Geometry-dependent divergence in the gold-catalyzed redox cascade cyclization of *o*-alkynylaryl ketoximes and nitrones leading to isoindoles†

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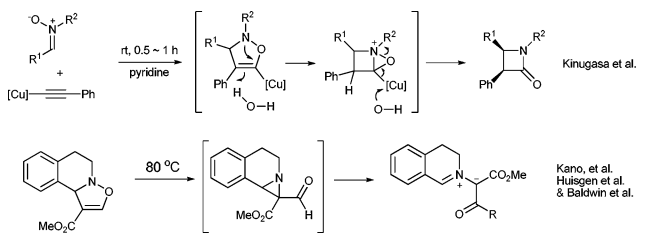
We report geometry-dependent cyclizations of *o*-alkynylaryl ketoximes and nitrones catalyzed by gold complexes. (*E*)-Ketoximes undergo *N*-attack to give isoquinoline-*N*-oxides. In sharp contrast, (*Z*)-ketoximes undergo unprecedented *O*-nucleophilic attack, followed by a redox cascade leading to a novel catalytic entry to isoindoles of diverse scope. The structure of an isoindole was unambiguously supported by X-ray crystallography. We demonstrated the generality of the isoindole synthesis from either (*Z*)-oximes or nitrones, and presented a mechanistic model of this redox cascade based on the reaction profiles of various substrates.

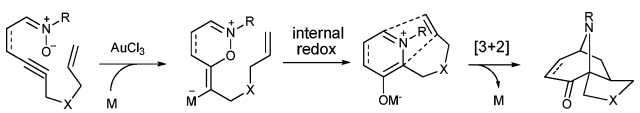
1. Introduction

Oximes and nitrones often function as stable precursors of amino compounds through the reductive cleavage of the N–O bond.[1] Besides, the cleavage of the N–O bond mediates a variety of redox processes, including conversions of oximes into amides,[2a–c] nitriles[2d,e] and enamides,[2f] *N*-substitutions of *O*-acyl (or sulfonyl) oximes,[2g–i] and [3,3]-sigmatropic rearrangements of oximes and nitrones.[2j,k] Redox reactions involving nitrones have scarcely been precedented, particularly when compared to their structural isomers, oxaziridines,[3] presumably due to the thermodynamic stability of the former. A conspicuous exception in this perspective is the Kinugasa reaction between a nitrone and a terminal acetylene, which was proposed to proceed through an initial dipolar cycloaddition of a nitrone onto a Cu-acetylide (Scheme 1).[4] Another relevant formal redox process is the rearrangement of a 2,3-dihydroisoxazole, formed from a dipolar cycloaddition of a nitrone with an alkyne, into an acyl aziridine reported by Takahashi and Kano,[5a] and Huisgen *et al.*,[5b] of which the mechanism was clarified by Baldwin and Pudussery *via* isolation of acyl aziridine intermediates.[5c] In addition, Eberbach *et al.* have reported a series of interesting cyclization reactions of closely related enynyl and enallenyl nitrone substrates.[6]



Scheme 1 Intramolecular redox reactions involving a nitrone and alkynes.

Despite the relative scarcity of precedents, there are several desirable characteristics in the use of oximes and nitrones as oxidants: (1) they are readily available, hydrolytically stable, non-toxic and non-explosive; (2) their redox chemistry can often be performed under a mild reaction condition with the aid of metal catalysis, and furthermore, (3) the imine, formed as a putative intermediate of a redox reaction of the oxime or nitrone, can be re-incorporated into the reaction in a cascade fashion, thus rendering the overall process completely atom-economical.[7] In this regard, we recently reported a gold-catalyzed generation of the azomethine ylide from the intramolecular redox reaction between alkynes and nitrones based on a concept that combines the exceptional carbophilic Lewis acidity of gold complexes[8] and the potential ability of a nitrone as an oxidant (Scheme 2).[9] More recently, Nakamura *et al.* reported a remarkable cascade cyclization through N–O bond cleavage of oximes catalyzed by a Cu(I) complex, leading to β-lactams.[10] To further showcase its generality, and to extend the mechanistic insights and synthetic implications of this gold-catalyzed N–O cleaving redox cascade, we wish to describe an intramolecular redox cyclization of *o*-alkynylaryl ketoximes and nitrones, leading to the general synthesis of isoindoles (Scheme 3). Isoindoles can be potential precursors of porphyrin analogs or pyrroles with extended conjugation and therefore, should find important applications in material science.[11] However, they are rather unstable and their preparatory methods are still limited, especially in a catalytic fashion.[11h–j] Here, we disclose that the mechanism of this Au-catalyzed redox is strictly geometry-dependent and thus, both (*Z*)-oximes as well as nitrones readily undergo redox cyclization into isoindoles, as demonstrated by the synthesis of a variety of isoindoles under relatively mild conditions.



Scheme 2 Intramolecular redox–dipolar cycloaddition (IR-DC) cascade.

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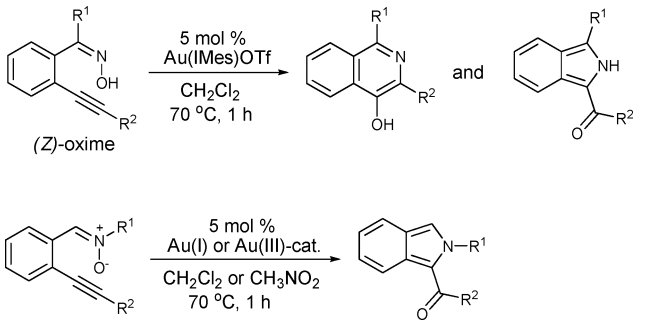
† Electronic supplementary information (ESI) available: ^{1}H and ^{13}C NMR spectra of starting materials and products, X-ray crystallographic data of **3e**, as well as Table S1 and S2. CCDC 738725. For ESI and crystallographic data in CIF or other electronic format, see DOI: 10.1039/b910757f

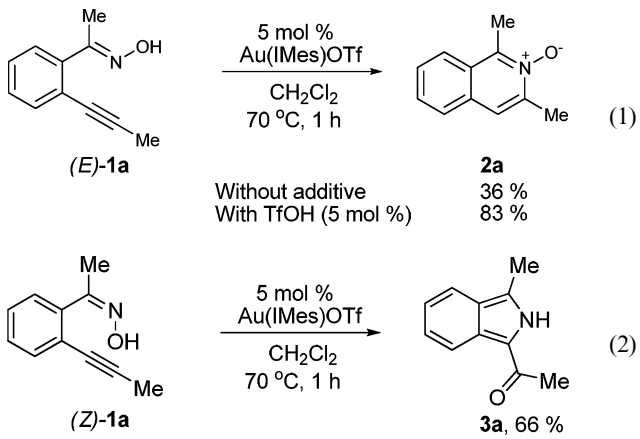


Scheme 3 Isoindole synthesis *via* redox cyclization of oximes and nitrones.

2. Results and discussion

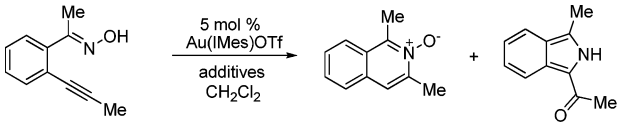
2.1. Geometry-dependent reaction profiles and attempted *in situ* *E–Z* isomerization

In our previous studies on the cyclization of *o*-alkynylaryl aldoximes catalyzed by electrophilic metal complexes,[12] we have shown that they undergo an efficient cyclization into isoquinoline-*N*-oxides with either Au(I) or Ag(I) catalysts *via* 6-*endo*-dig *N*-attack of the (*E*)-oxime. We projected that the absence of *O*-attack that we observed in the redox reaction of a nitrone (Scheme 2) is due to the geometrical constraints of the (*E*)-oxime. Therefore, our initial efforts were focused on the cyclization of ketoximes, in which (*Z*)-geometry is more available than that of aldoxime. As expected, when the carefully separated (*E*)-**1a** (formed as a major isomer of E : Z = 10 : 1 mixture) was treated with Au(IMes)OTf (5%) in CH_2Cl_2 (70 °C, sealed vial), 36% of isoquinoline-*N*-oxide **2a** was isolated as the only identifiable product (Eqn 1). With 5 mol% of TfOH as a co-catalyst, the yield further increased to 83% (*vide infra*, Table 1). In sharp contrast, (*Z*)-**1a** transformed into isoindole **3a** in 66% yield under identical conditions (Eqn 2). In both cases, the formation of **3a** from (*E*)-**1a** (or **2a** from the reaction of (*Z*)-**1a**) could not be observed even, in trace amount.



