Experimental Section

DMP (2.0 equiv) was added in one portion to a solution of **7a** (0.1 mmol) in benzene (4 mL) or BTF.[6] The solution was heated at reflux (or at 80–85 °C for the reactions in BTF) for about 30 min at which point TLC indicated complete consumption of starting material. Dilution with EtOAc followed by washing with 5% aq. $NaHCO_3$ (2 ×) and brine, drying over $MgSO_4$, and concentration led to crude **7b**. Pure **7b** was isolated in 40% yield after column chromatography (silica gel, EtOAc:hexane 1:2) (see Table 3 for selected physical properties).

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Table 3. Data for selected compounds.

7b: colorless needles, m.p. 135–136 °C (methanol); $R_f = 0.37$ [silica, EtOAc:hexane 1:2]; IR (film): $\tilde{\nu}_{max} = 2965$, 2922, 1694, 1576, 1512, 1437, 1383, 1302, 1260, 1227, 1163, 1115, 866, 814 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.96$ (d, $J = 3.5$ Hz, 1H), 6.80–6.71 (m, 2H), 4.77–4.70 (m, 1H), 3.87 (dd, $J = 5.5$, 1.2 Hz, 1H), 2.96 (dd, $J = 17.2$, 8.6 Hz, 1H), 2.83–2.73 (m, 1H), 2.58 (q, $J = 7.6$ Hz, 2H), 2.24 (d, $J = 17.3$ Hz, 1H), 2.13–1.97 (m, 2H), 1.70–1.50 (m, 2H), 1.95 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.6$, 144.0, 142.0, 128.0, 120.5, 121.1, 115.7, 78.6, 57.6, 39.7, 32.4, 29.0, 28.5, 15.5; HRMS (MALDI-FTMS), calcd for $C_{15}H_{18}NO_2$ $[(M+H)^+]$: 244.1338, found 244.1332

24b: $R_f = 0.65$ [silica, EtOAc:hexane 1:1]; IR (film): $\tilde{\nu}_{max} = 2919$, 2850, 1709, 1501, 1437, 1260, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.95$ (dd, $J = 7.0$, 2.6 Hz, 1H), 7.00–6.94 (m, 2H), 6.89 (dd, $J = 7.4$, 2.2 Hz, 1H), 5.83–5.72 (m, 1H), 5.23 (dd, $J = 18.3$, 1.1 Hz, 1H), 5.22 (d, $J = 9.2$ Hz, 1H), 4.34 (dd, $J = 10.5$, 3.3 Hz, 1H), 4.10–4.02 (m, 1H), 3.94–3.88 (m, 2H), 3.79 (t, $J = 10.5$ Hz, 1H), 3.61 (t, $J = 9.4$ Hz, 1H), 3.11 (dd, $J = 9.4$, 5.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 156.8$, 144.4, 132.6, 127.8, 123.4, 121.5, 120.6, 118.4, 116.6, 66.9, 47.8, 46.4, 43.6; HRMS (MALDI-FTMS), calcd for $C_{13}H_{15}N_2O_2$ $[(M+H)^+]$: 231.1133, found 231.1128

29: colorless needles, m.p. 108–109 °C (hexane:diethyl ether 2:1); $R_f = 0.18$ [silica, EtOAc:hexane 1:4]; IR (film): $\tilde{\nu}_{max} = 3296$, 3084, 2920, 2850, 1761, 1731, 1679, 1649, 1526, 1461, 1408, 1267, 1238, 1179, 1144, 1079, 1032, 1008, 908, 885 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.44$ (d, $J = 8.8$ Hz, 1H), 8.06 (d, $J = 7.9$ Hz, 1H), 8.02 (dd, $J = 7.9$, 1.5 Hz, 1H), 7.73 (br s, 1H), 7.47(t, $J = 7.9$ Hz, 1H), 7.22 (dt, $J = 7.9$, 1.5 Hz, 1H), 6.84 (dd, $J = 8.8$, 2.5 Hz, 1H), 6.81 (d, $J = 1.5$ Hz, 1H), 5.92–5.82 (m, 1H), 5.12 (d, $J = 16.9$ Hz, 1H), 5.04 (d, $J = 10.2$, 1H), 3.89 (s, 3H), 2.50 (br s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.7$, 165.4, 148.7, 146.8, 142.1, 137.2, 134.5, 133.7, 132.0, 128.5, 126.2, 120.5, 116.3, 114.0, 104.7, 95.1, 56.4, 37.5, 29.9; HRMS (MALDI-FTMS), calcd for $C_{19}H_{18}INO_4Na$ $[M+Na^+]$: 474.0178, found 474.0178

