Synthesis of 3-Carbamoyl-*β*-lactams *via* Manganese(III) Promoted Cyclization of *N*-Alkenylmalonamides

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Manganese(III) promoted cyclization of *N*-alkenylmalonamides gave 3-(aryl/alkylaminocarbonyl)-*β*-lactams as well as 3-(aryl/alkylaminothiocarbonyl)-*β*-lactams. The relative configuration of the obtained products was unambiguously determined by X-ray crystallography. The proposed method is very useful for the one-pot synthesis of a number of 3-(aryl/alkylaminocarbonyl)-*β*-lactams, especially those containing an aminothiocarbonyl moiety, which are not selectively accessible by other methods.

Keywords:

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Introduction. – For the period of almost seven decades, which is when the first documented use of penicillin began, the *β*-lactam system has been at the center of interest of organic chemistry. Of course, the main stream of research is related to the potential applications of *β*-lactams as an effective antimicrobial chemotherapeutic. However, purely synthetic applications are also known, for example, the '*Ojima β*-lactam Synthon Method' for the preparation of peptides [1], amino acids [2], and hydroxy acids [3].

So far, many different methods for the preparation of the 2-oxoazetidine ring have been developed, for example: carbodiimide coupling of *β*-amino acids [4], condensation with PPh_3 pyridine disulphide developed by *Ohno* and co-workers [5], *Grignard* reagent mediated cyclization of silyl esters of amino acids [6], cyclizations using an epoxide system and anion stabilizing group [7], intramoleular electrophilic addition to olefins [8], or radical cyclization of 3-oxoenamides [9]. However, it should be noted that the first method used for the preparation of *β*-lactams *via* the cycloaddition of ketenes to imines proposed by *Staudinger* at the beginning of the 19th century [10], after lots of modification and improvements, is still one of the most popular methods for the preparation of these compounds.

Recently, we have reported a variation of the *Staudinger* method for the preparation of 3-carbamoyl-β-lactams by addition of aldimines to carbamoyl-ketenes generated from 5-[hydroxy(arylamino)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione [11]. Despite many advantages arising mainly from the simplicity of this method, we were not able to obtain models of 3-carbamoyl-β-lactams with alkyl groups or sulfur in carbamoyl fragment.

As mentioned already, an alternative way of forming β-lactams may be the cyclization of enamides, which was demonstrated by *Trogolo et al.* [9] in the oxidative cyclization of 3-oxoenamides. On the other hand, we have recently developed a method for the preparation of *N*-alkenyl malonodiamides and *N*-alkenyl thiomalonodiamides **3** from carbamoyl and thiocarbamoyl *Meldrum*'s acids **1**, respectively [12].

Considering the above facts, we decided to check if oxidative cyclization of **3** allows bypassing the limitations, which we came across in our previous method of preparing 3-carbamoyl-β-lactams. Radical cyclization of carbonyl derivatives containing an active α-position promoted by transition metals is a well-known and broadly applied method [13]; however, to the best of our knowledge, this method has up to now not been used for the cyclization of malonodiamides, and particularly for their thio-derivatives.

Results and Discussion. – In this article, we present the synthesis of *β*-lactams **4** and **5** with a retro-amide and retro-thioamide side chain based on the Mn^{III}-promoted oxidative cyclization of suitable malonodiamides (*Scheme 1*).

Scheme 1

As a first experiment, we performed the reaction of *N*-isopropyl-*N*'-phenyl-*N*-[(1*Z*)-2-phenylprop-1-enyl]malonamide (**3a**) with 2 equiv. of $Mn(OAc)_3 \cdot H_2O$ using typical conditions for radical cyclization reactions with Mn^{III}, *i.e.*, 70° and AcOH as a solvent [13]. After purification, we obtained two main products, the first, **4a**, containing a vinyl moiety, in 30% yield and the second, **5a**, without elimination of AcOH, in 41% yield (*Table*, *Entry 1*) accompanied by traces of unreacted starting material. At this moment, we tried to optimize the conditions used. First, we checked the optimal temperature and observed that while gradually increasing the temperature up to 50°, there was no reaction observed even for an extended reaction time, whereas at the threshold of 65 – 70°, the reaction run with noticeable rate and consumption of Mn^{III} takes around 0.5 h. On the other hand, conducting the reaction in boiling AcOH caused a very fast reaction; Mn^{III} was consumed just after addition, but the yield of **4a** and **5a** remain in the same range (*Entry 2*). Moreover, we observed that the portionwise addition of $Mn(OAc)_3 \cdot H_2O$ to the hot reaction mixture allowed finding the moment,

when an additional amount of oxidizer is no longer consumed at a fast rate. In the case of **1**, the optimal amount of $Mn(OAc)_3 \cdot H_2O$ was *ca.* 1.6 equiv.

Table

In all above experiments after quenching the reaction, a small amount of unreacted **3** was observed on TLC. Therefore, in the next experiment, we checked whether using an excess of oxidizing reagent might improve the reaction yield: the use of 4 equiv. of $Mn(OAc)_3 \cdot H_2O$ required an extended time of 4 h for complete consumption of oxidant, and the yield of **4a** and **5a** was significantly reduced (*Entry 3*), suggesting that the already obtained *β*-lactams underwent subsequent oxidation, which causes a decrease in yield. Solvents have an important influence on the oxidation with $Mn(OAc)_3 \cdot H_2O$; usually highly polar protic solvents are used and in most cases AcOH is the solvent of choice; however, sometimes alcohols are used [13]. Therefore, we conducted two experiments in which **3a** and **3e**, respectively, were oxidized with 2 equiv. of $Mn(OAc)_3 \cdot H_2O$ in boiling MeOH for 0.5 h. After purification, we obtained products **4** and **5** in much lower yields than in the reactions carried out in AcOH (*Entries 4* and *5 vs. Entries 1* and *6*).

Results obtained on a series of *N*-alkenyl malonodiamides are shown in the *Table*. When R^1 was an alkyl group, only the product after elimination, **4**, was obtained,

whereas introduction of any aryl group as R^1 led to the formation of both **4** and **5**. Probably, if R^1 is an alkyl group, the higher basicity of the amide O-atom cause a fast intramolecular deprotonation. For the higher overall yield of *β*-lactams in the case of cyclization of **3** with R^1 = aryl, the *π*-interaction between two aromatic rings during radical ring closure may be responsible.