We initially hoped to find a suitable condition that induces facile *in situ* *E–Z* isomerization of ketoximes under the reaction conditions, so that the cyclization of the (*E*)-oxime might give the corresponding isoindole. Thus, various additives (5 mol%), including Brønsted acid (TfOH), base (n-Bu_4NOH), $Cu(OTf)\cdot C_6H_6$ and $Cu(OTf)_2$, were examined along with Au(IMes)OTf (5 mol%) as a catalyst in CH_2Cl_2 (Table 1). In all trials, the formation of isoindole **3a** from (*E*)-**1a** was not observed (Table 1). Notably, however, a dramatically improved yield of **2a** (83%) under a much milder condition (rt) was observed when the reaction was conducted with 5 mol% of TfOH as a co-catalyst along with 5 mol% of Au(I) catalyst (entries 1 and 2). This is presumably due to the facilitation of the catalyst turnover by the acid additive.[13] In the presence of 10% of TfOH alone without Au(I) catalyst, the cyclization into **2a** did not occur effectively (15%), but the recovered starting (*E*)-**1a** isomerized into its equilibrium ratio (*E* : *Z* = 10 : 1) (entry 3). However, even with 2 equiv. of TfOH and Au(I) catalyst, the formation of **3a** was not observed (entry 4), indicating a much higher rotational barrier around C=N bond compared to that of cyclization into isoquinoline-*N*-oxide **2a**.[14] Other Lewis acids (entries 5–8) or base (entry 9) similarly failed to isomerize the C=N bond *in situ*.

Table 1 Attempted *in situ* isomerization–cyclization of (*E*)-**1a**



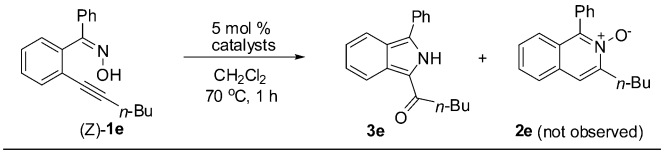
Entry	Additive[a]	Conditions[b,c]	Conv. (%)[d]	**2a** (%)[d]
1	None	70 °C, 1 h	>95	36
2	TfOH[e]	rt, 1.5 h	>95	83
3	TfOH (10%)[e,f]	70 °C, 1 h	20 (10 : 1)[g]	15
4	TfOH (2 equiv.)[e]	rt, 2 h	>95	94
5	$Cu(OTf)\cdot C_6H_6$	70 °C, 0.5 h	>95	63
6	$Cu(OTf)_2$	70 °C, 1.5 h	>95	63
7	$Cu(OTf)\cdot C_6H_6$ (1 equiv.)	rt, 1.5 h	Dec.[h]	—
8	$Cu(OTf)_2$ (1 equiv.)	rt, 1.5 h	Dec.[h]	—
9	n-Bu_4NOH[i]	70 °C, 1.5 h	60	52

[a] 5 mol% of additives, unless otherwise noted. [b] Reactions were conducted at 70 °C in a sealed vial. [c] The reaction was quenched by addition of Et_3N. [d] The conversion and the yield of **2a** were based on the crude NMR. [e] A stock solution (1.0 M in CH_2Cl_2) was used. [f] In the absence of Au catalyst. [g] *E* : *Z* ratio of the recovered **1a** in parenthesis. [h] Decomposed. [i] 3.0 M solution in MeOH.

2.2. Optimization and scope of the isoindole formation from (*Z*)-ketoximes

We screened various metals as catalysts for the optimization of isoindole formation from (*Z*)-**1e** (Table 2). At rt, little or no conversion was observed with any of the catalysts we examined. However, upon heating to 70 °C, various metals transformed (*Z*)-ketoximes into isoindole **3e** with varying efficiencies (entries 1–8). Among those, Au(IMes)OTf was the most effective, providing **3e** in 73% yield (entry 3). It is noteworthy that $AuCl_3$ gave only a modest yield of **3e** from a messy mixture (entry 2). The structural assignment of **3e** was supported by X-ray crystallography (Fig. 1). Further efforts were made to optimize the yield of **3e**: (1) by changing the gold counter-anion (entries 9–12), (2) by changing the solvents (Table S1, ESI†), or (3) by changing the ligand (Table S2, ESI†). Somewhat inferior yields were obtained from these trials, but Au(IMes)SbF_6, Au(IPr)OTf, and [*t*-Bu_2P(*o*-biphenyl)Au]OTf in CH_2Cl_2 or Au(IMes)OTf in CH_3NO_2 gave comparably good yields. Importantly, there was no isoquinoline-*N*-oxide observed in these trials, even in a trace amount. The use of TfOH (5%) co-catalyst along with Au(I), also did not produce any isoquinoline-*N*-oxide **2e**, confirming the C=N

Table 2 Screening of metal catalysts for the conversion of (*Z*)-**1e** into **3e**



Entry	Catalyst	Conv. (%)[a]	**3e** (%)[a]
1	AuCl	17	15
2	$AuCl_3$	75	44
3	[Au(IMes)]OTf	>95	73
4	$PtCl_2$	18	8
5	$In(OTf)_3$	18	11
6	$Zn(OTf)_2$	8	8
7	$Cu(OTf)_2$	67	Dec.[b]
8	AgOTf	46	32
9	$[Au(IMes)]NTf_2$	>95	65
10	$[Au(IMes)]ClO_4$	>95	65
11	$[Au(IMes)]BF_4$	>95	65
12	$[Au(IMes)]SbF_6$	>95	69
13	[Au(IMes)]OTf/TfOH[c]	>95	59

[a] Yields were based on the crude NMR spectra. [b] Decomposed. [c] 5 mol% of TfOH was used as an additive.

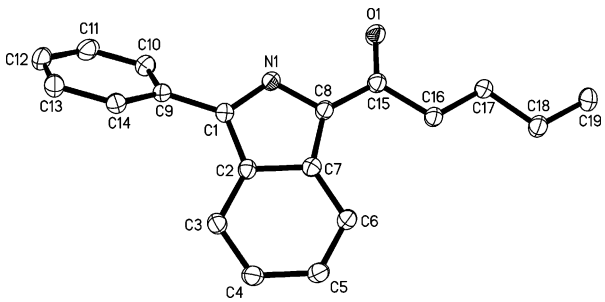
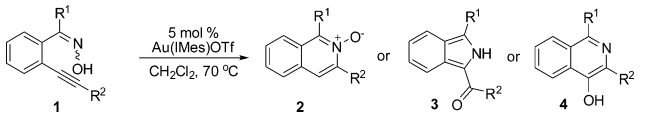


Fig. 1 A view of one of the four independent molecules of the isoindole in the crystal structure of isoindole **3e**. Ellipsoids are drawn at the 30% probability level.

rotational barrier is much higher than the cyclization to isoindole **3e** (entry 13). When the reaction was conducted at 150 °C without any catalyst as a control experiment, no reaction took place and an extensive decomposition occurred over 24 h, supporting that this redox cyclization is a metal-catalyzed process and *not* a thermal isomerization of 2,3-dihydroisoxazoles (*vide infra* in Scheme 5).[5,6b]

We next examined the generality of this geometry-dependent divergence with the following examples in Table 3. The ketoximes used in this study were carefully separated by chromatography and were separately subjected to the reaction conditions shown in Table 3. In all cases examined, (*E*)-oximes gave isoquinoline-*N*-oxides **2**, whereas (*Z*)-oximes gave isoindoles **3** uneventfully (entries 1–8). When the alkynyl terminus is substituted with an alkenyl group, good yields of the corresponding isoindoles were obtained (entries 11 and 12). Interestingly, (*Z*)-oximes **1c** and **1h** with a phenyl acetylene unit (entries 6 and 13), produced yet more products, which were assigned as 4-hydroxyisoquinolines **4c** and **4i**, respectively.[15] The structural assignment of these products was also supported by the following related transformation of (*E*)-**1j** bearing a (*Z*)-acrylate unit (Eqn 3). The obtained product **4j** is consistent with the structure shown, based on the absence of an ethoxy group, non-polar behaviour in TLC ($R_f = 0.65$, EtOAc–Hex = 1 : 1 on silica gel), and IR, ^1H, ^{13}C and COSY-NMR spectra.

