 2H, H_{Ar}), 7.32–7.16 (m, 3H, H_{Ar}), 6.19 (s, 1H, CH), 3.96–3.83 (m, 1H, CH cyclohexyl), 2.13–1.01 (m, 10H). ¹³C NMR (50 MHz, DMSO- d_6) δ 168.9 (Cq), 153.8 (Cq), 147.6 (Cq), 141.0 (Cq), 136.0 (Cq), 128.8 (CH_{Ar}), 128.6 (CH_{Ar}), 127.6 (CH_{Ar}), 126.0 (CH_{Ar}), 124.6 (CH_{Ar}), 123.9 (CH_{Ar}), 123.5 (CH_{Ar}), 120.8 (CH_{Ar}), 61.9 (CH), 51.4 (CH), 28.8 (CH₂), 25.2 (CH₂), 24.7 (CH₂). MS (EI) *m/z* (relative intensity) 380 (M⁺+1, 14), 379 (M⁺, 95), 298 (100), 226 (45). HRMS (EI) *m/z* calcd for C₂₁H₂₁N₃O₄ [M⁺] 379.1532, found 379.1541.

4.2.8. 3-Cyclohexyl-5-(*p*-nitrophenyl)-1-(*p*-methylphenyl)imidazolidin-2,4-dione **6b**. White solid (0.56 g, 95%). Mp 182–184 °C (EtOH/ DMF). IR (KBr, cm⁻¹) 3007, 1774, 1711, 1517, 1345. ¹H NMR (200 MHz, DMSO-d₆) δ 8.17 (d, *J*=8.4 Hz, 2H, H_{Ar}), 7.63 (d, *J*=8.4 Hz, 2H, H_{Ar}), 7.37 (d, *J*=8.0 Hz, 2H, H_{Ar}), 7.08 (d, *J*=8.0 Hz, 2H, H_{Ar}), 6.14 (s, 1H, CH), 3.92–3.81 (m, 1H, CH cyclohexyl), 2.17 (s, 3H, CH₃), 2.11–1.13 (m, 10H). ¹³C NMR (50 MHz, DMSO-d₆) δ 169.1 (Cq), 153.8 (Cq), 147.6 (Cq), 141.2 (Cq), 133.9 (Cq), 133.4 (Cq), 129.3 (CH_{Ar}), 129.1 (CH_{Ar}), 128.6 (CH_{Ar}), 127.6 (CH_{Ar}), 124.9 (Cq), 123.9 (CH_Ar), 123.5 (CH_Ar), 121.0 (CH_{Ar}), 62.0 (CH), 51.3 (CH), 28.8 (CH₂), 28.7 (CH₂), 25.2 (CH₂), 24.7 (CH₂), 20.2 (CH₃). MS (EI) *m*/*z* (relative intensity) 393 (M⁺, 90), 338 (95), 359 (52), 352 (49), 288 (100), 198 (61). HRMS (EI) *m*/*z* calcd for C₂₂H₂₃N₃O₄ [M⁺] 393.1689, found 393.1700.

4.2.9. 3-Benzyl-5-(m-nitrophenyl)-1-(p-methylphenyl)imidazolidin-2,4-dione **6c**. White solid (0.44 g, 75%). Mp 162–163 °C (EtOH/ DMF). IR (KBr, cm⁻¹) 3007, 1772, 1715, 1525, 1351. ¹H NMR (40 MHz, CDCl₃) δ 8.09–8.04 (m, 2H, H_{Ar}), 7.50–7.49 (m, 1H, H_{Ar}), 7.40 (t, *J*=7.9 Hz, 1H, H_{Ar}), 7.35–7.33 (m, 2H, H_{Ar}), 7.24–7.16 (m, 5H, H_{Ar}), 6.99–6.97 (m, 2H, H_{Ar}), 5.46 (s, 1H, CH), 4.71 (d, *J*=14.4 Hz, 1H, CH₂ benz), 4.63 (d, *J*=14.4 Hz, 1H, CH₂ benz), 2.15 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 168.7 (Cq), 154.1 (Cq), 148.5 (Cq), 135.4 (Cq), 135.1 (Cq), 135.0 (Cq), 133.0 (Cq), 132.7 (CH_{Ar}), 130.2 (CH_{Ar}), 129.8 (CH_{Ar}), 128.7 (CH_{Ar}), 63.2 (CH), 43.0 (CH₂), 20.7 (CH₃). MS (EI) *m/z* (relative intensity) 402 (M⁺+1, 21), 401 (M⁺, 99), 240 (64), 132 (38), 91 (100). HRMS (EI) *m/z* calcd for C₂₃H₁₉N₃O₄ [M⁺] 401.1375, found 401.1364.

4.2.10. 3-Benzyl-5-(m-nitrophenyl)-1-(p-fluorophenyl)imidazolidin-2,4-dione **6d**. White solid (0.56 g, 92%). Mp 169–170 °C (EtOH/ DMF). IR (KBr, cm⁻¹) 3003, 1782, 1698, 1537, 1372, 1179. ¹H NMR (200 MHz, CDCl₃) δ 8.22–8.16 (m, 2H, H_{Ar}), 7.62–7.25 (m, 9H, H_{Ar}), 7.03–6.94 (m, 2H, H_{Ar}), 5.54 (s, 1H, CH), 4.81 (d, *J*=14.3 Hz, 1H, CH₂ benz), 4.72 (d, *J*=14.3 Hz, 1H, CH₂ benz). ¹³C NMR (50 MHz, CDCl₃) δ 168.5 (Cq), 159.9 (d, ¹*J*=246.1 Hz, Cq), 154.2 (Cq), 148.7 (Cq), 135.3 (Cq), 134.8 (Cq), 132.7 (CH_{Ar}), 131.8 (d, ⁴*J*=3.0 Hz, Cq), 130.5 (CH_{Ar}), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.3 (CH_{Ar}), 124.3 (CH_{Ar}), 122.4 (d, ³*J*=8.1 Hz, CH_{Ar}), 122.1 (CH_{Ar}), 116.3 (d, ²*J*=22.8 Hz, CH_{Ar}), 63.5 (CH), 43.2 (CH₂). MS (EI) *m/z* (relative intensity) 405 (M⁺, 11.6), 404 (42), 390 (33), 376 (100), 57 (89), 55 (48). HRMS (EI) *m/z* calcd for C₂₂H₁₆FN₃O₄ [M⁺] 405.1125, found 405.1132.

4.2.11. 3-Benzyl-5-(m-nitrophenyl)-1-(m-trifluoromethylphenyl)imidazolidin-2,4-dione **6e**. White solid (0.64 g, 95%). Mp 170–172 °C (i-PrOH/DMF). IR (KBr, cm⁻¹) 3011, 1775, 1724, 1532, 1354. ¹H NMR (400 MHz, CDCl₃) δ 8.20–8.18 (m, 2H, H_{Ar}), 7.90 (s, 1H, H_{Ar}), 7.62–7.29 (m, 10H, H_{Ar}), 5.60 (s, 1H, CH), 4.81 (d, *J*=14.4 Hz, 1H, CH₂ benz), 4.75 (d, *J*=14.4 Hz, 1H, CH₂ benz). ¹³C NMR (50 MHz, CDCl₃) δ 168.1 (Cq), 154.0 (Cq), 148.7 (Cq), 136.4 (Cq), 135.0 (Cq), 134.3 (Cq), 132.5 (CH_{Ar}), 128.7 (CH_{Ar}), 128.4 (CH_{Ar}), 124.4 (CH_{Ar}), 129.9 (CH_{Ar}), 128.9 (CH_{Ar}), 122.6 (CH_{Ar}), 121.8 (CH_{Ar}), 121.7(q, ³*J*=3.7 Hz, CH_{Ar}), 116.8 (q, ³*J*=3.9 Hz, CH_{Ar}), 62.9 (CH), 43.3 (CH₂). ¹⁹F NMR (400 MHz, CDCl₃) δ –63.2. MS (EI) *m/z* (relative intensity) 456 (M⁺+1, 100), 455 (M⁺, 34), 425 (82), 406 (54). HRMS (EI) *m/z* calcd for C₂₃H₁₆F₃N₃O₄ [M⁺] 455.1093, found 455.1088.

4.2.12. 3-Benzyl-5-(*m*-nitrophenyl)-1-(*m*-fluorophenyl)imidazolidin-2,4-dione **6f**. White solid (0.50 g, 82%). Mp 142–143 °C (EtOH). IR (KBr, cm⁻¹) 3033, 1775, 1714, 1532, 1367. ¹H NMR (400 MHz, CDCl₃) δ 8.10–8.08 (m, 2H, H_{Ar}), 7.52–7.43 (m, 2H, H_{Ar}), 7.32–7.09 (m, 7H, H_{Ar}), 6.98–6.96 (m, 1H, H_{Ar}), 6.73–6.68 (m, 1H, H_{Ar}), 5.44 (s, 1H, CH), 4.70 (d, *J*=14.4 Hz, 1H, CH₂ benz), 4.63 (d, *J*=14.3 Hz, 1H, CH₂ benz). ¹³C NMR (100 MHz, CDCl₃) δ 168.2 (Cq), 162.9 (d, ¹*J*=246.6 Hz, Cq), 153.9 (Cq), 148.7 (Cq), 137.3 (d, ³*J*=10.5 Hz, Cq), 135.1 (Cq), 134.5 (Cq), 132.4 (CH_{Ar}), 130.6 (CH_{Ar}), 130.5 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 128.3 (CH_{Ar}), 124.3 (CH_{Ar}), 121.8 (CH_{Ar}), 114.9 (d, ⁴*J*=3.0 Hz, CH_{Ar}), 11.9 (d, ²*J*=21.1 Hz, CH_{Ar}), 107.6 (d, ²*J*=26.8 Hz, CH_{Ar}), 63.0 (CH), 43.2 (CH₂). MS (EI) *m*/*z* (relative intensity) 405 (M⁺, 8.9), 404 (30), 390 (20), 376 (100), 138 (72), 91 (71). HRMS (EI) *m*/*z* calcd for C₂₂H₁₆FN₃O₄ [M⁺] 405.1125, found 405.1127.

