Oxidation of Alcohols with *o*-Iodoxybenzoic Acid (IBX) in DMSO: A New Insight into an Old Hypervalent Iodine Reagent

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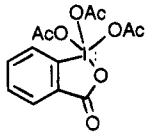
The ultracentennial 10-I-4 iodinane oxide IBX (**3**; *o*-iodoxybenzoic acid; 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide) represents a new oxidizing reagent that successfully joins to the large family of known oxidants. IBX, in contrast to other valuable oxidants, is inexpensive to prepare and easy to handle, can tolerate moisture and water, and generally gives very good yields. Furthermore, IBX is mild and chemoselective (primary alcohols are converted into aldehydes with no overoxidation to acids; 1,2-diols are converted to α-ketols or α-diketones without oxidative cleavage; amino alcohols are oxidized to amino carbonyls, without protection of the amino group; sensitive heterocycles are not affected; various other functional groups are compatible with IBX oxidation). IBX is versatile (it works in various solvents and it is highly sensitive to temperature variations), and its solutions in DMSO are stable enough to carry out the oxidation reaction easily.

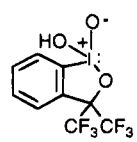
Introduction

There has been considerable interest, during the last decade, in hypervalent iodine derivatives[1] both in terms of defining their structures[1a,c,d] and for their recognized versatility in preparative organic synthesis.[1,2] Of the various iodo-based reagents, the 12-I-5 Dess–Martin periodinane[1b,c] (DMP, **1**) has attracted particular attention because it is one of the mildest reagents available for the oxidation of alcohols to carbonyls. This oxidation represents a pivotal reaction in organic chemistry, and several methods are known, covering a variety of experimental conditions. However, this reaction still continues to receive considerable attention in the search for new oxidants with particular features.[3]



DMP 1

Recently, three 10-I-4 iodinane oxides (**2**;[1c,2a] IBX, **3**[4d,e] and **4**[1c,2b]) have been used to convert alcohols into carbonyls. These iodinane oxides (**2-4**) seem to share some oxidizing properties with DMP (**1**), *e.g.*, they oxidize primary alcohols to aldehydes without overoxidation to carboxylic acids,[1c,4d] and one of them (**4**) has been claimed[2b] as the actual oxidant in aged but still effective batches of DMP. However, **2** and **3** (IBX) clearly differ from **1** (DMP) in the oxidation of 1,2-diols.[2a,4d] Thus, DMP cleaves the glycol C–C bond,[1c,2a] while **2** and IBX oxidize them to α-ketols or α-diketones without cleavage of the 1,2-diol bond.[2a,4d]



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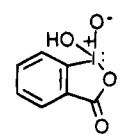
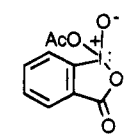


IBX 3



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In this paper, we wish to report the oxidizing properties of IBX (**3**) toward different classes of alcohols, such as alkyl and benzyl alcohols, diols, and thio and amino alcohols (Table 1). We also report the different reaction conditions compatible with its use (Tables 1 and 2).

Results and Discussion

IBX[4] (**3**; *o*-iodoxybenzoic acid; 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide) was first prepared in 1893,[4a] but it is only recently that two of us have shown[4d] that IBX in DMSO was capable of efficiently oxidizing alcohols to the corresponding carbonyl compounds at ambient temperature in a few hours (Table 1). Even more recently, the versatility of IBX in DMSO has been emphasized[4e] by Corey and Palani for the highly selective oxidation of 1,4-bis-primary or 1,4-primary–secondary diols to γ-lactols, a conversion which could not previously be accomplished in one step.

A possible mechanism for the oxidation of alcohols by IBX involves, as already suggested by Dess and Martin[1c]

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(1) Reviews and leading papers: (a) Nguyen, T. T.; Martin, J. C. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 1, pp 563–572. (b) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. (c) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277. (d) Dess, D. B.; Wilson, S. R.; Martin, J. C. *J. Am. Chem. Soc.* **1993**, *115*, 2488. (e) Prakash, O.; Saini, N.; Sharma, P. W. *Synlett* **1994**, 221. (f) Varvoglis, A. *Synthesis* **1984**, 709. (g) Varvoglis, A. *The Organic Chemistry of Polycoordinated Iodine;* VCH: Weinheim, New York, Basel, Cambridge, 1992. (h) Moriarty, R. M.; Vaid R. K. *Synthesis* **1990**, 431.