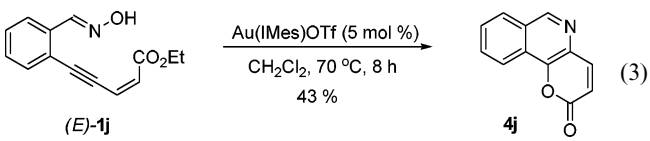
Table 3 Cyclization of (*E*)- and (*Z*)-ketoximes[a]



Entry	Oxime	R^1, R^2	Time/h	**2**/**3**/**4** (%)[b]
1	(*E*)-**1a**	Me, Me	2	**2a**, 83
2	(*Z*)-**1a**		1	**3a**, 66
3	(*E*)-**1b**	Me, *n*-Bu	2	**2b**, 91
4	(*Z*)-**1b**		0.5	**3b**, 42
5	(*E*)-**1c**	Me, Ph	2	**2c**, 46
6	(*Z*)-**1c**		12	**3c**, 30/**4c**, 41
7	(*E*)-**1d**	*n*-Pr, Me	1	**2d**, 94
8	(*Z*)-**1d**		1.5[c]	**3d**, 49
9	(*Z*)-**1e**	Ph, *n*-Bu	1	**3e**, 62
10	(*Z*)-**1f**	Ph, Me	0.5	**3f**, 65
11	(*Z*)-**1g**	Ph, 1-cyclohexenyl	5	**3g**, 63
12	(*Z*)-**1h**	Me, 1-cyclohexenyl	1.5[c]	**3h**, 73
13	(*Z*)-**1i**	Ph, Ph	10[c]	**3i**, 36/**4i**, 41

[a] *Conditions:* (for (*E*)-oximes): TfOH (5%) and Au(IMes)OTf (5%) in CH_2Cl_2 at rt; (for (*Z*)-oximes): Au(IMes)OTf (5%) in CH_2Cl_2 at 70 °C (sealed vessel). [b] Isolated yields of **2**–**4** after chromatography. [c] 10 mol% of catalyst was used.

This represents an interesting example of *in situ* isomerization of (*E*)-oximes before it can cyclize by *O*-nucleophilic attack.



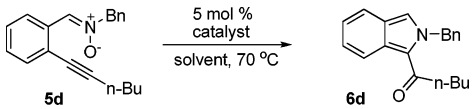
(3)

2.3. Optimization and scope of the nitrone cyclization

One apparent drawback in the isoindole synthesis from (*Z*)-ketoximes is the low availability of the (*Z*)-ketoxime, which often forms as a minor component in the equilibrium, especially when R^1 is an alkyl group. From the chemo-divergence in Table 1 and 2, a nitrone would be a logical starting material, because the (*Z*)-isomer is the exclusive form in nitrones. Thus, we screened a variety of reaction conditions for the cyclization of nitrones into isoindoles (Table 4). The efforts to find the optimized condition was less successful than in the case of (*Z*)-oximes. Although reasonable conversions and rates were achieved with some metal salts (entries 3, 4, 6 and 8), the reaction was typically plagued by extensive decomposition, and only a low yield of isoindole **6d** was obtained in dichloromethane as the solvent. The facile decomposition of the isoindoles of type **6**, as compared to type **3**, is not surprising, because the absence of a substituent at the 3-position of the isoindole would render **6** very susceptible to decomposition *via* undesired conjugate additions. Upon changing solvents into nitromethane, however, up to 58% of isoindole **6d** was obtained with [*t*-Bu_2P(*o*-biphenyl)Au]OTf catalyst. Although the yield of nitrone **6d** was modest, the overall yield from the carbonyl precursor significantly improved compared to (*Z*)-oximes, and isoindoles without the C3-substituent could be readily synthesized.

We next investigated the generality of this cyclization of nitrones **5** into isoindoles **6**, using substrates with different substituents at the aryl core and alkynyl terminus, and as *N*-substituents (Table 5).[16] Substrates with an *N*-alkyl group, and an alkyl group

Table 4 Screening of metal catalyst for the cyclization of nitrone **5d**[a]



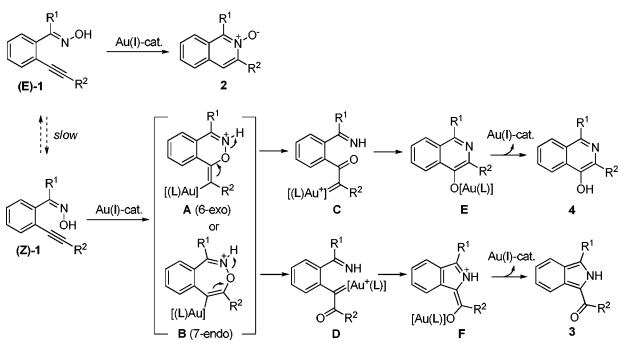
Entry	Catalyst	Solvent	Time	Conv. (%)	Yield (%)[b]
1	$Zn(OTf)_2$	CH_2Cl_2	3 h	0	—
2	$Cu(OTf)_2$	CH_2Cl_2	3 h	52	11
3	$PtCl_2$	CH_2Cl_2	1 h	>95	32
4	$AuCl_3$	CH_2Cl_2	1 h	>95	28
5	$Au(PPh_3)OTf$	CH_2Cl_2	3 h	60	16
6	[Au(**L**)] OTf[c]	CH_2Cl_2	1.5 h	>95	29
7	Au(IMes)OTf	CH_2Cl_2	3 h	54	13
8	Au(IPr)OTf	CH_2Cl_2	0.5 h	>95	24
9	$[P(C_6F_5)_3Au]OTf$	CH_2Cl_2	3 h	87	28
10	[Au(**L**)] OTf[c]	CH_3NO_2	0.5 h	>95	58
11	Au(IPr)OTf	CH_3NO_2	0.5 h	>95	48
12	$PtCl_2$	CH_3NO_2	2 h	74	42
13	$AuCl_3$	CH_3NO_2	0.5 h	>95	38

[a] *Conditions:* catalyst (5%) at 70 °C (sealed vessel), unless otherwise noted. [b] Crude NMR yield. [c] **L** = *t*-Bu_2P(*o*-biphenyl).

at the alkynyl position, generally underwent a smooth reaction (entries 1–4). When substrates with different electron demands at the aryl core were tested, trifluoromethyl-substituted **5e** smoothly cyclized, albeit in a modest yield (entry 5). However, more electron-rich **5f** underwent a sluggish reaction and under forced conditions (70 °C, 3 h) decomposed slowly into an intractable mixture (entry 6). Generally, the reaction of substrates with an aryl group at the alkynyl terminus was difficult due to a facile decomposition of the isoindole products. For example, in entries 7 and 8, we managed to isolate the corresponding isoindoles **6g** and **6h** in low yields, but these materials decomposed in hours upon storage at 4 °C. Interestingly, pyridinyl substrates **5i** and **5j** underwent a smooth cyclization leading to 6*H*-pyrrolo[3,4-*b*]pyridine derivatives (entries 9 and 10). Substrate **5k** bearing an alkenyl tether between the nitrone and the alkyne functionality also smoothly participated in the cyclization to afford the corresponding pyrrole derivative (entry 11).

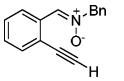
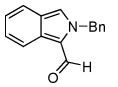
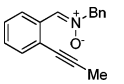
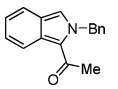
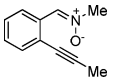
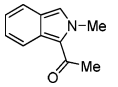
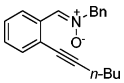
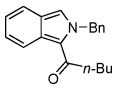
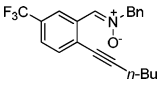
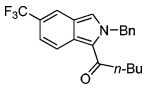
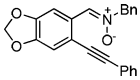
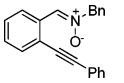
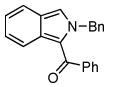
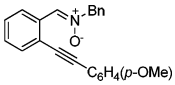
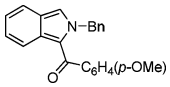
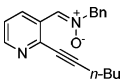
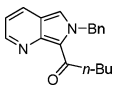
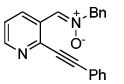
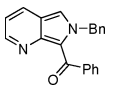
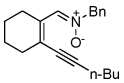
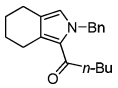
2.4. Mechanistic scenarios

The possible mechanism for the current redox cyclization into isoindoles from (*Z*)-ketoximes can be envisioned as in Scheme 4, following a corollary of the N–O bond redox in the generation of



Scheme 4 Possible mechanism of isoindole formation: 6-*exo*-dig or 7-*endo*-dig cyclization followed by N–O bond redox.