30: colorless needles, m.p. 63–64 °C (hexane:diethyl ether 2:1); $R_f = 0.10$ [silica, 1:4 ethyl acetate:hexane]; IR (film): $\tilde{\nu}_{max} = 3355$, 3073, 2979, 2920, 2850, 1761, 1679, ,1602, 1526, 1491, 1408, 1367, 1267, 1202, 1185, 1150, 1114, 1032, 956, 897 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.37$ (d, $J = 8.8$ Hz, 1H), 7.69 (br s, 1H), 6.67 (dd, $J = 8.8$, 2.4 Hz, 1H), 6.63 (d, $J = 2.4$ Hz, 1H), 5.91–5.78 (m, 1H), 5.11 (d, $J = 17.6$ Hz, 1H), 5.04 (d, $J = 10.3$ Hz, 1H), 3.85 (s, 3H), 2.48 (br s, 4H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.3$, 169.7, 148.2, 146.4, 136.8, 125.5, 120.0, 115.8, 113.5, 104.3, 55.8, 37.1, 29.4, 21.1; HRMS (FAB), calcd for $C_{14}H_{17}NO_4Na$ $[M+Na^+]$: 286.1055, found 286.1050

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[3] Compounds **3b** and **4b** are formed as single regioisomers, whereas **5b** and **6b** are mixtures. Efforts to understand this peculiar finding are underway.

[4] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-133866. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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[7] A. Ogawa, D. P. Curran, *J. Org. Chem.* **1997**, *62*, 450–451.

[8] Studies to determine whether DMP, its hydrolysis product,[2c] or both are the active oxidants in this reaction are underway.

[9] A multistep route to this type of diene is known, however the reaction requires the presence of chlorine substituents on the aryl ring, see: H. W. Heine, B. J. Barchiesi, E. A. Williams, *J. Org. Chem.* **1984**, *49*, 2560–2565.

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New Synthetic Technology for the Rapid Construction of Novel Heterocycles—Part 2. The Reaction of IBX with Anilides and Related Compounds**

K. C. Nicolaou,* Yong-Li Zhong, and Phil S. Baran

In the preceding communication[1] we disclosed a new cascade reaction for the preparation of novel heterocycles. The present discovery arose while optimizing that process, namely, the reaction of Dess–Martin periodinane (DMP) with anilides. When we attempted to access the polycycles reported[1] using IBX[2] we observed astoundingly efficient cyclization to *N*-phenyl γ-lactams. Herein, we report that the reaction of IBX with anilides leads not only to γ-lactams, but also to a variety of other heterocycles including oxazolidinones, thiooxazolidinones, and cyclic ureas in high yields (Scheme 1).

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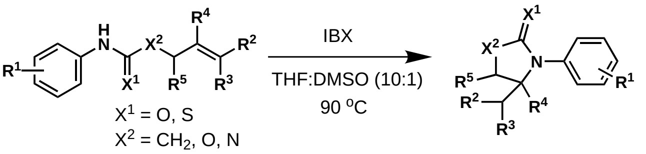


Scheme 1. Synthesis of novel heterocycles by treatment of unsaturated aryl amides, carbamates, thiocarbamates, and ureas with IBX. IBX = *o*-iodoxybenzoic acid; 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide; a precursor to DMP.