(2) (a) Grieco, P. A.; Collins, J. L.; Moher, E. R.; Fleck, T. J.; Gross, R. S. *J. Am. Chem. Soc.* **1993**, *115*, 6078. (b) Meyer, S. D. M.; Schreiber, S. L. *J. Org. Chem.* **1994**, *59*, 7549.

(3) See, for example: (a) Banwell, M. G.; Bridges, V. S.; Dupuche, J. R.; Richards, S. L.; Walter, J. M. *J. Org. Chem.* **1994**, *59*, 6338. (b) Asensio, G.; Gonzales Nuñes, M. E.; Bernardini, C. B.; Mello, R.; Adam, W. *J. Am. Chem. Soc.* **1993**, *115*, 7250.

(4) The acronyms "IBX" and "IBA", for iodoxybenzoic acid and iodosobenzoic acid, respectively, were coined by Katritzky.[4b] (a) Hartman, C.; Meyer, V. *Chem. Ber.* **1893**, *26*, 1727. (b) Katritzky, A. R.; Duell, B. L.; Gallos, J. K. *Org. Magn. Reson.* **1989**, *27*, 1007. (c) Katritzky, A. R.; Savage, G. P.; Gallos, J. K.; Dupont, Durst H. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1515. (d) Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994**, *35*, 8019. (e) Corey, E. J.; Palani, A. *Tetrahedron Lett.* **1995**, *36*, 3485.

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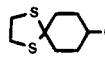
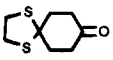
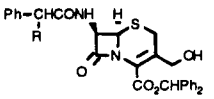
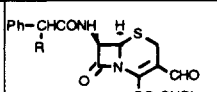
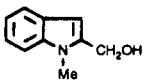
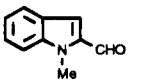
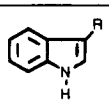
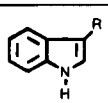
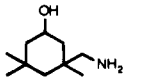
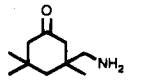
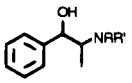
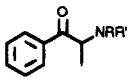
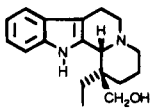
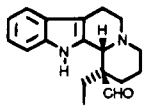
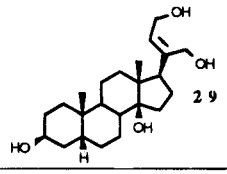
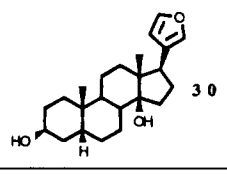
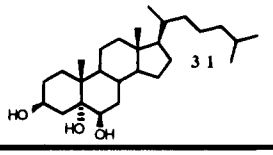
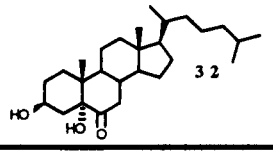
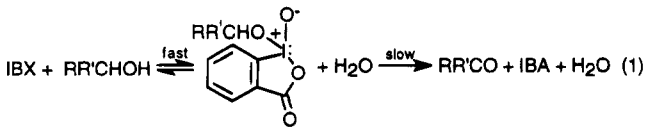
Table 1. IBX Oxidation of Alcohols