The ^{1}H-NMR spectra of the prepared *β*-lactams **4** and **5** showed coupling constants for H–C(3) and H–C(4) in the range 2.0 – 2.5 Hz in all cases, which indicates the exclusive formation of *trans* products. Moreover, the X-ray crystal structures obtained for selected compounds **4** and **5** also indisputably prove the *trans* configurations of the products (*Fig. 1*).

Fig. 1.

As one can see, the *β*-lactam **5** has an additional stereogenic center, hence taking into account that only *trans β*-lactams were observed as products of our reaction, the aforementioned product **5** should exist as four diastereoisomers, (1'*R*,3*R*,4*R*), (1'*S*,3*S*,4*S*), (1'*R*,3*S*,4*S*), and (1'*S*,3*R*,4*R*). Indeed, in one case (*Entry 11*), it was possible to separate the two pairs of enantiomers. At this moment, a question arises about assigning an absolute configuration for each pair. At the beginning, we performed

NOESY experiments as well as conformational analysis performed with HyperChem® software using OPLS force field. On the NOESY spectrum of the pair of enatiomers eluated from column chromatography as a first **5g'**, we observed an interaction between both *β*-lactam ring H-atoms and the Me group of the side chain, whereas the spectrum for the second pair of diastereoisomers **5g''** showed interactions between the *β*-lactam H–C(3) and the Me group as well between the H–C(3) and the amid NH. The calculated lowest energy conformations revealed that one diasteroisomer has short interatomic distances between *β*-lactam ring H-atoms and the Me group of *ca.* 0.24 nm, while the second diasteroisomer has short interatomic distances between H–C(3) H-atom and the Me group as well between the H–C(3) and the amid NH of 0.22 and 0.24 nm, respectively (*Fig. 2*). Comparing distances between H-atoms in the lowest energy conformation with the results of the NOESY experiments strongly suggest that **5g'** has to be a pair of (1'*R*,3*R*,4*R*) and (1'*S*,3*S*,4*S*) isomers and **5g''** of (1'*R*,3*S*,4*S*) and (1'*S*,3*R*,4*R*) isomers. Fortunately, **5g'** gave crystals suitable for X-ray crystallography, and the X-ray data confirmed our previous suppositions (*Fig. 1*). In the cases of **5a** and **5h**, it was not possible to separate the diastereoisomers chromatographically, however, slow crystallization allowed to obtain enough good crystals for X-ray crystallography of one pair of less soluble enantiomers from each mixture. As a digression, we can add that

in the case of model **h** (*Entry 12*) besides two main products **4h** and **5h** also the unexpected product **6h** with free OH group in the side chain was isolated.

Fig. 2.

Another question that we decided to resolve was whether other salts of transition metals could be used in this oxidative cyclization by checking two systems: the first was $Cu(OAc)_2$ in AcOH as a solvent at 70° or at boiling point. In both cases, even using an extended reaction time, no trace of *β*-lactams was obtained (*Entries 13* and *14*). When we used a mixture of 1 equiv. of $Cu(OAc)_2$ together with 1.6 equiv. of $Mn(OAc)_3$, *β*-lactams **4a** and **5a** were obtained in a yield slightly lower than in the experiment when only $Mn(OAc)_3$ was used (*Entry 15 vs. Entry 1*). As the second oxidative system, we used $Co(OAc)_2$ in hot AcOH. In this case, we obtained the required *β*-lactam, however in a significantly reduced yield (*Entry 16*).

Overall yields of the prepared 3-carbamoyl-*β*-lactams range from 37 to 71% and may be considered as modest. However, it should be emphasized that in the present synthesis *N*-alkenyl malonodiamides were used which are least prone to enolization, while it is known that radical formation occurs from the enolic form of malonic acid derivatives [9b][14]. Therefore, three experiments were carried out with the addition of

a base (pyridine or MeONa) to the reaction mixture (*Entries 17 – 19*). Only the introduction of pyridine as a base for the enolization did not disrupt the oxidation-cyclization process. However, enhancement of the yield is minimal (*Entries 17 vs. 1* and *18 vs. 6*).

The most interesting question that arose during our experiments was whether the *N*-alkenyl thiomalonoenamides can be also radically cyclized to give 3-thiocarbamoyl-*β*-lactams. To the best of our knowledge, a general selective method for the preparation of 3-thiocarbamoyl-*β*-lactams is not known. Moreover, for this class of compounds only one example is known [15].

The main problem during oxidative cyclization of *N*-alkenyl thiomalonoenamides **3** may arise from the possible desulfurization, which for thioamides is easily feasible with various oxidating agents like, for example, oxone, Ag^{I} [16] salts, or Na_2O_2 [17]. Fortunately, the performed experiments have shown that radical cyclization of **3** (X = S) with $Mn(OAc)_3 \cdot H_2O$ occurs with good yield in a short time leading to the formation of 3-thiocarbamoyl-*β*-lactams **4** and **5** (X = S, *Entries 20 – 23*). However, slightly higher amounts of oxidant are required to complete the reaction, most probably due to some desulfurization side reactions.

In summary, we have developed a new method for the preparation of 3-carbamoyl-*β*-lactams and 3-thiocarbamoyl-*β*-lactams, which are not available on other

ways. The method is fast and selective, and the products are obtained in moderate yields. The structure of the prepared compounds was confirmed by X-ray crystallography.