This simple reaction represents a fundamentally new strategy for the construction of molecular diversity relevant to biological screening and drug discovery

Specifically, we have found that a plethora of simple as well as complex anilides with an alkene functionality participate in an IBX-mediated cyclization reaction leading to a variety of novel structures (Table 1). Significantly, the reaction is unbiased to substitution on the aryl moiety.[3] Reactions with substrates which harbor electron-donating groups (e.g. entry 6), electron-withdrawing groups (e.g. entries 4 and 7), halides (e.g. entries 2, 4, 7, 11, 13, 15, 17, and 18), and sterically encumbered groups (e.g., entry 8) situated at the *ortho*, *meta* or *para* positions all proceed smoothly and in high yields. An X-ray crystal structure of one of the obtained products, complex heterocycle **16b**, is shown in Figure 1.[4]

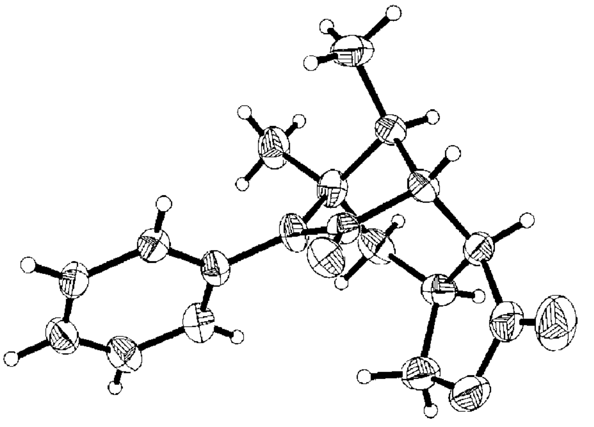


Figure 1. X-ray crystal structure of **16b**.

Considering the plethora of readily available phenyl isocyanates, allylic alcohols, and allylic amines, we recognized the diverse array of building blocks that could potentially be funneled into this new reaction. The generality of this two-step sequence for the construction of molecular diversity is demonstrated in Table 2. Remarkably, oxazolidinones (**19b**–**26b**, entries 1–8), thiooxazolidinones (**33b**, entry 9) and cyclic ureas (**34b**, **35b**, entries 10, 11) are readily available from the corresponding carbamates, thiocarbamates and open-chain ureas, respectively, using this straightforward protocol. Hydrolysis of the oxozolidinones (NaOH/EtOH) permits access to *cis*-*N*-phenyl 1,2-amino alcohols (**27**–**32**, Table 2). The challenging task of establishing quaternary centers (e.g. Table 1, entries 16, 17; Table 2, entries 2, 5, 7), including spiro compounds such as **25b**, proceeds smoothly without loss of efficiency. The procedure is operationally extremely simple and involves dissolution of the substrate and IBX in

Table 1. IBX-mediated cyclization of aryl carbamoyl alkenes to form heterocycles.

