New Reactivity Patterns of the β-Lactam Ring: Tandem C3–C4 Bond Breakage–Rearrangement of 4-Acyl- or 4-Imino-3,3-dimethoxy-2-azetidinones Promoted by $SnCl_2 \cdot 2H_2O$

Benito Alcaide,* Yolanda Martín-Cantalejo, Julián Rodríguez-López, and Miguel A. Sierra

Departamento de Química Orgánica I, Facultad de Química, Universidad Complutense, 28040-Madrid, Spain

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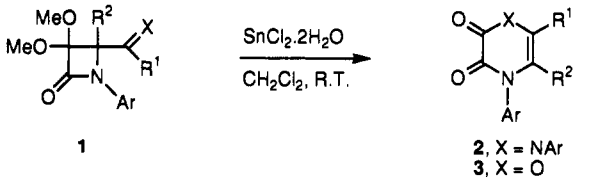
Introduction

Besides their use in the synthesis of β-lactam antibiotics,[1] 2-azetidinones are versatile building blocks because ring cleavage of any of the four single bonds of the β-lactam system is enhanced by ring strain.[2] Thus, access to diverse structural types of natural or synthetic compounds lacking the β-lactam ring have been reported by cleavage of the 2-azetidinone ring through any of the four possibilities.[3] In this context, our recently reported stereoselective synthesis of vinyl ethers starting from *N*-(arylidene)- or *N*-(alkylidene)amino-2-azetidinones may be illustrative.[4]

In our ongoing project directed at the synthesis and synthetic applications of functionalized 2-azetidinones[5] and at the development of new modes of reactivity of the 2-azetidinone ring,[4,5g] we thought that the presence of groups with the ability to stabilize a positive charge at position 3 of the β-lactam ring might promote cationic rearrangements in the presence of acids, through a C3–C4 bond breakage. Initially, we focussed our attention on 3,3-dimethoxyazetidin-2-ones analogous to **1** but lacking additional nucleophilic groups. Disappointingly, compounds **1** bearing aryl or alkyl substituents at C4 of the 2-azetidinone ring were resistant to reaction in the presence of protic or Lewis acids and external nucleophiles. However, when 4-imino- or 4-acyl-2-azetidinones **1** having an additional nucleophilic group were reacted in the presence of $SnCl_2 \cdot 2H_2O$[6] a smooth rearrangement was observed leading cleanly to new pyrazine and/or 1,4-oxazine derivatives **2** and **3** (Scheme I). Reported here is the study of this novel acid-catalyzed rearrangement of the β-lactam ring involving the cleavage of the C3–C4 bond. As far as we know, the only related acid-catalyzed rearrangement of monocyclic β-lactams, namely the conversion of 3-(acylamino)-1,4-diphenyl-2-azetidinones to 3-(acylamino)-1,2-diphenyl-5-imidazolines in refluxing xylene in the presence of iodine, was reported by Bird,[7] while the rearrangement of penicillin to penillonic acid is known to occur in the bicyclic series.[8] Mechanisms involving carbocationic intermediates were proposed for these processes. In addition, C3–C4 bond cleavage through carbanion intermediates was reported to account for the base-promoted hydrolysis of β-lactams having nitrogen substituents at C4 and two phenyl substituents at C3.[9]

Scheme I



1

2, X = NAr
3, X = O

Results and Discussion

First, 4-acyl β-lactams **1c–e** were reacted with different protic and Lewis acids. The best results were obtained by working with an equimolar amount of $SnCl_2 \cdot 2H_2O$ in CH_2Cl_2 at room temperature (Table I).[10] Disappearance of

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(2) For reviews, see: (a) Manhas, M. S.; Wagle, D. R.; Chiang, J.; Bose, A. K. *Heterocycles* **1988**, *27*, 1755. (b) Kano, S. J. *J. Synth. Org. Chem. Jpn.* **1978**, *36*, 581. (c) Ojima, I.; Hatanaka, N. *J. Synth. Org. Chem. Jpn.* **1982**, *40*, 209. (d) Ojima, I. In *Asymmetric Reactions and Processes in Chemistry*; Eliel, E. L., Otsuka, S., Eds.; *ACS Symp. Ser.* **1982**, *185*, 109. For leading references, see also: (e) Wasserman, H. H.; Leadbetter, M. R.; Kopka, I. E. *Tetrahedron Lett.* **1984**, *25*, 2391. (f) Wasserman, H. H.; Matsuyama, H. *J. Am. Chem. Soc.* **1981**, *103*, 461. (g) Combie, L.; Jones, R. C.; Osborne, S.; Mat-Zin, Ab. R. *J. Chem. Soc., Chem. Commun.* **1983**, 959. (h) Ojima, I.; Pei, Y. *Tetrahedron Lett.* **1992**, *33*, 887.