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Experimental Part

General. All solvents used in this study were dried over appropriate drying agents and distilled prior to use. Commercially available reagents were purchased from *Sigma-Aldrich.* Commercially unavailable reagents were prepared using literature procedures: *5-[hydroxy(phenylamino)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione* (**1a**) [18], *5-[hydroxy(ethylamino)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione* (**1b**) [11], *5-{hydroxy[(3-chlorophenyl)amino]methylidene}-2,2-dimethyl-1,3-dioxane-4,6-dione* (**1d**) [11], *5-{hydroxy[(4-nitrophenyl)amino]methylidene}-2,2-dimethyl-1,3-dioxane-4,6-dione* (**1f**) [19], *5-[(methylamino)sulfanylmethylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione* (**1g**) [20], *isopropyl(2-phenylpropylidene)amine* (**2a**) and tert-*butyl(2-phenylpropylidene)amine* (**2b**) [21], N-*alkenyl malonodiamides* and N-*alkenyl thiomalonodiamides*, **3a** – **3c**, **3f**, **3i**, and **3j** [12]. TLC: *Merck Kieselgel 60 F_{254}*. Flash column chromatography (FC): *Zeochem ZEOprep 60/40-63*. M.p.: *Warsztat*

Elektromechaniczny W-wa; uncorrected. NMR Spectra: *Varian Unity Plus 500* (^{1}H: 500 and ^{13}C: 125 MHz) or *Varian Gemini 200* (^{1}H: 200 and ^{13}C: 50 MHz); δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. HR-ESI-MS: *MicroMas Quattro LCT* mass spectrometer; in *m*/*z*.

5-[Hydroxy(butylamino)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1c**). Following the typical procedure in [18][11] for **1a** and **1b** using *Meldrum*'s acid (0.72 g, 5 mmol), anh. DMF (5 ml), Et_3N (1.4 ml, 10 mmol), butylisocyanate (0.495 g, 5 mmol) Yield 0.729 g (60%). M.p. 69 – 71°. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.96 (*t*, *J* = 7.1, 3 H); 1.25 – 1.46 (*m*, 2 H); 1.49 – 1.70 (*m*, 2 H); 1.71 (*s*, 6 H); 3.41 (*q*, *J* = 6.2, 2 H); 9.27 (br. *s*, 1 H); 13.80 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 14.0; 20.4; 26.7; 31.6; 40.6; 73.3; 105.0; 121.7; 164.8; 170.7; 170.8. HR-ESI-MS: 266.1007 ([*M* + Na]$^+$, $C_{11}H_{17}NNaO_5^+$; calc. 266.1004).

5-{Hydroxy[(4-methoxyphenyl)amino]methylidene}-2,2-dimethyl-1,3-dioxane-4,6-dione (**1e**). Following the typical literature procedure [18][11] for **1a** and **1b** using *Meldrum*'s acid (0.72 g, 5 mmol), anh. DMF (5 ml), Et_3N (1.4 ml, 10 mmol), 4-methoxyphenylisocyanate (0.745 g, 5 mmol). Yield 0.646 g (44%). M.p. 130 – 132°. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.77 (*s*, 6 H); 3.83 (*s*, 3 H); 6.92 (*d*, *J* = 9.3, 2 H); 7.35 (*d*, *J* = 9.3, 2 H); 11.02 (br. *s*, 1 H); 15.55 (br. *s*, 1 H).

5-[(Ethylamino)sulfanylmethylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1h**). Following the typical procedure in [20] for **1g** using *Meldrum*'s acid (0.72 g, 5 mmol), anh. DMF (5 ml), Et_3N (1.4 ml, 10 mmol), ethylisothiocyanate (0.435 g, 5 mmol), Yield 0.196 g (17%). M.p. 58 – 60°. ^{1}H-NMR (200 MHz, $CDCl_3$): 1.36 (*t*, *J* = 7.3, 3 H); 1.72 (*s*, 6 H); 3.48 – 3.62 (*m*, 2 H); 11.30 (br. *s*, 1 H); 14.20 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 13.4; 26.0; 40.0; 82.2; 103.6; 164.6; 170.1; 179.7. HR-ESI-MS: 254.0464 ([*M* + Na]$^+$, $C_9H_{13}NNaO_4S^+$; calc. 254.0463).

tert-*Butyl*-N'-*butyl*-N-*[(1Z)-2-phenylprop-1-enyl]malonamide* (**3d**). Following the typical procedure in [12] for **3a** – **3c**, **3f**, **3i**, and **3j** using **1c** (0.486 g, 2 mmol), anh. toluene (10 ml), and **2b** (0.756 g, 4 mmol). Yield 0.455 g (69%). ^{1}H-NMR (200 MHz, $CDCl_3$): (*t*, *J* = 7.2, 3 H); 1.30 – 1.69 (*m*, 4 H); 1.46 (*s*, 9 H); 2.01 (*s*, 2 H); 3.21 – 3.35 (*m*, 4 H); 6.30 (*s*, 1 H); 7.34 – 7.39 (*m*, 5 H); 7.81 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 13.7; 15.7; 20.1; 28.4; 31.5; 39.1; 42.7; 59.5; 125.3; 126.1; 128.3; 128.6; 139.5; 140.1; 166.5; 169.5. HR-ESI-MS: 353.2191 ([*M* + Na]$^+$, $C_{20}H_{30}N_2NaO_2^+$; calc. 353.2205).

N-*Isopropyl*-N'-*butyl*-N-*[(1E)-2-phenylprop-1-enyl]malonamide* (**3e**). Following the typical procedure in [12] using **1c** (0.486 g, 2 mmol), anh. toluene (10 ml), and **2a** (0.7 g, 4 mmol). Yield 0.480 g (76%). ^{1}H-NMR (200 MHz, $CDCl_3$): 0.92 (*t*, *J* = 7.1, 3 H); 1.15 (*d*, *J* = 6.8, 6 H); 1.30 – 1.56 (*m*, 4 H); 1.98 (*d*, *J* = 1.3, 3 H); 3.22 – 3.31 (*q*, *J* =

6.8, 2 H); 3.28, (*s*, 3 H); 4.90 (*quint.*, *J* = 6.8, 1 H); 6.23 (*s*, 1 H); 7.33 – 7.44 (*m*, 5 H); 7.93 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 13.7; 15.9; 19.8; 20.1; 31.5; 39.1; 40.6; 46.8; 121.0; 126.1; 128.4; 128.6; 139.4; 142.0; 166.2; 168.4. HR-ESI-MS: 359.2051 ([*M* + Na]$^+$, $C_{19}H_{28}N_2NaO_2^+$; calc. 339.2048).