4.2.13. 3-Cyclohexyl-5-(*p*-aminophenyl)-1-phenylimidazolidin-2,4dione **7a**. White solid (0.22 g, 53%). Mp 215–216 °C (EtOH). IR (KBr, cm⁻¹): 3456, 3374, 3059, 3044, 1767, 1706. ¹H NMR (200 MHz, DMSO- d_6) δ 7.48–6.93 (m, 7H, H_{Ar}), 6.49 (m, 2H, H_{Ar}), 5.67 (br s, 1H, CH), 5.18 (br s, 2H, NH₂), 3.91–3.84 (m, 1H, CH cyclohexyl), 2.14–1.06 (m, 10H). ¹³C NMR (50 MHz, DMSO- d_6) δ 170.9 (Cq), 153.9 (Cq), 149.0 (Cq), 136.4 (Cq), 128.5 (CH_{Ar}), 127.9 (CH_{Ar}), 124.1 (CH_{Ar}), 121.1 (CH_{Ar}), 120.4 (Cq), 113.9 (CH_{Ar}), 62.5 (CH), 50.9 (CH), 28.9 (CH₂), 28.8 (CH₂), 25.3 (CH₂), 24.8 (CH₂). MS (EI) *m/z* (relative intensity) 350 (M+1, 100), 349 (M⁺, 73), 267 (25), 195 (91), 196 (28). HRMS (EI) *m/z* calcd for C₂₁H₂₃N₃O₂ [M⁺] 349.1790, found 349.1792.

4.2.14. 3-Cyclohexyl-5-(*p*-aminophenyl)-1-(*p*-methylphenyl)imidazolidin-2,4-dione **7b**. White solid (0.30 g, 69%). Mp 182–183 °C (EtOH). IR (KBr, cm⁻¹): 3444, 3368, 3037, 1700, 1624. ¹H NMR (400 MHz, CDCl₃) δ 7.33–7.30 (m, 2H, H_{Ar}), 7.08–7.02 (m, 4H, H_{Ar}), 6.62–6.59 (m, 2H, H_{Ar}), 5.20 (s, 1H, CH), 4.05–3.97 (m, 1H, CH cyclohexyl), 3.69 (br s, 2H, NH₂), 2.25 (s, 3H, CH₃), 2.23–2.10 (m, 2H), 1.85–1.59 (m, 5H), 1.39–1.16 (m, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 170.8 (Cq), 154.6 (Cq), 147.0 (Cq), 134.2 (Cq), 134.0 (Cq), 129.5 (CH_{Ar}), 127.9 (CH_{Ar}), 122.9 (Cq), 120.7 (CH_{Ar}), 115.5 (CH_{Ar}), 63.5 (CH), 51.9 (CH), 29.4 (CH₂), 29.2 (CH₂), 25.8 (CH₂), 25.7 (CH₂), 25.0 (CH₂), 20.8 (CH₃). MS (EI) *m*/*z* (relative intensity) 364 (M⁺+1, 10), 363 (M⁺, 45), 362 (41), 281 (31), 245 (38), 211 (33), 210 (52), 209 (81), 147 (45), 106 (100). HRMS (EI) m/z calcd for $C_{22}H_{25}N_3O_2$ [M⁺] 363.1947, found 363.1755.

4.2.15. 3-Benzyl-5-(m-aminophenyl)-1-(p-methylphenyl)imidazolidin-2,4-dione **7c**. White solid (0.42 g, 94%). Mp 152–154 °C (EtOH). IR (KBr, cm⁻¹): 3471, 3377, 3029, 1715, 1698. ¹H NMR (200 MHz, CDCl₃) δ 7.47–7.05 (m, 10H, H_{Ar}), 6.68–6.56 (m, 3H, H_{Ar}), 5.30 (s, 1H, CH), 4.81 (d, *J*=14.4 Hz, 1H, CH₂ benz), 4.71 (d, *J*=14.4 Hz, 1H, CH₂ benz), 3.12 (br s, 2H, NH₂), 2.26 (s, 3H, CH₃). ¹³C NMR (50 MHz, CDCl₃) δ 169.9 (Cq), 147.0 (Cq), 135.8 (Cq), 134.3 (Cq), 134.1 (Cq), 130.2 (CH_{Ar}), 129.6 (CH_{Ar}), 128.7 (CH_{Ar}), 128.6 (CH_{Ar}), 128.0 (CH_{Ar}), 120.2 (CH_{Ar}), 116.8 (CH_{Ar}), 115.9 (CH_{Ar}), 113.1 (CH_{Ar}), 64.4 (CH), 42.8 (CH₂), 20.7 (CH₃). MS (EI) *m/z* (relative intensity) 372 (M⁺+1, 6.3), 371 (M⁺, 0.8), 137 (11), 69 (31), 83 (29), 55 (61), 57 (100). HRMS (EI) *m/z* calcd for C₂₃H₂₁N₃O₂ [M⁺] 371.1634, found 371.1632.

4.2.16. 3-Benzyl-5-(m-aminophenyl)-1-(p-fluorophenyl)imidazolidin-2,4-dione **7d**. White solid (0.35 g, 77%). Mp 61–64 °C (cyclohexane). IR (KBr, cm⁻¹): 3462, 3371, 3032, 1772, 1711. ¹H NMR (400 MHz, CDCl₃) δ 7.45–7.40 (m, 4H, H_{Ar}), 7.35–7.29 (m, 3H, H_{Ar}), 7.12–7.08 (m, 1H, H_{Ar}), 6.97–6.93 (m, 2H, H_{Ar}), 6.63–6.59 (m, 2H, H_{Ar}), 6.52 (t, *J*=2.0 Hz, 1H, H_{Ar}), 5.26 (s, 1H, CH), 4.80 (d, *J*=14.4 Hz, 1H, CH₂ benz), 4.72 (d, *J*=14.4 Hz, 1H, CH₂ benz), 3.69 (br s, 2H, NH₂). ¹³C NMR (100 MHz, CDCl₃) δ 169.6 (Cq), 159.4 (d, ¹*J*=244.8 Hz, Cq), 154.4 (Cq), 147.3 (Cq), 135.6 (Cq), 133.6 (Cq), 132.5 (d, ⁴*J*=2.6 Hz, Cq), 130.2 (CH_{Ar}), 128.7 (CH_{Ar}), 128.0 (CH_{Ar}), 122.0 (CH_{Ar}), 121.9 (d, ³*J*=8.0 Hz, CH_{Ar}), 116.5 (CH_{Ar}), 115.8 (CH_{Ar}), 115.7 (d, ²*J*=22.5 Hz, CH_{Ar}), 64.6 (CH), 42.8 (CH₂). ¹⁹F NMR (400 MHz, CDCl₃) δ –117.8. MS (EI) *m/z* calcd for C₂₂H₁₈FN₃O₂ [M⁺] 375.1383, found 375.1374.

4.2.17. 3-Benzyl-5-(m-aminophenyl)-1-(m-trifluoromethylphenyl) imidazolidin-2,4-dione **7e**. White solid (0.44 g, 87%). Mp 146–147 °C (EtOH). IR (KBr, cm⁻¹): 3490, 3401, 3013, 1716, 1698. ¹H NMR (400 MHz, CDCl₃) δ 7.93 (s, 1H, H_{Ar}), 7.36–7.14 (m, 8H, H_{Ar}), 6.97 (t, *J*=7.8 Hz, 1H, H_{Ar}), 6.52–6.41 (m, 3H, H_{Ar}), 5.18 (s, 1H, CH), 4.69 (d, *J*=14.5 Hz, 1H, CH₂ benz), 4.61 (d, *J*=14.5 Hz, 1H, CH₂ benz), 3.45 (br s, 2H, NH₂). ¹³C NMR (100 MHz, CDCl₃) δ 169.3 (Cq), 154.3 (Cq), 147.4 (Cq), 137.0 (Cq), 135.4 (Cq), 133.2 (Cq), 131.3 (q, ²*J*=32.5 Hz, Cq), 130.3 (CH_{Ar}), 129.4 (CH_{Ar}), 128.7 (CH_{Ar}), 128.6 (CH_{Ar}), 128.1 (CH_{Ar}), 123.6 (q, ³*J*=4.0 Hz, CH_{Ar}), 116.2 (CH_{Ar}), 120.8 (q, ³*J*=3.8 Hz, CH_{Ar}), 116.5 (q, ³*J*=4.0 Hz, CH_{Ar}), 116.2 (CH_{Ar}), 115.9 (CH_{Ar}), 112.5 (CH_{Ar}), 64.0 (CH), 42.8 (CH₂). ¹⁹F NMR (400 MHz, CDCl₃) δ –63.0. MS (EI) *m/z* (relative intensity) 425 (M⁺, 21), 278 (44), 84 (77), 59 (81), 57 (100), 55 (62). HRMS (EI) *m/z* calcd for C₂₃H₁₈F₃N₃O₂ [M⁺] 425.1351, found 425.1356.

