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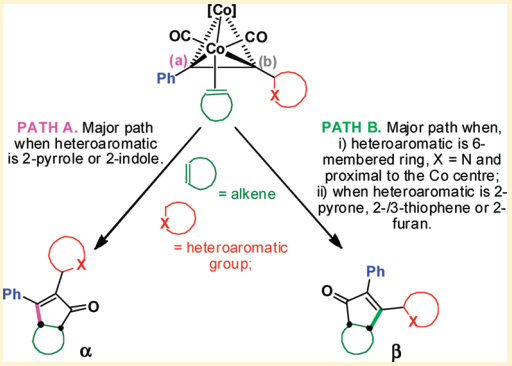
Regiochemistry in Cobalt-Mediated Intermolecular Pauson−Khand Reactions of Unsymmetrical Internal Heteroaromatic Alkynes with Norbornene

Benjamin E. Moulton, Adrian C. Whitwood, Anne K. Duhme-Klair, Jason M. Lynam, and Ian J. S. Fairlamb*

Department of Chemistry, University of York, Heslington, York, YO10 5DD, U.K.

Supporting Information

ABSTRACT: The intermolecular Pauson−Khand (PK) reactions of sterically comparable (2-phenylethynyl)heteroaromatic compounds with norbornene, mediated by $Co_2(CO)_8$ to give cyclopentenone products, were examined in this study. A synthetic protocol utilizing focused-microwave dielectric heating proved indispensable in the efficient synthesis of the PK cyclopentenone products. "π-Deficient" heteroaromatic substrates, e.g., 2-pyrones, and some "π-excessive" heteroaromatics such as 2- and 3-thiophene and 2-furan favor the β-position in the newly formed cyclopentenone ring. Other π-excessive heteroaromatics such as 2-pyrrole or 2-indole favor the α-position. A π-excessive 3-indole derivative gave a nearly equal mixture of regioisomers. The position of the nitrogen in pyridyl-containing alkyne substrates also affects the regiochemical outcome of the PK reaction. A 2-pyridyl alkyne, possessing a proximal nitrogen, influences the regioselectivity relative to a 4-pyridyl variant quite dramatically, favoring the β-position in the newly formed cyclopentenone ring. A 2-pyrimidylalkyne exhibits similar behavior to the 2-pyridylalkyne. Compounds that do not participate in PK reactions with norbornene include (2-phenylethynyl)imidazoles and the related benzimidazoles, which promote rapid decomposition of the in situ generated (μ_2-alkyne)$Co_2(CO)_6$ complexes. This stands in contrast with other nitrogen-containing heteroaromatics, e.g., pyrrole-, indole-, and pyrimidine-derived compounds, which effectively undergo PK reactions. Overall, the type of heteroaromatic group dramatically influences PK regioselectivity, which can in part be explained by rationalization of the current reaction mechanism, but not fully.

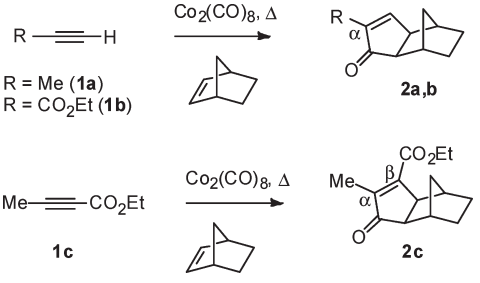


INTRODUCTION

The Pauson−Khand (PK) reaction,[1,2] the [2 + 2 + 1] cycloaddition reaction of an alkyne, alkene, and CO, the latter from $Co_2(CO)_8$, provides an efficient route to structurally diverse cyclopentenones, with many examples appearing in natural product syntheses.[3] Excellent regioselectivities are apparent for certain intermolecular PK reactions[4] (**1** → **2**, Scheme 1).

Experimental and theoretical studies have provided insight into the mechanism and origins of the regioselectivity; the latter aspect is an issue where unsymmetrical mono- (terminal) or disubstituted (internal) alkynes[5] are employed. Mechanistically, a reaction pathway was proposed by Magnus and Schore in 1985 (Scheme 2)[6] that involves CO dissociation from the in situ generated (μ_2-alkynyl)$Co_2(CO)_6$ complex (**I** → **II**) formed by reaction of the alkyne with $Co_2(CO)_8$ (step 1), creating a vacant coordination site for alkene coordination (step 2, **II** → **III**). The next step involves an irreversible insertion of the alkene π-bond into a Co−C bond starting from intermediate **IV** (step 3, **IV** → **V** → **VI**), followed by CO insertion which generates a 6-membered cobaltacycle **VII** (step 4). Reductive elimination (step 5) and subsequent loss of the dicobalt(0)carbonyl fragment (step 6) reveals the cyclopentenone product (**VII** → **VIII** → **IX**).

Scheme 1. Pauson−Khand Reaction with Unsymmetrical Terminal and Internal Alkynes



The regiochemistry observed in the cycloadduct product from the substituted alkyne (and/or alkene) can be explained by the steric crowding that evolves during C−C bond formation in step 3. Considering steric effects alone, larger substituents (R_L) appear at the α-position in the cyclopentenone ring. This has been observed in reactions of either propyne **1a** or ethyl propiolate **1b**

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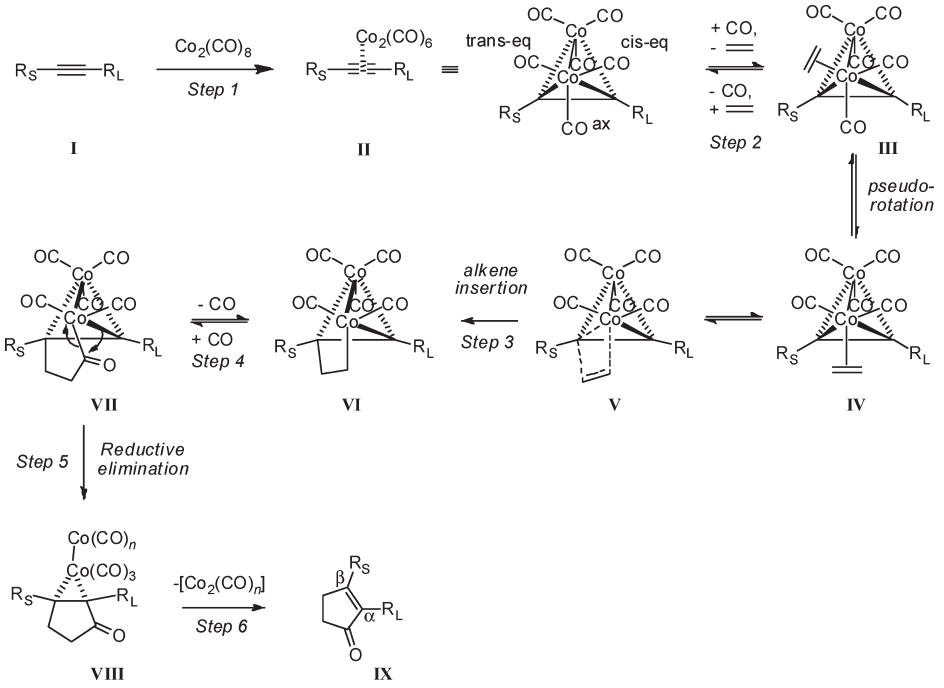
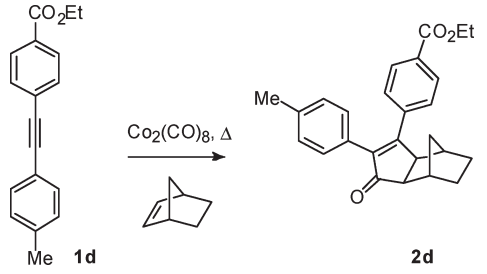
Scheme 2. General Accepted Mechanism for the Intermolecular PK Reaction[a]



[a] R_L = large variable substituent; R_S = small variable substituent; trans-eq refers to the equatorial CO ligand which is opposite to the large variable substituent, R_L; cis-eq refers to the equatorial CO ligand which is on the same side as the large variable substituent, R_L.

Scheme 3. "Push−pull" Internal Alkyne Leading to a Regioselective Intermolecular PK Reaction



with norbornene in the presence of $Co_2(CO)_8$ to give **2a** and **2b**, respectively (see Scheme 1).[7] Electronic effects can also alter the regiochemical outcome. For example, a similar reaction with ethyl butynoate **1c** resulted in the electron-accepting ester group residing at the β-position, exclusively (to give **2c**).

For a more sterically equivalent "push−pull" internal alkyne,[8] ethyl 4-(4′-methylphenylethynyl)benzoate **1d** (Scheme 3), PK reaction with $Co_2(CO)_6$ and norbornene gave one regioisomer (**2d**), where the electron-donating aryl group was found at the α-position and the electron-deficient aryl group at the β-position.[9]

Gimbert and Greene determined that electronic differences imposed by the alkyne substituents of the $(\mu_2\text{-}R^1C_2R^2)Co_2(CO)_6$ complex leads to the discriminate loss of a CO ligand, which then controls the regiochemistry of the reaction by affecting the relative position of alkene coordination (steps 2 → 3 in Scheme 2).[9] DFT calculations indicate that the equatorial CO ligands are the most labile and hence most likely to dissociate from $(\mu_2\text{-}R^1C_2R^2)Co_2(CO)_6$ complexes. Furthermore, the barrier for rotation in a $(\mu_2\text{-propyne})Co_2(\eta^2\text{-ethene})(CO)_5$ complex was found to be relatively low and can be overcome at room temperature (the η^2-ethene can move easily between equatorial and axial sites on cobalt).[10] The lowest lying transition state for alkene insertion affording the most stable cobaltacycle originates from the complex where the alkene is found inserting from the axial position.[11]

Further DFT calculations employing three alkynes (propyne, methyl 2-butynoate, and methyl propiolate) showed that alkene insertion is affected by the alkyne bond polarization.[12] The alkyne carbon carrying the most electron density was that involved in the alkene insertion step (step 3, Scheme 2) and subsequent C−C bond formation, even in cases where geometrical constraints were found less favorable.

Direct evidence for the formation of $(\mu_2\text{-alkyne})Co_2(CO)_5(\eta^2\text{-alkene})$ complexes (e.g., mimicking intermediate **IV** in Scheme 2) has attracted recent attention (e.g., by ESI-MS detection[13] or characterization in the solid state). For example, Evans and McGlinchey reported an arrested intermediate from an "enyne-type" substrate giving an $(\mu_2\text{-alkyne})Co_2(CO)_5(\eta^2\text{-alkene})$ complex.[14] Fox and co-workers reported the highly regioselective intermolecular PK reactions of chiral cyclopropenes,[15] which revealed the first examples of Co-complexes derived from the putative alkene-insertion intermediate. Crucially, the high regioselectivity was found to not derive from a selective alkene insertion step. Kinetic discrimination following alkene insertion affects the regiochemical outcome by allowing a minor diastereomer to give a ring-opened dinuclear cobalt complex, which does not deliver a PK product.

Use of decarbonylation agents (e.g., *N*-oxides, sulfides and sulfoxides, including synergistic effects[16]) under conventional heating[17] or microwave[18] and ultrasound[19] conditions promote PK reactions. Pryce, Browne, and co-workers recently reported that visible light (~410 nm) promoted the PK reaction of norbornene

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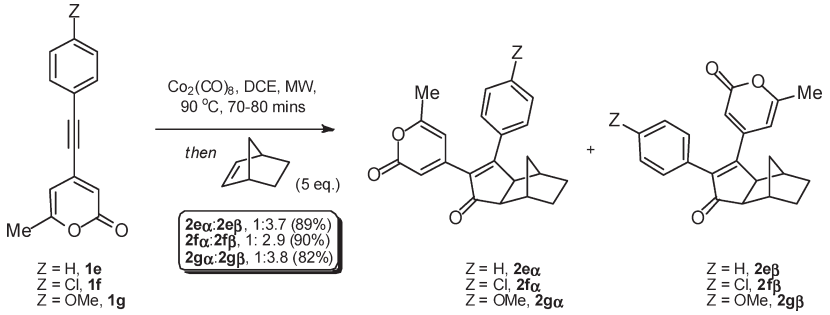
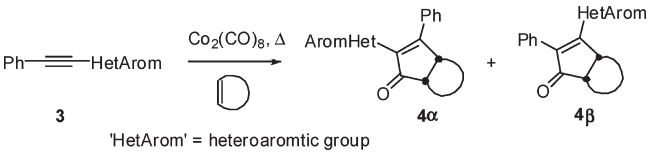
Scheme 4. Intermolecular Pauson−Khand Reactions of Alkynylated 2-Pyrones



Scheme 5. Intermolecular Pauson−Khand Reactions of Internal Alkynes 3 To Give 4α and 4*β*



with terminal alkynes (giving α-cycloadducts, as is the case for the thermal process).[20] The reaction occurs at ambient temperature, without addition of decarbonylation agents, in nonpolar solvents (e.g., toluene, hexane). The visible light promotes CO dissociation, facilitating the alkene insertion step.