Table 5 The scope of the isoindole formation from the nitrone[a]

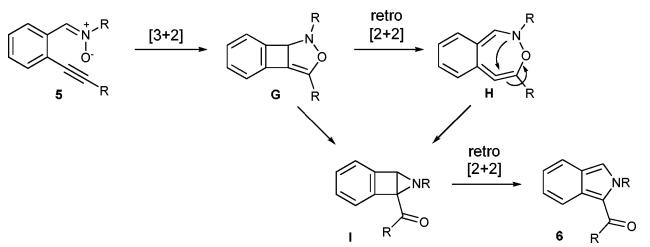
Entry	Substrate		Conditions: Time	**6** (%)[b]	
1		**5a**	A, 70 °C 1 h		**6a** 55%
2		**5b**	A, 70 °C 1 h		**6b** 53%
3		**5c**	B, rt 0.3 h		**6c** 57%
4		**5d**	B, 70 °C 0.5 h		**6d** 52%
5		**5e**	B, 70 °C 0.5 h		**6e** 43%
6		**5f**	B, 70 °C 3 h	Dec.	
7		**5g**	B, 70 °C 3 h		**6g** 32%
8		**5h**	B, rt 0.6 h		**6h** 30%
9		**5i**	A, 70 °C 0.3 h		**6i** 35%
10		**5j**	A, 70 °C 4 h		**6j** 40%
11		**5k**	B, 70 °C 0.5 h		**6k** 55%

[a] Unless otherwise mentioned, the following conditions were used. *Condition A:* Au(IPr)OTf (5%) in CH_3NO_2; *condition B:* [*t*-Bu_2P(*o*-biphenyl)Au]OTf (5%) in CH_3NO_2. [b] Isolated yields after chromatography.

azomethine ylides from nitrones.[9a] A notable feature in this mechanism is the divergence into isoindole **3** and 4-hydroxyisoquinoline **4** for (*Z*)-oximes bearing a phenyl substituent at the alkynyl position (R^2). For (*Z*)-**1c** and (*Z*)-**1i** (R^2 = Ph), a mixture of **3** and **4** were obtained (Table 3, entries 6 and 13), while all substrates with R^2 = alkyl gave single isomeric products **3**. This observation can be rationalized based on the following. Intermediate **C**, formed *via* the faster 6-*exo*-dig cyclization and the following redox, represents a Au-carbenoid, which could be envisioned as a gold-stabilized carbenium ion.[17,18] Therefore, the presence of a phenyl group at R^2 would stabilize **C** to afford 4-hydroxyisoquinoline **4** as a

mixture with **3**. In the absence of such a cation-stabilizing group, the slower 7-*endo*-dig cyclization and the following redox become the dominant pathway, leading to isoindole **3**. A similar 7-*endo* cyclization mechanism was also invoked by Hashmi *et al*.[19a] in the intramolecular oxygen transfer reaction between epoxides and alkynes.[19]

A similar mechanism could be envisioned for the isoindole formation from nitrones. However, given the complexity of the N–O bond redox processes,[4–6] one of the alternative mechanisms for the reaction of nitrone–alkyne substrates could be envisioned as that in Scheme 5. Initial intramolecular [3 + 2] dipolar cycloaddition between the nitrone and the alkyne, followed by retro-[2 + 2] electrocyclization, would provide a strained allene **H**,[6] which then rearrange into acyl aziridine **I**.[5] Instead, direct thermal rearrangement of **G** into acyl aziridine **I** could also be considered and the following retro-[2 + 2] electrocyclization would then furnish the desired isoindole **6**. However, we disfavor this alternative mechanism, because they involve rather strained intermediates **G–I**. In addition, a control experiment for the conversion of nitrone **5d** in the absence of any catalyst in CH_3NO_2 at 150 °C led to gradual decomposition of the starting material, with no noticeable isoindole formation. In sharp contrast, the Au(I)-catalyzed conversion of nitrone **5h** into **6h** occurs even at room temperature, with a significant conversion (Table 5, entry 8). Thus, a thermal rearrangement of 4-isoxazoline **G**, in this case, is a less likely option. Therefore, the isoindole formation from nitrones most likely follows a *gold-catalyzed* redox pathway that was depicted in Scheme 4 for (*Z*)-oximes.



Scheme 5 Alternative mechanism: initial [3 + 2] cycloaddition and thermal rearrangements.

3. Conclusions

Herein, we have demonstrated a novel isoindole synthesis starting from (*Z*)-ketoximes. The key mechanistic feature of this redox cyclization is that the mechanistic divergence into isoquinoline-*N*-oxides or isoquinoline is strictly dictated by the geometry of the starting ketoxime. A reaction profile of a range of (*Z*)-ketoximes and nitrones provides further mechanistic support for the proposed N–O bond redox mechanism.[21] In addition to the formation of isoindoles, we have observed the formation of 4-hydroxyisoquinoline derivatives (**4c**, **4i** and **4j**), which also fits into the currently proposed mechanistic model and reveals another controlling element in the redox reaction of nitrones. Currently, work aimed at trapping and utilizing the imine intermediate in a more synthetically useful fashion is under way in our laboratory, which should provide more direct evidence of the involvement of α-oxo carbenoids and imines as reactive species.

4. Experimental

General details

Anhydrous solvents (dichloromethane and nitromethane) were distilled from calcium hydride. All commercially available reagents were used as received without further purification. Ketoximes were prepared either by stirring a mixture of a ketone, $NH_2OH{\cdot}HCl$ (2 equiv.) and pyridine (5 equiv.) in ethanol at room temperature, or by treating a mixture of ketone and $NH_2OH{\cdot}HCl$ (1.5 equiv.) with NaOAc (2 equiv.) in CH_2Cl_2. A similar procedure was used for the preparation of nitrones except, in this case, that $BnNH_2OH$ or $MeNH_2OH{\cdot}HCl$ was used instead of hydroxylamine salt. Flash column chromatography was performed with 230-400 mesh silica gel. ^1H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer with TMS as an internal standard.

Characterization of substrates

(*E*)-1a. δ_H ($CDCl_3$, 400 MHz): 9.60 (1H, broad s), 7.60-7.40 (1H, m), 7.40-7.30 (3H, m), 2.32 (3H, s), 2.05 (3H, s); δ_C ($CDCl_3$, 100 MHz): 158.3, 140.4, 133.7, 129.1, 128.8, 128.3, 123.1, 91.2, 79.0, 16.0, 5.2.

(*Z*)-1a. δ_H ($CDCl_3$, 400 MHz): 8.23 (1H, broad s), 7.57-7.40 (1H, H), 7.40-7.22 (2H, m), 7.22-7.12 (1H, m), 2.20 (3H, s), 2.04 (3H, s); δ_C ($CDCl_3$, 100 MHz): 157.1, 138.7, 133.2, 128.9, 128.2, 127.5, 121.9, 90.2, 78.2, 21.8, 5.2.

(*E*)-1b. δ_H ($CDCl_3$, 400 MHz): 9.68 (1H, broad s), 7.49-7.39 (1H, m), 7.37-7.30 (1H, m), 7.30-7.22 (2H, m), 2.41 (2H, t, *J* 7.3), 2.32 (3H, s), 1.58 (2H, quintet, *J* 7.3), 1.45 (2H, sextet, *J* 7.7), 0.93 (3H, t, *J* 7.3); δ_C ($CDCl_3$, 100 MHz): 158.3, 140.4, 133.7, 129.0, 128.7, 128.2, 123.2, 95.8, 79.8, 31.2, 22.7, 19.9, 16.0, 14.2.

(*Z*)-1b. δ_H ($CDCl_3$, 400 MHz): 7.54-7.40 (1H, m), 7.38-7.24 (2H, m), 7.22-7.09 (1H, m), 2.40 (2H, t, *J* 7.0), 2.21 (3H, s), 1.57 (2H, quintet, *J* 7.0), 1.46 (2H, sextet, *J* 7.3), 0.93 (3H, t, *J* 7.0); δ_C ($CDCl_3$, 100 MHz): 157.2, 138.8, 133.1, 128.9, 128.1, 127.4, 122.0, 94.8, 79.0, 31.3, 22.6, 21.8, 19.8, 14.3.

(*E*)-1c. δ_H ($CDCl_3$, 400 MHz): 9.40 (1H, broad s), 7.68-7.54(1H, m), 7.54-7.44 (2H, m), 7.44-7.10 (6H, m), 2.40 (3H, s); δ_C ($CDCl_3$, 100 MHz): 158.2, 140.6, 133.7, 132.2, 129.2, 129.12, 129.08, 129.01, 128.96, 123.8, 122.4, 94.4, 88.7, 16.1.

(*Z*)-1c. δ_H ($CDCl_3$, 400 MHz): 8.20 (1H, broad s), 7.71-7.55 (1H, m), 7.55-7.45 (2H, m),7.45-7.35 (2H, m), 7.28-7.35 (3H, m), 7.17-7.35 (1H, m), 2.25 (3H, s); δ_C ($CDCl_3$, 100 MHz): 156.7, 139.0, 133.0, 132.3, 129.1, 129.0, 128.9, 127.7, 123.7, 121.2, 93.5, 88.0, 21.9.

(*E*)-1d. δ_H ($CDCl_3$, 400 MHz): 9.70 (1H, broad s), 7.54-7.32 (1H, m), 7.34-7.16 (3H, m), 2.85 (2H, t, *J* 7.7), 2.04 (3H, s), 1.52 (2H, sextet, *J* 7.4), 0.93 (3H, t, *J* 7.4); δ_C ($CDCl_3$, 100 MHz): 161.8, 139.6, 133.6, 129.8, 128.9, 128.2, 123.4, 90.8, 78.9, 30.9, 19.8, 14.9, 5.2.