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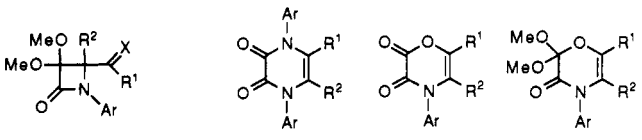
(9) Bose, A. K.; Kugajevsky, I. *Tetrahedron* **1967**, *23*, 957.

(10) Other Lewis acids such as $ZnCl_2$, ZnI_2, $TiCl_4$, and $AlCl_3$ were unable to promote the rearrangement.

0022-3263/93/1958-4767$04.00/0

Table I



1 2 3 4

	yield (%)[a,b] of 2	yield (%)[a,b] of 3	yield (%)[a,b] of 4
1a, $R^1 = R^2 = H$; X = NAr	**2a**, 95	–	–
1b, $R^1 = R^2 = Me$, X = NAr	**2b**, 99	–	–
1c, $R^1 = R^2 = H$; X = O	–	**3c**, 75[c]	**4c**, 44[c]
1d, $R^1 = R^2 = Me$; X = O	–	**3d**, 88	–
1e, $R^1 = Ph$, $R^2 = H$; X = O	–	**3e**, 95	–
1f, $R^1 = H$, $R^2 = Me$; X = $(OMe)_2$	–	–	**4f**, 95

[a] In pure, isolated material. [b] In all cases Ar = *p*-$MeOC_6H_4$, except for compounds **1f** and **4f** (Ar = Ph). [c] Compounds **3c** and **4c** were obtained under separate reactions.

the starting material occurred after a few hours. Standard workup gave the reaction product which was then purified by either crystallization or column chromatography. Compounds **1** bearing a ketal functionality at the 3 position of the four-membered ring may, in principle, be hydrolyzed to 3-oxo β-lactams, which in turn are important synthetic intermediates.[11] However, the isolated materials showed spectroscopic data which differed widely from that expected for 3-oxo β-lactams. Thus, compounds **3** have resonances attributable to olefinic protons in the region of 6.41–6.83 ppm in their ^1H NMR spectra while the only resonance attributable to a carbonyl group in their ^{13}C NMR spectra appears at 160.0–149.8 ppm, far away from the 190.0–200.0 ppm expected for an oxo group in a 3-oxo β-lactam.[11c,12] Spectroscopic data for compounds **3** are in good accordance with that expected for 1,4-dihydrooxazine derivatives. Specially illustrative is the reaction of compound **1c**. Depending on the reaction time compound **3c** or its precursor, cyclic orthoester **4c**, were selectively obtained.[13] Thus rearrangement to the six membered ring occurs prior to hydrolysis of the ketal group.

In order to prove the generality of the process above, the reactions of 4-imino β-lactams **1a,b** with $SnCl_2 \cdot 2H_2O$ were carried out next (Table I). In these cases a clean, almost quantitative conversion to reaction products was obtained. The spectroscopic data of the reaction products were in good accordance with pyrazine-2,3-dione derivatives **2**. These results confirm that imine groups attached to the position 4 of the β-lactam ring are also suitable to give the C3–C4 fragmentation–rearrangement process. Clearly, in these cases the rearrangement competes favorably with the hydrolysis of the imino group, which is not the case when aqueous hydrochloric acid is used (see below).