Our interest in this area stems from a preliminary study[21] detailing the microwave-assisted cobalt-mediated PK reactions of three internal alkynes containing a 2-pyrone (**1e**−**g**) with norbornene to give the regioisomeric cyclopentenone products **2eα**−**gα** and **2e*β***−**g*β*** (Scheme 4). The π-deficient 2-pyrone moiety is found to preferentially occupy the β-position in the cyclopentenone product. Also, the factors affecting CO lability in various (μ_2-alkyne)$Co_2(CO)_6$ complexes have been of interest to us (tangentially as therapeutic CO-releasing molecules).[22]

Despite the synthetic examples described above, the intermolecular PK reactions of unsymmetrical internal alkynes with appropriate alkenes have yet to be comprehensively investigated. We have therefore examined a series of sterically equivalent, or near-equivalent, internal alkynes as substrates for intermolecular PK reactions. The use of (2-phenylethynyl)heteroaromatic compounds in PK reactions is fairly rare in the literature, this despite several (μ_2-alkynyl)$Co_2(CO)_6$ complexes being known (Scheme 5).[23] From the (2-phenylethynyl)heteroaromatic compounds **3** investigated as part of this study, and other similar compounds, we can reveal that the type of heteroaromatic group significantly affects the regiochemical outcome of intermolecular PK reactions mediated by cobalt (for sterically similar heteroaromatic components). Also, the position of the nitrogen atom in pyridyl-containing alkynes dramatically affects the regiochemical outcome of the reaction.

RESULTS

The internal alkynes, required for the PK reactions, were prepared by a very useful Sonogashira cross-coupling protocol (Table 1).[24] The precatalyst $PdCl_2(PPh_3)_2$ (1 mol %) was employed for most of the couplings, and a Pd/Cu ratio (1:3) was found to be beneficial.

The *N*-methyl derivatives of 2-pyrrole **3a**, 2-indole **3b**, and 3-indole **3c** were prepared in satisfactory yields (entries 1−3). The imidazole derivative **3d** was accessed in 19% yield (entry 4), while the benzimidazole **3e** was obtained in 58% yield (entry 5). The pyrimidine derivative **3f**, which enables the heteroaromatic ring size to be evaluated in comparison with **3e**, proceeded in 54% yield (entry 6). The three pyridine regioisomers **3g**−**i** were all obtained in good yields (entries 7−9). These derivatives allow the relative position of the nitrogen atom to be probed, whereas quinoline **3j** offers a sterically distinct but electronically similar alternative to the pyridine ring system (88% yield, entry 10). Thiophenes **3k** and **3l** were obtained in acceptable yields, although different catalyst systems were used (entries 11 and 12). A 2-furan derivative **3m** needed to be prepared by Stille coupling of 1-(2,2-dibromovinyl)benzene with (2-tributylstannyl)furan using catalytic $Pd_2(dba)_3$ (dba = (*E*,*E*)-dibenzylidene acetone); in situ base-mediated elimination gave **3m** in 61% yield (entry 13). A series of electron-deficient 2-pyrone derivatives were prepared for comparison with reported alkynes **1e**−**g**.[21] We were particularly interested in evaluating terminal alkyne **3o** [available by silyl deprotection of **3n** in 56% yield (entry 14)]. Alkyne **3p** represents a complementary analogue to **1e** (entry 15), as both contain a 2-pyrone group, which was obtained in 91% yield. The "push−pull" pyrrole-2-pyrone derivative **3q** allows a highly polarized alkyne[25] to be tested in the reaction, obtained in an acceptable yield of 55% (entry 16).

PK Reactions of Internal Heteroaromatic Alkynes. The library of internal alkynes **3a**−**q** were reacted with $Co_2(CO)_8$ and norbornene under focused microwave dielectric heating conditions. Norbornene was selected as the primary alkene based on its high reactivity[27] toward cobaltacycle formation. Following a screen of reaction conditions, we settled on Evans' microwave conditions[18a] for the PK reaction. The protocol involves stirring equimolar quantities of the internal alkyne and $Co_2(CO)_8$ in 1,2-dichloroethane (DCE) at room temperature (ca. 22 °C) for 1 h in a microwave tube, preforming the (μ_2-alkynyl)$Co_2(CO)_6$ complex in situ (in all cases). Norbornene (5 equiv) was then added and the reaction mixture heated to 90 °C in a sealed tube under microwave irradiation[28] until complete consumption of the (μ_2-alkynyl)$Co_2(CO)_6$ complex was observed (by TLC). It is important to note that because of pressure build-up in the reaction vessel the mixture was vented every 10 min for the first hour of the reaction.

In the first example, the π-excessive pyrrole alkyne substrate **3a** reacted with $Co_2(CO)_8$ and norbornene affording a mixture of both regioisomers in 73% combined yield (entry 1, Table 2). The major regioisomeric product of the reaction (**4aα**) formed crystals suitable for study by X-ray diffraction after being allowed

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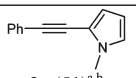
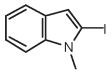
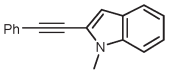
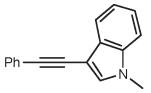
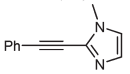
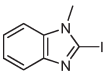
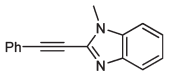
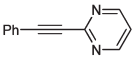
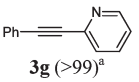
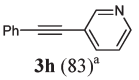
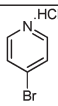
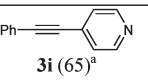
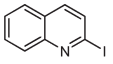
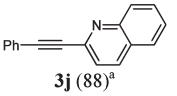
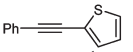
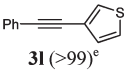
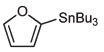
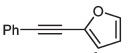
Table 1. Synthesis of (2-Phenylethynyl)heteroaromatic Substrates 3a−q by Sonogashira Cross-Coupling

Entry	ArX	Alkyne	Product / %
1			 **3a** (51)[a,b]
2			 **3b** (63)[a]
3			 **3c** (46)[a]
4			 **3d** (19)[a,c]
5			 **3e** (58)[a,c]
6			 **3f** (54)[a,c]
7			 **3g** (>99)[a]
8			 **3h** (83)[a]
9			 **3i** (65)[a]
10			 **3j** (88)[a]
11			 **3k** (53)[d]
12			 **3l** (>99)[e]
13			 **3m** (61)[f]
14			R = TMS, **3n** (49)[g] R = H, **3o** (56)[h]
15			**3p** (91)[a]
16			**3q** (55)[a]

[a] Terminal alkyne (1.1 equiv), $PdCl_2(PPh_3)_2$ (1 mol %), CuI (3 mol %), Et_3N (1.5 equiv), MeCN, reflux, 16 h. [b] Reaction run at room temperature (ca. 22 °C). [c] Reaction run at 110 °C in toluene. [d] $Pd(OAc)_2/P(o\text{-}C_6H_4Me)_3$ (1 mol % Pd; 2 mol % ligand) used in place of $PdCl_2(PPh_3)_2$. [e] $Pd(PPh_3)_4$ (1 mol %) used in place of $PdCl_2(PPh_3)_2$.[26] [f] Reaction by Stille coupling, $Pd_2(dba)_3$ (0.025 mmol, 2.5 mol % Pd), $P(p\text{-}C_6H_4OMe)_3$ (0.15 mmol), DMF, 80 °C, 10 h. [g] 10% Pd/C (20 wt.%), PPh_3 (25 wt %), CuI (4 mol %), Et_3N/CH_3CN (5:3, v/v), reflux 16 h. [h] Deprotection of **3n** was accomplished using TBAF (1 equiv) in THF at −78 °C for 30 min affording **3o** in 56% yield.

to stand in $CDCl_3$ over several weeks (see the Supporting Information). The X-ray crystal structure shows that the major regioisomeric product contains the *N*-methylpyrrole moiety in the α-position.

The π-excessive 2-indole alkyne substrate **3b** reacted with $Co_2(CO)_8$ and norbornene, affording a mixture of regioisomers in favor of **4bα**, with 87% combined yield (entry 2). The ratio of **4bα**:**4bβ** is similar, but not identical, to reactions of **3a**. The 3-indole alkyne substrate **3c** gave **4cα** and **4cβ** in a combined yield of 76% (entry 3), but surprisingly in an almost equal ratio. For the imidazole and benzimidazole alkynes **3d** and **3e** no reaction was observed (entries 4 and 5); note that the (μ_2-alkynyl)$Co_2(CO)_6$ complexes of **3d** and **3e** can be formed and characterized. However, a small amount of the known lactone **5** (Figure 1), which is derived from the carbonylative dimerization of two molecules of norbornene,[29] was formed under the reaction conditions in a yield of 2−7% with respect to the quantity of norbornene added. In a control reaction, heating $Co_2(CO)_8$ and norbornene at 90 °C for 20 min, under focused microwave heating, gave **5** in 19% yield. Therefore, under the PK reaction conditions used, the (μ_2-alkynyl)$Co_2(CO)_6$ complexes of **3d** and **3e** are unstable, readily decompose, and do not form PK cyclo-adducts of norbornene.

2-Pyrimidylalkyne **3f** favors formation of predominantly one regioisomer (entry 6). Pyrimidine is more electron-deficient than pyridine,[30] and the major regioisomer was assigned as **4fβ** (on the basis of $^1H-^1H$ NOESY studies).

Three pyridyl-containing alkynes, **3g**, **3h** and **3i**, containing the nitrogen at each of the 2-, 3-, and 4-positions, respectively, were investigated (entries 7−9). The ratio of regioisomers obtained from these PK reactions was dependent on the position of the nitrogen atom. For the 2-pyridyl substrate **3g**, a 9:1 ratio of regioisomers was observed in a combined yield of 71% (entry 7), which mirrors the regioselectivity observed using **3f** (entry 6).

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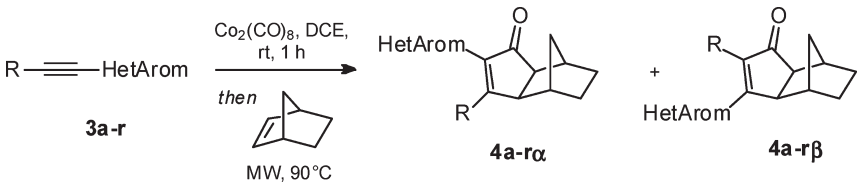
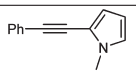
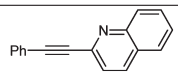
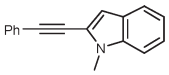
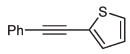
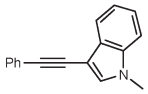
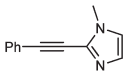
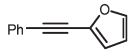
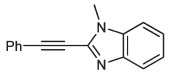
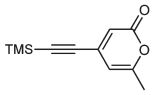
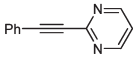
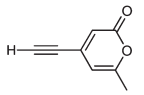
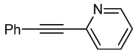
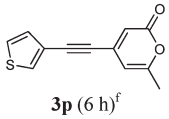
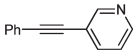
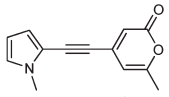
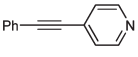
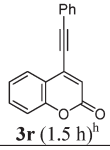
Table 2. Reaction Times and Yields Obtained from PK Reactions of Various (2-Phenylethynyl)heteroaromatic Substrates (3a−q and Reported 3r[32])[a]



Entry	Alkyne (**3**)	4α /%	4β / %	Entry	Alkyne	4α /%	4β / %
1	 **3a** (3.3 h)	54[b]	19	10	 **3j** (1 h)	19[b]	57
2	 **3b** (6.3 h)	58	29	11	 **3k** (4.5 h)	23	52
3	 **3c** (6.3 h)	39	37	12	 **3l** (3.5 h)	30	62[b]
4	 **3d** (0.3 h)[c]	-	-	13	 **3m** (1 h)	20	68
5	 **3e** (1 h)[c]	-	-	14	 **3n** (24 h)	-	17
6	 **3f** (0.5 h)	4	75	15	 **3o** (2.8 h)	32[e]	-
7	 **3g** (1.5 h)	7	64	16	 **3p** (6 h)[f]	47	45
8	 **3h** (1.5 h)	33	58[b]	17	 **3q** (3.3 h)[g]	82	4
9	 **3i** (0.5 h)	94 {2.4:1}[d]		18	 **3r** (1.5 h)[h]	28	51

[a] Reaction conditions: (i) $Co_2(CO)_8$ (1 equiv), internal alkyne (1 equiv, **3a**−**r**), DCE, room temperature, 1 h; (ii) norbornene (5 equiv) added, 90 °C, MW, reaction time indicated in the internal alkyne column in brackets (cycloadduct numbering correlates with terminal alkyne, e.g., **3a** and **4a**; unless otherwise specified, the heteroaromatic group indicates its position in the cycloadduct. [b] Regioisomeric outcome proven by X-ray crystallography. [c] No cyclopentenone products observed (by TLC), only enol lactone **5** in 2−7% yield (based on consumption of norbornene). [d] The regiochemistry could not be determined. [e] The (μ_2-**3o**)$Co_2(CO)_6$ complex was prepared and characterized first and then subjected to the PK reaction (the 2-pyrone group is found exclusively in the α-position). [f] Cycloadducts α and β are indicated by the position of the thienyl group. [g] Cycloadducts α and β are indicated by the position of the 2-pyrrole group. [h] Reported PK reaction, see ref 32.

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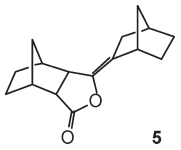


5

Figure 1. Side product formed in PK reactions of norbornene, $Co_2(CO)_8$, and internal alkynes **3d** or **3e**.

The 3-pyridyl substrate **3h** gave a 91% combined yield and regioisomeric ratio of 1.8:1, while the 4-pyridyl substrate **3i** gave a yield of 94% and regioisomeric ratio of 2.4:1. The large difference between the 2-pyridyl substrate and the 3- and 4-pyridyl substrates is of particular note. From the reaction of 3-pyridyl substrate **3h**, crystals of the major regioisomeric product were found suitable for study by X-ray diffraction (by slow evaporation from a CH_2Cl_2 solution), which confirmed the structure as **4hβ** (see the Supporting Information).

