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Allene Substitution-Controlled Switching of Dimerization to Cycloisomerization in the Pd^{II}-Catalyzed Reaction of Terminal α-Allenones

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Keywords: Allenes / Cyclization / Heterocycles / Palladium / Substituent effects

In this contribution, we describe the role of steric interactions in Pd^{II}-catalyzed reactions of terminal α-allenones, which has not previously been invoked in discussions of these versatile compounds. By adopting $[PdCl_2(MeCN)_2]$ as catalyst, the cycloisomerization/dimerization ratio of α-allenones is controlled by the substitution of the allene compound: unsubstituted allenones mainly afford dimerization, whereas allenones bearing an internal substituent favor the formation of cycloisomerization products. Thus, for the first time the mode of reaction (cycloisomerization vs. dimerization) of α-allenones is substrate-directable.

Introduction

Of the various heterocyclic structures, polysubstituted furans are among the most important, because of their presence in natural and synthetic substances, pharmaceuticals, and fragances.[1] A second feature of furans receiving increasing attention stems from the realisation that they represent readily accessible and highly flexible building blocks for the construction of a wide-range of other compounds including natural products.[2] On the other hand, during the past decades the allene moiety has developed from almost a rarity to an established member of the weaponry utilized in modern organic synthetic chemistry, by taking advantage of its inherent chirality and high reactivity in such diverse transformations as addition, cyclization/cycloaddition, cycloisomerization, and cross-coupling reactions.[3] Allenones are of particular interest since they undergo selective cycloisomerization or dimerization reactions to afford furans. Marshall and co-workers discovered the Rh^I- or Ag^I-catalyzed selective cycloisomerization of α-allenones to substituted furans,[4] while Hashmi and co-workers reported the Pd^{II}-catalyzed dimerization of terminal α-allenones to afford 2,4-disubstituted furans.[5] More recently, the cycloisomerization of α-allenones catalyzed by Au^{III},[6] or by a palladatricyclo[4.1.0.0(2,4)]heptane catalyst have also been reported.[7] Thus, it appears that the only known efficient method for controlling the mode of reaction (cycloisomerization vs. dimerization) of α-allenones is the case of choice of catalyst. However, substrate-directable reactions are an important class of selective organic transformations, and understanding their mechanism of direction is paramount to their utility.[8] Following our commitment in heterocyclic and allene chemistry,[9] we report herein that by adopting Pd^{II}-catalyzed conditions, the cycloisomerization/dimerization ratio of α-allenones is controlled by the substitution of the allene compound: unsubstituted allenones mainly afford dimerization, whereas allenones bearing an internal substituent favor the formation of cycloisomerization products.

Results and Discussion

The starting substrates, unsubstituted α-allenones **2a**–**f** and substituted α-allenones **3a**–**l**, were obtained from the appropriate carbaldehyde **1a**–**f** following sequential coupling/oxidation protocols. α-Allenones **2** were obtained from carbaldehydes **1** by zinc-mediated carbonyl–propargylation followed by Dess–Martin oxidation with concomitant propargyl to allene rearrangement (Scheme 1, Table 1). α-Allenones **3** were readily prepared in good overall yield beginning from the appropriate carbaldehyde **1** (Scheme 2, Table 2) via regiocontrolled indium-mediated Barbier-type carbonyl–allenylation reaction in aqueous media,[10] followed by Dess–Martin oxidation.

First, the general reactivity of α-allenones toward the bond reorganization was tested with aromatic substrates **2a**, **3a**, and **3b** by the use of $[PdCl_2(MeCN)_2]$ as catalyst (Scheme 3). As expected, the Pd^{II}-catalyzed reaction of unsubstituted α-allenone **2a** yielded the dimer **4a** bearing a furan ring, which is the result of a cycloisomerization fol-

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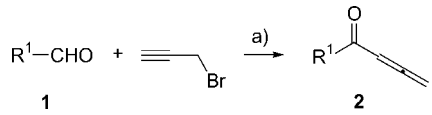
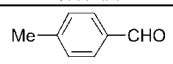
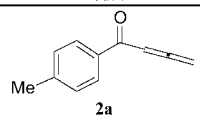
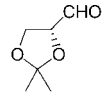
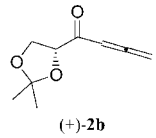
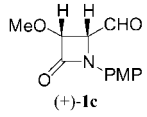
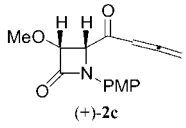
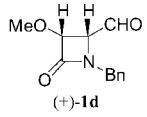
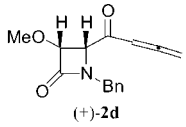
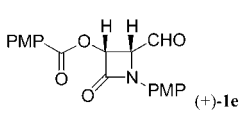
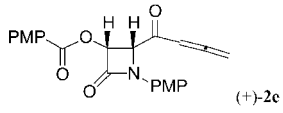
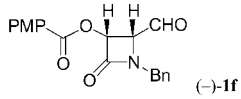
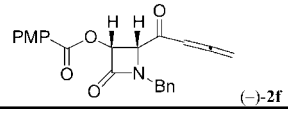
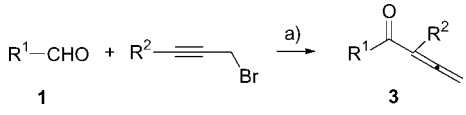