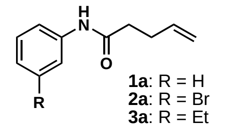
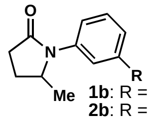
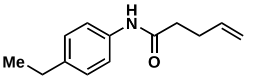
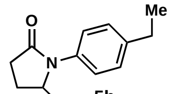
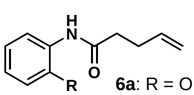
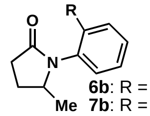
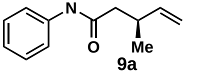
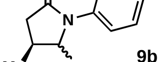
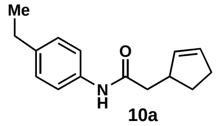
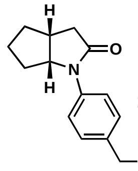
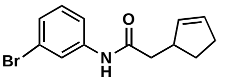
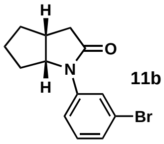
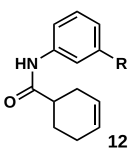
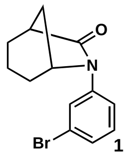
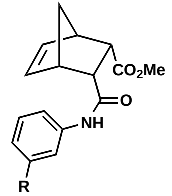
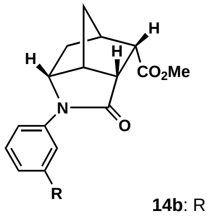
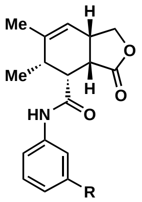
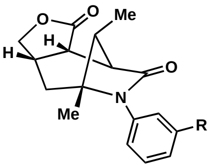
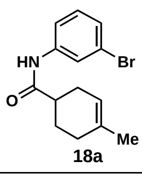
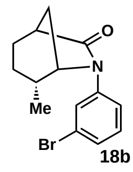
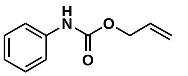
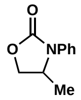
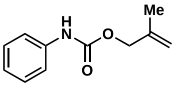
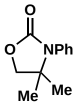
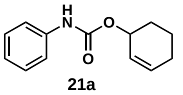
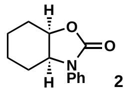
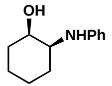
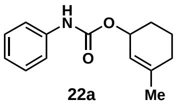
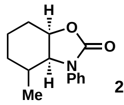
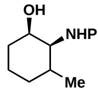
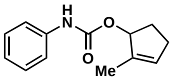
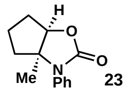
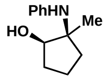
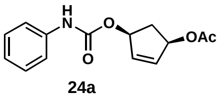
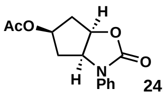
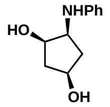
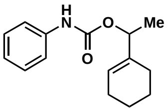
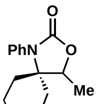
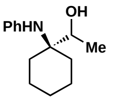
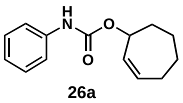
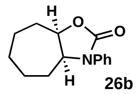
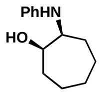
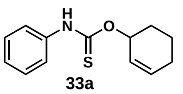
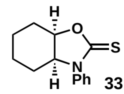
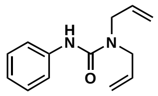
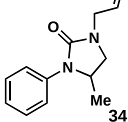
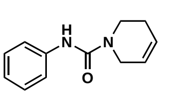
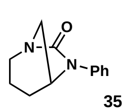
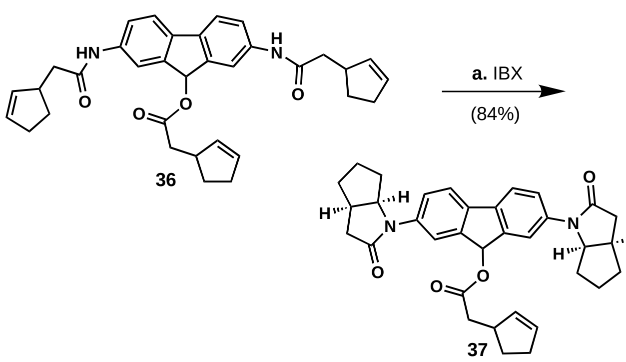
Entry	Substrate	Product	Yield [%]
1 2 3 4	 **1a**: R = H **2a**: R = Br **3a**: R = Et **4a**: R = F	 **1b**: R = H **2b**: R = Br **3b**: R = Et **4b**: R = F	86 79 89 80
5	 **5a**	 **5b**	90
6 7 8	 **6a**: R = OMe **7a**: R = F **8a**: R = *t*Bu	 **6b**: R = OMe **7b**: R = F **8b**: R = *t*Bu	88 80 70
9	 **9a**	 **9b** [ca. 1:1]	90
10	 **10a**	 **10b**	90
11	 **11a**	 **11b**	86
12 13	 **12a**: R = H **13a**: R = Br	 **12b**: R = H **13b**: R = Br	90 84
14 15	 **14a**: R = H **15a**: R = Br	 **14b**: R = H **15b**: R = Br	93 89
16 17	 **16a**: R = H **17a**: R = Br	 **16b**: R = H **17b**: R = Br	88 86
18	 **18a**	 **18b**	82

Table 2. IBX-mediated cyclization of carbamates, thiocarbamates, and open-chain ureas to form oxazolidinones, thiooxazolidinones, and cyclic ureas and synthesis of 1,2-amino alcohols.

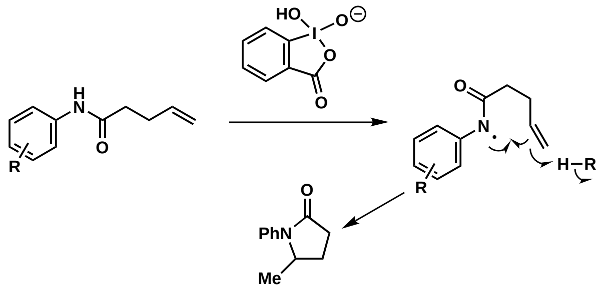
Entry	Substrate	Product	Yield [%]	1,2-amino alcohol	Yield [%]
1	 **19a**	 **19b**	88	—	–
2	 **20a**	 **20b**	90	—	–
3	 **21a**	 **21b**	85	 **27**	94
4	 **22a**	 **22b**	72	 **28**	92
5	 **23a**	 **23b**	88	 **29**	98
6	 **24a**	 **24b**	95	 **30**	95
7	 **25a**	 **25b** [one diastereomer]	76	 **31**	90
8	 **26a**	 **26b**	83	 **32**	95
9	 **33a**	 **33b**	86	—	–
10	 **34a**	 **34b**	90	—	–
11	 **35a**	 **35b**	70	—	–