The quinolinyl alkyne derivative **3j** (entry 10) was expected to share similar electronic properties with 2-pyridyl substrate **3g**, although the steric bulk is perhaps increased. The regioisomeric ratio for **4jα**/**4jβ** was determined to be 1:3, so the larger quinoline group had diminished the regioselectivity relative to **3g**. The minor regioisomeric product gave crystals suitable for study by X-ray diffraction (after being allowed to stand in $CDCl_3$), which confirmed the structure as **4jα** (see the Supporting Information).

For both the 2-thienylalkyne (**3k**) and 3-thienylalkyne (**3l**) derivatives, a regioisomeric ratio of ca. 2:1 was observed; each reaction also proceeded in good product yield (entries 11 and 12). The X-ray crystal structure of the major regioisomeric product from the reaction of **3l** confirms its structure as **4lβ** (see the Supporting Information). A comparison of the ^{1}H NMR spectroscopic data of the products from both reactions indicates that the regiochemical outcome of the reaction is the same for both **3k** and **3l**.

2-Furanylalkyne **3m** reacted with norbornene in the PK reaction exceptionally well, affording the products in 88% yield (ratio of **4mα**/**4mβ** = 1:3.4; entry 13). The regioisomeric structures of **4mα** and **4mβ** were confirmed by comparison of the spectroscopic data of **4kα**/**4kβ** and **4lα**/**4lβ**. Trimethylsilylalkynyl-2-pyrone **3n** proved to be a poor substrate for the PK reaction (entry 14). Loss of the intermediate (μ_2-alkynyl)$Co_2(CO)_6$ was seen only after 24 h of microwave irradiation, with two products formed, as shown by TLC. However, only one product could be purified and characterized fully. By comparison of the ^{1}H NMR spectroscopic data with the reported data obtained for **2eα**−**gα** and **2eβ**−**gβ**,[21] it is proposed that the 2-pyrone group is positioned β to the carbonyl group (**4nβ**). This regioisomeric product is also biased by the preference for the bulky TMS group for the α-position in the cyclopentenone ring system. A negligible amount of the other regioisomer (**4nα**) was formed, for which full structural characterization was not possible.

It is important to note that alkynyl-2-pyrone **3o** is quite unstable. The intermediate (μ_2-**3o**)$Co_2(CO)_6$ complex was purified by flash chromatography on silica gel (in 52% yield). The reaction of (μ_2-**3o**)$Co_2(CO)_6$ (entry 15), under the standard microwave conditions, led to the isolation of one regioisomeric product (**4oα**) in 32% yield. A two-dimensional ^{1}H−^{1}H COSY experiment showed cross-peaks between the proton in the β-position of the cyclopentenone ring and the H-3a proton of the cyclopentenone framework, confirming the proposed structure of the regioisomer.

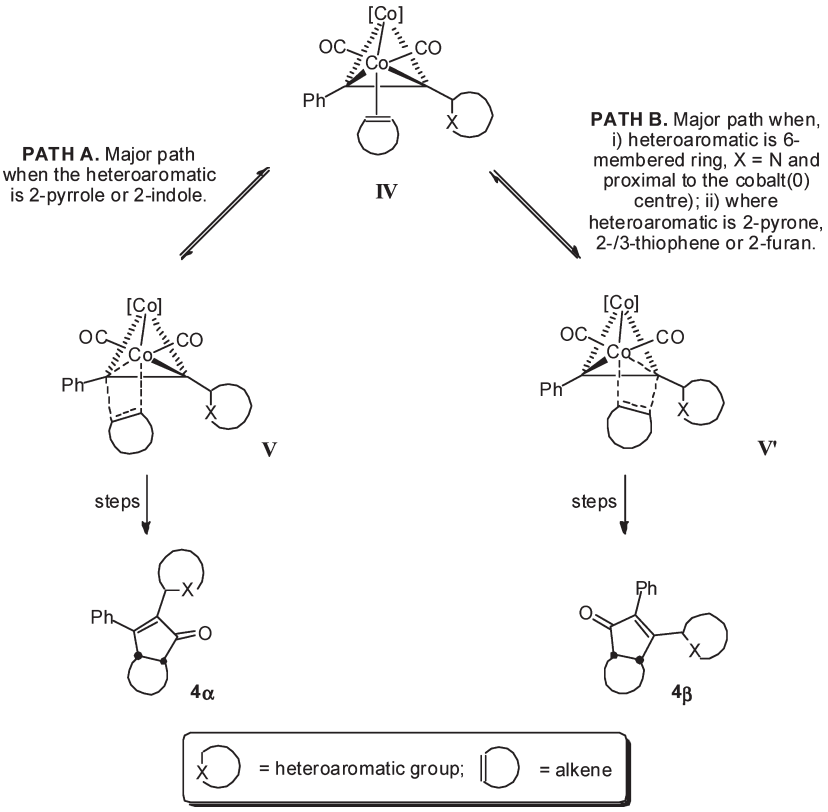
The PK reactions of 3-thienylalkynyl-2-pyrone **3p** and 2-pyrrolealkynyl-2-pyrone **3q** were conducted for comparison purposes with the other 2-pyrone substrates **3n** and **3o** (entries 16 and 17), in addition to the reported alkynyl-2-pyrones.[21] Alkyne **3p** afforded two regioisomeric products in a combined yield of 92% and a surprising 1:1 ratio. Alkyne **3q** afforded two regioisomeric products in a combined yield of 86% and ratio of 19.7:1 in favor of **4qα** (entry 17). Two-dimensional ^{1}H−^{1}H NOESY spectra of **4pα** and **4pβ** confirmed contacts between the norbornene unit and the β-positioned 2-pyrone group (in **4pα**), together with cross-peaks between the β-positioned thienyl group and norbornene (in **4pβ**), which allowed the structures of the regioisomers to be unambiguously assigned.

DISCUSSION

The regiochemical outcome of the intermolecular PK reactions of (2-phenylethynyl)heteroaromatic substrates with norbornene mediated by $Co_2(CO)_8$ is significantly affected by the type of heteroaromatic group. Moreover, the reaction times for the differing alkyne substrates vary significantly, and perhaps explain the lack of PK reactions reported for these types of substrates (despite a large number of (μ_2-HetAromC$_2$Ph)$Co_2(CO)_6$ complexes being reported in the literature[23]). Focused microwave dielectric heating has allowed us, in most cases, to synthesize the PK products derived from these internal alkynes, norbornene and $Co_2(CO)_8$, in reasonable reaction times. Sterically comparable heteroaromatic moieties significantly influence the regioselectivity of the PK reaction. The π-deficient heteroaromatics, e.g., 2-pyrones (**1e**, **3n**, **3p** and **3q**; note: exception of **3o** vide infra), favor the β-position in the newly formed cyclopentenone ring, which is in keeping with the reported PK reactions of **1e**−**g**.[21] The regiochemical outcome of **3n**, **3p**, and **3q** is also influenced by the other alkyne substituent. The π-excessive heteroaromatics, e.g., pyrrole (**3a**) and indole (**3b**), favor the α-position of the newly formed cyclopentenone ring. The 2- and 3-thiophenyl and 2-furan derivatives generally exhibit a bias toward the β-regioisomeric cyclopentenone products. However, indole derivative **3c** gave a near 1:1 mixture of regioisomeric products **4cα** and **4cβ**. While one could argue that steric effects are operative in PK reactions of either **3a** or **3b**, these steric effects are arguably removed in **3c** as the alkyne is at the 3-position relative to the *N*-methyl substituent. Therefore, in this unique case, the π-excessive 3-indole derivative does not give **4cα** as the major regioisomer; on the basis of electronic (and steric) arguments it would be expected to do so.

The presence of a proximal nitrogen on the alkyne heteroaromatic group was found to exert a profound effect on the regiochemical outcome of the PK reaction. For example, the position of the nitrogen in pyridyl-containing alkyne substrates (**3g**−**i**) gave quite different regiochemical outcomes. One may consider that the electronic character of the pyridyl ring system is likely affected as a consequence (2- and 4-pyridyl systems being more electron-deficient than 3-pyridyl systems). The regioselectivity is highest for 2-pyridyl substrate **3g** (giving mostly **4 gβ**), which crucially does not mirror the behavior of **3i**. The position of the sulfur atom in **3k** and **3l** does not affect the regiochemical outcome in the same way. While not obvious, it is possible that the proximal nitrogen atom in **3g** influences either the alkene coordination or insertion steps. The regiochemical outcome

Scheme 6. Heteroaromatic Group Effects on the Regioselectivity in the Intermolecular PK Reaction Mediated by $Co_2(CO)_8$[a]



[a] The Roman numerals used in this scheme mirror those used in Scheme 2; [Co] = $Co(CO)_3$.

from the reaction of 2-pyrimidylalkyne **3f** mirrors that of **3g**, giving preferentially **4fβ**. In studies reported by Itami and Yoshida, the directing effect of the 2-pyridylsilyl group was demonstrated in the Ru-catalyzed intermolecular Pauson−Khand-type reaction of alkenyl(2-pyridyl)silane, alkyne, and carbon monoxide.[31] While the 2-pyridyl group was located on the alkene and not the alkyne, it serves to highlight that a 2-pyridyl group can affect PK regioselectivity. In our work, it is also interesting to note differences between the 2-pyridyl and 2-quinoline substrates (**3g** and **3j**, respectively). It was expected that steric factors could dominate the regioisomeric outcome from the PK reaction of **3j** with norbornene (e.g., the bulky quinoline group ought to give **4jα** as the major regioisomer). However, the major regioisomeric product was still found to be **4jβ**. From the reported reaction of 4-(2-phenylethynyl)-2*H*-chromen-2-one **3r** with norbornene, mediated by $Co_2(CO)_8$ (Table 2, entry 18),[32] we know that the electron-deficient 2*H*-chromen-2-one (coumarin) gives more of the α-regioisomer **4rα** (relative to **3j**). Therefore, there could be a subtle steric difference between **3g** and **3j**, as evidenced by their regiochemical outcome in the PK reaction. Moreover, a similar difference is seen for the reported PK reactions of **1e** (2-pyrone) and **3r** (coumarin) with norbornene, mediated by $Co_2(CO)_8$.

For the (2-phenylethynyl)heteroaromatic substrates that do not participate in PK reactions with norbornene, e.g., (2-phenylethynyl)imidazole **3d** and the related benzimidazole compound **3e**, rapid decomposition of the in situ generated (μ_2-HetArom-C_2Ph)$Co_2(CO)_6$ complexes[33] likely occurs prior to alkene insertion. ^{1}H NMR spectra of (μ_2-**3d**/**3e**)$Co_2(CO)_6$ complexes in CD_2Cl_2 exhibit broad proton signals which we tentatively attribute to slippage of the cobalt(0) center onto the (benz)imidazole ring system, leading to decomposition under the microwave conditions. This stands in contrast to the 2-pyrrole, 2-indole, 3-indole, and pyrimidine substrates (**3a**−**c** and **3f**, respectively), which effectively undergo PK reactions with norbornene.

The 2-pyrone terminal alkyne **3o** gave **4oα** as the only regioisomer, which is an expected outcome based on steric arguments alone (this outcome parallels the reactivity of ethyl propiolate **1b**).[7] The modest yield from this reaction is attributed to the instability of **3o** and its associated (μ_2-**3o**)$Co_2(CO)_6$ complex under the microwave conditions used.

The regiochemical outcome of the PK reaction of 3-thienylalkynyl-2-pyrone **3p** with $Co_2(CO)_8$ and norbornene was expected to mirror the equivalent reaction with **1e**. However, a 1:1 mixture of **4pα** and **4pβ** were formed. It is unclear why there is no bias for one particular regioisomer. For 2-pyrrolealkynyl-2-pyrone **3q**, the regiochemical outcome of the PK reaction with $Co_2(CO)_8$ and norbornene behaved as expected, giving **4qα** as the major product.

We can broadly classify the effect of the different heteroaromatic moieties (where the other alkyne substituent is phenyl) in the current working model for the mechanism of the cobalt(0)−carbonyl-mediated intermolecular PK reactions of internal alkynes with alkenes (Scheme 6). Alkene insertion likely occurs at the *cis*-equatorial sites in complexes **II** → **III** (see Scheme 2),[34] and pseudorotation then places the alkene in the axial position (**IV**, Scheme 6), which is appropriately disposed to insert into one of two Co−C bonds, either distal (via **V**) or proximal (via **V′**) to the heteroaromatic group, which then gives α- and β-regioisomeric cyclopentenones, respectively.

It would be an understatement to suggest that a subtle combination of steric and electronic factors control the regioselectivity

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in intermolecular PK reactions of unsymmetrical internal alkynes, norbornene, and $Co_2(CO)_8$. Dynamic ligand effects could influence the cobalt center substantially, either by cobalt slippage on to the organic "heteroaromatic/aromatic" group, or in some cases, direct coordination. The aromatic stabilization energy of a given type of heteroaromatic/aromatic group may also be important.[35]

Concerning the reaction mechanism, the important findings reported by Overgaard and Platts[36] should perhaps be given more attention. The study indicates that the traditional view of the Co−Co bond in (μ_2-alkyne)$Co_2(CO)_6$ complexes may be incorrect (findings that affect how we view the precise structure of intermediate species **II**−**IV** in the current working mechanism).[37] It is suggested that the Co−Co bond is better thought of as a singlet diradical species (Co−Co bond order ∼0.25). Together with our observations, the potential involvement of Co radical/"pseudoradical" species would have profound implications for the mechanism of the PK reaction.