Entry	Alcohol	IBX (equiv)[a]	Product	Time (h)	Yield[b] %
1	 **5**	1.1	 **6**	24	92
2	 **7**	1.1	 **8**	24	78
3	 **9**: R = H	1.1	 **10**: R = H	8	91
4	**11**: R = NHBoc	1.1	**12**: R = NHBoc	12	94
5	 **13**	1.5	 **14**	8	89
6	 **15**: R = CH_2OH	1.1	 **16**: R = CHO	8	98
7	**17**: R = CH_2CH_2OH	1.1	**18**: R = CH_2CHO	6	79
8	 **19**	1.1[c]	 **20**	5	91[d]
9	**21**: R=R'=H	5[c]	**22**: R=R'=H	3.5	89
10	 **23**: R=H, R'=Me	5[c]	 **24**: R=H, R'=Me	2.5	90
11	**25**: R=R'=Me	5[c]	**26**: R=R'=Me	24	90
12	**25**: R=R'=Me	10	**26**: R=R'=Me	48	92
13	 **27**	1.5	 **28**	24	91
14	 **29**	1.5	 **30**	3.5	86[e]
15	 **31**	1.5	 **32**	0.75	85[e]

[a] Mmol of IBX/mmol of alcohol. [b] Yields of isolated compounds (flash chromatography or crystallization) [c] TFA (1.1 equiv) added to reaction mixture. [d] Compound characterized as acetamido derivative. [e] About 10% of 3-oxo derivative was isolated as byproduct.

for iodinane oxide **2**, an equilibrium as shown in eq 1,



where the concentration of the reactive intermediate decreases with increasing water concentration. Indeed, when the oxidation of alcohols[5] with IBX was monitored by ^{1}H-NMR, it was possible to observe the presence of transient peaks consistent with the proposed intermediates.

IBX in DMSO is a mild oxidant, and a variety of functional groups are compatible with its use. In particular, the chemoselective oxidation[6] of alcohols in the presence of thioethers and amines is noteworthy (Table 1). Accordingly, alcohols are cleanly oxidized by IBX in the presence of thioethers and 1,3-dithiolane (Table 1, entries 1–4). Moreover, in the case of thiochroman-4-ol (**5**), even if the oxidation conditions were forced using 10 equiv of IBX (ambient temperature, 120 h), the only

(5) The IBX oxidation of simple primary and secondary alcohols and the complex formation between IBX and *t*-BuOH was monitored by ^{1}H-NMR (DMSO-d_6, 300 MHz). A downfield shift for the intermediate complex is uniformly observed. A similar behavior is described by Dess and Martin for DMP complexes.[1c] Studies are in progress, and a detailed report will be published elsewhere.

Table 2. Oxidation of Benzoin (33) to Benzil (34)

entry	solvent[a]	time[b] (h)
1	THF[c] + Δ	2
2	THF + 3 equiv of DMSO	40
3	THF + 9 equiv DMSO	6
4	THF[d] + 9 equiv of DMSO +)))	3
5	THF[c] + 9 equiv of DMSO + Δ	0.2
6	CH_3CN + 9 equiv of DMSO	10
7	EtOAc + 9 equiv of DMSO	16

[a] The reaction slurries were thermostated at 22 °C. [b] Reaction times for complete disappearance (TLC) of **33**. Benzil (**34**) was isolated in yields greater than 90% in every experiment. [c] Reaction at reflux temperature. [d] The reaction was carried out in a water ultrasonic[20] cleaning bath (Transsonic TP690). The water was thermostated at 22 °C, the reaction flask was placed in a vortex.

reaction product was thiochroman-4-one (**6**), with no evidence of sulfoxide or sulfone byproducts. The 3-hydroxymethyl group of cephem derivatives (Table 1, entries 3 and 4) is easily oxidized to aldehyde, without overoxidation and/or double bond isomerization.

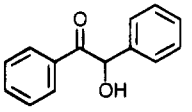
Moreover, IBX can be successfully used to oxidize amino alcohols to amino carbonyls. The oxidation of amino alcohols is a general synthetic problem that usually requires the protection of the amine as a nonbasic derivative.[7] To this end, the most widely used methodology is the Swern oxidation[8] that requires anhydrous conditions and low temperature, while other oxidants have been used in particular cases (*e.g.*, Jones reagent,[9] DMP,[10] and MnO_2[11]). IBX oxidizes alcohols selectively in the presence of primary, secondary, and tertiary amines in good yields (Table 1, entries 8–13). Primary and secondary amines must be temporarily protonated[3b,7] *in situ* with acid (*e.g.*, trifluoroacetic acid, 1–1.5 equiv); otherwise, low yields of the desired amino carbonyl compounds are obtained. Tertiary amines do not require protonation during the oxidation reaction, although the presence of trifluoroacetic acid appears to speed up the oxidation (consider, for example, the oxidation of **25** (Table 1, entries 11 and 12)). It is worth emphasizing that 1,2-amino alcohols, as well as 1,2-diols, are cleanly oxidized without C–C bond cleavage (Table 1, entries 9–12).