THF:DMSO (10:1) in a sealed tube and heating at 90 °C for a number of hours. The reaction is impervious to air or water, producing the desired products even using water as a co-solvent. The high efficiency and reliability of this IBX-mediated reaction was not diminished even in the case of bis-amide **36**, wherein cyclization occurred to furnish the polycycle **37** in 84% yield (Scheme 2).



Scheme 2. Facile generation of complex polycycle **37** from the simple bis-amide **36**. a) IBX (4.0 equiv), THF:DMSO (10:1), 90 °C, 24 h, 84%.

Based on preliminary experimental results we choose to depict the IBX-mediated cyclization as proceeding through an amide-centered reactive intermediate, such as a radical (Scheme 3). The precise steps leading to these intermediates cannot be confidently defined at present, nor can the exact nature of this intermediate. IBX may somehow interact with anilides to produce a species which behaves as an amidyl radical,[5] thus engaging the proximate olefin in a 5-*exo-trig* fashion followed by hydrogen abstraction, presumably from the solvent. In contrast with mechanistic studies for the reaction of alcohols with IBX,[6] NMR studies on the present reaction indicate that anilides do not form stable intermediates with this reagent.[7] The complexes of anilides with IBX might, therefore, be short-lived. Additional evidence for the radicaloid[8] character of the reaction is seen in Table 1, entry 9 in which case a 1:1 ratio of diastereoisomers was obtained indicating a disordered transition state, as expected from such a pathway.



Scheme 3. Tentative mechanistic proposal of the IBX-mediated cyclization of aryl carbamoyl alkenes.

As with the reaction of DMP with amides, discussed in the preceding communication,[1] the present process has (so far) only been demonstrated to proceed with anilides, suggesting the requirement for a proper electronic environment surrounding the nitrogen.[9] Although the reason for this rather peculiar requirement remains unknown, we suspect that the aryl moiety of these systems assumes an active (more than just a stabilizing) role in the reaction, just as it does in the case of DMP.

The structural types produced by the reactions reported in this and the preceding communication[1] are found in innumerable natural products and medicinally important compounds[10] and as such these processes may find important applications in organic synthesis. Furthermore, the extraordinary ease with which the starting materials for these reactions can be prepared, coupled with the striking complexity which is attainable in one step, makes this protocol ideal for the generation of manifold libraries of relevant compounds for biological screening and chemical biology purposes. Additional studies to delineate the precise mechanism by which periodinanes interact with anilides, efforts to expand the scope of these reactions to other substrates, and the development of solid-phase strategies incorporating these new reactions are underway. Finally, these disclosures underscore the importance of total synthesis in catalyzing the discovery and development of new and enabling technologies for organic synthesis, biology, and medicine.

Experimental Section

IBX (2.0 equiv) was added to a solution of **16a** (0.1 mmol) in THF:DMSO (10:1, 4 mL total volume). The solution was placed in a sealed tube and heated for 12 h at 90 °C, followed by another addition of IBX (2.0 equiv) and heating for a further 12 h period at the same temperature. The reaction mixture was diluted with EtOAc and washed with 5% aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated. After purification by preparative thin layer chromatography (PTLC, silica, EtOAc:hexane 1:2), compound **16b** was obtained in 88% yield (see Table 3 for selected physical properties).

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Table 3. Data for selected compounds.