Scheme 1. Regioselective preparation of α-allenic ketones **2**. Reagents and conditions: a) (i) Zn, THF, NH_4Cl (aq. satd.), room temp.; (ii) Dess–Martin periodinane, CH_2Cl_2, room temp.

Table 1. Regioselective preparation of unsubstituted α-allenic ketones **2**.[a]

Substrate	Product
 **1a**	 **2a**
 (–)-**1b**	 (+)-**2b**
 (+)-**1c**	 (+)-**2c**
 (+)-**1d**	 (+)-**2d**
 (+)-**1e**	 (+)-**2e**
 (–)-**1f**	 (–)-**2f**

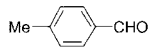
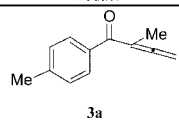
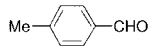
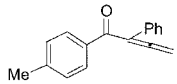
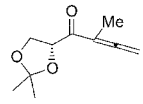
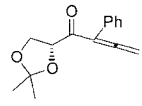
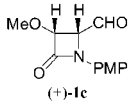
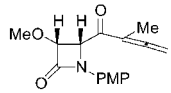
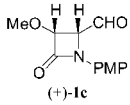
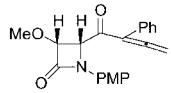
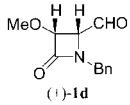
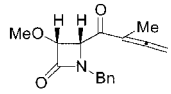
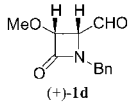
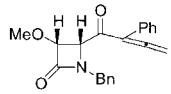
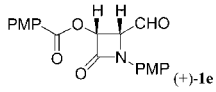
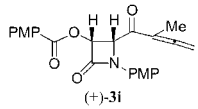
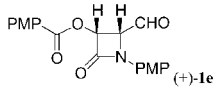
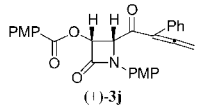
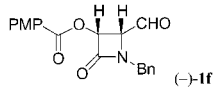
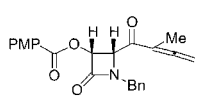
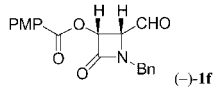
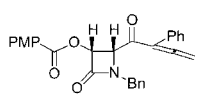
[a] Yield of pure, isolated product with correct analytical and spectroscopic data. PMP = 4-$MeOC_6H_4$.



Scheme 2. Regioselective preparation of α-allenic ketones **3**. Reagents and conditions: a) (i) In, THF, NH_4Cl (aq. satd.), room temp.; (ii) Dess–Martin periodinane, CH_2Cl_2, room temp.

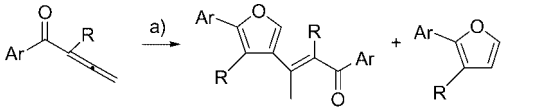
lowed by allenone coupling. Interestingly, the reaction of α-allenone **3b** bearing an internal methyl substituent gave in reasonable yield and very high selectivity the monomer **5a** which bears a furan ring, which is just the result of a cycloisomerization. Gratifyingly, the reaction of phenyl-substituted α-allenone **3c** afforded in good yield the furan **5b** as the sole product. On the basis of the markedly different behavior observed for the above systems, we suggest that

Table 2. Regioselective preparation of substituted α-allenic ketones **3**.[a]

Substrate	R^2	Product
 **1a**	Me	 **3a**
 **1a**	Ph	 **3b**
 (–)-**1b**	Me	 (+)-**3c**
 (–)-**1b**	Ph	 (+)-**3d**
 (+)-**1c**	Me	 (+)-**3e**
 (+)-**1c**	Ph	 (+)-**3f**
 (+)-**1d**	Me	 (+)-**3g**
 (+)-**1d**	Ph	 (+)-**3h**
 (+)-**1e**	Me	 (+)-**3i**
 (+)-**1e**	Ph	 (+)-**3j**
 (–)-**1f**	Me	 (+)-**3k**
 (–)-**1f**	Ph	 (+)-**3l**

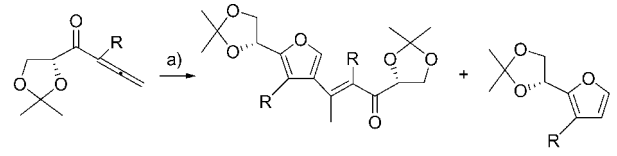
[a] Yield of pure, isolated product with correct analytical and spectroscopic data. PMP = 4-$MeOC_6H_4$.

the allene substituents play an important role in the process, such as preventing the dimerizacion reaction by steric interactions. Thus, for the first time the mode of reaction (cycloisomerization vs. dimerization) of α-allenones is substrate-directable.