Interestingly, oxidizable heteroaromatic compounds (furan,[4d] pyridine,[4d] indole) are not affected during IBX oxidation. The oxidation of indolyl alcohols is noteworthy (Table 1, entries 5–7, 13). Indoles, in particular those with an unsubstituted NH group, are known to be unstable in the presence of oxidizing reagents,[12] but oxidation of indolyl alcohols with IBX required no protection of the indole NH (*e.g.*, NTos or $NSiR_3$).

IBX also shows selectivity in the oxidation of polyalcohols (primary allylic *vs* secondary alcohol; *trans*-1,2-diol *vs* secondary alcohol (Table 1, entries 14 and 15)), although this behavior may depend on particular features of the substrate. Indeed, the same reactions (**29** to **30** and **31** to **32**) have been performed with triethylamine–SO_3 complex[13] and NBS,[14] respectively. Corey and Palani observed[4e] the general oxidation of 1,4-diols to γ-lactols, without overoxidation to lactones. Other functional groups compatible with IBX are double bonds,[4d] both conjugated and isolated, carboxylic acids,[4d] as well as carboxylic esters and carboxamides (Table 1). Phenols and anilines, however, do not withstand the presence of IBX: complex and dark colored reaction mixtures are obtained.

IBX is easily prepared from inexpensive, commercially available reagents *i.e.*, 2-iodobenzoic acid and inorganic oxidants such as potassium permanganate,[4a] potassium bromate,[1b,4d] or chlorine.[4b] IBX dissolves readily in DMSO,[4d,15] while it is virtually insoluble in other organic solvents such as sulfolane, DMF, MeCN, $CHCl_3$, CH_2Cl_2, acetone, and THF. Thus, IBX oxidations are usually carried out in DMSO solution at room temperature. The dissolution of IBX in DMSO takes 5–20 min, and clear solutions up to 1.5 M are obtainable. In our laboratory, preparative oxidation reactions are usually run with 0.3–1.0 M solutions and have been performed with 0.1–500 mmol of IBX. The compound to be oxidized can be added to the reaction mixture either before or after IBX, and a cosolvent such as THF, MeCN, or EtOAc may be used. The rate of oxidation is accelerated by using an excess of IBX, *e.g*, 5–10 equiv. This expedient is particularly useful in the case of amino alcohols, whose oxidation may require long reaction times. (Table 1, entries 11 and 12).

IBX, contrary to DMP,[16] is completely stable to moisture, and the oxidation can be performed in an open flask without any particular precaution, *e.g.*, inert atmosphere or dry solvent. Indeed, the oxidation of benzoin **33** to benzil **34** needed 2 h, both in commercial and in carefully



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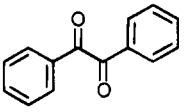

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dried DMSO.[17] In DMSO–H_2O 9/1 the oxidation of **33** to **34** required 10 h; thus, although water significantly decreases the concentration of the intermediate, it does

(6) The behavior of hypervalent iodo reagents toward amino and mercapto alcohols is not well defined. Periodinanes react with amines to give either imines (see: Amey, R. L.; Martin, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 5294) or unidentified products.[1c] However, DMP oxidizes alcohols selectively in nucleosides derivatives.[10] Amides undergo Hofmann rearrangement to amines in the presence of the iodine(III) reagents $PhI(OAc)_2$ and $PhI(O_2CCF_3)_2$ (see: Almond, M. R.; Stimmel, J. B.; Thompson, E. A.; Loudon, G. M. *Organic Syntheses;* Wiley: New York, 1993; Collect. Vol. VIII, p 132). The oxidation with DMP of an alcohol containing a thioether moiety was reported to be unsuccessful (see: Linderman R. J.; Graves, D. M. *Tetrahedron Lett.* **1987**, *28*, 4259), while $PhI(O_2CCF_3)_2$ is efficiently used for the deprotection of thioketals and thioacetals to carbonyl (see: Stork, G.; Zhao, K. *Tetrahedron Lett.* **1989**, *30*, 287).