16b: X-ray crystal structure given (see Figure 1). Colorless cubic crystals, m.p. 238–239 °C, (acetone-hexane); $R_f = 0.37$ [silica, EtOAc:hexane 1:2]; IR (film): $\tilde{\nu}_{max} = 2968, 2865, 1767, 1675, 1589, 1490, 1379, 1169, 1014, 866, 761, 693\ cm^{-1}$; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.40-7.33$ (m, 2H), 7.27–7.22 (m, 1H), 7.19–7.15 (m, 2H), 4.40 (t, $J = 7.2$ Hz, 1H), 4.07 (dd, $J = 7.2$, 5.2 Hz, 1H), 3.12 (m, 1H), 2.93 (dd, $J = 8.0$, 4.4 Hz, 1H), 2.69 (d, $J = 3.6$ Hz, 1H), 2.16 (d, $J = 12.0$ Hz, 1H), 2.00–1.92 (m, 2H), 1.62 (s, 1H), 1.24–1.11 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 176.0$, 173.2, 136.1, 129.2, 129.1, 126.8, 125.2, 123.5, 71.3, 64.9, 64.4, 48.3, 45.7, 40.9, 35.4, 31.8, 20.8, 13.7; HRMS (MALDI-FTMS), calcd for $C_{17}H_{20}NO_3$ $[(M+H)^+]$: 286.1443, found 286.1443

24b: $R_f = 0.25$ [silica, ethyl acetate:hexane 1:1]; $[\alpha]_D^{23} = -175°$ ($c = 0.04$, $CHCl_3$); IR (film): $\tilde{\nu}_{max} = 2920, 2848, 1736, 1598, 1499, 1401, 1242, 1206, 1164, 1122, 1087, 1011\ cm^{-1}$; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.59$ (d, $J = 7.9$ Hz, 1H), 7.47 (dd, $J = 7.9$, 7.3 Hz, 2H), 7.24 (t, $J = 7.3$ Hz, 1H), 5.36 (t, $J = 4.3$ Hz, 1H), 5.24 (t, $J = 7.0$ Hz, 1H), 5.01 (t, $J = 7.0$ Hz, 1H), 2.59 (dd, $J = 15.9$, 2.9 Hz, 1H), 2.35 (dd, $J = 15.4$, 2.8 Hz, 1H), 2.18 (m, 1H), 2.04 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.0$, 154.9, 137.7, 129.7 (2C), 125.0, 120.5 (2C), 77.8, 75.4, 61.1, 40.3, 37.4, 21.6; HRMS (MALDI-FTMS), calcd for $C_{14}H_{15}NO_4Na$ $[M+Na^+]$: 284.0899, found 284.0910

30: $R_f = 0.4$ [silica, ethyl acetate:methylene chloride 1:1]; $[\alpha]_D^{23} = -250°$ ($c = 0.1$, $CHCl_3$); IR (film): $\tilde{\nu}_{max} = 3380, 2361, 1602, 1503, 1432, 1321, 1262, 1099, 751\ cm^{-1}$; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.19$ (dd, $J = 8.7$, 7.5 Hz, 2H), 6.67 (t, $J = 8.7$ Hz, 1H), 6.66 (d, $J = 7.5$ Hz, 2H), 4.34–4.30 (m, 2H), 4.17 (br s, 1H), 3.68 (ddd, $J = 11.5$, 7.3, 4.2 Hz, 1H), 2.86 (br s, 1H), 2.60 (ddd, $J = 15.2$, 9.2, 7.0 Hz, 1H), 2.07 (dq, $J = 13.8$, 1.6 Hz, 1H), 1.96 (ddd, $J = 15.2$, 5.7, 4.2 Hz, 1H), 1.65 (ddt, $J = 13.8$, 7.3, 2.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 146.4$, 129.5 (2C), 119.1, 114.3 (2C), 72.4, 72.1, 59.0, 41.9, 41.2; HRMS (MALDI-FTMS), calcd for $C_{11}H_{16}NO_2$ $[(M+H)^+]$: 194.1181, found 194.1183

[1] K. C. Nicolaou, Y.-L. Zhong, P. S. Baran, *Angew. Chem.* **2000**, *112*, 1026–1029; *Angew. Chem. Int. Ed.* **1999**, *38*, **2000**, *112*, 1026–1029.