(*Z*)-1d. δ_H ($CDCl_3$, 400 MHz): 8.40 (1H, broad s), 7.46 (1H, d, *J* 7.7), 7.39-7.20 (2H, m), 7.13 (1H, d, *J* 7.0), 2.53 (2H, t, *J* 7.7), 2.03 (3H, s), 1.49 (2H, sextet, *J* 7.4), 0.94 (3H, t, *J* 7.4); δ_C ($CDCl_3$, 100 MHz): 160.2, 138.0, 133.1, 128.8, 128.0, 122.3, 90.1, 78.7, 37.7, 20.2, 14.4, 5.2.

(*Z*)-1e. δ_H ($CDCl_3$, 400 MHz): 9.00 (1H, s), 7.62-7.48 (1H, m), 7.48-7.42 (2H, m), 7.42-7.36 (2H, m), 7.36-7.28 (4H, m), 2.18 (2H, t, *J* 7.0), 1.46-1.04 (4H, m), 0.76 (3H, t, *J* 7.3); δ_C ($CDCl_3$, 100 MHz): 157.8, 136.2, 135.5, 132.5, 129.5, 128.8, 128.7, 128.4, 127.6, 127.2, 123.3, 94.8, 78.7, 30.5, 21.8, 19.2, 13.7.

(*Z*)-1f. δ_H ($CDCl_3$, 400 MHz): 8.14 (1H, broad s), 7.58-7.50 (1H, m), 7.50-7.43 (2H, m), 7.42-7.36 (2H, m), 7.36-7.28 (3H, m), 7.28-7.22 (1H, m), 1.85 (3H, s); δ_C ($CDCl_3$, 100 MHz,): 158.3, 136.7, 136.1, 133.0, 130.0, 129.2, 129.1, 128.9, 128.1, 127.7, 123.8, 90.6, 78.3, 4.9.

(*Z*)-1g. δ_H ($CDCl_3$, 400 MHz): 8.80 (1H, broad s), 7.62-7.52 (1H, m), 7.52-7.44 (2H, m), 7.44-7.38 (2H, m). 7.36-7.26 (4H, m), 5.91 (1H, m), 2.16-1.98 (2H, m), 1.98-1.82 (2H, m), 1.64-1.35 (4H, m); δ_C ($CDCl_3$, 100 MHz,): 158.2, 136.5, 136.1, 136.0, 132.7, 130.0, 129.4, 129.3, 129.0, 128.2, 127.8, 123.6, 121.2, 95.9, 85.5, 29.3, 26.3, 22.8, 22.1.

(*Z*)-1h. δ_H ($CDCl_3$, 400 MHz): 7.91 (1H, broad s), 7.60-7.40 (1H, m), 7.40-7.26 (2H, m), 7.24-7.12 (1H, m), 6.18 (1H, m), 2.21 (3H, s), 2.32-2.17 (2H, m), 2.17-2.04 (2H, m), 1.78-1.50 (4H, m); δ_C ($CDCl_3$, 100 MHz,): 156.5, 138.3, 135.8, 132.3, 128.4, 127.9, 127.1, 121.3, 120.9, 95.0, 84.9, 29.2, 26.0, 22.5, 21.7, 21.3.

(*Z*)-1i. δ_H ($CDCl_3$, 400 MHz): 8.20 (1H, broad s), 7.76-7.60 (1H, m), 7.58-7.50 (2H, m), 7.50-7.41 (2H, m), 7.41-7.28 (4H, m), 7.28-7.18 (5H, m); δ_C ($CDCl_3$, 100 MHz): 158.2, 136.8, 136.0, 132.9, 132.2, 130.1, 129.6, 129.4, 129.1, 128.9, 128.82, 128.78, 127.8, 123.6, 123.0, 93.9, 88.1.

(*E*-oxime, *Z*-alkene) 1j. δ_H ($CDCl_3$, 400 MHz): 8.86 (1H, s), 7.97 (1H, broad s), 7.92-7.81 (1H, broad s), 7.63-7.48 (1H, m), 7.41-7.30 (2H, m), 6.39 (1H, d, *J* 11.4), 6.18 (1H, d, *J* 11.3), 4.31 (2H, q, *J* 7.0), 1.33 (3H, t, *J* 7.0); δ_C ($CDCl_3$, 100 MHz): 165.4, 149.5, 134.6, 133.6, 130.1, 129.4, 125.7, 122.99, 122.96, 98.4, 92.0, 61.3, 30.3, 14.9.

5c. δ_H ($CDCl_3$, 400 MHz): 9.25 (1H, d, *J* 7.7), 7.94 (1H, s), 7.42 (1H, d, *J* 7.3), 7.36-7.24 (2H, m), 3.90 (3H, s), 2.11 (3H, s); δ_C ($CDCl_3$, 100 MHz): 134.0, 132.9, 131.7, 130.4, 128.6, 127.9, 123.8, 92.8, 77.8, 55.6, 5.2.

5d. δ_H ($CDCl_3$, 400 MHz): 9.26 (1H, d, *J* 7.4), 7.98 (1H, s), 7.54-7.46 (2H, m), 7.46-7.38 (4H, m), 7.37-7.26 (2H, m), 5.10 (2H, s), 2.36 (2H, t, *J* 7.0), 1.62-1.36 (4H, m), 0.97 (3H, t, *J* 7.4); δ_C ($CDCl_3$, 100 MHz): 133.9, 133.4, 132.6, 131.6, 130.4, 130.1, 129.5, 128.5, 128.0, 124.1, 97.4, 72.2, 31.2, 22.6, 19.7, 14.2.

5e. δ_H ($CDCl_3$, 400 MHz): 9.64 (1H, s), 8.00 (1H, s), 7.58-7.46 (4H, m), 7.46-7.34 (3H, m), 5.10 (2H, s), 2.39 (2H, t, *J* 7.0), 1.62-1.30 (4H, m), 0.97 (3H, t, *J* 7.0); δ_C ($CDCl_3$, 100 MHz): 133.4, 133.0, 132.2, 132.1, 130.4 (q, $J_{C\text{-}F}$ 32.7), 130.2, 129.8, 129.7, 127.3, 126.7 (q, $J_{C\text{-}F}$ 3.8), 124.8 (q, $J_{C\text{-}F}$ 3.8), 124.3 (q, $J_{C\text{-}F}$ 266), 100.3, 77.7, 72.6, 31.3, 22.7, 19.8, 14.2.

5f. δ_H ($CDCl_3$, 400 MHz): 8.98 (1H, s), 8.21 (1H, s), 7.97 (1H, s), 7.48-7.57 (3H, m), 7.39-7.28 (4H, m), 6.94 (1H, s), 6.03 (2H, s), 5.08 (2H, s)

5g. δ_H ($CDCl_3$, 400 MHz): 9.38 (1H, d, *J* 7.7), 8.04 (1H, s), 7.55 (1H, dd, 7.4, 0.7), 7.52 (2H, d, *J* 23.9), 7.42-7.33 (10H, m), 5.13(2H, s); δ_C ($CDCl_3$, 100 MHz): 133.6, 133.0, 132.9, 132.2, 131.8, 130.5, 130.3, 129.8, 129.7, 129.5, 129.4, 129.0, 128.3, 123.2, 123.1, 96.0, 87.0, 72.5.

5h. $_H$ ($CDCl_3$, 400 MHz): 9.33 (1H, d, *J* 11.7), 8.05 (1H, s), 7.54-7.49 (3H, m), 7.41-7.32 (7H, m), 6.91 (2H, *J* d, 8.8), 5.12 (2H, s), 3.87 (3H, s); δ_C ($CDCl_3$, 100 MHz,): 160.6, 133.7, 133.1, 132.7, 131.6, 130.5, 130.2, 130.0, 129.1, 128.2, 123.5, 115.3, 114.7, 96.1, 85.8, 72.4, 56.0.

5i. δ_H ($CDCl_3$, 400 MHz): 9.54 (1H, d, *J* 8.0), 8.46 (1H, d, *J* 4.4), 7.97 (1H, s), 7.55-7.47 (2H, m), 7.47-7.36 (3H, m), 7.22 (1H, dd, *J* 4.8, 8.1), 5.10 (2H, s), 2.38 (2H, t, *J* 6.6), 1.56 (2H, quint, *J* 7.4), 1.46 (2H, sextet, *J* 7.7), 0.95 (3H, t, *J* 7.3); δ_C ($CDCl_3$, 100 MHz): 150.5, 142.7, 134.6, 133.1, 131.3, 130.0, 129.5, 129.4, 128.3, 122.8, 97.4, 78.3, 72.2, 30.6, 22.5, 19.4, 14.0.