(7) Kocienski, P. J. *Protective Groups*; Thieme Verlag: Stuttgart, 1994; Chapters 1 and 6.

(8) (a) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165. (b) Denmark, S. E.; Forbes, D. C.; Hays, D. S.; DePue, J. S; Wilde, R. G. *J. Org. Chem.* **1995**, *60*, 1391.

(9) Roush, W. R.; Walts, A. E. *J. Am. Chem. Soc.* **1984**, *106*, 721.

(10) Samano, V.; Robins, M. J. *J. Org. Chem.* **1990**, *55*, 5186.

(11) Martinez, S. J.; Dalton, L.; Joule, J. A. *Tetrahedron* **1984**, *40*, 3339.

(12) (a) Sundberg, R. J. *The Chemistry of Indoles*; Academic Press: New York, London, 1970; pp 282–315. (b) Moriarty and Prakash reported an interesting oxidative cleavage of **17** to 3-(methoxymethyl)-indole with $PhI(OAc)_2$ (see: Moriarty, R. M.; Prakash, O. *Acc. Chem. Res.* **1986**, *19*, 244).

(13) Ferland J. M. *Can. J. Chem.* **1974**, *52*, 1652.

(14) Fieser, L. F.; Rajagopalan, S. *J. Am. Chem. Soc.* **1949**, *71*, 3938.

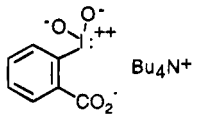
(15) At rt, IBX solutions in DMSO are stable for about 1 week. After 12 days, it is possible to detect (^{1}H-NMR, 300 MHz) IBX reduction to IBA (≈10%) and 2-iodobenzoic acid (≈5%) and corresponding oxidation of DMSO to dimethyl sulfone.

(16) The problem of DMP sensibility to moisture has been deeply studied by Schreiber;[2b] see, in particular, the relative humidity problem during summertime discussed in the Experimental Section.

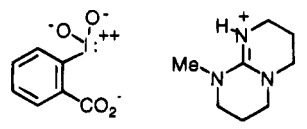
(17) Commercial DMSO: Merck "pro analysi" code no. 1.02952. Dried DMSO: Merck "pro analysi" distilled and stored (24 h) over activated (200 °C) 4 Å molecular sieves.

not preclude the reaction even when it is present in large amounts. Moreover, although IBX only dissolves in DMSO, it is possible to perform IBX oxidations in other solvents, thus avoiding the tedious workup problems typical of DMSO (Table 2). IBX is able to oxidize alcohols (*e.g.*, **33** to **34**) in THF, simply by refluxing the reaction mixture (Table 2, entry 1) or by adding at ambient temperature a few equivalents of DMSO (3–9 equiv) to accelerate the reaction (Table 2, entries 2 and 3). *It is worth highlighting that, despite its virtual insolubility in THF, IBX*[18] *was able to oxidize* ***33*** *without the need of dissolution in DMSO.*

Finally two quaternary ammonium salts, **35**[1c,d] and **36**, were prepared to enhance the solubility of IBX in organic solvents other than DMSO. Although both **35** and **36** are more soluble than IBX, they are still only sparingly soluble in acetone, EtOAc, $CHCl_3$, or CH_2Cl_2. However, they dissolve readily in MeCN, EtOH, and H_2O. Unfortunately, **35** and **36** are unable to oxidize alcohols at ambient temperature (*e.g.*, phenethyl alcohol or 3-(hydroxymethyl)pyridine), other than benzyl alcohol (DMSO, rt, 48 h, 50%).[19]