Scheme 3. Substrate controlled switching of dimerization to cycloisomerization in aromatic α-allenic ketones. Reagents and conditions: a) 5 mol-% $[PdCl_2(MeCN)_2]$, MeCN, room temp., **4a**: 8 h; **5a**: 3 h; **5b**: 3 h. Ar = *p*-tolyl.

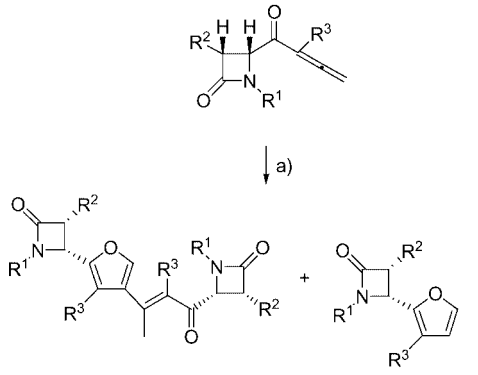
Because total control is observed for the dimerization and cycloisomerization reactions of aromatic α-allenones in the presence of catalytic amounts of $[PdCl_2(MeCN)_2]$, it was decided to test the effect of the nature of the α-allenone on the Pd^{II}-catalyzed process. To study whether or not the switching of dimerization to cycloisomerization could be applied to aliphatic derivatives, unsubstituted α-allenones **2b**–**f** and substituted α-allenones **3c**–**l** were treated under similar conditions. In fact, useful control was observed, because internally substituted α-allenones gave good or total selectivities in favor of cycloisomerization products (Scheme 4 and Scheme 5). The role of the bulky β-lactam ring is noticeable for the unsubstituted α-allenones **2c**–**f**, because considerable amounts of the unexpected cycloisomerization products are normally obtained. On the other hand, the stereochemical integrity at the proximal stereocenters was retained in the course of the process. Enantiopure 2-azetidinone-tethered furans **4e**–**j** and **5e**–**o** are of special interest, because they can be regarded as hybrids of two different pharmacophoric subunits, β-lactam and furan ring. The *E* configuration of the tri- or tetrasubstituted double bond in dimers **4** was assigned by NMR spectroscopic methods, on the basis of qualitative homonuclear NOE difference spectra.



Scheme 4. Substrate controlled switching of dimerization to cycloisomerization in aliphatic enantiopure α-allenic ketones. Reagents and conditions: a) 5 mol-% $[PdCl_2(MeCN)_2]$, MeCN, room temp., **4c**: 6 h; **5c**: 6 h; **5d**: 4 h.

It seems that the reactivity in this type of Pd^{II}-catalyzed reactions is determined by the presence or absence of a substituent at the internal allene carbon atom, as the allenones

(+)-**2c**: R^1 = PMP, R^2 = MeO, R^3 = H
(+)-**3e**: R^1 = PMP, R^2 = MeO, R^3 = Me
(+)-**3f**: R^1 = PMP, R^2 = MeO, R^3 = Ph
(+)-**2d**: R^1 = Bn, R^2 = MeO, R^3 = H
(+)-**3g**: R^1 = Bn, R^2 = MeO, R^3 = Me
(+)-**3h**: R^1 = Bn, R^2 = MeO, R^3 = Ph
(+)-**2e**: R^1 = PMP, R^2 = PMPCOO, R^3 = H
(+)-**3i**: R^1 = PMP, R^2 = PMPCOO, R^3 = Me
(+)-**3j**: R^1 = PMP, R^2 = PMPCOO, R^3 = Ph
(+)-**2f**: R^1 = Bn, R^2 = PMPCOO, R^3 = H
(+)-**3k**: R^1 = Bn, R^2 = PMPCOO, R^3 = Me
(+)-**3l**: R^1 = Bn, R^2 = PMPCOO, R^3 = Ph