5j. δ_H ($CDCl_3$, 400 MHz): 9.61 (1H, dd, *J* 1.1, 8.4), 8.55 (1H, dd, *J* 1.5, 4.8), 8.03 (1H, s), 7.52-7.47 (2H, m), 7.47-7.41 (3H, m), 7.41-7.34 (5H, m), 7.30 (1H, dd, *J* 8.1, 4.8), 5.13 (2H, s); δ_C ($CDCl_3$, 100 MHz): 150.9, 142.3, 135.0, 133.1, 132.6, 131.1, 130.3, 130.1, 129.9, 129.8, 129.0, 128.8, 123.6, 122.1, 95.3, 86.5, 72.7.

5k. δ_H ($CDCl_3$, 400 MHz): 8.32-8.10 (1H, m), 7.46-7.30 (5H, m), 4.85 (2H, s), 2.85 (2H, m), 2.28 (2H, t, *J* 6.6), 2.22 (2H, s), 1.57 (4H, t, *J* 2.9), 1.44-1.30 (4H, m), 0.92 (3H, t, *J* 7.3); δ_C ($CDCl_3$, 100 MHz): 136.1, 134.1, 133.9, 130.0, 129.5, 129.3, 127.0, 99.3, 80.4, 71.6, 32.3, 31.4, 27.2, 22.6, 22.2, 19.9, 14.2.

Representative cyclization of (*E*)-ketoximes into isoquinoline-*N*-oxides. To solution of (*E*)-**1a** (40 mg, 0.231 mmol) in CH_2Cl_2 (2.0 mL) was added Au(IMes)Cl (6.2 mg, 0.0115 mmol), AgOTf (3.0 mg, 0.0115 mmol) and TfOH (0.12 mL of 0.10 M solution in CH_2Cl_2, 0.0115 mmol), and the mixture was stirred for 1 h at rt. The reaction was terminated by addition of Et_3N (5 drops), the mixture was concentrated under vacuum, and the residue was purified by silica gel chromatography (MeOH–CH_2Cl_2 = 1 : 30) to give 33.2 mg (83%) of **2a** as a pale brown solid (R_f = 0.4, MeOH–CH_2Cl_2 = 1 : 10).

Representative cyclization of (*Z*)-ketoximes into isoindoles. To solution of (*Z*)-**1a** (40 mg, 0.231 mmol) in CH_2Cl_2 (2.0 mL) was added Au(IMes)Cl (6.2 mg, 0.0115 mmol) and AgOTf (3.0 mg, 0.0115 mmol). The resulting mixture was heated at 70 °C for 1 h, then cooled to rt and the reaction was quenched by the addition of Et_3N (5 drops). The mixture was concentrated under vacuum and the residue was purified by silica gel chromatography (EtOAc–Hex = 1 : 10) to give 26.4 mg (66%) of **3a** as white solid (R_f = 0.3, EtOAc–Hex = 1 : 4).

Representative cyclization of nitrones into isoindoles. To solution of **5d** (40 mg, 0.137 mmol) in CH_3NO_2 (1.4 mL) was added [*t*-Bu_2P(*o*-biphenyl)Au]Cl (3.6 mg, 0.00685 mmol) and AgOTf (1.8 mg, 0.00685 mmol). The resulting mixture was heated at 70 °C for 30 min, then cooled to rt, and was quenched by the addition of Et_3N (5 drops). The mixture was concentrated under vacuum and the residue was purified by silica gel chromatography (EtOAc–Hex = 1 : 4) to afford 20.8 mg (52%) of **6d** as a white solid.

Characterization of products

2a. Pale brown solid (mp 61-62 °C);[20a] ν_{max} (film)/cm^{-1}: 3052, 2975, 2923, 1736 w, 1556 m, 1503 s, 1333 s, 1227 s; δ_H ($CDCl_3$,

400 MHz): 7.91 (1H, d, *J* 8.0), 7.70 (1H, d, *J* 8.2), 7.64-7.44 (3H, m), 2.92 (3H, s), 2.67 (3H, s); δ_C ($CDCl_3$, 100 MHz): 146.2, 146.1, 129.4, 128.7, 128.5, 128.3, 127.2, 124.5, 121.5, 19.1, 14.1; HRMS (EI^+) Calc. (M^+) 173.0841 found 173.0839.

3a. Brown solid (mp 199-202 °C); ν_{max} (film)/cm^{-1}: 3151, 3045, 2920, 1733 w, 1599 s, 1458 s, 1326 m, 1290 m, 1233 m; δ_H ($CDCl_3$, 400 MHz): 11.70 (1H, broad s), 7.84 (1H, d, *J* 8.4), 7.67 (1H, d, *J* 8.4), 7.36 (1H, t, *J* 7.3), 7.11 (1H, t, *J* 7.3), 2.70 (3H, s), 2.69 (3H, s); δ_C ($CDCl_3$, 100 MHz): 184.6, 131.6, 129.0, 127.6, 125.9, 121.9, 121.8, 121.0, 120.3, 28.1, 12.1; HRMS (EI^+) Calc. (M^+) 173.0841 found 173.0840.

2b. Pale brown solid (mp 77-79 °C); ν_{max} (film)/cm^{-1}: 3057, 2958, 2933, 2869, 1731 w, 1558 m, 1503 m, 1354 s, 1231 s, 1210 s; δ_H ($CDCl_3$, 400 MHz): 7.90 (1H, d, *J* 8.1), 7.71 (1H, d, *J* 8.3), 7.64-7.50 (2H, m), 7.48 (1H, s), 3.06 (2H, t, *J* 7.4), 2.91 (3H, s), 1.80 (2H, quintet, *J* 7.3), 1.50 (2H, sextet, *J* 7.3), 1.00 (3H, t, *J* 7.3); δ_C ($CDCl_3$, 100 MHz): 149.7, 146.1, 129.3, 128.6, 128.4, 128.1, 127.4, 124.4, 120.4, 31.4, 29.8, 23.3, 14.6, 14.1; HRMS (EI^+) Calc. (M^+) 215.1310 found 215.1310.

3b. Dark brown solid (mp 133-135 °C); ν_{max} (film)/cm^{-1}: 3182, 3062, 2949, 2927, 2868, 1706 m, 1587 s, 1596 m, 1460 s, 1227 m; δ_H ($CDCl_3$, 400 MHz): 11.85 (1H, broad s), 7.83 (1H, d, *J* 8.4), 7.67 (1H, d, *J* 8.4), 7.35 (1H, t, *J* 7.7), 7.10 (1H, t, *J* 7.7), 3.02 (2H, t, *J* 7.3), 2.72 (3H, s), 1.85 (2H, quintet, *J* 7.3), 1.51 (2H, sextet, *J* 7.3), 0.99 (3H, t, *J* 7.3); δ_C ($CDCl_3$, 100 MHz): 188.1, 131.5, 128.4, 127.5, 125.9, 121.9, 121.6, 120.8, 120.5, 40.0, 28.0, 23.5, 14.7, 12.7; HRMS (EI^+) Calc. (M^+) 215.1310 found 215.1311.

2c. White solid (mp 143-144 °C); ν_{max} (film)/cm^{-1}: 3406 m br, 3055, 2923, 2853, 1732 w, 1595 w, 1499 s, 1352 s, 1399 s, 1290 m, 1222 s; δ_H ($CDCl_3$, 400 MHz): 7.94 (1H, d, *J* 8.4), 7.86-7.72 (3H, m), 7.67 (1H, s), 7.62 (1H, t, *J* 7.4), 7.55 (1H, t, *J* 7.4), 7.53-7.38 (3H, m), 2.97 (3H, s); δ_C ($CDCl_3$, 100 MHz): 147.4, 146.3, 134.4, 130.5, 129.7, 129.35, 129.27, 129.0, 128.8, 128.7, 128.0, 124.5, 123.2, 14.3; HRMS (EI^+) Calc. (M^+) 235.0997 found 235.0996;

3c. Brown crystal (mp 189-190 °C); ν_{max} (film)/cm^{-1}: 3180, 3150, 3054, 2921, 2851, 1721 w, 1621 m, 1566 s, 1531 m, 1457 s, 1437 m, 1330 s, 1234 s; δ_H ($CDCl_3$, 400 MHz): 7.90-7.76 (2H, m), 7.65 (1H, d, *J* 8.11), 7.63-7.46 (3H, m), 7.15 (1H, t, *J* 7.5), 7.11-7.04 (2H, m), 6.99 (1H, s), 2.78 (3H, s); δ_C ($CDCl_3$, 100 MHz): 183.3, 141.1, 140.5, 135.4, 131.6, 130.2, 129.2, 129.1, 127.5, 126.2, 122.8, 122.3, 121.5, 120.9, 120.5, 18.4 (additional peaks were observed, presumably due to intramolecular hydrogen bonding); HRMS (EI^+) Calc. (M^+) 235.0997 found 235.0998.