4.2.18. 3-Benzyl-5-(m-aminophenyl)-1-(m-fluorophenyl)imidazolidin-2,4-dione **7f**. White solid (0.29 g, 64%). Mp 118–120 °C (EtOH). IR (KBr, cm⁻¹): 3453, 3419, 1762, 1703. ¹H NMR (400 MHz, CDCl₃) δ 7.36–6.97 (m, 9H, H_{Ar}), 6.66–6.42 (m, 4H, H_{Ar}), 5.13 (s, 1H, CH), 4.67 (d, *J*=14.5 Hz, 1H, CH₂ benz), 4.59 (d, *J*=14.5 Hz, 1H, CH₂ benz), 3.57 (br s, 2H, NH₂). ¹³C NMR (100 MHz, CDCl₃) δ 169.3 (Cq), 162.7 (d, ¹*J*=245.2 Hz, Cq), 154.3 (Cq), 147.3 (Cq), 138.0 (d, ³*J*=10.7 Hz, Cq), 135.5 (Cq), 133.4 (Cq), 130.6 (CH_{Ar}), 130.4 (d, *J*=9.3 Hz, CH_{Ar}), 128.6 (CH_{Ar}), 128.5 (CH_{Ar}), 128.0 (CH_{Ar}), 116.5 (CH_{Ar}), 116.2 (CH_{Ar}), 115.1 (d, ⁴*J*=2.9 Hz, CH_{Ar}), 64.1 (CH), 42.7 (CH₂). MS (EI) *m/z* (relative intensity) 376 (M⁺+1, 44), 375 (M⁺, 100), 214 (49), 213 (53), 91 (44). HRMS (EI) *m/z* calcd for C₂₂H₁₈FN₃O₂ [M⁺] 375.1383, found 375.1381.

4.2.19. N-Cyclohexyl 2-[N-(p-chlorophenoxyacetyl)-N-[4-(3-cyclohexyl-2,4-dioxo-1-phenylimidazolidin-5-yl)phenylamino]-2-(p-tolyl)acetamide **10a**. White solid (0.34 g, 45%, EtOH/DMF). IR (KBr, cm⁻¹): 3267, 3081, 1772, 1715, 1680, 1645, 1504, 1491, 1410. ¹H NMR (200 MHz, CDCl₃) δ 7.39–7.08 (m, 11H, H_{Ar}), 6.90–6.79 (m, 4H, H_{Ar}),

6.75–6.64 (m, 2H, H_{Ar}), 5.98 (s, diast.2, 0.34H, CH), 5.94 (s, diast.1, 0.66H, CH), 5.41–5.34 (m,1H, NH), 5.31 (s, 1H, diast.2, 0.34H, CH), 5.28 (s, diast.1, 0.66H, CH), 4.39–4.20 (m, 2H, CH₂), 4.09–3.91 (m, 1H, CH), 3.85–3.66 (m, 1H, CH), 2.25 (s, diast.1, 2H, CH₃), 2.15 (s, diast.2, 1H, CH₃), 1.94–0.90 (m, 20H). ¹³C NMR (50 MHz, CDCl₃) δ 169.3 (Cq), 168.2 (Cq, diast.2), 168.1 (Cq, diast.1), 167.6 (Cq), 156.5 (Cq), 154.3 (Cq), 138.8 (Cq, diast.1), 138.6 (Cq, diast.2), 138.5 (Cq, diast.2), 138.4 (Cq, diast.1), 136.3 (Cq), 134.0 (CH_{Ar}), 131.3 (CH_{Ar} diast.2), 131.2 (CH_{Ar}, diast.1), 130.5 (Cq), 130.2 (CH_{Ar}), 130.1 (Cq), 129.2 (CH_{Ar}), 129.1 (CH_{Ar}), 129.0 (CH_{Ar}), 127.4 (CH_{Ar}), 126.2 (Cq), 124.7 (CH_{Ar}, diast.1), 124.6 (CH, diast.2), 62.9 (CH), 52.2 (CH), 48.9 (CH), 32.7 (CH₂), 29.3 (CH₂), 29.1 (CH₂), 25.8 (CH₂), 25.4 (CH₂), 24.9 (CH₂), 24.8 (CH₂), 24.7 (CH₂), 21.1 (CH₃, diast.1), 21.0 (CH₃, diast.2).

4.2.20. N-Benzyl 2-[N-(p-chlorophenoxyacetyl)-N-[4-(3-cyclohexyl-2,4-dioxo-1-phenylimidazolidin-5-yl)phenylamino]-2-(p-tolyl)acet*amide* **10b**. White solid (0.41 g, 54%, EtOH/DMF). IR (KBr, cm⁻¹): 3265, 3066, 1770, 1710, 1667, 1599. ¹H NMR (200 MHz, CDCl₃) δ 7.38–7.11 (m, 15H, H_{Ar}), 6.84–6.62 (m, 7H, H_{Ar}), 6.13–6.04 (m, 1H, CH), 6.02 (s, diast.1, 0.5H, NH), 5.99 (s, diast.2, 0.5H, NH), 5.31 (s, diast.1, 0.5H, CH), 5.28 (s, diast.2, 0.5H, CH), 4.52-4.38 (m, 2H, CH₂), 4.40-4.18 (m, 2H, CH₂), 4.08-3.92 (m, 1H, CH cyclohexyl), 2.23 (s, diast.2, 1.5H, CH₃), 2.14 (s, diast.2, 1.5H, CH₃), 2.10–1.14 (m,10H). ¹³C NMR (50 MHz, CDCl₃) δ 167.0 (Cq), 167.4 (Cq), 156.2 (Cq), 154.0 (Cq), 138.4 (Cq), 138.3 (Cq, diast.1), 138.2 (Cq, diast.2), 137.4 (Cq), 135.9 (Cq), 133.8 (Cq), 130.9 (Cq, diast.1), 130.8 (Cq, diast.2), 129.9 (CH_{Ar}), 129.8 (CH_{Ar}), 128.9 (CH_{Ar}), 128.7 (CH_{Ar}), 128.2 (CH_{Ar}), 127.2 (CH_{Ar}), 127.1(CH_{Ar}), 127.0 (CH_{Ar}), 125.9 (Cq), 124.4 (Cq, diast.1), 124.3 (Cq, diast.2), 119.9 (CHAr), 115.7 (CHAr), 66.6 (CH2), 64.9 (CH, diast.1), 64.6 (CH, diast.2), 62.7 (CH), 52.0 (CH), 43.5 (CH₂), 29.1 (CH₂), 29.0 (CH₂), 25.6 (CH₂), 24.8 (CH₂), 20.9 (CH₃, diast.1), 20.8 (CH₃, diast.2).

4.2.21. N-Cyclohexyl 2-[N-(p-chlorophenoxyacetyl)-N-[4-(3cyclohexyl-2,4-dioxo-1-p-tolyl-imidazolidin-5-yl)phenylamino]-2phenylacetamide 10c. White solid (0.51 g, 69%, EtOH/DMF). IR (KBr, cm⁻¹): 3263, 3062, 1772, 1711, 1681. ¹H NMR (200 MHz, CDCl₃) δ 7.26–6.96 (m, 15H, H_{Ar}), 6.66 (d, J=8.9 Hz, 2H, H_{Ar}), 5.98 (s, 1H, CH), 5.48 (d, J=6.8 Hz, diast.1, 0.5H, NH), 5.45 (d, J=6.8 Hz, diast.2, 0.5H, NH), 5.25 (s, diast.1, 0.5H, CH), 5.23 (s, diast.2, 0.5H, CH), 4.38-4.20 (m, 2H, CH₂), 4.05-3.90 (m, 1H, CH cyclohexyl), 3.84-3.67 (m, 1H, CH Cyclohexyl), 3.30 (s, diast.1, 1.5H, CH₃), 3.29 (s, diast.2, 1.5H, CH₃), 2.30-0.97 (m, 20H). ¹³C NMR (50 MHz, CDCl₃) δ 169.5 (Cq, diast.1), 169.4 (Cq, diast.2), 168.0 (Cq), 167.7 (Cq), 156.5 (Cq), 154.3 (Cq), 138.5 (Cq), 134.5 (Cq, diast.1), 134.4 (Cq, diast.2), 134.2 (Cq, diast.2), 134.1 (Cq, diast.1), 133.6 (Cq, diast.1), 133.5 (Cq), 133.4 (Cq, diast.2), 130.2 (CHAr), 130.1 (CHAr), 129.5 (CHAr), 129.4 (CHAr), 129.1 (CHAr), 128.5 (Cq, diast.1), 128.4 (Cq, diast.2), 128.3 (CHAr), 127.5 (CHAr), 126.2 (Cq), 120.7 (CHAr), 120.4 (CHAr), 116.0 (CH_{Ar}), 66.8 (CH), 65.1 (CH, diast.1), 65.0 (CH, diast.2), 63.2 (CH, diast.2), 63.0 (CH, diast.1), 52.1 (CH), 48.9 (CH), 32.6 (CH₂), 29.3 (CH₂), 29.1 (CH₂), 29.0 (CH₂) 25.7 (CH₂), 25.3 (CH₂), 24.9 (CH₂), 24.7 (CH₂), 24.6 (CH₂), 20.7 (CH₃).