N-*tert-butyl*-N'-*(4-metoxyphenyl)*-N-*[(1*E*)-2-phenylprop-1-enyl]malonamide* (**3g**). Following the typical procedure in [12] using **1e** (0.586 g, 2 mmol), anh. toluene (10 ml), and **2b** (0.756 g, 4 mmol). Yield 0.311 g (41%). ^{1}H-NMR (500 MHz, $CDCl_3$): 1.50 (*s*, 9 H); 2.04 (*s*, 3 H); 3.36 (*d*, *J* = 17.1, 1 H); 3.40 (*d*, *J* = 17.1, 1 H); 3.78, (*s*, 3 H); 6.33 (*s*, 1 H); 6.85 (*d*, *J* = 8.7, 2 H); 7.26 – 7.50 (*m*, 7 H); 9.99 (br. *s*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 16.0; 28.6; 43.0; 55.7; 60.4; 114.2; 121.9; 125.2; 126.3; 128.6; 128.8; 131.4; 139.5; 140.6; 156.5; 164.7; 169.7. HR-ESI-MS: 403.1994 ([*M* + Na]$^+$, $C_{23}H_{28}N_2NaO_3^+$; calc. 403.1998).

N-*tert-butyl*-N'-*(4-nitrophenyl)*-N-*[(1*E*)-2-phenylprop-1-enyl]malonamide* (**3h**). Following the typical procedure in [12] for using **1f** (0.616 g, 2 mmol), anh. toluene (10 ml), and **2b** (0.756 g, 4 mmol). Yield 0.150 g (19%). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.51 (*s*, 9 H); 2.04 (*d*, *J* = 1.4, 3 H); 3.43 (*d*, *J* = 1.6, 2 H); 6.33 (*d*, *J* = 1.4, 1 H); 7.38 – 7.44 (*m*, 5 H); 7.77 (*d*, *J* = 9.1, 2 H); 8.20 (*d*, *J* = 9.1, 2 H); 10.95 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 16.3; 28.9; 42.8; 60.7; 119.9; 125.1; 125.5; 126.5; 129.1; 129.2; 139.5;

141.2; 144.2; 165.8; 169.5. HR-ESI-MS: 418.1741 ([*M* + Na]$^+$, $C_{22}H_{25}N_3NaO_4^+$; calc. 418.1743).

N-*tert-butyl-3-(ethylamino)*-N-*[(1*E*)-2-phenylprop-1-enyl]-3-thioxopropanamide* (**3k**). Following the typical procedure in [12] using **1h** (0.462 g, 2 mmol), anh. toluene (10 ml), and **2b** (0.756 g, 4 mmol). Yield 0.387 g (61%). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.29 (*t*, *J* = 7.4, 3 H); 1.46 (*s*, 9 H); 2.03 (*d*, *J* = 1.4, 3 H); 3.68 – 3.80 (*m*, 4 H); 6.30 (*d*, *J* = 1.4, 1 H); 7.34 – 7.42 (*m*, 5 H); 10.12 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 13.0; 16.0; 28.4; 40.8; 49.8; 59.7; 124.9; 126.2; 128.3; 128.6; 139.4; 140.5; 169.7; 194.8. HR-ESI-MS: 341.1672 ([*M* + Na]$^+$, $C_{18}H_{26}N_2NaOS^+$; calc. 341.1664).

N-*Isopropyl-3-(ethylamino)*-N-*[(1*E*)-2-phenylprop-1-enyl]-3-thioxopropanamide* (**3l**). Following the typical procedure in [12] using **1h** (0.462 g, 2 mmol), anh. toluene (10 ml), and **2a** (0.700 g, 4 mmol). Yield 0.320 g (51%). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.16 (*d*, *J* = 6.6, 6 H); 1.30 (*t*, *J* = 7.3, 3 H); 2.00 (*s*, 3 H); 3.64 – 3.78 (*m*, 2 H); 3.81 (*s*, 2 H); 4.87 (*quint.*, *J* = 6.8, 1 H); 6.23 (*s*, 1 H); 7.36 – 7.48 (*m*, 5 H); 10.20 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 13.4; 16.7; 20.2; 41.4; 47.5; 48.3; 121.1; 126.7; 128.9; 129.1; 139.8; 143.0; 169.1; 194.8. HR-ESI-MS: 327.1514 ([*M* + Na]$^+$, $C_{17}H_{24}N_2NaOS^+$; calc. 327.1507).

Radical Cyclization of N-*Alkenyl Malonodiamides and* N-*Alkenyl Thiomalonodiamides* (**3**). *General Procedure.* A soln. of **3** (1 mmol) in AcOH (10 ml) was heated to 70°. Then, $Mn(OAc)_3 \cdot H_2O$ (1.6 – 2.3 mmol; amount specified in the *Table*) was added. The mixture was stirred and heated to 70° for 30 min. The hot mixture was poured into 50 ml of cold H_2O, and extracted with CH_2Cl_2 (5 × 20 ml). The combined org. layer was washed with 5% aq. $NaHCO_3$ (2 × 10ml) and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residue was purified.

1-Isopropyl-2-oxo-N-*phenyl-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4a**). Purification by FC (AcOEt/hexane 1:3). ^{1}H-NMR (200 MHz, $CDCl_3$):1.27 (*d*, *J* = 6.6, 3 H); 1.44 (*d*, *J* = 6.8, 3 H); 3.69 – 3.77 (*m*, 1 H); 3.79 (*d*, *J* = 2.1, 1 H); 4.90 (*d*, *J* = 2.1, 1 H); 5.49 (*s*, 1 H); 5.65 (*s*, 1 H); 7.10 – 7.63 (*m*, 10 H); 8.25 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 20.8; 21.4; 47.1; 56.4; 62.5; 115.1; 120.5; 125.0; 126.7; 128.8; 129.2; 129.4; 137.8; 138.6; 146.1; 163.9; 165.5. HR-ESI-MS: 357.1575 ([*M* + Na]$^+$, $C_{21}H_{22}N_2NaO_2^+$; calc. 357.1579).