A final comment is required concerning a very recent report[38] which shows that a push−pull system, namely methyl 4-(4′-methoxyphenylethynyl)benzoate, reacted with norbornadiene and $Co_2(CO)_8$, which gave a mixture of regioisomeric cycloadducts (2.5:1). The major regioisomer was that where the electron donating aryl group was found in the α-position and the electron-withdrawing aryl group in the β-position (as expected). However, this outcome is markedly different from the reaction of **1d**, norbornene,[39] and $Co_2(CO)_8$ (Scheme 3), where the exclusive formation of only one regioisomeric product was observed.[9] These two outcomes, along with some of the findings detailed in our study, serve to highlight that the factors governing the regioselectivity in the intermolecular PK reactions are both subtle and complex.

In summary, we have probed the regioselectivity of the PK reaction by altering the heteroaromatic group in a series of unsymmetrical internal alkynes. Further mechanistic studies are required to fully understand the regiochemical observations made in this and in other studies. The following questions are of interest: (i) How does the heteroaromatic group affect the Co−Co bond order in complexes such as **I** (and subsequent intermediate species in the reaction mechanism)? (ii) What is the relevance and propagation of single electron cobalt species in PK reactions? (iii) How does varying the alkene substrate affect the regiochemical outcome from the reaction of "push−pull" internal alkynes and $Co_2(CO)_8$? Our findings relating to these questions will be reported in due course.

EXPERIMENTAL SECTION

General Methods. See the Supporting Information.

General Procedure for Sonogashira Cross-Coupling Reactions. The aryl bromide/iodide (1 equiv), the terminal acetylene (1.1 equiv), $PdCl_2(PPh_3)_2$ (precatalyst, 1 mol %), CuI (cocatalyst, 3 mol %), and dry acetonitrile (1.5 mL/mmol) were added to an oven-dried Schlenk tube charged with a magnetic stirrer bar. Dry triethylamine (1.5 equiv) was added, and the reaction was heated at reflux for 16 h. On completion, the reaction mixture was washed with H_2O, extracted with DCM, dried over $MgSO_4$, and filtered and the solvent removed in vacuo. The crude products were purified either by chromatography on silica gel, using hexane/EtOAc (1:0 to 7:3, v/v) as the eluent, or by recrystallization from hot EtOH.

*1-Methyl-2-(2-phenylethynyl)-1H-pyrrole (**3a**) (Entry 1, Table1).* Synthesized according to the general Sonogashira procedure, except it was performed at room temperature, with iodobenzene (143 mg, 0.08 mL, 0.76 mmol) and 1-methyl-2-ethynyl-1*H*-pyrrole (80 mg, 0.70 mmol), to afford the title compound as a dark oil (70 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.74 (s, 3H), 6.12 (dd, J = 3.8, 2.7 Hz, 1H), 6.49 (dd, J = 3.8, 1.7 Hz, 1H), 6.69 (dd, J = 2.7, 1.7 Hz, 1H), 7.31−7.36 (m, 3H), 7.48−7.51 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 34.6 (CH_3), 81.3 (4°), 93.0 (4°), 108.2 (CH), 114.8 (CH), 115.7 (4°), 123.4 (4°), 123.8 (CH), 127.9 (CH), 128.3 (CH), 131.1 (CH). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2961, 2205, 1604, 1322, 1094, 1011. LR(ESI-MS) m/z: 182 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{13}H_{12}N$ 182.0964, found 182.0959 $[M + H]^+$.

*1-Methyl-2-(2-phenylethynyl)-1H-indole (**3b**) (Entry 2, Table 1).* Synthesized according to the general Sonogashira procedure, except it was performed at 60 °C, with 2-iodo-1-methyl-1*H*-indole (350 mg, 1.4 mmol) and phenylacetylene (153 mg, 0.16 mL, 0.15 mmol) to afford the title compound as a yellow solid (203 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 (s, 3H), 6.85 (s, 1H), 7.14 (ddd, J = 8.0, 6.3, 1.7 Hz, 1H), 7.26−7.33 (m, 2H), 7.37−7.42 (m, 3H), 7.57−7.63 (m, 3H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 30.8 (CH_3), 81.2 (4°), 95.3 (4°), 107.5 (CH), 109.5 (CH), 120.2 (CH), 121.1 (CH), 122.2 (4°), 122.8 (4°), 123.1 (CH), 127.4 (CH), 128.6 (CH), 128.7 (4°), 131.5 (CH), 137.4 (4°). LR(ESI-MS) m/z: 232 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{17}H_{14}N$ 232.1121, found 232.1129 $[M + H]^+$.

*1-Methyl-3-(2-phenylethynyl)-1H-indole (**3c**) (Entry 3, Table 1).* Synthesized according to the general Sonogashira procedure, except it was performed at 60 °C, with 3-iodo-1-methyl-1*H*-indole (350 mg, 1.4 mmol) and phenylacetylene (153 mg, 0.16 mL, 0.15 mmol) to afford the title compound as a dark oil (147 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 3H), 7.23 (ddd, J = 7.9, 6.8, 1.3 Hz, 1H), 7.28−7.37 (m, 6H), 7.55−7.58 (m, 2H), 7.83 (ddd, J = 7.9, 1.3, 0.8 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 33.1 (CH_3), 83.1 (4°), 91.0 (4°), 97.0 (4°), 109.5 (CH), 120.2 (CH), 120.3 (CH), 122.7 (CH), 124.3 (4°), 127.4 (CH), 128.3 (CH), 129.1 (4°), 131.2 (CH), 132.2 (CH), 136.2 (4°). LR(ESI-MS) m/z: 232 {MH^+, 100}. HR(ESI-MS) m/z: calcd for $C_{17}H_{14}N$ 232.1121, found 232.1123 $[M + H]^+$.

*1-Methyl-2-(2-phenylethynyl)-1H-imidazole (**3d**) (Entry 4, Table 1).* Synthesized according to the general Sonogashira procedure, with 1-methyl-2-bromo-1*H*-imidazole (832 mg, 4.0 mmol) and phenylacetylene (449 mg, 0.48 mL, 4.4 mmol), and purification by chromatography on silica gel using petroleum ether/EtOAc (1:1, v/v) as the eluent to afford the title compound as a brown solid (137 mg, 19%). Mp = 52−56 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.79 (s, 3H), 6.93−6.97 (br s, 1H), 7.08−7.13 (br s, 1H), 7.35−7.39 (m, 3H), 7.55−7.57 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 33.7 (CH_3), 78.7 (4°), 92.8 (4°), 121.6 (4°-br), 122.0 (CH), 128.6 (CH), 129.1 (CH), 129.9 (CH), 131.8 (CH), 132.6 (4°-br). IR ν_{max} (CH_2Cl_2, cm^{-1}): 1570, 1458, 1411, 1339, 1108. LR(ESI-MS) m/z: 183 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{12}H_{11}N_2$ 183.0917, found 183.0916 $[M + H]^+$.

*1-Methyl-2-(2-phenylethynyl)-1H-benzo[d]imidazole (**3e**)[40] (Entry 5, Table 1).* Synthesized according to the general Sonogashira procedure, except it was performed at room temperature, with 1-methyl-2-bromo-1*H*-benzo[*d*]imidazole (438 mg, 1.7 mmol) and phenylacetylene (173 mg, 0.21 mL, 1.9 mmol) to afford the title compound as a yellow/brown solid (229 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.91 (s, 3H), 7.23−7.34 (m, 3H), 7.36−7.42 (m, 3H), 7.62−7.64 (m, 2H), 7.78 (ddd, J = 7.0, 1.3, 1.3 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 30.7 (CH_3), 78.7 (4°), 94.9 (4°), 109.4 (CH), 120.1 (CH), 121.2 (4°), 122.8 (CH), 123.8 (CH), 128.5 (CH), 129.6 (CH), 132.0 (CH), 134.8 (4°), 137.6 (4°), 143.0 (4°). LR(ESI-MS) m/z: 233 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{16}H_{13}N_2$ 233.1073, found 233.1074 $[M + H]^+$.

*2-(2-Phenylethynyl)pyrimidine (**3f**)[41] (Entry 6, Table 1).* Synthesized according to the general Sonogashira procedure, with 2-bromopyrimidine (477 mg, 3.0 mmol) and phenylacetylene (336 mg, 0.36 mL, 3.3 mmol) but at 110 °C in toluene, to afford the title compound as a brown

solid (293 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (dt, J = 4.9, 1.1 Hz, 1H), 7.34−7.41 (m, 3H), 7.64−7.67 (m, 2H), 8.75 (dd, J = 4.9, 1.1 Hz, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 87.9 (4°), 88.0 (4°), 119.6 (CH), 121.3 (4°), 128.4 (CH), 129.7 (CH), 132.6 (CH), 153.3 (4°), 157.3 (CH). LR(ESI-MS) m/z: 181 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{12}H_9N_2$ 181.0760, found 181.0765 $[M + H]^+$.

*2-(2′-Phenylethynyl)pyridine (**3g**)*[42] *(Entry 7, Table 1).* Synthesized according to the general Sonogashira procedure, except it was performed at 60 °C, with 2-bromopyridine (632 mg, 0.39 mL, 4.0 mmol) and phenylacetylene (449 mg, 0.48 mL, 4.4 mmol) to afford the title compound as a brown oil (716 mg, quant). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22 (ddd, J = 7.7, 4.9, 1.1 Hz, 1H), 7.33−7.37 (m, 3H), 7.51 (dt, J = 7.7, 1.1, 1.1 Hz, 1H), 7.57−7.61 (m, 2H), 7.67 (dt, J = 7.7, 7.7, 1.8 Hz, 1H), 8.61 (ddd, J = 4.9, 1.8, 1.1 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 88.5 (4°), 89.1 (4°), 122.2 (4°), 122.7 (CH), 127.1 (CH), 128.3 (CH), 128.9 (CH), 132.0 (CH), 136.1 (CH), 143.4 (4°), 150.0 (CH). LRCI-MS m/z: 180 {$(MH)^+$, 100}.

*3-(2′-Phenylethynyl)pyridine (**3h**)*[42] *(Entry 8, Table 1).* Synthesized according to the general Sonogashira procedure, with 3-bromopyridine (632 mg, 0.39 mL, 4.0 mmol) and phenylacetylene (449 mg, 0.48 mL, 4.4 mmol), to afford the title compound as a brown solid (537 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (ddd, J = 7.9, 4.9, 0.9 Hz, 1H), 7.35−7.39 (m, 3H), 7.53−7.57 (m, 2H), 7.81 (ddd, J = 7.9, 2.2, 1.7 Hz, 1H), 8.55 (dd, J = 4.9, 1.7 Hz, 1H), 8.77 (dd, J = 2.2, 0.9 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 85.9 (4°), 92.6 (4°), 120.4 (4°), 122.5 (4°), 123.0 (CH), 128.4 (CH), 128.8 (CH), 131.7 (CH), 138.4 (CH), 148.5 (CH), 152.2 (CH). LR(ESI-MS) m/z: 180 {$(MH)^+$, 100}.

*4-(2′-Phenylethynyl)pyridine (**3i**)*[43] *(Entry 9, Table 1).* Synthesized according to the general Sonogashira procedure, except it was performed at 60 °C, with 4-bromopyridine·HCl (583 mg, 3.0 mmol) and phenylacetylene (337 mg, 0.36 mL, 3.3 mmol), to afford the title compound as an off-white solid (347 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35−7.39 (m, 5H), 7.53−7.56 (m, 2H), 8.59 (dd, J = 4.6, 1.4 Hz, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 86.6 (4°), 94.0 (4°), 122.0 (4°),125.5 (CH), 128.5 (CH), 129.20 (CH), 131.5 (4°), 131.8 (CH), 149.7 (CH). LR(CI-MS) m/z: 180 {$(MH)^+$, 100}.

*2-(2-Phenylethynyl)quinoline (**3j**)*[44] *(Entry 10, Table 1).* Synthesized according to the general Sonogashira procedure, with 2-bromoquinoline (400 mg, 1.6 mmol) and phenylacetylene (176 mg, 0.19 mL, 1.7 mmol), to afford the title compound as light brown powder (316 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37−7.40 (m, 3H), 7.55 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.65−7.68 (m, 2H), 7.73 (ddd, J = 8.6, 6.9, 1.6 Hz, 1H), 7.80 (dd, J = 8.1, 1.6 Hz, 1H), 8.12−8.15 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 89.3 (4°), 89.9 (4°), 122.1 (4°), 124.3 (CH), 127.1 (CH), 127.1 (4°), 127.5 (CH), 128.4 (CH), 129.1 (CH), 129.3 (CH), 130.0 (CH), 132.2 (CH), 136.1 (CH), 143.6 (4°), 148.2 (4°). LR(ESI-MS) m/z: 230 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{17}H_{12}N$ 230.0964, found 230.0967 $[M + H]^+$.