4.2.22. N-Cyclohexyl 2-[N-(p-chlorobenzoyl)-N-[4-(3-cyclohexyl-2,4dioxo-1-p-tolyl-imidazolidin-5-yl)phenylamino]-2-phenylacetamide **10d.** White solid (0.56 g, 79%, EtOH/DMF). IR (KBr, cm⁻¹): 3276, 3086, 1771, 1713, 1651. ¹H NMR (400 MHz, CDCl₃) δ 7.25–6.93 (m, 17H, H_{Ar}), 6.05 (s, 1H, CH), 5.57 (*d*, *J*=8.1 Hz, diast.2, 0.08H, NH), 5.53 (d, *J*=8.1 Hz, diast.1, 0.92H, NH), 5.11 (s, 1H, CH), 3.99–3.91 (m, 1H, CH cyclohexyl), 3.86–3.77 (m, 1H, CH cyclohexyl), 2.30 (s, 3H, CH₃), 2.17–1.81 (m, 6H), 1.72–1.54 (m, 5H), 1.36–0.95 (m, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 169.7 (Cq), 169.5 (Cq), 168.1 (Cq), 154.3 (Cq), 141.8 (Cq), 135.5 (Cq), 134.5 (Cq), 134.4 (Cq), 134.0 (Cq), 133.5 (Cq), 132.7 (Cq), 131.0 (CH_{Ar}), 130.1 (CH_{Ar}), 130.0 (CH_{Ar}), 129.5 (CH_{Ar}), 128.6 (CH_{Ar}), 127.8 (CH_{Ar}), 127.1 (CH_{Ar}), 120.5 (CH_{Ar}), 66.6 (CH), 63.2 (CH), 52.0 (CH), 48.9 (CH), 32.8 (CH₂), 29.3 (CH₂), 29.0 (CH₂), 25.8 (CH₂), 25.4 (CH₂), 24.9 (CH₂), 24.8 (CH₂), 24.7 (CH₂), 20.8 (CH₃).

4.2.23. N-Cyclohexyl 2-[N-(2-chloroacetyl)-N-[4-(3-cyclohexyl-2,4dioxo-1-p-tolvl-imidazolidin-5-vl)phenvlaminol-2-(p-tolvl)acetamide **10e**. White solid (0.27 g, 40%, EtOH). IR (KBr, cm⁻¹): 3269, 3034, 1773, 1714, 1677, 1647. ¹H NMR (400 MHz, CDCl₃) δ 7.20–7.00 (m, 7H, H_{Ar}), 6.80–6.68 (m, 5H, H_{Ar}), 5.85 (s, diast.2, 0.40H, CH), 5.82 (s, diast.1, 0.60H, CH), 5.39 (d, J=8.1 Hz, diast.2, 0.40H, NH), 5.39 (d, J=8.1 Hz, diast.1, 0.60H, NH), 5.21 (s, diast.2, 0. 40H, CH), 5.18 (s, diast.1, 0.60H, CH), 3.97-3.89 (m, 1H, CH cyclohexyl), 3.77-3.65 (m, 3H, CH cyclohexyl+CH₂), 2.25 (s, diast.2, 1.20H, CH₃), 2.24 (s, diast.1, 1.80H, CH₃), 2.18 (s, 3H, CH₃), 1.86–1.46 (m, 11H), 1.30–0.87 (m, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 169.7 (Cq), 168.4 (Cq, diast.2), 168.4 (Cq, diast.1), 166.7 (Cq, diast.2), 166.6 (Cq, diast.1), 154.6 (Cq), 139.5 (Cq), 138.7 (Cq), 134.8 (Cq), 134.4 (Cq), 133.9 (Cq), 131.5 (Cq), 130.8 (Cq), 130.4 (CH_{Ap}, diast.1), 130.3 (CH_{Ap}, diast.2), 129.9 (CH_{Ap}, diast.1), 129.8 (CHAr, diast.2), 129.3 (CHAr, diast.1), 129.3 (CHAr, diast.2), 127.7 (CHAr), 120.7 (CHAr, diast.1), 120.6 (CHAr, diast.2), 65.6 (CH), 63.4 (CH, diast.2), 63.3 (CH, diast.1), 52.4 (CH), 49.1 (CH), 42.9 (CH₂), 33.0 (CH₂), 33.0 (CH₂), 29.5 (CH₂), 29.4 (CH₂), 26.0 (CH₂), 26.0 (CH₂), 25.6 (CH₂), 25.2 (CH₂), 25.0 (CH₂), 24.9 (CH₂), 21.3 (CH₃), 21.1 (CH₃).

4.2.24. N-Cyclohexyl 2-[N-(3-phenylpropargyl)-N-[4-(3-cyclohexyl-2,4dioxo-1-p-tolyl-imidazolidin-5-yl)phenylamino]-2-phenylacetamide **10f**. White solid (0.30 g, 42%, EtOH). IR (KBr, cm⁻¹): 3269, 3061, 1771, 1713, 1648, 1605. ¹H NMR (200 MHz, CDCl₃) δ 7.34–6.91 (m, 18H, H_{Ar}), 6.01 (br s, 1H, CH), 5.75–5.71 (m, 1H, NH), 5.26 (s, diast.1, 0.65H, CH), 5.24 (s. diast.2, 0.35H, CH), 4.06-3.90 (m, 1H, CH cyclohexyl), 3.87-3.71 (m, 1H, CH cyclohexyl), 2.27 (s, diast.1, 1.95H, CH₃), 2.15 (s, diast.2, 1.05H, CH₃), 2.30-0.93 (m, 20H). ¹³C NMR (50 MHz, CDCl₃) δ 169.6 (Cq, diast.1), 169.56 (Cq, diast.2), 167.8 (Cq), 154.7 (Cq, diast.2), 154.5 (Cq, diast.1), 140.5 (Cq), 134.4 (Cq), 134.3 (Cq), 133.9 (Cq), 133.8 (Cq), 132.7 (CH_{Ar}), 131.9 (CH_{Ar}), 130.2 (CH_{Ar}), 130.1 (CH_{Ar}), 129.5 (CH_{Ar}), 128.6 (CH_{Ar}), 128.5 (CH_{Ar}), 128.4 (CH_{Ar}), 126.9 (CH_{Ar}), 126.8 (CH_{Ar}), 120.7 (CH_{Ar}), 120.3 (CH_{Ar}), 119.9 (Cq), 92.5 (Cq), 82.4 (Cq), 64.9 (CH, diast.2), 64.8 (CH, diast.1), 63.6 (CH, diast.1), 63.4 (CH, diast.2), 52.1 (CH), 48.8 (CH), 32.7 (CH₂), 32.7 (CH₂), 29.3 (CH₂), 29.1 (CH₂), 25.8 (CH₂), 25.4 (CH₂), 25.0 (CH₂), 24.8 (CH₂), 24.7 (CH₂), 20.8 (CH₃).

4.2.25. N-Cyclohexyl 2-[N-(p-nitrophenylacetyl)-N-[3-(3-benzyl-2,4dioxo-1-(p-tolyl)-imidazolidin-5-yl)phenylamino]-2-phenylacetamide **10g**. White solid (0.57 g, 76%, EtOH/DMF). IR (KBr, cm⁻¹): 3361, 3031, 1715, 1682, 1650, 1519, 1345. ¹H NMR (400 MHz, CDCl₃) δ 8.00–7.96 (m, 2H, H_{Ar}), 7.71 (s, diast.2, 0.34H, H_{Ar}), 7.55 (s, diast.1, 0.66H, H_{Ar}), 7.37-6.67 (m, 19H, HAr), 6.03 (s, diast.1, 0.66H, CH), 5.90 (s, diast.2, 0.34H, CH), 5.38-5.07 (m, 2H, NH+CH), 4.74-4.60 (m, 2H, CH₂), 3.77-3.67 (m, 1H, CH cyclohexyl), 3.32-3.19 (m, 2H, CH₂), 2.16 (s, 3H, CH₃), 1.88–0.86 (m, 10H). ¹³C NMR (100 MHz, CDCl₃) δ 169.9 (Cq, diast.2), 169.7 (Cq, diast.1), 169.4 (Cq), 168.2 (Cq, diast.2), 168.1 (Cq, diast.1), 154.0 (Cq), 146.7 (Cq), 142.4 (Cq, diast.1), 142.3 (Cq, diast.2), 140.2 (Cq), 140.0 (Cq), 135.7 (Cq), 135.6 (Cq), 131.6 (Cq), 130.4 (CH_{Ar}), 130.1 (CH_{Ar}), 129.6 (CH_{Ar}), 128.7 (CH_{Ar}), 128.6 (CH_{Ar}), 128.4 (CH_{Ar}), 128.1 (CH_{Ar}), 123.4 (CH_{Ar}), 120.7 (CH_{Ar}), 65.2 (CH, diast.1), 64.4 (CH, diast.2), 63.8(CH, diast.1), 63.1 (CH, diast.2), 48.9 (CH), 42.9 (CH₂), 41.6 (CH₂, diast.2), 41.4 (CH₂, diast.1), 32.7 (CH₂), 25.4 (CH₂), 24.8 (CH₂), 24.7 (CH₂), 20.7 (CH₃).