1-Isopropyl-2-oxo-N-*phenyl-4-(1-acetoxy-1-phenylethyl)azetidine-3-carboxamide* (**5a**; mixture of diasteroizomers). Purification by FC (AcOEt/hexane 3:5). M.p. 152 – 160°. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.22 (*d*, *J* = 6.8, 3 H); 1.41 (*d*, *J* = 6.8, 3 H); 1.99 (*s*, 3 H); 2.14 (*s*, 3 H); 3.41 (*quint.*, *J* = 6.8, 1 H); 3.60 (*d*, *J* = 2.0, 1 H), 4.20 (*d*,

J = 2.0, 1 H); 7.05 (*t*, *J* = 7.3, 1 H); 7.22 – 7.31 (*m*, 2 H); 7.32 – 7.42 (*m*, 7 H); 7.60 (br. *s*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 19.7; 20.7; 21.4; 22.5; 47.8; 56.3; 63.1; 83.2; 120.3; 124.9; 125.1 (minor); 125.4 (major); 128.7; 129.1 (minor); 129.2 (major); 129.3 (major); 129.4 (minor); 137.7; 140.5; 163.3; 165.0; 169.2. HR-ESI-MS: 417.1802 ([*M* + Na]$^+$, $C_{23}H_{26}N_2NaO_4^+$; calc. 417.1790).

1-tert-Butyl-2-oxo-N-*ethyl-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4b**). Purification by FC (AcOEt/hexane 3:5). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.14 (*t*, *J* = 7.3, 3 H); 1.35 (*s*, 9 H); 3.26 – 3.37 (*m*, 2 H); 3.50 (*d*, *J* = 2.1, 1 H); 4.81 (*d*, *J* = 2.1, 1 H); 5.56 (*s*, 1 H); 5.59 (*s*, 1 H); 6.30 (br. *s*. 1 H); 7.30 – 7.40 (*m*, 3 H); 7.57 – 7.62 (*m*, 2 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 14.6; 27.9; 34.4; 55.2; 55.8; 61.7; 114.2; 126.2; 128.2; 128.6; 138.6; 147.5; 165.3; 165.7. HR-ESI-MS: 323.1732 ([*M* + Na]$^+$, $C_{18}H_{24}N_2NaO_2^+$; calc. 323.1735).

1-Isopropyl-2-oxo-N-*ethyl-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4c**). Purification by FC (AcOEt/hexane 1:2). ^{1}H-NMR (500 MHz, $CDCl_3$): 1.15 (*t*, *J* = 7.3, 3 H); 1.23 (*d*, *J* = 6.3, 3 H); 1.39 (*d*, *J* = 6.8, 3 H); 3.23 – 3.31 (*m*, 1 H); 3.33 – 3.39 (*m*, 1 H); 3.56 (*d*, *J* = 2.0, 1 H); 3.68 (*quint.*, *J* = 6.3, 1 H); 4.80 (*d*, *J* = 2.0, 1 H); 5.45 (*s*, 1 H); 5.61 (*s*, 1 H); 6.28 (br. *s*, 1 H); 7.30 – 7.41 (*m*, 3 H); 7.58 – 7.60 (*m*, 2 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 14.8; 20.6; 21.2; 34.7; 46.6; 56.1; 61.8; 114.4; 126.4; 128.5; 128.8;

138.4; 146.0; 165.5. HR-ESI-MS: 309.1572 ([*M* + Na]$^+$, $C_{17}H_{22}N_2NaO_2^+$; calc. 309.1579).

1-tert-Butyl-2-oxo-N-*butyl-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4d**). Purification by FC (AcOEt/hexane 1:2). ^{1}H-NMR (200 MHz, $CDCl_3$): 0.90 (*t*, *J* = 7.0, 3 H); 1.34 (*s*, 9 H); 1.27 – 1.53 (*m*, 4 H); 3.24 – 3.30 (*m*, 1 H); 3.49 (*d*, *J* = 2.1, 1 H); 4.80 (*d*, *J* = 2.1, 1 H); 5.45 (*s*, 1 H); 5.61 (*s*, 1 H); 6.35 (br. *s*, 1 H); 7.30 – 7.39 (*m*, 3 H); 7.57 – 7.61 (*m*, 2 H). ^{13}C-NMR (50 MHz, CDCl3): 13.7; 19.9; 27.9; 31.4; 39.2; 55.1; 55.8; 61.7; 114.1; 126.2; 128.2; 128.6; 138.6; 147.5; 165.4; 165.8. HR-ESI-MS: 351.2041 ([*M* + Na]$^+$, $C_{20}H_{28}N_2NaO_2^+$; calc. 351.2048).

1-Isopropyl-2-oxo-N-*butyl-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4e**). Purification by FC (AcOEt/hexane 1:2). ^{1}H-NMR (200 MHz, $CDCl_3$): 0.91 (*t*, *J* = 7.2, 3 H); 1.21 (*d*, *J* = 6.7, 3 H); 1.40 (*d*, *J* = 6.8, 3 H); 1.20 – 1.54 (*m*, 4 H); 3.22 – 3.35 (*m*, 2 H); 3.56 (*d*, *J* = 2.2, 1 H); 3.68 (*quint.*, *J* = 6.7, 1 H); 4.80 (*d*, *J* = 2.2, 1 H); 5.45 (*s*, 1 H); 5.61 (*s*, 1 H); 6.27 (br. *s*, 1 H); 7.26 – 7.42 (*m*, 3 H); 7.56 – 7.63 (*m*, 2 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 13.7; 20.0; 20.3; 20.9; 31.4; 39.3; 46.4; 55.9; 61.6; 114.1; 126.2; 128.2; 128.6; 138.2; 145.8; 165.3; 165.4. HR-ESI-MS: 337.1902 ([*M* + Na]$^+$, $C_{19}H_{26}N_2NaO_2^+$; calc. 337.1892).

1-tert-butyl-2-oxo-N-*(3-chlorophenyl)-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4f**). Purification by FC (AcOEt/hexane 1:2). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.40 (*s*, 9 H); 3.75 (*d*, *J* = 2.1, 1 H); 5.00 (*d*, *J* = 2.1, 1 H); 5.61 (*s*, 1 H); 5.65 (*s*, 1 H); 7.00 – 7.30 (*m*, 3 H); 7.36 – 7.52 (*m*, 3 H); 7.53 – 7.65 (*m*, 3 H); 8.70 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 28.4; 56.0; 56.1; 62.6; 115.1; 118.1; 120.3; 124.9; 126.6; 128.8; 129.2; 130.2; 135.0; 138.8; 139.0; 147.5; 163.9; 166.0. HR-ESI-MS: 405.1351 ([*M* + Na]$^+$, $C_{22}H_{23}ClN_2NaO_2^+$; calc. 405.1346).