*2-(2′-Phenylethynyl)thiophene (**3k**)*[45] *(Entry 11, Table 1).* Synthesized according to the general PK procedure, except it was performed at 60 °C, with 2-bromothiophene (652 mg, 0.39 mL, 4.0 mmol), phenylacetylene (449 mg, 0.48 mL, 4.4 mmol), and $Pd(OAc)_2$ (1 mol %) and tri-*o*-tolylphosphine (2 mol %) as catalyst system (in place of $PdCl_2(PPh_3)_2$), to afford the title compound as a white solid (392 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01−7.04 (m, 1H), 7.29 (s, 1H), 7.31 (dd, J = 1.7, 1.2 Hz, 1H), 7.34−7.38 (m, 3H), 7.53−7.54 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 82.6 (4°), 93.0 (4°), 122.9 (4°), 123.3 (4°), 127.1 (CH), 127.2 (CH), 128.3 (CH), 128.4 (CH), 131.4 (CH), 131.9 (CH). LR(CI-MS) m/z: 184 {M^+, 100}, 202 {$(MNH_4)^+$, 21}.

*3-(2′-Phenylethynyl)thiophene (**3l**)*[46] *(Entry 12, Table 1).* Synthesized according to the general Sonogashira procedure, except it was performed at 60 °C, with 3-bromothiophene (326 mg, 0.19 mL, 2.0 mmol), phenylacetylene (250 mg, 0.24 mL, 2.2 mmol), and $Pd(PPh_3)_4$ (1 mol %) as catalyst (in place of $PdCl_2(PPh_3)_2$), to afford the title compound as a white solid (368 mg, quant). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (dd, J = 5.0, 1.2 Hz, 1H), 7.30 (dd, J = 5.0, 3.0 Hz, 1H), 7.32−7.36 (m, 3H), 7.51−7.54 (m (with overlapping dd, J = 3.0, 1.2 Hz), 3H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 84.5 (4°), 88.8 (4°), 122.3 (4°), 123.2 (4°), 125.3 (CH), 128.2 (CH), 128.3 (CH), 128.6 (CH), 129.9 (CH), 131.5 (CH). LR(CI-MS) m/z: 184 {(M^+), 100}.

*2-(2′-Phenylethynyl)furan (**3m**) (Entry 13, Table 1).* 1-(2,2-Dibromovinyl)benzene (262 mg, 1.0 mmol), (2-tributylstannyl)furan (375 mg, 0.33 mL, 1.05 mmol), *N*,*N*-diisopropylethylamine (194 mg, 0.26 mL, 1.5 mmol), $Pd_2(dba)_3$ (21 mg, 0.025 mmol), and tris(4-methoxyphenyl)phosphine (53 mg, 0.15 mmol) were dissolved in DMF (5 mL) and the mixture heated at 80 °C for 10 h. The mixture was then diluted with Et_2O (20 mL), washed with H_2O (3 × 15 mL), dried over $MgSO_4$, and filtered before the solvent was removed in vacuo. Purification by chromatography on silica gel, using hexane/EtOAc (99:1, v/v) as the eluent, afforded the title compound as a clear oil (103 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.44 (dd, J = 3.4, 1.9 Hz, 1H), 6.67 (dd, J = 3.4, 0.8 Hz, 1H), 7.34−7.37 (m, 3H), 7.44 (dd, J = 1.9, 0.8 Hz, 1H), 7.51−7.55 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 79.4 (4°), 93.2 (4°), 111.1 (CH), 115.2 (CH), 122.3 (4°), 128.4 (CH), 128.7 (CH), 131.4 (CH), 137.1 (4°), 143.6 (CH). LR(ESI-MS) m/z: 139 {85}, 168 {M^+, 100}. HR(ESI-MS) m/z: calcd for $C_{12}H_8O$ 168.0575, found 168.0571 $[M]^+$.

*4-Ethynyl-6-methyl-2H-pyran-2-one (**3o**)*[47] *(Entry 14, Table 1).* Compound **3n** (350 mg, 1.7 mmol) was dissolved in THF (1.5 mL) and cooled to −78 °C. TBAF (1.8 mL of 1.0 M solution in THF) was added dropwise and the solution stirred for 30 min with the temperature maintained at −78 °C. When TLC showed complete consumption of starting material, H_2O (3 mL) was added and the mixture extracted with hexane (3 × 10 mL). The solvent was dried over $MgSO_4$ and filtered and the solvent removed in vacuo to afford the title compound as a white solid (126 mg, 0.9 mmol, 56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.23 (d, J = 0.9, 0.7 Hz, 3H), 3.47 (s, 1H), 5.97 (dq, J = 1.4, 0.9 Hz, 1H), 6.27 (dq, J = 1.4, 0.7 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 19.9 (CH_3), 79.4 (4°), 86.3 (CH), 105.2 (CH), 116.1 (CH), 137.8 (4°), 161.8 (4°), 162.3 (4°). LR(CI-MS) m/z: 135 {$(MH)^+$, 88}, 152 {$(MNH_4)^+$, 100}.

*6-Methyl-4-(2-(thiophene-3-yl)ethynyl)-2H-pyran-2-one (**3p**) (Entry 15, Table 1).* Synthesized according to the general Sonogashira procedure, with 4-bromo-6-methyl-2-pyrone[48] (325 mg, 1.7 mmol) and 3-ethynylthiophene (204 mg, 0.19 mL, 1.9 mmol), to afford the title compound as a pale brown crystalline solid (307 mg, 91%). Mp = 112−114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.24 (dd, J = 0.9, 0.7 Hz, 3H), 6.03 (dq, J = 1.4, 0.9 Hz, 1H), 6.27 (dq, J = 1.4, 0.7 Hz, 1H), 7.19 (dd, J = 5.0, 1.2 Hz, 1H), 7.34 (dd, J = 5.0, 3.0 Hz, 1H), 7.63 (dd, J = 3.0, 1.2 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 19.9 (CH_3), 85.3 (4°), 93.9 (4°), 105.3 (CH), 114.1 (CH), 120.5 (4°), 126.1 (CH), 129.8 (CH), 131.5 (CH), 138.9 (4°), 161.9 (4°), 162.2 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2211, 1723, 1634, 1547, 1512, 1446, 1384, 1359, 1313, 1216, 1138, 1030. LR(ESI-MS) m/z: 217 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{12}H_9O_2S$ 217.0318, found 217.0315 $[M + H]^+$.

*6-Methyl-4-(2-(1-methyl-1H-pyrr-2-yl)ethynyl)-2H-pyran-2-one (**3q**) (Entry 16, Table 1).* Synthesized according to the general Sonogashira procedure, with 4-bromo-6-methyl-2-pyrone[48] (229 mg, 1.2 mmol) and 1-methyl-2-ethynyl-1*H*-pyrrole (140 mg, 1.3 mmol), to afford the title compound as a brown powder (143 mg, 55%). Mp = 109−113 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.24 (dd, J = 0.9, 0.7 Hz, 3H), 3.72 (s, 3H), 5.99 (dq, J = 1.4, 0.9 Hz, 1H), 6.15 (dd, J = 3.9, 2.6 Hz, 1H), 6.18 (dq, J = 1.4, 0.7 Hz, 1H), 6.61 (dd, J = 3.9, 1.7 Hz, 1H), 6.77 (dd, J = 2.6, 1.7 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 19.9 (CH_3), 34.7 (CH_3), 91.0 (4°), 91.8 (4°), 104.9 (CH), 109.2 (CH), 111.9 (CH), 113.9 (4°), 118.3 (CH), 126.2 (CH), 139.0 (4°), 161.7 (4°), 162.4 (4°).

LR(ESI-MS) m/z: 214 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{13}H_{12}NO_2$ 214.0863, found 214.0870 $[M + H]^+$.

General Procedure for the Pauson–Khand (PK) Reactions. The alkyne (0.5 mmol), dicobalt(0) octacarbonyl (0.171 g, 0.5 mmol), and DCE (2 mL) were added to a microwave tube and charged with a magnetic stirrer bar. The reagents were stirred for 1 h at ambient temperature, after which time norbornene (0.235 g, 2.5 mmol) was added and the reaction was placed in the microwave reactor (100 W, 90 °C). Any pressure build-up was released from the vessel at 10 min intervals during the first hour of the reaction. The reaction was followed by TLC analysis (silica gel) and heated until the intermediate (μ_2-alkyne)$Co_2(CO)_6$ complex was no longer detected. On completion of the reaction, the solvent was removed in vacuo and the reaction mixture purified by chromatography on silica gel, using hexane/EtOAc (1:0 to 7:3, v/v) as the eluent, to afford the desired cycloadduct(s).

Compounds ***4aα*** *and* ***4aβ*** *from* ***3a*** *(Entry 1, Table 2).* Synthesized according to the general PK procedure except on 2.8 mmol scale, with **3a** (50 mg, 2.8 mmol), to afford **4aα** as a yellow solid (45 mg, 54%) and **4aβ** as a light brown solid (16 mg, 19%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-(1-Methyl-1*H*-pyrr-2-yl)-3-phenyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4aα**). Mp = 122–125 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.03 (d, J = 10.6 Hz, 1H), 1.20 (d, J = 10.6 Hz, 1H), 1.40–1.47 (m, 2H), 1.63–1.73 (m, 2H), 2.19 (br, 1H), 2.50 (d, J = 5.6 Hz, 1H), 2.60 (br, 1H), 3.14 (s, 3H), 3.25 (d, J = 5.6 Hz, 1H), 6.10 (dd, J = 3.6, 1.9 Hz, 1H), 6.18 (dd, J = 3.6, 2.6 Hz, 1H), 6.65 (dd, J = 2.6, 1.9 Hz, 1H), 7.27–7.29 (m, 2H), 7.30–7.35 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.8 (CH_2), 29.0 (CH_2), 31.8 (CH_2), 34.4 (CH_3), 39.0 (CH), 39.4 (CH), 50.2 (CH), 54.0 (CH), 108.4 (CH), 110.4 (CH), 123.4 (CH), 124.2 (4°), 128.2 (CH), 128.6 (CH), 129.9 (CH), 135.1 (4°), 135.3 (4°), 170.0 (4°), 208.7 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1691, 1620, 1526, 1445, 1336, 1198, 1157, 1088. LR(ESI-MS) m/z: 304 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{21}H_{22}NO$ 304.1696, found 304.1696 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-(1-Methyl-1*H*-pyrr-2-yl)-2-phenyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4aβ**). Mp = >89 °C dec. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.03 (d, J = 10.5 Hz, 1H), 1.19 (d, J = 10.5 Hz, 1H), 1.42–1.38 (m, 2H), 1.69–1.64 (m, 2H), 2.19 (br, 1H), 2.48 (d, J = 5.6 Hz, 1H), 2.60 (br, 1H), 2.86 (s, 3H), 2.86 (d, J = 5.6 Hz, 1H), 6.24 (dd, J = 3.8, 2.6 Hz, 1H), 6.47 (dd, J = 3.8, 1.7 Hz, 1H), 6.63 (dd, J = 2.6, 1.7 Hz, 1H), 7.24–7.21 (m, 3H), 7.31–7.26 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.86 (CH_2), 28.91 (CH_2), 31.7 (CH_2), 35.3 (CH_3), 39.0 (CH), 39.5 (CH), 51.8 (CH), 54.2 (CH), 109.2 (CH), 112.7 (CH), 126.7 (CH), 127.6 (CH), 128.4 (CH), 128.8 (CH), 129.6 (4°), 133.0 (4°), 139.2 (4°), 161.9 (4°), 207.8 (4°). ν_{max} (CH_2Cl_2, cm^{-1}): 2960, 2876, 1790, 1685, 1613, 1595, 1492, 1374, 1343, 1291, 1199, 1162. LR(ESI-MS) m/z: 304 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{21}H_{22}NO$ 304.1696, found 304.1704 $[M + H]^+$.

Compounds ***4bα*** *and* ***4bβ*** *from* ***3b*** *(Entry 2, Table 2).* Synthesized according to the general PK procedure, except on 2.5 mmol scale, with **3b** (58 mg, 2.5 mmol), to afford **4bα** as a yellow solid (51 mg, 58%) and **4bβ** as a yellow solid (26 mg, 29%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-(1-Methyl-1*H*-inden-2-yl)-3-phenyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4bα**). Mp = >165 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.09 (d, J = 10.5 Hz, 1H), 1.28 (d, J = 10.5 Hz, 1H), 1.42–1.53 (m, 2H), 1.61–1.78 (m, 2H), 2.24 (br, 1H), 2.58 (d, J = 5.5 Hz, 1H), 2.65 (br, 1H), 3.30 (s, 3H), 3.36 (d, J = 5.5 Hz, 1H), 6.50 (s, 1H), 7.10 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.21 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.24–7.35 (m, 6H), 7.60 (d, J = 7.9 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 28.8 (CH_2), 29.0 (CH_2), 30.7 (CH_3), 31.9 (CH_2), 39.1 (CH), 39.5 (CH), 50.5 (CH), 54.1 (CH), 103.1 (CH), 109.5 (CH), 119.5 (CH), 120.9 (CH), 121.6 (CH), 128.2 (4°), 128.4 (CH), 128.7 (CH), 130.4 (CH), 131.5 (4°), 134.4 (4°), 134.7 (4°), 137.8 (4°), 171.0 (4°), 208.3 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1694, 1626, 1527, 1465, 1393, 1344. LR(ESI-MS) m/z: 354 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{25}H_{24}NO$ 354.1852, found 354.1854 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-(1-Methyl-1*H*-inden-2-yl)-2-phenyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4bβ**). Mp = >71 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (d, J = 10.5 Hz, 1H), 1.28 (d, J = 10.5 Hz, 1H), 1.42–1.53 (m, 2H), 1.61–1.78 (m, 2H), 2.24 (br, 1H), 2.58 (d, J = 5.5 Hz, 1H), 2.65 (br, 1H), 3.30 (s, 3H), 3.36 (d, J = 5.5 Hz, 1H), 6.50 (s, 1H), 7.10 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.21 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.24–7.35 (m, 6H), 7.60 (d, J = 7.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.8 (CH_2), 28.9 (CH_2), 31.4 (CH_3), 31.7 (CH_2), 38.8 (CH), 39.6 (CH), 52.2 (CH), 54.2 (CH), 104.4 (CH), 109.9 (CH), 120.3 (CH), 121.1 (CH), 123.2 (CH), 127.9 (4°), 128.1 (CH), 128.4 (CH), 128.8 (CH), 132.0 (4°), 136.0 (4°), 139.0 (4°), 142.0 (4°), 161.3 (4°), 207.9 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1690, 1616, 1597, 1462, 1393, 1317. LR(ESI-MS) m/z: 354 {$(MH)^+$, 61}, 376 {$(MNa)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{25}H_{23}NNaO$ 376.1675, found 376.1672 $[M + Na]^+$.