4.2.26. *N*-Cyclohexyl 2-[*N*-(*p*-chlorobenzoyl)-*N*-[3-(3-benzyl-2,4dioxo-1-(*p*-tolyl)-imidazolidin-5-yl)phenylamino]-2-phenylacetamide **10h**. White solid (0.35 g, 49%, i-PrOH). IR (KBr, cm⁻¹): 3267, 3033, 1714, 1683. ¹H NMR (400 MHz, CDCl₃) δ 7.37–6.81 (m, 21H, H_{Ar}), 6.58 (br s, 1H, H_{Ar}), 6.19 (s, diast.1, 0.93H, CH), 6.13 (s, diast.2, 0.07H, CH), 5.58 (d, *J*=8.2 Hz, diast.2, 0.07H, NH), 5.42 (d, *J*=7.8 Hz, diast.1, 0.93H, NH), 5.10 (s, 1H, CH), 4.64 (s, 2H, CH₂), 3.83–3.73 (m, 1H, CH cyclohexyl), 2.24 (s, diast.1, 2.79H, CH₃), 2.10 (s, diast.2, 0.21H, CH₃), 1.93–1.50 (m, 5H), 1.34–0.91 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 169.9 (Cq), 168.8 (Cq), 168.2 (Cq), 154.0 (Cq), 141.1 (Cq), 135.7 (Cq), 135.3 (Cq), 134.5 (Cq), 134.1 (Cq), 133.5 (Cq), 132.8 (Cq), 132.0 (Cq), 130.6 (CH_Ar), 129.8 (CH_Ar), 129.6 (CH_Ar), 129.4 (CH_Ar), 129.1 (CH_Ar), 128.8 (CH_Ar), 128.7 (CH_Ar), 128.6 (CH_Ar), 128.5 (CH_Ar), 128.1 (CH_Ar), 127.8 (CH_Ar), 125.9 (CH_Ar), 120.1 (CH_Ar), 65.2 (CH), 63.2 (CH), 48.9 (CH), 42.9 (CH₂), 32.8 (CH₂), 32.9 (CH₂), 25.5 (CH₂), 24.8 (CH₂), 24.7 (CH₂), 20.8 (CH).

4.2.27. N-Cyclohexyl 2-[N-(p-nitrophenylacetyl)-N-[3-(3-benzyl-2,4dioxo-1-(p-fluorophenyl)-imidazolidin-5-yl)phenylamino]-2-(p-fluorophenyl)acetamide 10i. White solid (0.46 g, 60%, DMF). IR (KBr, cm⁻¹): 3344, 1771, 1708, 1679, 1647. ¹H NMR (400 MHz, CDCl₃) δ 8.03–8.00 (m, 2H, H_{Ar}), 7.78–7.64 (m, 1H, H_{Ar}), 7.40–6.61 (m, 17H, H_{Ar}), 6.41 (s, diast.1, 0.59H, H_{Ar}), 6.37 (s, diast.2, 0.41H, H_{Ar}), 6.07 (s, diast.1, 0.59H, CH), 5.96 (s, diast.2, 0.41, CH), 5.61 (s, diast.1, 0.59H, NH), 5.43 (s, diast.2, 0.41H, NH), 5.37 (s, diast.2, 0.41H, CH), 5.13 (s, diast.1, 0.59H, CH), 4.74 (s, diast.2, 0.82H, CH2), 4.70 (s, diast.1, 1.18H, CH₂), 3.77-3.73 (m, 1H, CH cyclohexyl), 3.40-3.32 (m, 2H, CH₂), 1.90–0.92 (m, 10H). ¹³C NMR (100 MHz, CDCl₃) δ 169.9 (Cq), 168.6 (Cq), 168.0 (Cq), 162.4 (d, ¹*J*=249.9 Hz, Cq), 159.4 (d, ¹*J*=249.0 Hz, Cq), 154.0 (Cq), 146.7 (Cq), 142.2 (Cq), 139.8 (Cq), 135.3 (Cq), 132.2 (CHAr), 131.9 (CHAr), 130.0 (CHAr), 129.6 (CHAr), 128.7 (CHAr), 128.2 (CHAr), 125.8 (CHAr), 123.4 (CHAr), 123.1 (Cq), 121.3 (CHAr), 115.8 (d, ²J=23.8 Hz, CH_{Ar}), 115.3 (d, ²J=21.5 Hz, CH_{Ar}), 63.9 (CH, diast.1), 63.7 (CH, diast.2), 63.4 (CH, diast.1), 63.2 (CH, diast.2), 48.9 (CH), 42.9 (CH₂), 41.4 (CH₂), 32.6 (CH₂), 25.3 (CH₂), 24.7 (CH₂), 24.6 (CH₂).

4.2.28. N-Cyclohexyl 2-IN-(3-phenylpropargyl)-N-I3-(3-benzyl-2.4dioxo-1-(p-fluorophenyl)-imidazolidin-5-yl)phenylamino]-2-(p-fluorophenyl)acetamide 10j. White solid (0.49 g, 67%, EtOH/H₂O). IR (KBr, cm⁻¹): 3212, 3068, 2211, 1777, 1716, 1639, 1601. ¹H NMR (400 MHz, CDCl₃) δ 7.37–7.10 (m, 13H, H_{Ar}), 7.00–6.93 (m, 4H, H_{Ar}), 6.86-6.64 (m, 5H, H_{Ar}), 6.09 (s, diast.2, 0.37H, CH), 6.03 (s, diast.1, 0.63H, CH), 5.79 (d, J=8.0 Hz, diast.1, 0.63H, NH), 7.75 (d, J=7.6 Hz, diast.2, 0.37H, NH), 5.35 (s, diast.2, 0.37H, CH), 5.29 (s, diast.1, 0.63H, CH), 4.73-4.53 (m, 2H, CH₂), 3.82-3.73 (m, 1H, CH Cyclohexyl), 1.93–1.79 (m, 2H), 1.69–1.55 (m, 3H), 1.36–0.96 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 169.2 (Cq, diast.1), 169.1 (Cq, diast.2), 168.0 (Cq, diast.1), 167.9 (Cq, diast.2), 162.8 (d, ¹J=248.6, Cq, diast.2, CF), 162.7 (d, ¹*J*=249.1, Cq, diast.1, CF), 159.7 (d, *J*=245.4, Cq, diast.1, CF), 159.6 (d, J=245.4, Cq, diast.2, CF), 155.0 (Cq, diast.1), 154.9 (Cq, diast.2), 154.5 (Cq, diast.2), 154.4 (Cq, diast.1), 140.5 (Cq, diast.1), 140.4 (Cq, diast.2), 135.8 (Cq), 133.9 (Cq, diast.1), 133.5 (Cq, diast.2), 132.9 (CH_{Ar}), 132.7 (CH_{Ar}), 132.6 (CH_{Ar}), 132.5 (CH_{Ar}), 132.3 (d, ⁴*J*=2.9 Hz, Cq), 132.2 (CH_{Ar}), 132.1 (CH_{Ar}), 130.5 (CH_{Ar}), 130.4 (CH_{Ar}), 129.8 (CH_{Ar}, diast.1), 129.6 (CH_{Ar}, diast.2), 129.5 (d, ⁴*J*=3.4 Hz, Cq), 129.0 (CH_{Ar}, diast.1), 128.9 (CH_{Ar}, diast.2), 128.8 (CH_{Ar}, diast.1), 128.7 (CH_{Ar}, diast.2), 128.6 (CHAr), 128.5 (CHAr), 128.3 (CHAr), 127.2 (CH, diast.1), 126.9 (CH, diast.2), 122.4 (d, ³J=8.0 Hz, CH_{Ar}), 122.1 (d, ³J=6.8 Hz, CH_{Ar}), 119.9 (*Cq*, *diast.2*), 119.8 (*Cq*, *diast.1*), 116.0 (d, ²*J*=22.7 Hz, *CH*, *diast.1*), 115.9 (d, ²J=22.7 Hz, CH, diast.2), 115.7 (d, ²J=21.6 Hz, CH, diast.1), 115.6 (d, ²J=21.6 Hz, CH, diast.2), 93.1 (Cq, diast.1), 92.9 (Cq, diast.2), 82.3 (Cq, diast.2), 82.2 (Cq, diast.1), 64.2 (CH, diast.1), 64.1 (CH, diast.2), 63.5 (CH), 49.2 (CH, diast.2), 49.1 (CH, diast.1), 43.1 (CH₂, diast.2), 43.0 (CH₂, diast.1), 33.0 (CH₂), 32.9 (CH₂), 25.6 (CH₂), 25.0 (CH₂), 24.9 (CH_2) . ¹⁹F NMR δ – 112.0 (diast.1, 0.63), –112.3 (diast.2, 0.37), –117.3.