1-tert-Butyl-2-oxo-N-*(4-metoxyphenyl)-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4g**). Purification by FC (AcOEt/hexane 1:3). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.40 (*s*, 9 H); 3.69 (*d*, *J* = 2.3, 1 H); 3.76 (*s*, 3 H); 4.99 (*d*, *J* = 2.3, 1 H); 5.62 (*s*, 1 H); 5.65 (*s*, 1 H); 6.85 – 6.89 (*m*, 2 H); 7.35 – 7.41 (*m*, 3 H); 7.50 – 7.60 (*m*, 4 H); 9.14 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 28.4; 55.8; 55.9; 56.4; 62.5; 114.5; 115.0; 122.1; 126.7; 128.7; 129.1; 129.6; 131.0; 139.0; 147.8; 157.0; 163.7. HR-ESI-MS: 401.1827 ([*M* + Na]$^+$, $C_{23}H_{26}N_2NaO_3^+$; calc. 401.1841).

*(3*R*,4*R*)-1-tert-Butyl-2-oxo*-N-*(4-metoxyphenyl)-4-[(1*R*)-1-acetoxy-1-phenylethyl]azetidine-3-carboxamide* and *(3*S*, 4*S*)-1-tert-Butyl-2-oxo*-N-*(4-metoxyphenyl)-4-[(1*S*)-1-acetoxy-1-phenylethyl]azetidine-3-carboxamide* (**5g'**). Purification by FC (AcOEt/hexane 2:3). ^{1}H-NMR (500 MHz, $CDCl_3$): 1.40 (*s*, 9 H);

2.06 (*s*, 3 H); 2.07 (*s*, 3 H); 3.34 (*d*, *J* = 2.0, 1 H); 3.77 (*s*, 3 H); 4.45 (*d*, *J* = 2.0, 1 H); 6.78 – 6.83 (*m*, 2 H), 7.30 – 7.48 (*m*, 7 H); 7.91 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 21.5; 22.7; 29.1; 55.8; 55.9; 56.3; 62.8; 83.3; 114.5; 121.9; 125.4; 126.9; 128.6; 131.0; 139.2; 156.9; 163.3; 166.6; 169.1. HR-ESI-MS: 461.2069 ([*M* + Na]$^+$, $C_{25}H_{30}N_2NaO_5^+$; calc. 461.2052).

*(3*S*,4*S*)-1-tert-Butyl-2-oxo*-N-*(4-metoxyphenyl)-4-[(1*R*)-1-acetoxy-1-phenylethyl]azetidine-3-carboxamide* and *(3*R*, 4*R*)-1-tert-Butyl-2-oxo*-N-*(4-metoxyphenyl)-4-[(1*S*)-1-acetoxy-1-phenylethyl]azetidine-3-carboxamide* (**5g''**). Purification by FC (AcOEt/hexane 2:3). ^{1}H-NMR (500 MHz, $CDCl_3$): 1.51 (*s*, 9 H); 1.96 (*s*, 3 H); 2.07 (*s*, 3 H); 3.40 (*d*, *J* = 2.4, 1 H); 3.72 (*s*, 3 H); 4.45 (*d*, *J* = 2.4, 1 H); 6.77 – 6.79 (*m*, 2 H); 7.19 – 7.22 (*t*, *J* = 7.3, 1 H); 7.27 – 7.33 (*m*, 4 H); 7.44 – 7.46 (*m*, 2 H); 8.44 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.8; 22.4; 29.4; 55.9; 56.1; 58.5; 63.4; 83.9; 114.8; 122.0; 122.1; 126.5; 128.8; 129.6; 142.5; 157.5; 164.1; 165.2; 169.7. HR-ESI-MS: 461.2069 ([*M* + Na]$^+$, $C_{25}H_{30}N_2NaO_5^+$; calc. 461.2052).

1-tert-Butyl-2-oxo-N-*(4-nitrophenyl)-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4h**). Purification by FC (AcOEt/hexane 1:2). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.42 (*s*, 9 H); 3.80 (*d*, *J* = 2.2, 1 H); 5.01 (*d*, *J* = 2.2, 1 H); 5.63 (*s*, 1 H); 5.68 (*s*, 1 H); 7.38 – 7.54 (*m*, 3 H); 7.56 – 7.64 (*m*, 4 H); 8.08 – 8.13 (*m*, 2 H); 9.09 (br. *s*, 1 H). ^{13}C-NMR (50

MHz, $CDCl_3$): 28.4; 56.0; 56.3; 62.7; 115.4; 119.6; 125.3; 126.6; 129.0; 129.3; 138.6; 143.7; 144.1; 147.2; 164.4; 165.8. HR-ESI-MS: 416.1594 ([*M* + Na]$^+$, $C_{22}H_{23}N_3NaO_4^+$; calc. 416.1586).

1-tert-Butyl-2-oxo-N-*(4-nitrophenyl)-4-(1-acetoxy-1-phenylethyl)azetidine-3-carboxamide* (**5h**; mixture of diasteroizomers). Purification by FC (AcOEt/hexane 1:2). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.38 (*s*, 9 H); 2.01 (*s*, 3 H); 2.05 (*s*, 3 H); 3.66 (*d*, *J* = 2.4, 1 H); 4.56 (*d*, *J* = 2.4, 1 H); 7.31 – 7.41 (*m*, 3 H); 7.42 – 7.54 (*m*, 2 H); 7.89 – 7.95 (*m*, 2 H); 8.19 – 8.25 (*m*, 2 H); 9.80 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 21.5; 22.5; 29.3; 56.2; 59.1; 62.5; 83.9; 120.3 (major); 120.2 (minor); 126.0; 128.0; 128.9; 129.1; 140.9; 144.5; 145.9; 164.7; 166.2; 169.4. HR-ESI-MS: 476.1783 ([*M* + Na]$^+$, $C_{24}H_{27}N_3NaO_6^+$; calc. 476.1798).