35



36

In conclusion, the ultracentennial[4a] 10-I-4 iodinane oxide *IBX (**3**) represents a new oxidizing reagent* that successfully joins to the large family of known oxidants. *IBX*, in contrast to other valuable oxidants,[3] *is inexpensive to prepare and easy to handle, can tolerate moisture and water, and generally gives very good yields. Furthermore, IBX is mild and chemoselective* (primary alcohols are converted into aldehydes with no overoxidation to acids; 1,2-diols are converted to α-ketols or α-diketones without oxidative cleavage; amino alcohols are oxidized to amino carbonyls, without protection of the amino group; 1,4-diols are highly selectively oxidized to γ-lactols;[4e] sensitive heterocycles are not affected; various other functional groups are compatible with IBX oxidation). *IBX is versatile* (it works in various solvents and it is highly sensitive to temperature variations), *and its solutions in DMSO are stable*[15]*enough to carry out the oxidation reaction easily.*

Experimental Section

Caution! IBX (**3**) has been reported to detonate[21] upon heavy impact and heating over 200 °C. Dess and Martin reported[1c] that heating and striking IBX (**3**) with a hammer did not cause any detonation. In our hands, using IBX at temperatures between 20 and 70 °C, no hazard has been experienced.

Compounds **5**, **7**, **15**, **17**, **19**, **21**, **23**, **25**, and **33** are commercially available and were used as obtained. Compounds **9**,[22] **11**,[22] **13**,[23] **27**,[24] **29**,[13] and **31**[14] were prepared using the cited procedures. Ammonium salt **35** was prepared as previously reported.[1c] The known products (**6**,[25] **8**,[26] **10**,[22] **12**,[22] **14**,[23] **16**,[25] **18**,[27] **22**,[28] **24**,[29] **26**,[30] **28**,[24] **30**,[31] **32**,[14] and **34**[25]) obtained by IBX oxidation were identified by comparison of their spectral and physical data to those of authenticated samples prepared by cited methods or with commercially available materials. IBX (**3**) was prepared according to the Dess–Martin procedure,[1b] with a minor modification during workup[4d] (the solid was rinsed with anhydrous acetone and Et_2O instead of EtOH). Analytical data for IBX (**3**) (IR, ^{1}H- and ^{13}C-NMR spectra, mp, and elemental analysis) have already been reported.[4d] Flash chromatography was performed using Kieselgel 60 (230–400 mesh, E. Merck). Combustion analyses were performed by Redox, Cologno Monzese, Italy.

Alcohol Oxidation with IBX in DMSO. 17β-Furyl-5β,14β-androstane-3β,14β-diol (30). IBX (520 mg, 1.9 mmol) was added to a solution of tetrol **29**[13] (500 mg, 1.32 mmol) in DMSO (5 mL). After 3.5 h, the reaction mixture was diluted with water (20 mL), filtered, and extracted with Et_2O (3 × 50 mL), and the organic layers were dried (Na_2SO_4) and evaporated. The crude product was purified by flash chromatography (*n*-hexane/EtOAc 6/4) to give **30** (407 mg, 1.13 mmol, 86%, mp 206–209 °C, (lit.[31] mp 207–209 °C)) and 17β-furyl-14β-hydroxy-5β,14β-androstan-3-one (50 mg, 0.14 mmol, 11%, mp 162–167 °C (lit.[32] mp 166–168 °C)).