Compounds ***4cα*** *and* ***4cβ*** *from* ***3c*** *(Entry 3, Table 2).* Synthesized according to the general PK procedure, except on 2.5 mmol scale, with **3c** (58 mg, 2.5 mmol), to afford **4cα** as a yellow solid (34 mg, 39%) and **4cβ** as a yellow solid (33 mg, 37%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-(1-Methyl-1*H*-inden-3-yl)-3-phenyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4cα**). Mp = >188 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00 (d, J = 10.4 Hz, 1H), 1.24 (d, J = 10.4 Hz, 1H), 1.43–1.50 (m, 2H), 1.64–1.71 (m, 2H), 2.17 (br, 1H), 2.52 (d, J = 5.4 Hz, 1H), 2.62 (br, 1H), 3.27 (d, J = 5.4 Hz, 1H), 3.82 (s, 3H), 6.64 (d, J = 8.0 Hz, 1H), 6.77 (t, J = 7.5 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 7.22–7.27 (m, 4H), 7.46 (d, J = 6.9 Hz, 2H), 7.51 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.90 (CH_2), 28.94 (CH_2), 31.7 (CH_2), 33.0 (CH_3), 38.8 (CH), 39.5 (CH), 50.5 (CH), 54.0 (CH), 105.4 (4°), 109.1 (CH), 119.1 (CH), 121.2 (CH), 121.3 (CH), 125.5 (4°), 128.3 (CH), 128.4 (CH), 129.1 (CH), 130.3 (CH), 135.9 (4°), 136.3 (4°), 137.0 (4°), 166.0 (4°), 209.5 (4°). ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2875, 1687, 1620, 1608, 1524, 1469, 1386, 1336, 1303, 1200, 1069. LR(ESI-MS) m/z: 354 {$(MH)^+$, 63}, 376 {$(MNa)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{25}H_{23}NNaO$ 376.1672, found 376.1673 $[M + Na]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-(1-Methyl-1*H*-inden-3-yl)-2-phenyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4cβ**). Mp = >192 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00 (d, J = 10.4 Hz, 1H), 1.31 (d, J = 10.4 Hz, 1H), 1.42–1.57 (m, 2H), 1.68–1.73 (m, 2H), 2.33 (br, 1H), 2.52 (d, J = 5.5 Hz, 1H), 2.61 (br, 1H), 3.45 (d, J = 5.5 Hz, 1H), 3.68 (s, 3H), 6.97 (s, 1H), 7.09 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H), 7.22–7.26 (m, 1H), 7.27–7.33 (m, 4H), 7.34–7.39 (m, 2H), 7.42 (d, J = 8.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 29.0 (CH_2), 29.1 (CH_2), 31.6 (CH_2), 33.3 (CH_3), 39.4 (CH), 39.6 (CH), 50.7 (CH), 54.0 (CH), 109.8 (CH), 110.8 (4°), 121.1 (CH), 121.7 (CH), 122.4 (CH), 126.2 (4°), 127.5 (CH), 128.8 (CH), 129.3 (CH), 132.8 (CH), 134.5 (4°), 137.2 (4°), 138.2 (4°), 165.8 (4°), 207.8 (4°). ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2875, 1673, 1613, 1584, 1570, 1522, 1474, 1465, 1366, 1317. LR(ESI-MS) m/z: 354 {$(MH)^+$, 100}, 376 {$(MNa)^+$, 81}. HR(ESI-MS) m/z: calcd for $C_{25}H_{24}NO$ 354.1852, found 354.1855 $[M + H]^+$.

Compounds ***4fα*** *and* ***4fβ*** *from* ***4f*** *(Entry 6, Table 2).* Synthesized according to the general PK procedure, with **3f** (90 mg, 5.0 mmol), to afford **4fα** as an off-white solid (4 mg, 3%) and **4fβ** as a white solid (114 mg, 75%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-Phenyl-2-(pyrimidin-2-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4fα**). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (d, J = 10.9 Hz, 1H), 1.38–1.48 (m, 3H), 1.63–1.73 (m, 2H), 2.17 (br, 1H), 2.58 (d, J = 5.4 Hz, 1H), 2.65 (br, 1H), 3.33 (d, J = 5.4 Hz, 1H), 7.22–7.30 (m, overlapped with residual $CDCl_3$, 5H), 7.33–7.36 (m, 3H), 8.79 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.9 (CH_2), 29.1 (CH_2), 31.9 (CH_2), 38.6 (CH), 39.7 (CH), 51.0 (CH), 54.7 (CH), 119.6 (CH), 128.5 (CH), 130.2 (CH), 157.4 (CH), 173.3 (4°). Remaining carbon peaks could not be observed even after extended collection times. IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 1696, 1624, 1559, 1424, 1354. LR(ESI-MS) m/z: 303 {$(MH)^+$,

46}, 325 {$(MNa)^+$, 100). HR(ESI-MS) *m/z*: calcd for $C_{20}H_{19}N_2O$ 303.1492, found 303.1498 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-Phenyl-3-(pyrimidin-2-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4fβ**). Mp = >175 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 (d, *J* = 10.6 Hz, 1H), 1.34 (d, *J* = 10.6 Hz, 1H), 1.38−1.49 (m, 2H), 1.61−1.74 (m, 2H), 2.31−2.35 (m, 1H), 2.53 (d, *J* = 5.5 Hz, 1H), 2.61−2.63 (m, 1H), 3.39 (d, *J* = 5.5 Hz, 1H), 7.18−7.20 (m, 3H), 7.25−7.29 (m, 3H), 8.72 (d, *J* = 4.9 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.6 (CH_2), 29.1 (CH_2), 31.6 (CH_2), 38.3 (CH), 39.9 (CH), 50.2 (CH), 54.2 (CH), 120.0 (CH), 127.9 (CH), 127.9 (CH), 129.1 (CH), 131.4 (4°), 146.3 (4°), 156.9 (CH), 164.1 (4°), 166.5 (4°), 209.6 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1698, 1566, 1556, 1421, 1359, 1244, 1198, 1170. LR(ESI-MS) *m/z*: 303 {$(MH)^+$, 100}, 325 {$(MNa)^+$, 25). HR(ESI-MS) *m/z*: calcd for $C_{20}H_{19}N_2O$ 303.1492, found 303.1500 $[M + H]^+$.

Compounds ***4gα*** *and* ***4gβ*** *from* ***4g*** *(Entry 7, Table 2).* Synthesized according to the general PK procedure, with **3g** (90 mg, 5.0 mmol), except purification. On completion of the reaction, the mixture was filtered through Celite with DCM (20 mL) and the solvent removed in vacuo. Chromatography on silica gel using DCM/MeOH (99:1, v/v) as the eluent afforded **4gα** as a white solid (11 mg, 7%) and **4gβ** as a white solid (96 mg, 64%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-Phenyl-2-(pyridin-2-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4gα**). Mp = 138−142 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.04 (d, *J* = 10.6 Hz, 1H), 1.32 (d, *J* = 10.6 Hz, 1H), 1.40−1.46 (m, 2H), 1.63−1.72 (m, 2H), 2.15 (br, 1H), 2.54 (d, *J* = 5.5 Hz, 1H), 2.63 (br, 1H), 3.28 (d, *J* = 5.5, Hz, 1H), 7.20 (ddd, *J* = 7.7, 5.0, 0.9 Hz, 1H), 7.24−7.30 (m, 5H), 7.31−7.34 (m, 1H), 7.67 (ddd, *J* = 7.8, 7.7 Hz, 1.9 Hz, 1H), 8.59 (ddd, *J* = 5.0, 1.9, 0.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.9 (CH_2), 29.1 (CH_2), 31.8 (CH_2), 38.6 (CH), 39.5 (CH), 50.9 (CH), 54.4 (CH), 122.6 (CH), 124.9 (CH), 128.3 (CH), 128.7 (CH), 129.9 (CH), 134.6 (4°), 136.2 (CH), 142.4 (4°), 149.9 (CH), 152.5 (4°), 172.3 (4°), 208.0 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1691, 1623, 1583, 1472, 1428, 1350, 1200, 1179. LR(ESI-MS) *m/z*: 302 {$(MH)^+$, 100}. HR-(ESI-MS) *m/z*: calcd for $C_{21}H_{20}NO$ 302.1539, found 302.1538 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-Phenyl-3-(pyridin-2-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4gβ**). Mp = 129−131 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.02 (d, *J* = 10.5 Hz, 1H), 1.25 (d, *J* = 10.5 Hz, 1H), 1.39−1.51 (m, 2H), 1.61−1.71 (m, 2H), 2.21 (br, 1H), 2.51 (d, *J* = 5.4 Hz, 1H), 2.61 (br, 1H), 3.49 (d, *J* = 5.4 Hz, 1H), 7.01 (ddd, *J* = 7.8, 1.0, 1.0 Hz, 1H), 7.18−7.121 (m, 3H), 7.30−7.34 (m, 3H), 7.45 (ddd, *J* = 7.8, 7.8, 1.8 Hz, 1H), 8.73 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.7 (CH_2), 29.1 (CH_2), 31.6 (CH_2), 38.4 (CH), 39.8 (CH), 50.0 (CH), 54.0 (CH), 123.5 (CH), 125.1 (CH), 128.1 (CH), 128.5 (CH), 129.2 (CH), 131.8 (4°), 135.7 (CH), 144.2 (4°), 149.9 (CH), 154.3 (4°), 169.0 (4°), 209.3 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2961, 2876, 1692, 1585, 1566, 1493, 1353, 1198, 1167. LR(ESI-MS) *m/z*: 302 {$(MH)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{21}H_{20}NO$ 302.1539, found 302.1532 $[M + H]^+$.

Compounds ***4hα*** *and* ***4hβ*** *from* ***3h*** *(Entry 8, Table 2).* Synthesized according to the general PK procedure, with **3h** (90 mg, 0.5 mmol), except purification. After chromatography on silica gel using DCM/MeOH (99:1, v/v) as the eluent, the solvent was removed in vacuo to give crude **4hα** first, which was passed through a small pad of silica using hexane/EtOAc (2:3, v/v) as the eluent to afford pure **4hα** as a white solid (50 mg, 33%). **4hβ** eluted from the first column, following **4hα**, affording an off-white solid (87 mg, 58%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-Phenyl-2-(pyridin-3-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4hα**). Mp = 116−119 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (d, *J* = 10.6 Hz, 1H), 1.21 (d, *J* = 10.6 Hz, 1H), 1.39−1.44 (m, 2H), 1.64−1.69 (m, 2H), 2.11 (br, 1H), 2.53 (d, *J* = 5.5 Hz, 1H), 2.61 (br, 1H), 3.23 (d, *J* = 5.5 Hz, 1H), 7.23−7.37 (m, 6H), 7.62 (ddd, *J* = 7.9, 2.1, 1.7 Hz, 1H), 8.36 (d, *J* = 1.7 Hz, 1H), 8.49 (dd, *J* = 4.8, 1.7 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 28.8 (CH_2), 28.9 (CH_2), 31.6 (CH_2), 38.2 (CH), 39.5 (CH), 51.2 (CH), 54.1 (CH), 123.2 (CH), 128.1 (4°), 128.3 (CH), 128.7 (CH), 129.9 (CH), 134.6 (4°), 136.8 (CH), 139.2 (4°), 148.7 (CH), 150.1 (CH), 171.9 (4°), 208.1 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2963, 2876, 1692, 1621, 1583, 1565, 1350, 1329, 1200, 1170, 1028. LR(ESI-MS) *m/z*: 302 {$(MH)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{21}H_{20}NO$ 302.1539, found 302.1544 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-Phenyl-3-(pyridin-3-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4hβ**). Mp = >136 °C dec. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.06 (d, *J* = 10.7 Hz, 1H), 1.23 (d, *J* = 10.7 Hz), 1.43 (m, 2H), 1.62−1.75 (m, 2H), 2.12 (br, 1H), 2.54 (d, *J* = 5.4 Hz, 1H), 2.63 (br, 1H), 3.22 (d, *J* = 5.4, Hz, 1H), 7.16 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.23 (br s, 1H), 7.29−7.33 (m, 3H), 7.55 (d, *J* = 7.8 Hz, 1H), 8.62 (br s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.7 (CH_2), 29.0 (CH_2), 31.6 (CH_2), 38.2 (CH), 39.5 (CH), 50.4 (CH), 54.1 (CH), 123.4 (br, CH), 128.2 (CH), 128.6 (CH), 129.2 (CH), 131.4 (4°), 135.7 (CH), 144.3 (4°), 149.3 (CH), 150.3 (4°), 165.9 (4°), 208.0 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1695, 1624, 1597, 1493, 1474, 1411, 1349, 1200, 1166, 1024. LR(ESI-MS) *m/z*: 302 {$(MH)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{21}H_{20}NO$ 302.1539, found 302.1536 $[M + H]^+$.