4c. Yellow oil;[20b] ν_{max} (film)/cm^{-1}: 3409 (3780~2800, s br), 3048, 2921, 2854, 1665 m, 1604 m, 1418 s, 1398 s, 1289 s, 1189 s; δ_H ($CDCl_3$, 400 MHz): 8.26 (1H, d, *J* 8.4), 8.07 (1H, d, *J* 8.5), 7.74 (2H, d, *J* 7.7), 7.71 (1H, t, *J* 7.7), 7.62 (1H, t, *J* 7.3), 7.54 (2H, t, *J* 7.3), 7.42 (1H, t, *J* 7.3), 5.78 (1H, broad s), 2.92 (3H, s); δ_C ($CDCl_3$, 100 MHz): 151.0, 143.1, 137.9, 135.1, 130.2, 130.0, 129.6, 129.0, 128.6, 128.4, 127.8, 126.4, 122.7, 22.6; HRMS (EI^+) Calc. (M^+) 235.0997 found 235.0998.

2d. Brown oil; ν_{max} (film)/cm^{-1}: 3054, 2961, 2929, 2871, 1543 m, 1500 s, 1461 m, 1356 s, 1324 s, 1235 s; δ_H ($CDCl_3$, 400 MHz): 7.89 (1H, d, *J* 8.4), 7.69 (1H, d, *J* 7.3), 7.63-7.44 (3H, m), 3.41 (2H, t, *J* 7.7), 2.66 (3H, s), 1.81 (2H, sextet, *J* 7.4), 1.12 (3H, t, *J* 7.4); δ_C ($CDCl_3$, 100 MHz): 149.6, 146.1, 129.4, 128.5, 128.4, 128.1, 127.2, 124.4, 121.6, 29.4, 20.6, 19.1, 15.2; HRMS (EI^+) Calc. (M^+) 201.1154 found 201.1155.

3d. Brown crystal (mp 135-136 °C); ν_{max} (film)/cm^{-1}: 3399, 3174, 3048, 2956, 2926, 2866, 1724 m, 1597 s, 1503 s, 1429 m, 1354 w, 1289 w, 1265 w, 1219 w; δ_H ($CDCl_3$, 400 MHz): 11.48 (1H, broad s), 7.85 (1H, d, *J* 8.4), 7.69 (1H, d, *J* 8.5), 7.35 (1H, t, *J* 7.0), 7.10 (1H, t, *J* 8.1), 3.05 (2H, t, *J* 7.3), 2.69 (3H, s), 1.82 (2H, sextet, *J* 7.4), 0.99 (3H, t, *J* 7.3); δ_C ($CDCl_3$, 100 MHz): 184.7, 140.6, 136.1, 135.4, 130.2, 128.9, 127.5, 125.5, 122.9, 121.9, 121.7, 120.3, 28.9, 28.1, 23.6, 14.6 (additional peaks were observed, presumably due to the intramolecular hydrogen bonding); HRMS (EI^+) Calc. (M^+) 205.1154 found 205.1154.

3e. Yellow crystal (mp 125-127 °C); ν_{max} (film)/cm^{-1}: 3259, 2958, 2930, 2871, 1703 s, 1612 m, 1453 s, 1410 w, 1346 w, 1315 w, 1194 w; δ_H ($CDCl_3$, 400 MHz): 11.00 (1H, broad s), 8.00 (1H, d, *J* 8.4), 7.91 (1H, d, *J* 8.4), 7.77 (2H, d, *J* 7.7), 7.53 (2H, t, *J* 7.3), 7.43 (1H, t, *J* 7.4), 7.40 (1H, t, *J* 7.3), 7.20 (1H, t, *J* 7.7), 3.05 (2H, t, *J* 7.7), 1.81 (2H, quintet, *J* 7.7), 1.50 (2H, sextet, *J* 7.4), 0.99 (3H, t, *J* 7.4); δ_C ($CDCl_3$, 100 MHz): 189.4, 131.6, 130.0, 129.2, 128.2, 127.4, 124.7, 123.4, 122.5, 120.7, 40.6, 27.7, 23.4, 14.7; HRMS (EI^+) Calc. (M^+) 277.1467 found 277.1466.

3f. Yellow solid (mp 61-63 °C);[20d] ν_{max} (film)/cm^{-1}: 3196, 3056, 2921, 2852, 1703, 1609 s, 1504 w, 1459 s, 1348 m, 1232 s; δ_H ($CDCl_3$, 400 MHz): 11.15 (1H, broad, s), 8.0 (1H, d, *J* 8.4), 7.93 (1H, d, *J* 8.4), 7.78 (2H, d, *J* 8.0), 7.53 (2H, t, *J* 7.4 Hz), 7.48-7.36 (2H, m), 7.21 (1H, t, *J* 7.7). 2.74 (3H, s); δ_C ($CDCl_3$, 100 MHz): 185.3, 132.1, 131.6, 129.9, 129.3, 128.9, 128.3, 127.5, 124.7, 123.4, 122.8, 122.5, 120.6, 28.4; HRMS HRMS (EI^+) Calc. (M^+) 235.0997 found 235.0996.

3g. Yellow solid (mp 139-142 °C); ν_{max} (film)/cm^{-1}: 3177, 3028, 2970, 2929, 2856, 1738 s, 1561 s, 1532 s, 1445 s, 1365 m, 1227 s; δ_H ($CDCl_3$, 400 MHz): 11.28 (1H, broad s), 7.97 (1H, d, *J* 8.4), 7.92 (1H, d, *J* 8.8), 7.79 (2H, d, *J* 7.3), 7.51 (2H, t, *J* 7.3), 7.41 (1H, t, *J* 7.3), 7.30 (1H, t, *J* 7.7), 7.17 (1H, t, *J* 7.7), 6.57 (1H, m), 2.62-2.42 (2H, m), 2.42-2.24 (2H, m), 1.96-1.50 (4H, m); δ_C ($CDCl_3$, 100 MHz): 186.7, 140.1, 136.3, 132.4, 131.8, 129.8, 129.1, 128.4, 126.9, 124.9, 123.5, 122.0, 121.9, 121.5, 26.4, 25.4, 23.0, 22.6; HRMS (EI^+) Calc. (M^+) 301.1467 found 301.1467;

3h. Dark brown solid (mp 137-140 °C); ν_{max} (film)/cm^{-1}: 3182, 3150, 3052, 2929, 2856, 1713 w, 1557 s, 1532 m, 1446 s, 1374 m, 1326 m, 1228 m; δ_H ($CDCl_3$, 400 MHz): 11.67 (1H, broad s), 7.83 (1H, d, *J* 8.8), 7.63 (1H, d, *J* 8.0), 7.26 (1H, t, *J* 8.2), 7.08 (1H, t, *J* 7.7), 6.49 (1H, m), 2.70 (3H, s), 2.62-2.44 (2H, m), 2.40-2.24 (2H, m), 1.94-1.72 (4H, m); δ_C ($CDCl_3$, 100 MHz): 185.7, 140.5, 139.9, 135.4, 135.0, 132.0, 130.2, 129.8, 127.1, 126.1, 122.8, 121.8, 121.4, 121.2, 120.0, 26.3, 25.6, 23.1, 22.7, 18.4 (additional peaks were observed, presumably due to hydrogen bonding); HRMS (EI^+) Calc. (M^+) 239.1310 found 239.1310.

3i. Yellow solid (mp 143-145 °C); ν_{max} (film)/cm^{-1}: 3195, 2923, 2851, 1731 m, 1586 m, 1455 s, 1303, 1235; δ_H ($CDCl_3$, 400 MHz): 11.60 (1H, broad s), 8.08-7.93 (1H, m), 7.93-7.74 (4H, m), 7.67-7.57 (1H, m), 7.57-7.48 (4H, m), 7.48-7.40(1H, m), 7.40-7.30(1H, m), 7.24-7.10(2H, m); δ_C ($CDCl_3$, 100 MHz): 184.5, 140.8, 133.8, 131.9, 131.5, 130.2, 130.0, 129.4, 129.1, 128.4, 127.3, 125.1, 123.8,

122.3, 122.2, 121.3; HRMS (EI$^+$) Calc. (M$^+$) 297.1155 found 297.1157.