Finally, β-lactam **1f** bearing an dimethoxymethyl group at the C4 position was tested. Again, a similar rearrangement to the six-membered oxazine occurs, but the reaction time was considerably longer than for **1a–e**. Moreover, the reaction of **1f** stopped at the stage of ortholactone **4f** which either remains unaltered at longer reaction times or decomposes when more energetic reaction conditions are used. Compound **4f** deserves some additional comments. When the ^1H and ^{13}C NMR spectra of ortholactone **4f** were recorded in $CDCl_3$ at room temperature (294 K) two separate sets of signals were observed in a 2/1 ratio which suggested the possible presence of two isomeric products. When the ^1H NMR spectra of **4f** was recorded in DMSO-d_6, the duplicity of signals still remained. However, coalescence of the signals was observed in spectra taken at higher temperatures. Molecular modeling showed that compound **4f** has two preferred conformations. The above effects observed in compound **4f** may be attributable to the interaction of the methyl group in **4f** with the *N*-phenyl moiety, interaction which is not present in **4c**, which shows one single set of resonances in both its ^1H and ^{13}C NMR spectra.

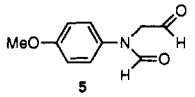
The above rearrangements also take place in the presence of protic acids (H_2SO_4 or HCl). However, yields were erratic and mixtures of the different reaction products were usually obtained. Thus, heterogeneous ($CHCl_3$/5% aqueous HCl) hydrolysis of β-lactam **1a**, yields, depending on the reaction time, mixtures of compounds **1c**, **2a**, **3c**, **4c**, and the decomposition product formed by hydrolysis of dione **3c**, the *N*-(*p*-anisyl)-*N*-(2-oxoethyl)formamide **5**. ^1H NMR monitoring of the reaction of **1a** shows that pyrazine **2a** is formed in the initial burst of the reaction, and its concentration remains mostly unchanged with time. Hydrolysis of the imino group to aldehyde **1c** competes favorably with rearrangement to pyrazine **2a**, and **1c** slowly rearranges to morpholine **3c** through ortholactone **4c**. Finally, compound **3c** is decomposed to **5**, after several days.

It seems clear from the above data that both imino and carbonyl groups in compounds **1** are prone to promote the rearrangement to compounds **2–4**. Reaction pathways in Scheme II may account for the observed reaction products. Both mechanistic rationalizations rest in coordination of tin (or the proton if a protic acid is used) to the starting material as the promoter of the rearrangement. Path A involves coordination of tin to the group at C4 to yield intermediate **6** which would evolve by C3–C4 bond breakage due to the enhanced reactivity of the double bond and the ability of the ketal to stabilize the emerging carbocation at C3 to give **7**. Annelation of intermediate **7** renders compounds **4**, which are further hydrolyzed giving the final products **2** and **3**, except for compound **1f** which yields exclusively ortholactone **4f** upon treatment with tin(II) chloride. Alternatively, compounds **1** upon dicoordination at the ketal functionality to yield **8**, may evolve through a concerted or stepwise six-electron rearrangement to compounds **4**.[14]

(11) See, for example: (a) Palomo, C.; Aizpurua, J. M.; Cossio, F. P.; García, J. M.; López, M. C.; Oiarbide, M. *J. Org. Chem.* **1990**, *55*, 2070. (b) Palomo, C.; Aizpurua, J. M.; López, M. C.; Arruekoetxea, N.; Oiarbide, M. *Tetrahedron Lett.* **1990**, *31*, 6425. (c) van der Veen, Bari, S. S.; Krishnan, L.; Manhas, M. S.; Bose, A. K. *J. Org. Chem.* **1989**, *54*, 5758. (d) Tufariello, J. J.; Pinto, D. J. P.; Milowsky, A. S.; Reinhardt, D. V. *Tetrahedron Lett.* **1987**, *28*, 5481. (e) Chiba, K.; Mori, M.; Ban, Y. *Tetrahedron* **1985**, *41*, 387. (f) Manhas, M. S.; Bari, S. S.; Bhawal, B. M.; Bose, A. K. *Tetrahedron Lett.* **1984**, *25*, 4733.

(12) Alcaide, B.; Martín-Cantalejo, Y., unpublished results.

(13) Compound **4c** was quantitatively converted into dihydrooxazine **3c** under the reaction conditions used obtaining **3c** directly from **1c**. Longer reaction time (24 h) promotes the formation of formamide **5**, through hydrolysis–decarboxylation of dione **3c**.