Compounds ***4iα*** *and* ***4iβ*** *from* ***3i*** *(Entry 9, Table 2).* Synthesized according to the general PK procedure, with **3i** (90 mg, 0.5 mmol), to afford **4iα** as a white solid (42 mg, 28%) and **4iβ** as a white solid (100 mg, 66%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-Phenyl-2-(pyridin-4-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4iα**). Selected peaks. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.00−1.06 (overlapping d's, *J* = 10.7 Hz, 1H), 1.16−1.22 (overlapping d's, *J* = 10.7 Hz, 1H), 1.35−1.44 (m, 2H), 1.59−1.74 (m, 2H), 2.05−2.10 (m, 1H), 2.53 (d, *J* = 5.5 Hz, 1H), 2.58−2.63 (br, 1H), 3.21 (d, *J* = 5.5 Hz, 1H), 7.10−7.20 (m, 3H), 7.22−7.37 (m, 4H), 8.50−8.80 (br s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.7 (CH_2), 28.9 (CH_2), 31.6 (CH_2), 38.2 (CH), 39.5 (CH), 51.1 (CH), 54.1 (CH), 128.3 (CH), 128.3 (CH), 128.6 (CH), 130.8 (CH), 134.3 (4°), 139.9 (4°), 141.8 (4°), 150.1 (CH), 172.6 (4°), 207.3 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2963, 2877, 1695, 1623, 1591, 1543, 1489, 1445, 1350, 1198, 1167. LR(ESI-MS) *m/z*: 302 {$(MH)^+$, 100}, 324 {$(MNa)^+$, 73}. HR(ESI-MS) *m/z*: calcd for $C_{21}H_{20}NO$ 302.1539, found 302.1544 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-Phenyl-3-(pyridin-4-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4iβ**). Mp = >148 °C dec. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.06 (d, *J* = 10.7 Hz, 1H), 1.21 (d, *J* = 10.7 Hz, 1H), 1.38−1.44 (m, 2H), 1.62−1.74 (m, 2H), 2.09 (br, 1H), 2.53 (d, *J* = 5.5 Hz, 1H), 2.63 (br, 1H), 3.15 (d, *J* = 5.5 Hz, 1H), 7.12−7.22 (m, 4H), 7.28−7.32 (m, 3H), 8.50−8.80 (br s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.7 (CH_2), 28.9 (CH_2), 31.6 (CH_2), 38.0 (CH), 39.6 (CH), 50.5 (CH), 54.1 (CH), 122.8 (br, CH), 128.4 (CH), 128.5 (CH), 129.1 (CH), 130.9 (4°), 143.0 (CH), 144.9 (4°), 150.3 (4°), 166.3 (4°), 208.1 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2963, 2877, 1695, 1623, 1591, 1543, 1489, 1445, 1350, 1198, 1167. LR(ESI-MS) *m/z*: 302 {$(MH)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{21}H_{20}NO$ 302.1539, found 302.1543 $[M + H]^+$.

Compounds ***4jα*** *and* ***4jβ*** *from* ***3j*** *(Entry 10, Table 2).* Synthesized according to the general PK procedure, with **3j** (115 mg, 5.0 mmol), to afford **4jα** as an off-white solid (33 mg, 19%) and **4jβ** as a white solid (99 mg, 57%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-Phenyl-2-(quinolyn-2-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4jα**). Mp = 206−211 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.08 (br d, *J* = 10.7 Hz, 1H), 1.40 (br d, *J* = 10.7 Hz, 1H), 1.42−1.50 (m, 2H), 1.67−1.75 (m, 2H), 2.22 (br, 1H), 2.59 (d, *J* = 5.6 Hz, 1H), 2.68 (br, 1H), 3.35 (d, *J* = 5.6 Hz, 1H), 7.20−7.24 (m, 2H), 7.28−7.32 (m, 3H), 7.52 (ddd, *J* = 7.8, 6.9, 0.9 Hz, 1H), 7.65 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.8 (CH_2), 29.1 (CH_2), 32.0 (CH_2), 38.7 (CH), 39.5 (CH), 51.0 (CH), 54.5 (CH), 122.6 (CH), 126.6 (CH), 127.3 (4°), 127.5 (CH), 128.3 (CH), 128.9 (CH), 129.3 (CH), 129.6

(CH), 130.0 (CH), 134.4 (CH), 136.2 (4°), 142.8 (4°), 148.3 (4°), 153.3 (4°), 172.8 (4°), 208.2 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2964, 2876, 1693, 1594, 1501, 1354. LR(ESI-MS) *m/z*: 352 {$(MH)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{25}H_{22}NO$ 352.1696, found 352.1703 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-Phenyl-3-(quinolyn-2-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4j*β***). Mp = 167−168 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.05 (d, *J* = 10.6 Hz, 1H), 1.31 (d, *J* = 10.6 Hz, 1H), 1.41−1.54 (m, 2H), 1.65−1.69 (m, 2H), 2.30 (br, 1H), 2.56 (d, *J* = 5.5 Hz, 1H), 2.65 (br, 1H), 3.66 (d, *J* = 5.5, Hz, 1H), 7.05 (d, *J* = 8.5 Hz, 1H), 7.23 (dd, *J* = 6.7 Hz, 3.0 Hz, 2H), 7.28−7.32 (m, 3H), 7.55−7.58 (m, 1H), 7.73−7.78 (m, 2H), 7.89 (d, *J* = 8.5 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.7 (CH_2), 29.2 (CH_2), 31.6 (CH_2), 38.6 (CH), 39.9 (CH), 50.4 (CH), 54.2 (CH), 122.3 (CH), 127.3 (CH), 127.5 (4°), 127.6 (CH), 128.2 (CH), 128.4 (CH), 129.4 (CH), 129.7 (CH), 130.0 (CH), 131.7 (4°), 135.4 (CH), 144.8 (4°), 148.3 (4°), 154.9 (4°), 169.4 (4°), 209.4 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1695, 1604, 1592, 1556, 1493, 1357, 1306, 1227, 1198, 1164. LR(ESI-MS) *m/z*: 352 {$(MH)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{25}H_{22}NO$ 352.1696, found 352.1695 $[M + H]^+$.

Compounds ***4kα*** *and* ***4kβ*** *from* ***3k*** *(Entry 11, Table 2).* Synthesized according to the general PK procedure, with **3k** (92 mg, 5.0 mmol), to afford **4kα** as a white solid (35 mg, 23%) and **4k*β*** as a cream solid (80 mg, 52%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-Phenyl-2-(thiophene-2-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4kα**). Mp > 165 °C dec. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 10.6 Hz, 1H), 1.23 (d, *J* = 10.6 Hz, 1H), 1.31−1.41 (m, 2H), 1.60−1.68 (m, 2H), 2.12 (br, 1H), 2.49 (d, *J* = 5.5 Hz, 1H), 2.61 (br, 1H), 3.03 (d, *J* = 5.5 Hz, 1H), 6.92 (dd, *J* = 5.0, 3.8 Hz, 1H), 7.22−7.25 (m, 2H), 7.34−7.37 (m, 2H), 7.41−7.44 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.7 (CH_2), 28.9 (CH_2), 31.6 (CH_2), 37.9 (CH), 39.6 (CH), 52.5 (CH), 54.0 (CH), 126.5 (CH), 126.5 (CH), 127.4 (CH), 127.6 (CH), 128.8 (CH), 129.2 (CH), 132.2 (4°), 135.6 (4°), 136.4 (4°), 169.4 (4°), 207.5 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2964, 2877, 1694, 1614, 1532, 1444, 1426, 1372, 1307, 1199. LR(ESI-MS) *m/z*: 307 {$(MH)^+$, 100}. HR-(ESI-MS) *m/z*: calcd for $C_{20}H_{19}OS$ 307.1151, found 307.1157 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-Phenyl-3-(thiophene-2-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4k*β***). Mp = 106−111 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 10.7 Hz, 1H), 1.31 (d, *J* = 10.7 Hz), 1.40−1.46 (m, 1H), 1.48−1.54 (m, 1H), 1.66−1.72 (m, 1H), 1.74−1.80 (m, 1H), 2.12 (d, *J* = 5.6 Hz, 1H), 2.55 (m, 1H), 2.59 (m, 1H), 3.17 (d, *J* = 5.6 Hz, 1H), 7.01 (dd, *J* = 5.1, 3.8 Hz, 1H), 7.23 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.33 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.38 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.39−7.45 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.7 (CH_2), 29.3 (CH_2), 32.1 (CH_2), 39.1 (CH), 40.2 (CH), 50.5 (CH), 54.2 (CH), 127.2 (CH), 128.4 (CH), 128.9 (CH), 129.5 (CH), 130.3 (CH), 130.4 (CH), 132.6 (4°), 138.0 (4°), 141.3 (4°), 161.2 (4°), 207.9 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1686, 1617, 1590, 1489, 1420, 1357, 1198, 1162. LR(ESI-MS) *m/z*: 307 {$(MH)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{20}H_{19}OS$ 307.1151, found 307.1153 $[M + H]^+$.

Compounds ***4lα*** *and* ***4lβ*** *from* ***3l*** *(Entry 12, Table 2).* Synthesized according to the general PK procedure, with **3l** (92 mg, 5.0 mmol), to afford **4lα** as a cream solid (46 mg, 30%) and **4l*β*** as a white solid (95 mg, 62%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-Phenyl-2-(thiophene-3-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4lα**). Mp = 142−146 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 10.5 Hz, 1H), 1.20 (d, *J* = 10.5 Hz, 1H), 1.34−1.42 (m, 2H), 1.64−1.66 (m, 2H), 2.09 (br, 1H), 2.47 (d, *J* = 5.5 Hz, 1H), 2.60 (br, 1H), 3.10 (d, *J* = 5.5 Hz), 6.80 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.14 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.32−7.36 (m, 2H), 7.36−7.39 (m, 3H), 7.66 (dd, *J* = 3.0, 1.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.8 (CH_2), 28.9 (CH_2), 31.6 (CH_2), 38.1 (CH), 39.5 (CH), 51.5 (CH), 54.1 (CH), 124.5 (CH), 125.4 (CH), 127.7 (CH), 128.0 (CH), 128.6 (CH), 129.3 (CH), 131.3 (4°), 136.2 (4°), 137.1 (4°), 169.5 (4°), 208.5 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1691, 1619, 1491, 1445, 1416, 1327, 1199. LR(ESI-MS) *m/z*: 307 {$(MH)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{20}H_{19}OS$ 307.1151, found 307.1157 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-Phenyl-3-(thiophene-3-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4l*β***). Mp = 159−162 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.07 (d, *J* = 10.6 Hz, 1H), 1.26 (d, *J* = 10.6 Hz, 1H), 1.40−1.51 (m, 2H), 1.65−1.78 (m, 2H), 2.37−2.39 (m, 1H), 2.49 (d, *J* = 5.6 Hz, 1H), 2.58−2.61 (m, 1H), 3.14 (d, *J* = 5.6 Hz, 1H), 6.91 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.19 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.21−7.24 (m, 2H), 7.33−7.36 (m, 1H), 7.37−7.41 (m, 2H), 7.48 (dd, *J* = 3.0, 1.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.7 (CH_2), 29.3 (CH_2), 31.9 (CH_2), 39.2 (CH), 39.6 (CH), 50.6 (CH), 54.0 (CH), 125.5 (CH), 127.6 (CH), 128.0 (CH), 128.0 (CH), 128.6 (CH), 129.2 (CH), 133.1 (4°), 136.5 (4°), 141.7 (4°), 162.9 (4°), 208.6 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2875, 1667, 1619, 1592, 1417, 1329, 1199, 1164. LR(ESI-MS) *m/z*: 307 {$(MH)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{20}H_{19}OS$ 307.1151, found 307.1152 $[M + H]^+$.