4i. Yellow oil; ν_{max} (film)/cm^{-1}: 3391(3700-2800, broad s), 3048, 2909, 2843, 1695 m, 1598 w, 1518 m, 1395 s, 1304 s; δ_H ($CDCl_3$, 400 MHz): 8.33 (1H, d, *J* 8.5), 8.07 (1H, d, *J* 8.5), 7.82 (2H, d, *J* 7.3), 7.78-7.66 (3H, m), 7.64-7.36 (7H, m), 5.90 (1H, broad s); δ_C ($CDCl_3$, 100 MHz): 153.6, 143.7, 140.4, 137.8, 135.7, 130.8, 130.2, 129.9, 129.7, 129.2, 128.9, 128.8, 127.9, 127.8, 122.5; HRMS (EI$^+$) Calcd for (M$^+$) 297.1154 found 297.1155.

4j. ν_{max} (film)/cm^{-1}: 3062, 2923, 2854, 1721 s, 1602, 1564, 1488, 1369, 1329, 1283, 1250; δ_H ($CDCl_3$, 400 MHz): 9.14 (1H, s), 8.52 (1H, d, *J* 8.1), 8.11 (1H, d, *J* 9.6), 8.07 (1H, d, *J* 8.5), 7.91 (1H, t, *J* 7.3), 7.81 (1H, t, *J* 7.3), 6.66 (1H, d, *J* 9.5); δ_C ($CDCl_3$, 100 MHz): 160.7, 150.1, 146.6, 132.2, 130.6, 130.5, 130.3, 130.1, 128.3, 126.3, 122.1, 118.5; HRMS (EI$^+$) Calcd for (M$^+$) 197.0477 found 197.0476.

6c. ν_{max} (film)/cm^{-1}: 3093, 3056, 3000, 2948, 1769, 1714 s, 1627, 1416, 1335, 1216, 1171; δ_H ($CDCl_3$, 400 MHz): 7.87 (1H, d, *J* 8.8), 7.64 (1H, d, *J* 8.4), 7.39 (1H, s), 7.31 (1H, app t, *J* 7.3), 7.12 (1H, app t, *J* 7.4 z), 4.27 (3H, s), 2.72 (3H, s); δ_C ($CDCl_3$, 100 MHz): 187.2, 129.9, 126.6, 125.4, 124.7, 122.4, 121.5, 120.5, 40.9, 31.1; HRMS (EI$^+$) Calcd for (M$^+$) 173.0841 found 173.0842.

6d. White crystal (mp 90-92 °C); ν_{max} (film)/cm^{-1}: 3064, 3033, 2958, 2932, 2872, 1716, 1614, 1394 cm^{-1}; δ_H ($CDCl_3$, 400 MHz): 7.87 (1H, d, *J* 8.8), 7.64 (1H, d, *J* 8.5), 7.46 (1H, s), 7.40-7.19 (4H, m), 7.19-7.02 (3H, m), 5.94 (2H, s), 2.02 (2H, t, *J* 7.3), 1.74 (2H, quintet, *J* 7.7 Hz), 1.29 (2H, sextet, *J* 7.3 Hz), 0.94 (3H, t, *J* 7.3 Hz); δ_C ($CDCl_3$, 100 MHz): 190.5, 138.1, 135.0, 129.5, 128.3, 128.0, 126.7, 124.9, 124.8, 122.5, 121.8, 121.3, 120.9, 55.5, 42.5, 27.5, 23.3, 14.7; HRMS (EI$^+$) Calcd for (M$^+$) 291.1623, found 291.1623.

6e. White crystal (mp 81-83 °C); ν_{max} (film)/cm^{-1}: 3112, 3066, 2959, 2933, 2872, 1719 s, 1637 s, 1547 m, 1496 s, 1448 s, 1334 s, 1263 s, 1172 s; δ_H ($CDCl_3$, 400 MHz): 7.98 (1H,s), 7.96 (1H, s), 7.58 (1H, s) 7.45 (1H, d, *J* 9.2), 7.28-7.20 (4H, m,), 7.12 (1H, d, *J* 6.6), 5.96 (2H, s), 3.02 (2H, t, *J* 7.3 Hz), 1.74 (2H, quintet, *J* 7.3 Hz), 1.39 (2H, sextet, *J* 7.4), 0.94 (3H, t, *J* 7.3); δ_c ($CDCl_3$, 100 MHz): 190.8, 137.4, 129.6, 129.5, 128.6, 128.1, 125.7, 125.2 (q, J_{C-F} = 271), 124.6 (q, J_{C-F} = 32 Hz), 123.2, 122.2 (q, J_{C-F} = 3.0), 121.9, 121.8, 120.1 (q, J_{C-F} = 5.4), 55.8, 42.6, 27.3, 23.2, 14.7; HRMS (EI$^+$) Calcd for (M$^+$) 359.1497, found 359.1502.

6g. δ_H ($CDCl_3$, 400 MHz): 7.69 (1H, d, *J* 6.9), 7.62-7.52 (2H, m), 7.45 (2H, t, *J* 7.7), 7.35-7.22 (7H, m), 7.04-7.94 (2H, m), 6.78 (1H, d, *J* 8.8), 5.97 (2H, s); ^{13}C NMR spectrum could not be taken due to its extreme instability (decomposed upon keeping at 4 °C in hours).

6h. Pale yellow oil; δ_H ($CDCl_3$, 400 MHz): 7.73 (2H, d, *J* 8.4), 7.58 (1H, d, *J* 6.6), 7.54 (1H, s), 7.54-7.48 (1H, m), 7.32-7.20 (4H, m), 7.05-7.06 (3H, m), 6.94 (2H, d, *J* 8.8), 5.92 (2H, s), 3.89 (3H, s); δ_C ($CDCl_3$, 100 MHz): δ 185.0, 162.7, 137.7, 133.9, 133.4, 131.8, 130.3, 128.9, 128.1, 127.7, 125.1, 124.4, 123.7, 122.2, 120.7, 122.1, 120.7, 120.6, 114.5, 113.7, 55.6, 54.0; Very unstable (slowly decomposed upon keeping at 4 °C overnight).

6i. ν_{max} (film)/cm^{-1}: 3090, 3031, 2955, 2926, 2869, 1730, 1626 s, 1548, 1440, 1329, 1277, 1193; δ_H ($CDCl_3$, 400 MHz): 8.69 (1H, dd, *J* 4.0, 1.4), 7.94 (1H, dd, *J* 8.0, 1.4), 7.37 (1H, s), 7.34-7.20 (3H, m), 7.16 (2H, d, *J* 6.6), 7.03 (1H, dd, *J* 8.5, 4.1), 5.98 (2H, s), 3.50 (2H, t, *J* 7.3), 1.71 (2H, quint, *J* 7.4), 1.39 (2H, sextet, *J* 7.7), 0.92 (3H, t, *J* 7.4 Hz); δ_C ($CDCl_3$, 100 MHz): 192.8, 150.9, 144.9, 137.6, 129.5, 129.4, 128.6, 128.3, 121.4, 121.2, 118.3, 117.5, 55.6, 42.0, 28.1, 23.2, 14.8.

6j. ν_{max} (film)/cm^{-1}: 3059, 3030, 2853, 1724, 1611 s, 1575, 1449, 1431, 1329, 1284, 1219, 1169; δ_H ($CDCl_3$, 400 MHz): 8. 47 (1H, dd, *J* 4.0, 1.4, Hz), 7.92 (1H, dd, *J* 8.4, 1.5 Hz), 7.88 (2H, broad d, *J* 6.9), 7.55 (1H, t, *J* 7.3), 7.48 (1H, s), 7.43 (2H, t, *J* 7.7), 7.35-7.26 (3H, m), 7.26-7.22 (2H, m), 6.96 (1H, dd, *J* 8.5, 4.4), 5.96 (2H, s); δ_C ($CDCl_3$, 100 MHz): 186.6, 151.2, 144.2, 140.5, 137.6, 132.7, 131.1, 129.5, 129.3, 128.8, 128.4, 121.8, 121.6, 118.5, 117.3, 55.1.

6k. Colorless oil; ν_{max} (film)/cm^{-1}: 3087, 3063, 2932, 2860, 1708 s, 1638 m, 1410 s, 1348 w, 1312 w; δ_H ($CDCl_3$, 400 MHz): 7.42-7.16 (3H, m), 7.08 (2H, d, *J* 7.0), 6.63 (1H, s), 5.50 (2H, s). 2.83 (2H, t, *J* 5.8 Hz, 2H), 2.63 (2H, t, *J* 7.4), 2.52 (2H, t, *J* 5.), 1.94-1.78 (2H, m), 1.78-1.68 (2H, m), 1.68-1.48 (2H, m), 1.29 (2H, sextet, *J* 7.3), 0.88 (3H, t, *J* 7.3); δ_C ($CDCl_3$, 100 MHz): 192.2, 139.7, 129.8, 129.1, 128.1, 127.7, 127.59, 127.56, 121.0, 53.6, 42.2, 27.3, 26.2, 24.5, 23.6, 23.2, 22.6, 14.7; HRMS (EI$^+$) Calcd for (M$^+$) 295.1936, found 295.1934.

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