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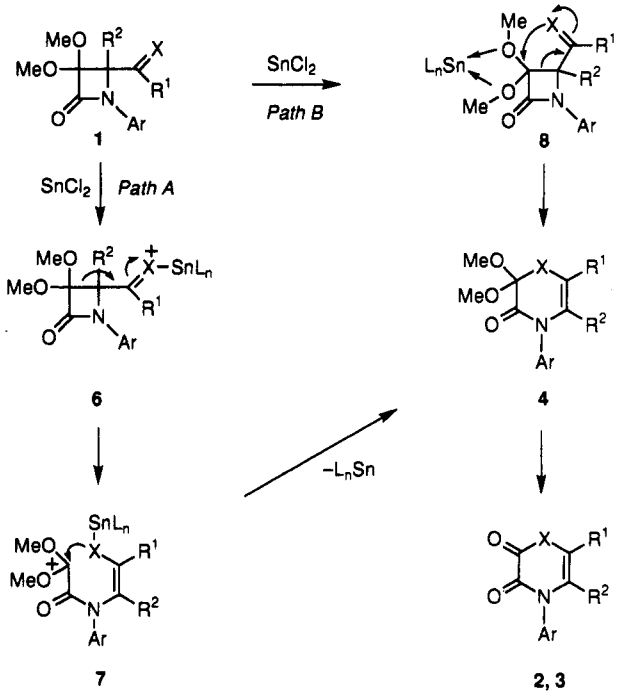
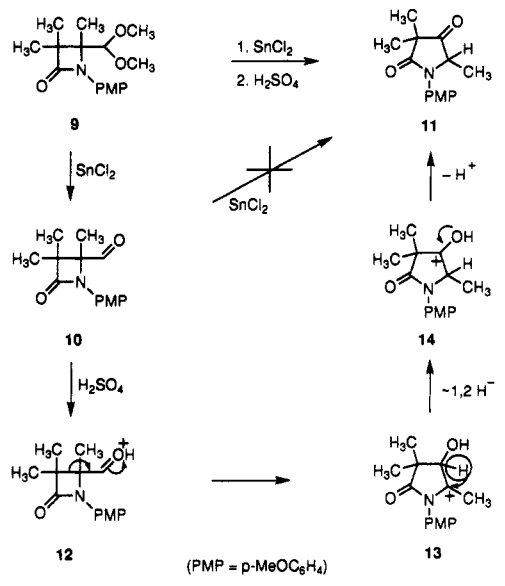
(14) For some recent references on the attack of nucleophiles to coordinated ketals see, for example: (a) Sammakia, T.; Smith, R. S. *J. Am. Chem. Soc.* **1992**, *114*, 10998. (b) Granja, J. R.; Castedo, L.; Mouriño, A. *J. Org. Chem.* **1993**, *58*, 125. (c) Molander, G. A.; Haar, J. P. *J. Am. Chem. Soc.* **1993**, *115*, 40.

Scheme II



Scheme III



The key feature of the process above is the presence of a ketal moiety at the C3 of the 2-azetidinone ring. Thus, the ketal group in β-lactam **9**, bearing two methyl groups at C3, is smoothly hydrolyzed by $SnCl_2 \cdot 2H_2O$ to the corresponding aldehyde **10**, the final reaction product in these conditions. When more energetic conditions were used (concentrated sulfuric acid), a new product, whose spectroscopic and analytical data are in good accordance with the structure of γ-lactam **11**, is formed. In this case, a different type of C3–C4 bond breakage, through the initial shift of the C3–C4 bond to the protonated aldehyde group to give the five-membered ring carbocationic intermediate **13**, occurs. A 1,2-hydride shift to form intermediate **14** followed by loss of a proton would give **11** (Scheme III).

The change in reaction pathway for compound **10** supports the decisive role of the methoxy groups at C3 in promoting the rearrangement of compounds **1**, but does not allow an unequivocal choice between the two reaction pathways in Scheme II. It can be argued, for example, that tin coordination of the carbonyl group of compounds **1c–e** should promote a reaction analogous to that observed in compound **10**. Subsequently, formation of five-membered ring compounds analogous to **11** should be observed in these cases. Since this is not the case, path B involving coordination at the ketal moiety should be responsible for the observed rearrangement. However, it is equally reasonable to propose that the ability of two methyl groups to stabilize a carbocation at C3 is not enough to promote the cationic rearrangement in Scheme II, two methoxy groups being needed indeed.

In conclusion, a novel, $SnCl_2 \cdot 2H_2O$-promoted carbocationic rearrangement of β-lactams, having a ketal functionality at the C3 carbon and a nucleophilic sp^2 (imino or carbonyl) group at C4 to yield novel pyrazine-2,3-diones or dihydro-1,4-oxazines derivatives, is reported. On the basis of experimental evidence, this process is thought to occur through C3–C4 bond breakage promoted by the ability of the ketal group to stabilize an emerging positive charge on the ketal carbon.