Amino Alcohol Oxidation with IBX + TFA in DMSO. 3-(Aminomethyl)-3,5,5-trimethylcyclohexanone (20). IBX (900 mg, 3.2 mmol) was added to a solution of amino alcohol **19** (500 mg, 2.9 mmol) and TFA (238 μL, 3.2 mmol) in DMSO (6.5 mL). After 5 h, the reaction mixture was diluted with water (20 mL), filtered, basified with Na_2CO_3, extracted with Et_2O (6 × 30 mL), dried (Na_2SO_4), and evaporated to give **20** as a foam. The compound was characterized as acetyl derivative (Ac_2O/CH_2Cl_2/TEA). The reaction mixture was diluted with CH_2Cl_2, washed with water, dried (Na_2SO_4), and evaporated. Purification by flash chromatography ($CHCl_3$/MeOH 97/3) and trituration with *i*-Pr_2O gave 3-(acetamidomethyl)-3,5,5-trimethylcyclohexanone (561 mg, 2.7 mmol, 91%, mp 81–83 °C): ^{1}H-NMR ($CDCl_3$, 300 MHz) δ (ppm) 5.55 (br, 1H), 3.25–3.10 (m, 2H), 2.30–2.05 (m, 4H), 2.03 (s, 3H), 1.70–1.45 (m, 2H), 1.08 (s, 3H), 1.06 (s, 3H), 1.04 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ (ppm) 23.4, 25.4, 29.8, 33.2, 35.7, 40.0, 47.3, 49.8, 51.1, 53.9, 170.2, 211.1; MS (EI) *m*/*z* (relative intensity) 211 (M^+, 1), 196 (1), 178 (2), 154 (4), 139 (100), 125 (36); IR (KBr) 3260, 3090, 2960, 2920, 1700, 1680 cm^{-1}. Anal. Calcd for $C_{12}H_{21}NO_2$: C, 68.25; H, 9.95; N, 6.64. Found: C, 68.37; H, 10.00; N, 6.60.

Benzoin (33) Oxidation with IBX in THF. Benzil (34; Table 2, Entry 1). IBX (1 g, 3.6 mmol) was added to a solution of **33** (540 mg, 2.5 mmol) in 10 mL of THF. The reaction mixture was refluxed for 2 h, and then it was diluted with THF (50 mL) and filtered. The solvent was evaporated to dryness. The crude was dissolved in EtOAc (15 mL), washed with water (3 × 5 mL), dried (Na_2SO_4), and evaporated to dryness. Crystallization from EtOH gave **34** (492 mg, 2.3 mmol, 92%, mp 94–95 °C) identical, in all respects, with a commercial sample.

1,3,4,6,7,8-Hexahydro-1-methyl-2*H*-pyrimido[1,2-*a*]-pyrimidinium 2-Iodoxybenzoate (36). IBX (1 g, 3.57

(18) In the solid state, IBX is a polymer strongly associated along the I–O bond; see: Gougoutas, J. Z. *Cryst. Struct. Commun.* **1981**, *10*, 489.

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(20) ***Caution!*** Explosion of sensitive or metastable system may be promoted by ultrasounds. See: Abdulla, R. F. *Aldrichim. Acta* **1988**, *21*, 30.

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mmol) was added to a solution of 1,3,4,6,7,8-hexahydro-1-methyl-2*H*-pyrimido[1,2-*a*]pyrimidine (513 μL, 3.57 mmol) in CH_3CN (20 mL). After 30 min, the mixture was evaporated and the crude treated with EtOAc (10 mL). The filtered solid was triturated with acetone (8.5 mL) to give **36** (1.2 g, 2.89 mmol, 80%, mp 156–158 °C): ^{1}H-NMR ($CDCl_3$, 300 MHz) δ (ppm) 8.58 (br, 1H), 8.40–8.18 (m, 2H), 7.82–7.62 (m, 2H), 3.40–3.20 (m, 8H), 3.03 (s, 3H), 2.10–1.85 (m, 4H).; ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ (ppm) 20.7, 21.0, 38.1, 38.8, 47.1, 47.9, 48.0, 123.8, 131.7, 132.7, 134.2, 134.2, 146.2, 151.3, 168.6; MS (EI) *m*/*z* (relative intensity) 248 (100), 231 (66), 203 (26), 153 (45); IR (KBr) 3320, 3240, 3180, 3160, 2970, 2940, 2870, 1640, 1600, 1560, 1350 cm^{-1}. Anal. Calcd for $C_{15}H_{20}IN_3O_4$: C, 41.58; H, 4.62; I, 29.32; N, 9.70. Found: C, 40.99; H, 4.59; I, 29.80; N, 9.31.

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