4.2.29. N-Cyclohexyl 2-[N-(p-chlorophenoxyacetyl)-N-[3-(3-benzyl-2,4-dioxo-1-(m-trifluoromethylphenyl)-imidazolidin-5-yl)phenyl-amino]-2-(p-tolyl)acetamide **10**I. White solid (0.42 g, 51%, EtOH/DMF). IR (KBr, cm⁻¹): 3347, 3033, 1771, 1713, 1668, 1603. ¹H NMR (200 MHz, CDCl₃) δ 7.82 (br s, 2H, H_{Ar}), 7.43–7.28 (m, 10H, H_{Ar}), 7.17–7.13 (m, 3H, H_{Ar}), 6.95–6.80 (m, 4H, H_{Ar}), 6.66–6.62 (m, 2H, H_{Ar}), 6.02 (s, 1H, CH), 5.40 (br s, 2H, NH+CH), 4.75 (s, 2H, CH₂), 4.10 (s, 2H, CH₂), 3.82–3.67 (m, 1H, CH cyclohexyl), 2.25 (s, diast.1, 2H,

CH₃), 2.17 (s, diast.2, 1H, CH₃), 1.90–1.55 (m, 5H), 1.42–0.92 (m, 5H). 13 C NMR (50 MHz, CDCl₃) δ 168.1 (Cq), 167.5 (Cq), 156.6 (Cq), 154.1 (Cq), 139.1 (Cq), 138.5 (Cq), 136.8 (Cq), 135.3 (Cq), 131.5 (CH_{Ar}), 130.3 (CH_{Ar}), 129.6 (CH_{Ar}), 129.2 (CH_{Ar}), 129.1 (CH_{Ar}), 128.8 (CH_{Ar}), 128.6 (CH_{Ar}), 128.3 (CH_{Ar}), 126.8 (Cq), 126.2 (Cq), 121.2 (Cq), 116.7 (Cq), 116.0 (CH_{Ar}), 66.6 (CH₂), 64.6 (CH), 63.2 (CH), 48.9 (CH), 43.1 (CH₂), 32.7 (CH₂), 25.5 (CH₂), 24.8 (CH₂), 24.7 (CH₂), 21.1 (CH₃).

4.2.30. N-Cyclohexyl 2-[N-(p-nitrophenylacetyl)-N-[3-(3-benzyl-2,4dioxo-1-(m-trifluoromethylphenyl)-imidazolidin-5-yl)phenylamino]-2-phenylacetamide 10m. White solid (0.59 g, 74%, EtOH/DMF). IR (KBr, cm⁻¹): 3364, 3032, 1772, 1718, 1649, 1600. ¹H NMR (400 MHz, CDCl₃) δ 7.96–6.10 (m, 22H, H_{Ar}), 6.05 (br s, diast.2, 0.24H, CH), 5.94 (br s, diast.1, 0.76H, CH), 5.54–5.10 (m, 2H, NH+CH), 4.75–4.66 (m, 2H, CH₂), 3.74–3.65 (m, 1H, CH cyclohexyl), 3.35–3.27 (m, 2H, CH₂), 1.84-1.51 (m, 5H), 1.24-0.79 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 169.8 (Cq), 168.6 (Cq), 168.2 (Cq, diast.1), 168.0 (Cq, diast.2), 154.0 (Cq), 153.9 (Cq), 146.7 (Cq), 142.3 (Cq), 140.4 (Cq), 136.9 (Cq, diast.1), 136.8 (Cq, diast.2), 135.3 (Cq, diast.1), 135.2 (Cq, diast.2), 133.6 (Cq), 131.4 (q, ²J=33.0 Hz, Cq), 130.3 (CH_{Ar}), 130.0 (CH_{Ar}), 129.6 (CH_{Ar}), 129.5 (CH_{Ar}), 128.8 (CH_{Ar}), 128.6 (CH_{Ar}), 128.4 (CH_{Ar}), 128.3 (CH_{Ar}), 123.5 (q, ¹J=272.5 Hz, Cq). 123.4 (CH_{Ar}), 122.6 (CH_{Ar}), 121.1 (CH_{Ar}), 116.451 (CH_{Ar}), 64.9 (CH, diast.1), 64.3 (CH, diast.2), 63.4 (CH, diast.1), 62.8 (CH, diast.2), 48.9 (CH), 43.0 (CH₂), 41.5 (CH₂, diast.1), 41.3 (CH₂, diast.2), 32.7 (CH₂), 32.6 (CH₂), 25.4 (CH₂), 25.3 (CH₂), 24.7 (CH₂), 24.6 (CH₂).

4.2.31. N-Cyclohexyl 2-[N-(p-chlorobenzoyl)-N-[3-(3-benzyl-2,4dioxo-1-(m-trifluoromethylphenyl)-imidazolidin-5-yl)phenylaminol-2-(p-chlorophenvl)acetamide **10n**. White solid (0.44 g, 54%, EtOH/ DMF). IR (KBr, cm⁻¹): 3359, 3035, 1772, 1719, 1684, 1631. ¹H NMR (200 MHz, CDCl₃) δ 7.96 (s, diast.1, 0.8H, H_{Ar}), 7.92 (s, diast.2, 0.2H, H_{Ar}), 7.37–6.89 (m, 20H, H_{Ar}), 6.21 (s, diast.1, 0.8H, CH), 6.15 (s, diast.2, 0.2H, CH), 5.73 (d, J=8.3 Hz, diast.2, 0.2H, NH), 5.63 (d, J=8.1 Hz, 0.8H, NH), 5.24 (s, 1H, CH), 4.78-4.70 (m, 2H, CH₂), 3.91-3.72 (m, 1H, CH cyclohexyl), 1.98–0.97 (m, 10H). ¹³C NMR (50 MHz, CDCl₃) δ 169.8 (Cq), 168.1 (Cq), 167.9 (Cq), 154.0 (Cq), 141.3 (Cq), 136.8 (Cq, diast.2), 136.7 (Cq, diast.1), 135.7 (Cq, diast.2), 135.6 (Cq, diast.1), 135.3 (Cq), 134.7 (Cq, diast.1), 134.6 (Cq, diast.2), 133.7 (Cq), 132.7 (Cq), 132.6 (Cq), 131.8 (CH_{Ar}), 131.6 (q, J=30.6 Hz, Cq), 129.8 (CH_{Ar}), 129.5 (CH_{Ar}), 128.9 (CHAr), 128.8 (CHAr), 128.6 (CHAr), 128.3 (CHAr), 127.9 (CHAr), 125.5 (CH_{Ar}), 125.4 (CH_{Ar}), 123.5 (q, J=272.8 Hz, Cq), 121.8 (CH_{Ar}),121.1 (q, J=4.0 Hz, CH_{Ar}), 116.4 (q, J=4.0 Hz, CH_{Ar}), 64.9 (CH, diast.2), 64.5 (CH, diast.1), 63.1 (CH, diast.2), 62.9 (CH, diast.1), 49.0 (CH), 43.0 (CH₂), 32.8 (CH₂), 25.4 (CH₂), 24.8 (CH₂), 24.7 (CH₂).

4.2.32. N-Cyclohexyl 2-[N-(3-phenylpropargyl)-N-[3-(3-benzyl-2,4dioxo-1-(m-trifluoromethylphenyl)-imidazolidin-5-yl)phenylamino]-2-(p-chlorophenyl)acetamide 100. White solid (0.28 g, 35%, EtOH). IR (KBr, cm⁻¹): 3276, 3064, 1777, 1722, 1684, 1649. ¹H NMR (400 MHz, CDCl₃) δ 8.11 (s, diast.1, 0.76H, H_{Ar}), 8.06 (s, diast.2, 0.24H, H_{Ar}), 7.35–6.81 (m, 21H, H_{Ar}), 6.09 (s, diast.1, 0.76H, CH), 6.03 (s, diast.2, 0.24H, CH), 5.88-5.83 (m, 1H, NH), 5.46 (s, diast.1, 0.76H, CH), 5.39 (s, diast.2, 0.24H, CH), 4.74 (d, J=14.4 Hz, diast.1, 0.76H, CH₂), 4.69 (d, J=14.3 Hz, diast.2, 0.24H, CH₂), 4.65 (d, J=14.4 Hz, diast.1, 0.76H, CH₂), 4.53 (d, J=14.3 Hz, diast.2, 0.24H, CH₂), 3.78-3.72 (m, 1H, CH cyclohexyl), 1.92-1.54 (m, 5H), 1.38-0.95 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 168.7 (Cq), 167.8 (Cq, diast.2), 167.7 (Cq, diast.1), 155.0(Cq, diast.2), 154.9 (Cq, diast.1), 154.4 (Cq), 140.6 (Cq, diast.2), 140.5 (Cq, diast.1), 137.0 (Cq, diast.2), 136.9 (Cq, diast.1), 135.6 (Cq), 134.9 (Cq, diast.2), 134.8 (Cq, diast.1), 133.3 (Cq), 132.9 (CH_{Ar}), 132.7 (CH_{Ar}), 132.4 (Cq), 132.1 (CH_{Ar}), 131.7 (q, ²J=32.4 Hz, Cq), 131.6 (CH_{Ar}), 130.4 (CH_{Ar}), 130.2 (Cq), 129.8 (CH_{Ar}), 129.6 (CH_{Ar}), 129.0 (CHAr), 128.9 (CHAr), 128.8 (CHAr), 128.7 (CHAr), 128.6 (CHAr), 128.5 (CH_{Ar}), 128.4 (CH_{Ar}), 127.0 (CH_{Ar}, diast.2), 126.7 (CH_{Ar}, diast.1), 123.8 (q, ¹J=272.8 Hz, Cq), 122.5 (CH_{Ar}, diast.2), 122.4 (CH_{Ar}, diast.1), 121.1 (Cq), 119.9 (CH_{Ar}), 117.2 (q, ³J=3.7 Hz, diast.1, CH_{Ar}), 117.1 (q,³