Experimental Section

General. General experimental data and procedure have been previously reported.[5g] Compounds **1a**, **1b**, **1f**, and **9** were prepared by standard lithium enolate–imine methodology.[5c] Compounds **1c** and **1d** were prepared by acid hydrolysis of **1a** and **1b**. Compound **1e** was prepared according to literature procedure.[5d] See supplementary material for full experimental procedure and spectroscopic data.

General Procedure for the Reaction of Compounds 1 with $SnCl_2 \cdot 2H_2O$. To a stirred suspension of $SnCl_2 \cdot H_2O$ (0.5 mmol) in CH_2Cl_2 (10 mL) cooled to 0 °C was added a solution of the corresponding β-lactam (0.5 mmol) in the same solvent (10 mL). The ice-water bath was removed, and the mixture was stirred at rt for the time indicated. After diluting with CH_2Cl_2 and filtering through Celite, the solvent was removed in vacuo. Whenever possible, crude products were purified by crystallization (solids) or flash chromatography (oils, silica gel, hexanes/EtOAc 4:1), after ^1H NMR examination.

1,4-Di-(*p*-anisyl)-2,3-dioxo-1,2,3,4-tetrahydropyrazine (2a). Reaction time: 20 h. From 100 mg (0.28 mmol) of **1a** and $SnCl_2 \cdot 2H_2O$ (62 mg, 0.28 mmol) was obtained 81 mg (95%) of compound **2a** after crystallization as a white solid: mp 296–297 °C (EtOAc); ^1H-NMR δ 3.84 (s, 6H, 2 × OCH_3), 6.37 (s, 2H, CH=CH), 6.98 (d, 4H, J = 9.0 Hz, Ar), 7.35 (d, 4H, J = 9.0 Hz, Ar); ^{13}C-NMR δ 159.3, 155.6, 132.1, 126.6, 114.6, 113.5, 55.4; IR (KBr) 1680; MS m/z 324 ($M^{+\cdot}$, parent), 296 (M − 28), 281, 267, 253, 148, 134, 92, 77. Anal. Calcd for $C_{18}H_{16}N_2O_4$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.53; H, 4.99; N, 8.69.

1,4-Di-(*p*-anisyl)-5,6-dimethyl-2,3-dioxo-1,2,3,4-tetrahydropyrazine (2b). Reaction time: 7 h. From 100 mg (0.25 mmol) of **1b** and $SnCl_2 \cdot 2H_2O$ (56 mg, 0.25 mmol) was obtained 81 mg (99%) of compound **2b** after crystallization as a white solid: mp >290 °C dec (EtOAc/hexanes); ^1H-NMR δ 1.81 (s, 6H, 2 × CH_3), 3.85 (s, 6H, 2 × OCH_3), 7.01 (d, 4H, J = 9.0 Hz, Ar), 7.16 (d, 4H, J = 9.0 Hz, Ar); ^{13}C-NMR δ 159.5, 156.3, 130.3, 128.7, 116.4, 114.8, 55.4, 16.5; IR (KBr) 1690; MS m/z 352 ($M^{+\cdot}$), 324 (M − 28), 148 (parent), 107, 92, 77. Anal. Calcd for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.25; H, 5.67; N, 7.86.

4-(*p*-Anisyl)-3,4-dihydro-2,2-dimethoxy-3-oxo-2*H*-1,4-oxazine (4c). Reaction time: 15 min. From 600 mg (1.62 mmol) of **1c** and $SnCl_2 \cdot 2H_2O$ (364 mg, 1.62 mmol) was obtained 189 mg (44%) of compound **4c** after crystallization as a white, crystalline solid: mp 61–63 °C (EtOAc/hexanes); ^1H-NMR δ 3.52 (s, 6H, 2 × OCH_3), 3.80 (s, 3H, OCH_3), 5.88 (d, 1H, J = 4.5 Hz, =CH), 6.22 (d, 1H, J = 4.5 Hz, =CH), 6.92 (d, 2H, J = 8.7 Hz, Ar), 7.24 (d, 2H, J = 8.7 Hz, Ar); ^{13}C-NMR δ 158.7, 158.0, 131.6, 126.6, 126.3, 114.4, 112.6, 108.8, 55.4, 51.2 (2C); IR (KBr) 1700. MS m/z 265 ($M^{+\cdot}$), 237 (M − 28), 234, 208 (parent), 206, 191, 134, 132, 92, 77,