1-tert-Butyl-2-oxo-N-*(4-nitrophenyl)-4-(1-hydroxy-1-phenylethyl)azetidine-3-carboxamide* (**6h**; mixture of diasteroizomers). Purification by FC (AcOEt/hexane 1:2). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.34 (*s*, 9 H); 1.79 (*s*, 3 H); 2.89 (br. *s*, 1H); 3.74 (*d*, *J* = 2.4, 1 H); 4.54 (*d*, *J* = 2.4, 1 H); 7.30 – 7.45 (*m*, 3 H); 7.59 – 7.64 (*m*, 2 H); 7.88 – 7.94 (*m*, 2 H); 8.20 – 8.26 (*m*, 2 H); 9.81 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 21.0; 29.1; 56.0; 59.4; 60.0; 86.6; 120.2; 120.3; 126.0; 127.1; 129.0; 141.0; 144.3; 145.9; 164.6; 166.3.

1-tert-Butyl-2-thioxo-N-*methyl-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4i**). Purification by FC (AcOEt/hexane 3:5). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.36 (*s*, 9 H); 3.16 (*d*, *J* = 4.8, 3 H); 3.77 (*d*, *J* = 2.0, 1 H); 5.14 (*d*, *J* = 2.0, 1 H); 5.59 (*s*, 1 H); 5.62 (*s*, 1 H); 7.33 – 7.37 (*m*, 3 H); 7.51 – 7.56 (*m*, 2 H); 8.50 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 28.5; 33.1; 55.8; 60.1; 67.5; 116.3; 127.1; 128.7; 129.0; 139.0; 147.7; 166.5; 196.0. HR-ESI-MS: 325.1343 ($[M + Na]^+$, $C_{17}H_{22}N_2NaOS^+$; calc. 325.1351).

1-Isopropyl-2-thioxo-N-*methyl-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4j**). Purification by FC (AcOEt/hexane 1:2). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.25 (*d*, *J* = 6.6, 3 H); 1.40 (*d*, *J* = 6.8, 3 H); 3.16 (*d*, *J* = 4.8, 3 H); 3.66 – 3.80 (*m*, 1 H); 3.81 (*d*, *J* = 2.3, 1 H); 5.09 (*d*, *J* = 2.3, 1 H); 5.51 (*s*, 1 H); 5.61 (*s*, 1 H); 7.26 – 7.38 (*m*, 3 H); 7.39 – 7.53 (*m*, 2 H); 8.38 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 20.4; 20.9; 32.6; 46.4; 59.7; 66.8; 116.1; 126.6; 128.2; 128.5; 138.2; 145.6; 165.6; 195.6. HR-ESI-MS: 311.1188 ($[M + Na]^+$, $C_{16}H_{20}N_2NaOS^+$; calc. 311.1194).

1-tert-Butyl-2-thioxo-N-*ethyl-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4k**). Purification by FC (AcOEt/hexane 1:3). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.24 (*t*, *J* = 7.3, 3 H); 1.37 (*s*, 9 H); 3.50 – 3.82 (*m*, 2 H); 3.74 (*d*, *J* = 1.7, 1 H); 5.17 (*d*, *J* = 1.7, 1 H); 5.58 (*s*, 1 H); 5.62 (*s*, 1 H); 7.33 – 7.37 (*m*, 3 H); 7.51 – 7.56 (*m*, 2 H); 8.43 (br. *s*, 1 H). ^{13}C-

NMR (50 MHz, $CDCl_3$): 12.8; 27.9; 40.7; 55.3; 59.5; 67.2; 115.6; 126.5; 128.2; 128.5; 138.5; 147.1; 166.0; 194.2. HR-ESI-MS: 339.1520 ([*M* + Na]$^+$, $C_{18}H_{24}N_2NaOS^+$; calc. 339.1507).

1-tert-Butyl-2-thioxo-N-*ethyl-4-(1-acetoxy-1-phenylethyl)azetidine-3-carboxamide* (**5k**; mixture of diasteroizomers). Purification by FC (AcOEt/hexane 2:3). ^{1}H-NMR (200 MHz, $CDCl_3$): 0.90 (*t*, *J* = 7.3, 3 H); 1.51 (*s*, 9 H); 1.93 (*s*, 3 H); 2.06 (*s*, 3 H); 3.12 – 3.45 (*m*, 2 H); 3.53 (*d*, *J* = 2.5, 3 H); 4.67 (*d*, *J* = 2.5, 1 H); 7.26 – 7.42 (*m*, 5 H); 8.33 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 13.2; 18.0; 22.4; 29.4; 41.0; 64.2; 64.3; 67.2; 83.9; 126.6; 128.7; 129.4; 142.1; 164.5; 169.4; 186.3. HR-ESI-MS: 399.1704 ([*M* + Na]$^+$, $C_{20}H_{28}N_2NaO_3S^+$; calc. 399.1718).

1-Isopropyl-2-thioxo-N-*ethyl-4-(1-phenylvinyl)azetidine-3-carboxamide* (**4l**). Purification by FC (AcOEt/hexane 1:3). ^{1}H-NMR (200 MHz, $CDCl_3$): 1.24 (*dt*, *J* = 1.0, *J* = 6.6, 3 H); 1.26 (*dd*, *J* = 1.0, *J* = 6.7, 3 H); 1.39 (*dd*, *J* = 1.0 *J* = 6.7, 3 H); 3.58 – 3.68 (*m*, 2 H); 3.70 – 3.78 (*m*, 1 H); 3.79 (*d*, *J* = 2.3, 1 H); 5.11 (*d*, *J* = 2.3, 1 H); 7.30 – 7.40 (*m*, 3 H); 7.41 – 7.52 (*m*, 2 H); 8.38 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 12.9; 20.4; 20.9; 40.6; 46.3; 59.7; 66.9; 116.1; 126.7; 128.2; 128.4; 128.5; 145.7; 165.6; 194.4. HR-ESI-MS: 325.1341 ([*M* + Na]$^+$, $C_{17}H_{22}N_2NaOS^+$; calc. 325.1350).