J=3.3 *Hz*, *diast.2*, *CH*_{Ar}), 93.2 (*Cq*, *diast.2*), 93.0 (Cq, diast.1), 82.2 (Cq), 63.7 (CH), 63.5 (CH), 49.2 (CH), 43.2 (CH₂, diast.1), 43.1 (*CH₂*, *diast.2*), 33.0 (CH₂), 32.9 (CH₂), 25.7 (CH₂), 25.0 (CH₂), 24.9 (CH₂).

4.2.33. N-Cyclohexyl 2-[N-(o-hydroxybenzoyl)-N-[3-(3-benzyl-2,4dioxo-1-(m-trifluoromethylphenyl)-imidazolidin-5-yl)phenylaminol-2-(p-tolvl)acetamide 10p. White solid (0.31 g. 40%. EtOH). IR (KBr. cm⁻¹): 3376, 3034, 1778, 1715, 1673, 1642. ¹H NMR (200 MHz, CDCl₃) δ 9.83 (br s, 1H, OH), 7.94 (s, 1H, H_{Ar}), 7.37–6.95 (m, 17H, H_{Ar}), 6.71 (d, *J*=8.4 Hz, 1H, H_{Ar}), 6.61 (d, *J*=7.5 Hz, 1H, H_{Ar}), 6.28–6.20 (m, 1.96H, H_{Ar}+0.96H diast.1, CH), 6.13 (s, diast.2, 0.04H, CH), 5.59 (d, J=7.9 Hz, 1H, NH), 5.28 (s, 1H, CH), 4.77 (d, J=14.5 Hz, 1H, CH₂), 4.68 (d, J=14.5 Hz, 1H, CH₂), 3.92–3.83 (m, 1H, CH cyclohexyl), 2.26 (s, diast.1, 2.88H, CH₃), 2.16 (s, diast.2, 0.12H, CH₃), 1.95–1.05 (m, 10H). ¹³C NMR (50 MHz, CDCl₃) δ 171.0 (Cq), 168.8 (Cq), 168.4 (Cq), 157.3 (Cq), 154.1 (Cq), 141.5 (Cq), 138.7 (Cq), 136.8 (Cq), 135.4 (Cq), 132.5 (Cq), 132.0 (CH_{Ar}), 131.3 (CH_{Ar}), 130.6 (CH_{Ar}), 130.5 (CH_{Ar}), 129.5 (CH_{Ar}), 129.3 (CH_{Ar}), 129.0 (CH_{Ar}), 128.8 (CH_{Ar}), 128.6 (CH_{Ar}), 128.2 (CH_{Ar}), 128.1 (CH_{Ar}), 125.3 (CH_{Ar}), 122.1 (CH_{Ar}), 121.0 (q, J=3.9 Hz, CH_{Ar}), 118.9 (CH_{Ar}), 118.2 (CH_{Ar}), 117.2 (CH_{Ar}), 116.5 (q, J=3.8 Hz, CH_{Ar}), 65.6 (CH), 63.2 (CH), 49.2 (CH), 43.0 (CH₂), 32.7 (CH₂), 25.4 (CH₂), 24.8 (CH₂), 24.7 (CH₂), 21.1 (CH₃).

4.2.34. N-Cyclohexyl 2-[N-(p-chlorophenoxyacetyl)-N-[3-(3-benzyl-2,4-dioxo-1-(m-fluorophenyl)-imidazolidin-5-yl)phenylamino]-2-(ptolyl)acetamide 10q. White solid (0.41 g, 53%, EtOH/DMF). IR (KBr, cm⁻¹): 3277, 3079, 1778, 1721, 1650, 1614. ¹H NMR (200 MHz, CDCl₃) δ 7.98–6.62 (m, 21H, H_{Ar}), 6.05 (br s, diast.1, 0.75H, CH), 5.98 (br s, *diast.2*, 0.25H, CH), 5.60–5.22 (m, 2H, CH+NH), 4.81–4.65 (m, 2H, CH₂), 4.24-4.03 (m, 2H, CH₂), 3.83-3.65 (m, 1H, CH cyclohexyl), 2.25 (s, diast.1, 2.25H, CH₃), 2.19 (s, diast.2, 0.75H, CH₃), 1.98-1.61 (m, 5H), 1.40–0.85 (m, 5H). ¹³C NMR (50 MHz, CDCl₃) δ 168.6 (Cq), 168.3 (Cq, diast.2), 168.0 (Cq, diast.1), 167.6 (Cq, diast.2), 167.5 (Cq, diast.1), 162.8 (d, J=246.1 Hz, Cq), 156.5 (Cq), 153.9 (Cq), 138.9 (Cq), 138.5 (Cq), 137.6 (d, J=10.5 Hz, Cq), 135.3 (Cq), 131.3 (CH_{Ar}), 130.3 (CH_{Ar}), 130.0 (CH_{Ar}), 129.2 (CH_{Ar}), 129.1 (CH_{Ar}), 128.9 (CH_{Ar}), 128.7 (CH_{Ar}), 128.5 (CH_{Ar}), 128.2 (CH_{Ar}), 126.6 (Cq), 126.1 (Cq), 116.0 (CH_{Ar}), 115.1 (CH_{Ar}), 111.4 (d, J=21.3 Hz, CH_{Ar}), 107.6 (d, J=26.9 Hz, CH_{Ar}), 66.5 (CH₂), 64.7 (CH, diast.2), 64.4 (CH, diast.1), 63.5 (CH, diast.2), 63.1 (CH, diast.1), 48.9 (CH), 42.9 (CH₂), 32.7 (CH₂), 25.4 (CH₂), 24.7 (CH₂), 24.7 (CH₂), 21.1 (CH₃).

4.2.35. N-Cyclohexyl 2-[N-(p-nitrophenylacetyl)-N-[3-(3-benzyl-2,4dioxo-1-(m-fluorophenyl)-imidazolidin-5-yl)phenylamino]-2phenylacetamide 10r. White solid (0.41 g, 54%, EtOH/DMF). IR (KBr, cm⁻¹): 3358, 3034, 1767, 1716, 1651, 1604, 1494, 1347. ¹H NMR (400 MHz, CDCl₃) δ 8.06–8.04 (m, 2H, H_{Ar}), 7.89–7.64 (m, 1H, H_{Ar}), 7.42-6.92 (m, 16H, H_{Ar}), 6.81-6.70 (m, 2H, H_{Ar}), 6.42 (br s, 1H, H_{Ar}), 6.14 (br s, diast.1, 0.65H, CH), 5.99 (br s, diast.2, 0.35H, CH), 5.42 (br s, 1H, NH), 5.19 (br s, diast.2, 0.35H, CH), 5.08 (br s, diast.1, 0.65H, CH), 4.74-4.71 (m, 2H, CH₂), 3.84-3.74 (m, 1H, CH cyclohexyl), 3.41 (d, *I*=15.4 Hz, 1H, CH₂), 3.3 7 (d, *I*=15.4 Hz, 1H, CH₂), 1.94–1.56 (m, 5H), 1.40-1.25 (m, 2H), 1.34-0.90 (m, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 170.1 (Cq), 168.6 (Cq), 168.4 (Cq), 163.1 (d, ¹*J*=246.1 Hz, Cq), 154.1 (Cq), 147.0 (Cq), 142.6 (Cq), 140.3 (Cq), 137.9 (d, ³J=8.9 Hz, Cq), 135.5 (Cq), 134.3 (Cq), 133.0 (Cq), 132.3 (CH_{Ar}), 131.8 (CH_{Ar}), 130.7 (CH_{Ar}), 130.4 (CH_{Ar}), 129.0 (CH_{Ar}), 128.9 (CH_{Ar}), 128.7 (CH_{Ar}), 125.7 (CH_{Ar}), 123.7 (CH_{Ar}), 114.9 (CH_{Ar}), 111.7 (d, ${}^{2}J$ =22.5 Hz, CH), 107.2 (d, ²J=25.7 Hz, CH), 65.3 (CH, diast.2), 64.6 (CH, diast.1), 63.7 (CH, diast.2), 63.2 (CH, diast.1), 49.2 (CH), 43.3 (CH₂), 41.7 (CH₂), 33.0 (CH₂), 25.6 (CH₂), 25.1 (CH₂), 25.0 (CH₂), 24.9 (CH₂).