59. Anal. Calcd for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 58.89; H, 5.86; N, 5.23.

3,4-Dihydro-2,2-dimethoxy-5-methyl-3-oxo-4-phenyl-2*H*-1,4-oxazine (4f). Reaction time: 65 h. From 120 mg (0.41 mmol) of **1f** and $SnCl_2 \cdot 2H_2O$ (92 mg, 0.41 mmol) was obtained 96 mg (95%) of compound **4f** after chromatography as a colorless oil: ^{1}H-NMR (minor) 1.71 (d, 3H, J = 1.5 Hz, CH_3), 3.63 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 6.00 (d, 1H, J = 1.5 Hz, CH=), 7.21–7.30 (m, 5H, Ar); (major) 1.66 (d, 3H, J = 1.2 Hz, CH_3), 3.63 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 6.10 (q, 1H, J = 1.2 Hz, CH=), 7.21–7.30 (m, 5H, Ar); ^{1}H-NMR (348 K, DMSO-d_6) δ 1.58 (s, 3H, CH_3), 3.59 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 6.38 (s, 1H, CH=), 7.26–7.41 (m, 5H, Ar); ^{13}C-NMR δ (minor) 163.0, 160.1, 143.2, 139.4, 129.2, 128.0, 126.6, 113.6, 60.1, 52.2, 29.6; (major) 163.5, 161.4, 145.7, 137.5, 129.0, 126.9, 125.3, 115.3, 60.1, 52.2, 29.6; IR ($CHCl_3$) 1700, 1640; MS m/z 249 ($M^{+\cdot}$), 217, 189, 161, 117 (parent), 77. Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.62; H, 6.07; N, 5.62. Found: C, 62.71; H, 6.00; N, 5.58.

4-(*p*-Anisyl)-3,4-dihydro-2,3-dioxo-2*H*-1,4-oxazine (3c). Reaction time: 2.5 h. From 600 mg (1.62 mmol) of **1c** and $SnCl_2 \cdot 2H_2O$ (364 mg, 1.62 mmol) was obtained 266 mg (75%) of compound **3c** after chromatography as a colorless oil: ^{1}H-NMR δ 4.86 (s, 3H, OCH_3), 6.41 (d, 1H, J = 4.8 Hz, =CH), 6.70 (d, 1H, J = 4.8 Hz, =CH), 6.98 (d, 2H, J = 9.0 Hz, Ar), 7.27 (d, 2H, J = 9.0 Hz, Ar); IR ($CHCl_3$) 1780, 1740, 1710. Anal. Calcd for $C_{11}H_9NO_4$: C, 60.28; H, 4.14; N, 6.39. Found: C, 59.87; H, 4.40; N, 6.41.

4-(*p*-Anisyl)-3,4-dihydro-5,6-dimethyl-2,3-dioxo-2*H*-1,4-oxazine (3d). Reaction time: 1.5 h. From 100 mg (0.34 mmol) of **1d** and $SnCl_2 \cdot 2H_2O$ (76 mg, 0.34 mmol) was obtained 74 mg (88%) of compound **3d** after chromatography as a white solid: mp 178–180 °C (MeOH/Et_2O); ^{1}H-NMR δ 1.65 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 6.97 (d, 2H, J = 9.0 Hz, Ar), 7.08 (d, 2H, J = 9.0 Hz, Ar); ^{13}C-NMR δ 160.0, 154.7, 151.7, 131.7, 128.8, 128.7, 115.5, 115.0, 55.5, 15.7, 14.8; IR (KBr) 1760, 1700, 1680; MS m/z 247 ($M^{+\cdot}$), 219 (M – 28), 148 (parent), 92, 77. Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.66. Found: C, 63.03; H, 5.38; N, 5.88.