1-Isopropyl-2-thioxo-N-*ethyl-4-(1-acetoxy-1-phenylethyl)azetidine-3-carboxamide* (**5l**; mixture of diasteroizomers). Purification by FC (AcOEt/hexane 2:3). ^{1}H-NMR (200 MHz, $CDCl_3$): 0.97 (*t*, *J* = 7.3, 3 H); 1.28 (*d*, *J* = 6.7, 3 H); 1.42 (*d*, *J* = 6.8, 3 H); 1.93 (*s*, 3 H); 2.10 (*s*, 3 H); 3.25 – 3.48 (*m*, 2 H); 3.50 – 3.70 (*m*, 1 H); 3.84 (*d*, *J* = 2.7, 1 H); 4.57 (*d*, *J* = 2.7, 1 H); 7.24 – 7.41 (*m*, 5 H); 8.60 (br. *s*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 13.2; 19.1; 21.1; 21.8; 22.4; 40.9 (minor); 41.1 (major); 47.7; 63.9 (minor); 64.0 (major); 66.7; 84.0; 126.4; 128.7; 129.4; 142.2; 164.8; 169.5; 196.2. HR-ESI-MS: 385.1564 ([*M* + Na]$^+$, $C_{19}H_{26}N_2NaO_3S^+$; calc. 385.1562).

Crystal Structure Determination[1]). Diffraction data were recorded on *KUMA KM4* diffractometer with graphite-monochromated MoK_α using a *Sapphire-2 CCD* detector (*Agilent Ltd.*). The structures were solved with direct methods and refined with the SHELX97 program package [22] with the full-matrix least-squares refinement based on F2. The data were corrected for absorption with the CrysAlis RED program [23]. All non-H-atoms were refined anisotropically. All H-atoms were positioned with idealized geometry and were refined isotropically with U_{iso}(H) = 1.2U_{eq}(C and N) for aromatic, CH_2, CH, and amine H-atoms (1.5 for Me H-atoms) using a riding model with C–H =

[1]) CCDC-903076 – 903079 contain the supplementary crystallographic data for **5a**, **5g'**, **4h**, and **5h**, respectively. These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif.

0.93 Å (aromatic H-atoms), 0.96 Å (Me H-atoms), 0.97 Å (CH_2 H-atoms) 0.98 Å (CH H-atoms), and 0.86 Å (N–H bonds).

Crystal Data of **5a**: $C_{23}H_{26}N_2O_4$, M_r 394.46; colorless block, size 0.23 × 0.18 × 0.15 mm; monoclinic, space group $C2/c$; a = 19.6870(17), b = 8.8802(4), c = 25.6299(13) Å, β = 98.177(5)°, V = 4435.2(5) Å^3; T = 20°, Z = 8, $\rho_{calc.}$ = 1.181 g cm^{-3}, μ(MoK_α) = 0.081 mm^{-1} ; F(000) = 1680, 13677 reflections in h (–23/24), k (–10/10), l (–21/31), measured in the range 2.40 ≤ Θ ≤ 28.72°, completeness Θ_{max} = 99.9%, 4354 independent reflections, R_{int} = 0.0437, 2209 reflections with $F_o > 4\sigma(F_o)$, 262 parameters, 0 restraints, R^1_{obs} = 0.0466, wR^2_{obs} = 0.1104, R^1_{all} = 0.0971, wR^2_{all} = 0.1245, goodness-of-fit = 0.841, largest difference peak and hole: 0.233/–0.134 e Å^{-3}.

Crystal Data of **5g'**: $C_{25}H_{27}N_2O_5$, M_r 435.49; colorless block, size 0.31 × 0.27 × 0.24 mm; orthorhombic, space group $P2_12_12_1$; a = 8.9667(3), b = 12.2729(5), c = 21.6290(11) Å, V = 2380.22(17) Å^3; T = 25°, Z = 4, $\rho_{calc.}$ = 1.215 g cm^{-3}, μ(MoK_α) = 0.085 mm^{-1} ; F(000) = 924, 15467 reflections in h (–11/10), k (–15/14), l (–26/26), measured in the range 2.50 ≤ Θ ≤ 28.55°, completeness Θ_{max} = 99.9%, 4676 independent reflections, R_{int} = 0.0269, 3226 reflections with $F_o > 4\sigma(F_o)$, 298 parameters, 1 restraints, R^1_{obs} = 0.0571, wR^2_{obs} = 0.1616, R^1_{all} = 0.0779, wR^2_{all} = 0.1749, goodness-of-fit = 0.962, largest difference peak and hole: 0.330/–0.183 e Å^{-3}.

Crystal Data of **4h**: $C_{22}H_{24}N_3O_4$, M_r 394.44; colorless block, size 0.10 × 0.05 × 0.4 mm; monoclinic, space group $P2_1/c$; a = 13.3919(13), b = 20.346(2), c = 7.9436(11) Å, β = 92.995(9)°, V = 2161.4(4) Å^3; T = 25°, Z = 4, $\rho_{calc.}$ = 1.212 g cm^{-3}, μ(MoK_α) = 0.085 mm^{-1} ; F(000) = 836, 13437 reflections in h (–16/16), k (–25/12), l (–9/9), measured in the range 2.51 ≤ Θ ≤ 28.63°, completeness Θ_{max} = 99.9%, 4234 independent reflections, R_{int} = 0.0649, 2013 reflections with $F_o > 4\sigma(F_o)$, 243 parameters, 0 restraints, R^1_{obs} = 0.0933, wR^2_{obs} = 0.2603, R^1_{all} = 0.1707, wR^2_{all} = 0.3243, goodness-of-fit = 1.073, largest difference peak and hole: 0.728/ –0.313 e Å^{-3}.

Crystal Data of **5h**: $C_{25.25}H_{30}N_3O_6$, M_r 471.52; colorless block, size 0.27 × 0.19 × 0.14 mm; triclinic, space group $P\bar{1}$; a = 9.7291(3), b = 15.6542(6), c = 18.4054(6) Å, α = 73.740(3), β = 80.503(3), γ = 82.990(3)°, V = 2645.63(16) Å^3; T = 20°, Z = 4, $\rho_{calc.}$ = 1.184 g cm^{-3}, μ(MoK_α) = 0.085 mm^{-1} ; F(000) = 1002, 26020 reflections in h (–11/11), k (–18/19), l (–22/22), measured in the range 2.32 ≤ Θ ≤ 28.51°, completeness Θ_{max} = 99.9%, 10385 independent reflections, R_{int} = 0.0209, 6247 reflections with $F_o > 4\sigma(F_o)$, 676 parameters, 8 restraints, R^1_{obs} = 0.0693, wR^2_{obs} = 0.1965, R^1_{all} = 0.1067, wR^2_{all} = 0.2373, goodness-of-fit = 1.022, largest difference peak and hole: 0.501/–0.187 e Å^{-3}.

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