Compounds ***4mα*** *and* ***4mβ*** *from* ***3m*** *(Entry 13, Table 2).* Synthesized according to the general PK procedure, with **3m** (84 mg, 5.0 mmol), to afford **4mα** as a cream solid (29 mg, 20%) and **4m*β*** as a cream solid (98 mg, 68%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-2-(Fur-2-yl)-3-phenyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4mα**). Mp = >134 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (d, *J* = 10.6 Hz, 1H), 1.16 (d, *J* = 10.6 Hz, 1H), 1.32−1.41 (m, 2H), 1.59−1.65 (m, 2H), 2.06 (br, 1H), 2.47 (d, *J* = 5.5 Hz, 1H), 2.58 (br, 1H), 3.12 (d, *J* = 5.5 Hz, 1H), 6.41 (dd, *J* = 3.4, 1.8 Hz, 1H), 7.02 (ddd, *J* = 3.4, 0.6, 0.5 Hz, 1H), 7.24 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.37−7.42 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.9 (CH_2), 28.9 (CH_2), 31.7 (CH_2), 35.3 (CH_3), 39.0 (CH), 39.5 (CH), 51.8 (CH), 54.2 (CH), 109.2 (CH), 112.7 (CH), 126.7 (CH), 127.6 (CH), 128.4 (CH), 128.8 (CH), 129.6 (4°), 133.0 (4°), 39.2 (4°), 161.9 (4°), 207.8 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1785, 1696, 1547, 1473, 1392, 1340, 1291, 1200, 1146. LR(ESI-MS) *m/z*: 313 {$(MNa)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{20}H_{18}NaO_2$ 313.1199, found 313.1189 $[M + Na]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-3-(Fur-2-yl)-2-phenyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one (**4m*β***). Mp = >133−136 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (d, *J* = 10.6 Hz, 1H), 1.26 (d, *J* = 10.6 Hz, 1H), 1.36−1.43 (m, 1H), 1.47−1.53 (m, 1H), 1.61−1.69 (m, 1H), 1.72−1.79 (m, 1H), 2.49 (d, *J* = 5.5 Hz, 1H), 2.52 (m, 1H), 2.56 (m, 1H), 3.14 (d, *J* = 5.5 Hz, 1H), 6.38 (dd, *J* = 3.6, 1.8 Hz, 1H), 6.43 (dd, *J* = 3.6, 0.7 Hz, 1H), 7.24−7.27 (m, 2H), 7.33−7.37 (m, 1H), 7.39−7.43 (m, 2H), 7.50 (dd, *J* = 1.8, 0.7 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 28.6 (CH_2), 29.3 (CH_2), 31.7 (CH_2), 39.5 (CH), 39.8 (CH), 48.3 (CH), 53.7 (CH), 112.2 (CH), 115.7 (CH), 128.1 (CH), 128.5 (CH), 129.1 (CH), 132.7 (4°), 139.8 (4°), 144.8 (CH), 150.5 (4°), 156.6 (4°), 208.1 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876, 1685, 1620, 1594, 1492, 1476, 1342, 1215, 1171, 1023. LR(ESI-MS) *m/z*: 313 {$(MNa)^+$, 100}. HR(ESI-MS) *m/z*: calcd for $C_{20}H_{18}NaO_2$ 313.1199, found 313.1199 $[M + Na]^+$.

Compound ***4n*β*** *from* ***3n*** *(Entry 14, Table 2).* Synthesized according to the general PK procedure, with **3n** (89 mg, 5.0 mmol), to afford **4n*β*** as a white solid (28 mg, 17%). While another product was observed by TLC analysis, it could not be isolated and characterized. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-4-(1-Oxo-2-trimethylsilyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-3-yl)-2*H*-pyran-2-one (**4n*β***). Mp = 161−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.11 (s, 9H), 0.95 (d, *J* = 10.6 Hz, 1H), 0.99 (d, *J* = 10.6 Hz, 1H), 1.22−1.31 (m, 2H), 1.55−1.68 (m, 2H), 2.12 (br, 1H), 2.24 (d, *J* = 5.6 Hz, 1H), 2.30 (s, 1H), 2.47 (br, 1H), 2.74 (d, *J* = 5.6 Hz, 1H), 5.86−5.87 (m, 1H), 5.92−5.94 (m, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = −0.80 (CH_3). 20.2 (CH_3), 28.2 (CH_2), 28.7 (CH_2), 31.2 (CH_2), 37.4 (CH), 39.5 (CH), 54.5 (CH), 54.6 (CH), 103.4 (CH), 109.6 (CH), 147.2 (4°), 155.1 (4°), 161.8 (4°), 162.7 (4°), 178.5 (4°), 213.4 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2962, 2876,

1727, 1690, 1641, 1588, 1544, 1383, 1315, 1249, 1215, 1198. LR(ESI-MS) m/z: 329 {$(MH)^+$, 40}, 351 {$(MNa)^+$, 100). HR(ESI-MS) m/z: calcd for $C_{19}H_{24}O_3SiNa$ 351.1387, found 351.1396 $[M + Na]^+$.

Compound **4oα** *from* **3o** *(Entry 15, Table 2).* Synthesized according to the general PK procedure except on 3.75 mmol scale, with **3o** (50 mg, 3.75 mmol) (note: the intermediate complex was purified first; see characterization data below), to afford **4oα** as a cream solid (31 mg, 32%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-4-(1-Oxo-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-2-yl)-6-methyl-2*H*-pyran-2-one (**4oα**). Mp = 142−147 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.00 (d, J = 10.8 Hz, 1H), 1.03 (d, J = 10.7 Hz, 1H), 1.29−1.41 (m, 2H), 1.62 (dddd, J = 11.3, 11.3, 3.9, 3.9 Hz, 1H), 1.73 (dddd, J = 11.3, 11.3, 4.0, 4.0 Hz, 1H), 2.25 (s, 3H), 2.31 (br, 1H), 2.36 (d, J = 5.4 Hz, 1H), 2.49 (br d, 1H), 2.74 (dd, J = 5.4, 3.0 Hz, 1H), 6.26 (s, 1H), 6.71 (s, 1H), 7.80 (d, J = 3.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.0 (CH_3), 28.2 (CH_2), 29.2 (CH_2), 31.4 (CH_2), 38.4 (CH), 39.6 (CH), 48.2 (CH), 55.0 (CH), 102.2 (CH), 109.5 (CH), 141.9 (4°), 145.6 (4°), 161.8 (4°), 163.1 (4°), 165.1 (CH), 207.2 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2963, 2877, 1722, 1638, 1608, 1548, 1411, 1332, 1305, 1185, 1131. LR(ESI-MS) m/z: 257 {$(MH)^+$, 100}, 279 {$(MNa)^+$, 43). HR(ESI-MS) m/z: calcd for $C_{16}H_{17}O_3$: 257.1172, found 257.1166 $[M + H]^+$. Data for the Intermediate Complex [μ_2-4-Ethynyl-6-methyl-2*H*-pyran-2-one]hexacarbonyl Dicobalt. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.27 (s, 3H), 5.93 (s, 1H), 6.28 (s, 1H), 6.33 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.0 (CH_3), 73.8 (CH), 82.9 (4°), 105.6 (CH), 110.8 (CH), 155.9 (4°), 161.6 (4°), 162.8 (4°), 198.2 (br, M−CO). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2101, 2065, 2037, 1713, 1632, 1567, 1363, 1310, 1273, 1263, 1223. LR(ESI-MS) m/z: 421 {$(MH)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{14}H_7Co_2O_8$ 420.8799, found 420.8791 $[M + H]^+$. Anal. Calcd for $C_{14}H_6Co_2O_8$: C, 40.03; H, 1.44. Found: C, 39.96; H, 1.48.

Compounds **4pα** *and* **4pβ** *from* **3p** *(Entry 16, Table 2).* Synthesized according to the general PK procedure, with **3p** (108 mg, 5.0 mmol), to afford **4pα** as an orange solid (79 mg, 47%) and **4pβ** as a white solid (76 mg, 45%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-4-[1-Oxo-2-(thiophene-3-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-3-yl]-2*H*-pyran-2-one (**4pα**). Mp = >163 °C dec. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.08 (d, J = 10.6 Hz, 1H), 1.09 (d, J = 10.6 Hz, 1H), 1.34−1.40 (m, 2H), 1.62−1.71 (m, 2H), 2.20 (s, 4H overlapping with H-4), 2.45 (d, J = 5.6 Hz, 1H), 2.59 (br, 1H), 2.91 (d, J = 5.6 Hz, 1H), 5.76 (s, 1H), 6.22 (s, 1H), 7.02 (dd, J = 5.0, 1.2 Hz, 1H), 7.28 (dd, J = 5.0, 3.0 Hz, 1H), 7.72 (dd, J = 3.0, 1.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.1 (CH_3), 28.5 (CH_2), 28.8 (CH_2), 31.6 (CH_2), 38.0 (CH), 39.6 (CH), 50.5 (CH), 53.9 (CH), 103.3 (CH), 110.9 (CH), 125.4 (CH), 126.7 (CH), 127.4 (CH), 129.9 (4°), 139.7 (4°), 152.4 (4°), 162.2 (4°), 162.4 (4°), 162.6 (4°), 207.5 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2963, 2877, 1726, 1701, 1638, 1544, 1297, 1205, 1144. LR(ESI-MS) m/z: 339 {$(MH)^+$, 100}, 361 {$(MNa)^+$, 59). HR(ESI-MS) m/z: calcd for $C_{20}H_{19}O_3S_1$ 339.1049, found 339.1055 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-4-[1-Oxo-3-(thiophene-3-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-2-yl]-2*H*-pyran-2-one (**4pβ**). Mp = 158−161 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.06 (d, J = 10.9 Hz, 1H), 1.11 (d, J = 10.9 Hz, 1H), 1.36−1.49 (m, 2H), 1.64−1.75 (m, 2H), 2.22 (s, 3H), 2.33 (br, 1H), 2.47 (d, J = 5.6 Hz, 1H), 2.56 (br, 1H), 3.13 (d, J = 5.6 Hz, 1H), 5.82 (s, 1H), 6.11 (s, 1H), 7.17 (d, J = 3.9 Hz, 1H), 7.36 (br s, 1H), 7.67 (br s, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 20.1 (CH_3), 28.5 (CH_2), 29.1 (CH_2), 31.9 (CH_2), 39.3 (CH), 39.7 (CH), 51.1 (CH), 54.2 (CH), 104.8 (CH), 112.6 (CH), 126.8 (CH), 127.3 (CH), 129.20 (CH), 135.1 (4°), 137.0 (4°), 149.4 (4°), 162.3 (4°), 162.6 (4°), 165.7 (4°), 206.3 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2963, 2877, 1723, 1692, 1640, 1606, 1547, 1418, 1321, 1294, 1198, 1145. LR(ESI-MS) m/z: 339 {$(MH)^+$, 100}, 361 {$(MNa)^+$, 75). HR(ESI-MS) m/z: calcd for $C_{20}H_{19}O_3S$ 339.1049, found 339.1055 $[M + H]^+$.

Compounds **4qα** *and* **4qβ** *from* **3q** *(Entry 17, Table 2).* Synthesized according to the general PK procedure, with **3q** (107 mg, 5.0 mmol), to afford the **4qα** as an orange solid (138 mg, 82%) and **4qβ** as an orange solid (7 mg, 4%). Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-4-[1-Oxo-2-(1-methyl-1*H*-pyrr-2-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-3-yl]-2*H*-pyran-2-one (**4qα**). Mp = 141−144 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.09 (s, 2H), 1.36−1.43 (m, 2H), 1.63−1.75 (m, 2H), 2.12 (t, J = 0.7 Hz, 3H), 2.27 (br, 1H), 2.48 (d, J = 5.6 Hz, 1H), 2.58 (br, 1H), 3.01 (d, J = 5.6 Hz, 1H), 3.35 (s, 3H), 5.49 (dq, J = 1.5, 0.9 Hz, 1H), 6.09 (dd, J = 3.7, 1.8 Hz, 1H), 6.16 (dd, J = 3.7, 2.7 Hz, 1H), 6.29 (dq, J = 1.5, 0.7 Hz, 1H), 6.72 (dd, J = 2.7, 1.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.1 (CH_3), 28.5 (CH_2), 28.9 (CH_2), 31.8 (CH_2), 34.9 (CH_3), 38.7 (CH), 39.4 (CH), 49.5 (CH), 53.9 (CH), 102.4 (CH), 109.0 (CH), 111.5 (CH), 112.4 (CH), 122.6 (4°), 125.1 (CH), 139.6 (4°), 150.6 (4°), 161.8 (4°), 162.7 (4°), 162.9 (4°), 207.9 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2963, 2877, 1720, 1701, 1637, 1548, 1484, 1315, 1227, 1197. LR(ESI-MS) m/z: 336 {$(MH)^+$, 3), 358 {$(MNa)^+$, 100}. HR(ESI-MS) m/z: calcd for $C_{21}H_{21}NNaO_3$ 358.1414, found 358.1420 $[M + H]^+$. Data for (3a*RS*,4*SR*,7*RS*,7a*SR*)-4-[1-Oxo-3-(1-methyl-1*H*-pyrr-2-yl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methano-inden-2-yl]-2*H*-pyran-2-one (**4qβ**). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.04−1.06 (m, 2H), 1.38−1.41 (m, 2H), 1.65−1.69 (m, 2H), 2.15 (s, 3H), 2.17 (br, 1H), 2.47 (d, J = 5.8 Hz, 1H), 2.57 (br, 1H), 3.08 (d, J = 5.8 Hz, 1H), 3.33 (s, 3H), 5.72−5.73 (br s, 1H), 6.24−6.25 (s, 1H), 6.27 (dd, J = 3.9, 2.5 Hz, 1H), 6.53 (dd, J = 3.9, 1.8 Hz, 1H), 6.82 (dd, J = 2.5, 1.8 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 20.1 (CH_3), 28.7 (CH_2), 28.9 (CH_2), 31.8 (CH_2), 35.9 (CH_3), 39.5 (CH), 39.7 (CH), 51.9 (CH), 54.3 (CH), 103.7 (CH), 110.3 (CH), 111.5 (CH), 115.0 (CH), 128.6 (4°), 129.1 (CH), 133.9 (4°), 148.6 (4°), 161.6 (4°), 163.1 (4°), 165.5 (4°), 205.6 (4°). IR ν_{max} (CH_2Cl_2, cm^{-1}): 2963, 2876, 1717, 1636, 1597, 1543, 1458, 1424, 1316, 1196. LR(ESI-MS) m/z: 336 {$(MH)^+$, 14}, 358 {$(MNa)^+$, 100). HR(ESI-MS) m/z: calcd for $C_{21}H_{21}NNaO_3$ 358.1414, found 358.1417 $[M + Na]^+$.

■ ASSOCIATED CONTENT

Supporting Information. General experimental details, ^{1}H and ^{13}C NMR spectra (images) for new compounds, and a summary of the X-ray diffraction data (four structures). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Tel: (+44) 1904 324091. Fax: (+44) 1904 322516. E-mail: ian.fairlamb@york.ac.uk.

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