4-(*p*-Anisyl)-3,4-dihydro-2,3-dioxo-6-phenyl-2*H*-1,4-oxazine (3e). Reaction time: 2 h. From 100 mg (0.30 mmol) of **1e** and $SnCl_2 \cdot 2H_2O$ (68 mg, 0.30 mmol) was obtained 84 mg (95%) of compound **3e** after crystallization as a pale yellow solid: mp 130–140 °C dec (EtOAc); ^{1}H-NMR δ 3.85 (s, 3H, OCH_3), 6.83 (s, 1H, =CH), 7.02 (d, 2H, J = 9.0 Hz, Ar), 7.35–7.59 (m, 7H, Ar); ^{13}C-NMR δ 159.6, 154.1, 149.8, 137.1, 130.8, 129.2, 129.1, 128.9, 126.4, 123.6, 114.7, 109.7, 55.5; IR (KBr) ν 1760, 1690; MS m/z ($M^{+\cdot}$), 267 (M – 28), 208, 180, 134 (parent), 107, 92, 77, 63. Anal. Calcd for $C_{17}H_{13}NO_4$: C, 69.15; H, 4.44; N, 4.74. Found: C, 69.23; H, 4.51; N, 4.60.

***N*-(*p*-Anisyl)-*N*-(2-oxoethyl)formamide (5).** Reaction time: 24 h. From 230 mg (0.87 mmol) of **1c** and $SnCl_2 \cdot 2H_2O$ (195 mg, 0.87 mmol) was obtained 59 mg (35%) of compound **5** after chromatography as a pale yellow oil: ^{1}H-NMR δ 3.79 (s, 3H, OCH_3), 4.49 (s, 2H, CH_2), 6.89 (d, 2H, J = 9.0 Hz, Ar), 7.18 (d, 2H, J = 9.0 Hz, Ar), 8.40 (s, 1H, CH=O), 9.63 (s, 1H, CH=O); ^{13}C-NMR δ 196.7, 163.4, 159.7, 134.4, 126.9, 115.7, 57.1, 56.4; IR ($CHCl_3$) 3350, 1740, 1670; MS m/z 193 ($M^{+\cdot}$), 164 (M – 29), 135 (parent), 108, 77. Anal. Calcd for $C_{10}H_{11}NO_3$: C, 62.16; H, 5.75; N, 7.24. Found: C, 62.19; H, 5.69; N, 7.31.

1-(*p*-Anisyl)-3,3-dimethyl-4-formyl-4-methylazetidin-2-one (10). Reaction time: 12 h. From 95 mg (0.34 mmol) of **9** and $SnCl_2 \cdot 2H_2O$ (76 mg, 0.34 mmol) was obtained 79 mg (95%) of compound **10** after crystallization as a white solid: mp 103–105 °C (EtOAc/hexanes); ^{1}H-NMR δ 1.30 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 6.86 (m, 2H, Ar), 7.26 (m, 2H, Ar), 9.95 (s, 1H, CH=O); ^{13}C-NMR δ 202.6, 170.3, 156.6, 129.8, 119.1, 114.5, 70.1, 57.7, 55.4, 19.0, 18.6, 13.8; IR (KBr) 1755, 1730. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 67.98; H, 6.93; N, 5.67. Found: C, 67.71; H, 7.06; N, 5.85.

Synthesis of 1-(*p*-Anisyl)-3,3,5-trimethylpyrrolidine-2,4-dione (11). A solution of 25 mg (0.1 mmol) of **10** in chloroform (5 mL) was vigorously stirred with 2 drops of concd H_2SO_4 at room temperature for 8 h. The reaction was quenched with water (2 mL), the aqueous layer was extracted with chloroform (3 × 10 mL), and all the organics were successively washed with 5% $NaHCO_3$ and water and dried ($MgSO_4$). After filtration and evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexanes/EtAcO 4:1), yielding **11** as a pale yellow oil: yield 75%; ^{1}H-NMR δ 1.31 (s, 3H, CH_3), 1.32 (d, 3H, J = 6.6 Hz, CH_3), 1.34 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 4.44 (q, 1H, J = 6.6 Hz, CH), 6.91 (m, 2H, Ar), 7.30 (m, 2H, Ar); ^{13}C-NMR δ 213.4, 174.5, 157.9, 128.7, 125.7, 114.5, 61.8, 55.5, 47.1, 21.6, 21.2, 16.2; IR ($CHCl_3$) 1770, 1700. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 67.98; H, 6.93; N, 5.67. Found: C, 68.03; H, 6.89; N, 5.73.

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Supplementary Material Available: Additional procedures and compound characterization data (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.