[2] First preparation of IBX: C. Hartman, V. Meyer, *Ber. Dtsch. Chem. Ges.* **1893**, *26*, 1727; for a superior route to IBX, see: M. Frigerio, M. Santagostino, S. Sputore, *J. Org. Chem.* **1999**, *64*, 4537–4538; introduction of the acronym "IBX": A. R. Katritzky, B. L. Duell, J. K. Gallos, *Org. Magn. Reson.* **1989**, *27*, 1007; use of IBX as a selective oxidant for alcohols: M. Frigerio, M. Santagostino, *Tetrahedron Lett.* **1994**, *35*, 8019–8022; E. J. Corey, A. Palani, *Tetrahedron Lett.* **1995**, *36*, 3485–3488.

[3] One exception is the nitro group, in which case the reaction did not proceed under the normal conditions.

[4] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-133867. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[5] a) A.-C. Callier, B. Quiclet-Sire, S. Z. Zard, *Tetrahedron Lett.* **1994**, *35*, 6109–6112; b) A.-C. Callier, B. Quiclet-Sire, S. Z. Zard, *Tetrahedron Lett.* **1995**, *36*, 8791–8794; c) M. Newcomb, J. L. Esker, *Tetrahedron Lett.* **1991**, *32*, 1035–1038; d) M. Newcomb, J. L. Esker, *Tetrahedron Lett.* **1993**, *34*, 6877–6880; e) A. J. Clark, J. L. Peacock, *Tetrahedron Lett.* **1998**, *39*, 6029–6032; f) A. J. Clark, R. P. Filik, J. L. Peacock, G. H. Thomas, *Synlett* **1999**, 441–443; g) A. J. Clark, R. J. Deeth, C. J. Samuel, H. Wongtap, *Synlett* **1999**, 444–446.

[6] S. De Munari, M. Frigerio, M. Santagostino, *J. Org. Chem.* **1996**, *61*, 9272–9279; M. Frigerio, M. Santagostino, S. Sputore, G. Palmisano, *J. Org. Chem.* **1995**, *60*, 7272–7276.

[7] A 0.05 mmol scale reaction was performed in [D$_6$]DMSO at varying temperatures (25–110 °C) in an NMR tube. No intermediates could be detected; only product formation and some decomposition of IBX was observed.

[8] B. B. Snider, *Chem. Rev.* **1996**, *96*, 339–363.

[9] The DMP cascade reaction[1] also requires anilides as substrates.

[10] A literature search using SciFinder (ACS) to probe the popularity of these structural types in natural products and medicinally important compounds led to over 50000 hits. The potential that these functionalities have for further elaboration to other scaffolds is nearly infinite. The following are some selected examples. Natural products: Yunnaneic acids A-D, uremic toxin-decreasing effects: T. Takashi, A. Nishimura, I. Kouno, G.-I. Nonaka, T.-J. Young, *J. Nat. Prod.* **1996**, *59*, 843–849; isoschizogamine, HIV inhibitor: J. Hajicek, J. Taimr, M. Budesinsky, *Tetrahedron Lett.* **1998**, *39*, 505–508; G. T. Tan, J. M. Pezzuoto, A. D. Kinghorn, S. H. Hughes, *J. Nat. Prod.* **1991**, *54*, 143–154. Medicinally important compounds: a) Therapeutic CNS agents: M. Varasi, F. Heidempergher, C. Caccia, P. Salvati (Pharmacia S.p.A., Italy), WO-A 95-EP1650; b) 5-HT3 antagonists: M. Varasi, F. Heidempergher, C. Arrigoni, C. Caccia (Farmitalis Carlo Erba S.R.L., Italy), WO-A 93-EP1498; c) antihyperlipidemics: S. Yano, T. Ohno, K. Ogawa, H. Yamada, T. Shirasaka, H. Kawamura, S. Watanabe (Taiho Pharmaceutical Co., Ltd., Japan), WO-A 930JP559; d) hypolipemics and hypoglycemics: H. Yanagisawa, K. Fujimoto, T. Fujita, K. Wada, M. Oguchi, T. Yoshioka, T. Fujiwara, H. Horikoshi (Sankyo Co., Japan) JP-A 95-162442; e) monoamine oxidase inhibitors: C. Banzati, A. Della Torre, P. Melloni, D. Pieraccioli, P. Salvadori, *J. Heterocycl. Chem.* **1983**, *20*, 139–140; f) antidepressants: (Erba, Carlo S.p.A., Italy) IT-B 75-30829.