4.2.36. N-Cyclohexyl 2-[N-(p-chlorobenzoyl)-N-[3-(3-benzyl-2,4-dioxo-1-(m-fluorophenyl)-imidazolidin-5-yl)phenylamino]-2-(p-chlorophenyl)acetamide **10s**. White solid (0.21 g, 28%, EtOH/DMF). IR (KBr, cm⁻¹): 3359, 3032, 1773, 1715, 1686, 1625. ¹H NMR (200 MHz, CDCl₃) δ 7.42–6.79 (m, 21H, H_{Ar}), 6.18 (s, diast.1, 0.86H, CH), 6.13 (s, diast.2, 0.14H, CH), 5.66 (d, J=8.1 Hz, diast.2, 0.14H, NH), 5.50 (d,

J=8.3 Hz, diast.1, 0.86H, NH), 5.15 (s, 1H, CH), 4.73 (s, 2H, CH₂), 3.90–3.75 (m, 1H, CH cyclohexyl), 2.02–0.98 (m, 10H). ¹³C NMR (50 MHz, CDCl₃) δ 169.9 (Cq), 168.3 (Cq), 167.9 (Cq), 162.8 (d, ¹*J*=245.9, Cq), 153.9 (Cq), 141.3 (Cq), 135.5 (d, ³*J*=13.2 Hz, Cq), 134.8 (Cq), 133.7 (Cq), 132.9 (Cq), 132.8 (Cq), 131.9 (CH_{Ar}), 131.8 (CH_{Ar}), 131.4 (Cq), 130.2 (d, ³*J*=9.2 Hz, CH_{Ar}), 129.9 (Cq), 129.8 (CH_{Ar}), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.2 (CH_{Ar}), 127.9 (CH_{Ar}), 125.6 (CH_{Ar}), 114.5 (d, ⁴*J*=3.3 Hz, CH_{Ar}), 111.4 (d, ²*J*=21.0 Hz, CH_{Ar}), 107.3 (d, ²*J*=26.9 Hz, CH_{Ar}), 64.7 (CH, *diast.2*), 64.5 (CH, diast.1), 63.4 (CH, *diast.2*), 63.1 (CH, diast.1), 49.0 (CH), 43.0 (CH₂), 32.8 (CH₂), 25.4 (CH₂), 24.8 (CH₂), 24.7 (CH₂).

4.2.37. N-Cyclohexyl 2-[N-(2-chloroacetyl)-N-[3-(3-benzyl-2,4dioxo-1-(m-fluorophenyl)-imidazolidin-5-yl)phenylamino]-2-(ptolyl)acetamide 10t. White solid (0.25 g, 37%, EtOH/DMF). IR (KBr, cm⁻¹): 3252, 3034, 1769, 1711, 1678, 1602. ¹H NMR (400 MHz, CDCl₃) δ 7.82 (br s, 1H, H_{Ar}), 7.47–6.37 (m, 16H, H_{Ar}), 6.16–4.98 (m, 3H, 2CH+NH), 4.70-4.52 (m, 2H, CH₂), 3.65-3.50 (m, 3H, CH+CH₂), 2.14 (s, diast.1, 2H, CH₃), 2.08 (s, diast.2, 1H, CH₃), 1.31-1.45 (m, 5H), 1.25–0.82 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 168.6 (Cq), 168.2 (Cq, diast.2), 167.9 (Cq, diast.1), 166.3 (Cq, diast.1), 166.1 (Cq, diast.2), 162.6 (d, J=246.1 Hz, Cq), 153.8 (Cq), 139.3 (Cq, diast.2), 139.2 (Cq, diast.1), 138.3 (Cq, diast.1), 138.2 (Cq, diast.2), 137.4 (d, J=10.6 Hz, Cq), 135.3 (Cq), 133.8 (Cq), 131.4 (CH_{Ar}), 130.1 (CH_{Ar}), 130.0 (CH_{Ar}), 129.9 (CH_{Ar}), 129.8 (CH_{Ar}), 129.1 (Cq), 128.9 (CH_{Ar}), 128.6 (CH_{Ar}), 128.4 (CH_{Ar}), 128.0 (CH_{Ar}), 115.1 (d, J=2.8 Hz, CH_{Ar}), 111.2 (d, J=21.4 Hz, CH_{Ar}), 107.5 (d, J=26.5 Hz, CH_{Ar}), 64.9 (CH, diast.1), 64.7 (CH, diast.2), 63.3 (CH, diast.1), 63.0 (CH, diast.2), 48.6 (CH), 42.7 (CH₂), 42.3 (CH₂), 32.5 (CH₂), 32.5 (CH₂), 25.3 (CH₂), 24.7 (CH₂), 24.5 (CH₂), 21.0 (CH₃, diast.1), 20.9 (CH₃, diast.2).

4.2.38. N-Cyclohexyl 2-[N-(3-phenylpropargyl)-N-[3-(3-benzyl-2,4dioxo-1-(m-fluorophenyl)-imidazolidin-5-yl)phenylamino]-2-(pchlorophenyl)acetamide 10u. White solid (0.41 g, 54%, EtOH/DMF). IR (KBr, cm⁻¹): 3273, 3088, 2212, 1776, 1722, 1684, 1632. ¹H NMR (400 MHz, CDCl₃) δ 7.46–6.85 (m, 21H, H_{Ar}), 6.75–6.61 (m, 1H, H_{Ar}), 6.08 (s, diast.1, 0.74H, CH), 6.02 (s, diast.2, 0.26H, CH), 5.78 (d, J=8.2 Hz, diast.2, 0.26H, NH), 5.69 (d, J=7.8 Hz, diast.1, 0.74H, NH), 5.37 (s, diast.1, 0.74H, CH), 5.32 (s, diast.2, 0.26H, CH), 4.73 (d, J=14.5 Hz, diast.1, 0.74H, CH₂), 4.65 (d, J=14.6, diast.2, 0.26H, CH₂), 4.64 (d, J=14.5 Hz, diast.1, 0.74H, CH₂), 4.41 (d, J=14.6 Hz, diast.2, 0.26H, CH₂), 3.83-3.72 (m, 1H, CH cyclohexyl), 1.94-1.55 (m, 5H), 1.37-0.94 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 168.5 (*Cq*, *diast.2*), 168.4 (Cq, diast.1), 167.5 (Cq, diast.2), 167.3 (Cq, diast.1), 162.7 (d, ¹J=245.7 Hz, Cq), 154.7 (Cq, diast.2), 154.6 (Cq, diast.1), 154.0 (Cq), 140.1 (Cq), 137.5 (d, ³*J*=10.6 Hz, Cq), 135.3 (Cq), 134.7 (*Cq*, *diast.2*), 134.6 (Cq, *diast.*1), 133.5 (Cq, diast.2), 133.2 (Cq, diast.1), 132.6 (CH_{Ar}), 132.5 (CH_{Ar}), 132.3 (CH_{Ar}), 132.1 (Cq), 131.8 (CH_{Ar}), 131.2 (CH_{Ar}), 130.1 (CH_{Ar}, diast.1), 130.0 (CHAn diast.2), 129.6 (Cq), 129.4 (CHAr), 128.7 (CHAr), 128.623 (CH_{Ar}, diast.2), 128.6 (CH_{Ar}, diast.1), 128.5 (CH_{Ar}, diast.2), 128.4 (CH_{Ar}, diast.1), 128.2 (CHAr, diast.2), 128.2 (CHAr, diast.1), 128.1 (CHAr), 126.6 $(CH_{Ar}, diast.2)$, 126.5 $(CH_{Ar}, diast.1)$, 119.7 (Cq, diast.1), 119.6 (Cq, diast.2), 114.7 $(d, {}^{4}J=2.8 \text{ Hz}, CH_{Ar})$, 111.3 $(d, {}^{2}J=20.3 \text{ Hz}, diast.2, CH_{Ar})$, 111.0 $(d, {}^{2}J=21.2 \text{ Hz}, diast.1, CH_{Ar})$, 107.7 $(d, {}^{2}J=26.8 \text{ Hz}, diast.1, CH_{Ar})$, 107.3 (d, ²J=22.7 Hz, diast.2, CH_{Ar}), 93.0 (Cq, diast.2), 92.8 (Cq, diast.1), 81.9 (Cq, diast.1), 81.8 (Cq, diast.2), 63.5 (CH, diast.2), 63.24 (CH, diast.1), 63.3 (CH), 48.9 (CH), 42.8 (CH₂), 32.7 (CH₂), 32.6 (CH₂), 25.4 (CH_2) , 24.7 (CH_2) , 24.6 (CH_2) . ¹⁹F NMR (400 MZ, CDCl₃) δ –110.6.

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Supplementary data

Crystallographic information file (CIF) of compound **10k** (CCDC 852635). Copies of ¹H and ¹³C NMR of the products and a plot of structure **10k**. Supplementary data related to this article can be found in the online version, at doi:10.1016/j.tet.2012.01.073. These data includes MOL files and InChiKeys of the most important compounds described in this article.

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