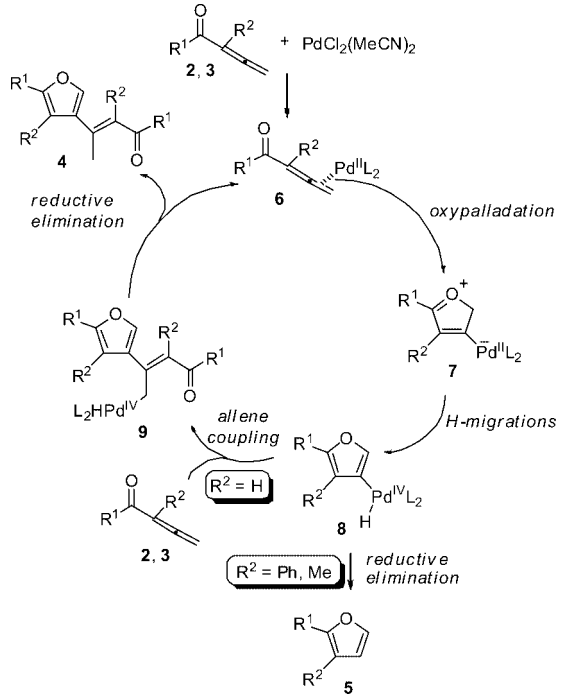
(+)-**4e**: R^3 = H (60%)
(+)-**4f**: R^3 = Me (7%)
(+)-**4g**: R^3 = H (70%)
(–)-**4h**: R^3 = H (64%)
(+)-**4i**: R^3 = Me (32%)
(+)-**4j**: R^3 = H (72%)

(+)-**5e**: R^3 = H (16%)
(+)-**5f**: R^3 = Me (45%)
(+)-**5g**: R^3 = Ph (81%)
(+)-**5h**: R^3 = H (9%)
(+)-**5i**: R^3 = Me (65%)
(+)-**5j**: R^3 = Ph (81%)
(+)-**5k**: R^3 = Me (50%)
(+)-**5l**: R^3 = Ph (72%)
(+)-**5m**: R^3 = H (10%)
(+)-**5n**: R^3 = Me (87%)
(+)-**5o**: R^3 = Ph (58%)

Scheme 5. Substrate controlled switching of dimerization to cycloisomerization in 2-azetidinone-tethered α-allenic ketones. Reagents and conditions: a) 5 mol-% $[PdCl_2(MeCN)_2]$, MeCN, room temp., **4e**: 4.5 h; **4g**: 5 h; **4h**: 5.5 h; **4j**: 6.5 h; **5f**: 3 h; **5g**: 6 h; **5i**: 4.5 h; **5j**: 6 h; **5k**: 6 h; **5l**: 5 h; **5n**: 5 h; **5o**: 5 h.

2a–**f** that are lacking a group gave dimerization, while the allenones **3b**, **3d**, **3f**, **3h**, **3j**, and **3l**, which bear a phenyl group at the internal allenic carbon exclusively underwent a cycloisomerization reaction. Allenones **3a**, **3c**, **3e**, **3g**, **3i**, and **3k**, bearing an internal methyl substituent yielded cycloisomerization adducts as the sole or major products. The pathway proposed in Scheme 6 looks valid for the formation of products **4** and **5**. This pathway resembles Hashmi's proposal.[5] It could be presumed that the initially formed allene-palladium complex **6** undergoes an intramolecular attack by the ketone group (oxypalladation), giving rise to the furan intermediate **7**, which after H-migrations affords the aromatic palladium species **8**. Palladafuran **8** may suffer a reductive elimination to yield furans **5**. Alternatively, intermediate **8** is trapped by another allenone molecule in a subsequent coupling process leading to dimers **4** via **9**. The

formation of the *E* isomer in alkene derivatives **4** is the consequence of an addition of the organometallic species to the allene side remote from the acyl group. It may be inferred that different steric effects in the organometallic species **8** may be responsible for the different reactivity preference, stabilizing one of the intermediates rather than the other. Dimerization falters in the presence of sterically encumbering allenones. Probably, dimerization via **9** is restricted by the steric hindrance of the R^2 substituent (R^2 = Me or Ph) when a second molecule of allenone **3** is trying to approach to the palladafuran **8**.



Scheme 6. Mechanistic explanation for the substrate controlled switching of dimerization to cycloisomerization in α-allenic ketones.

Conclusions

In conclusion, the presence of a substituent at the α-position in a terminal allenone has a profound influence on the reactivity, inducing a switching of dimerization to cycloisomerization in the Pd^{II}-catalyzed reaction. For instance, the presence of a phenyl group at the α-position of the allenone makes inert the substrate to the dimerization. These transformations are relevant from a synthetic standpoint, since for the first time the mode of reaction (cycloisomerization vs. dimerization) of α-allenones is substrate-directable, and from a biological perspective, since hybrid natural products have emerged as a promising approach to diversity oriented synthesis.

Experimental Section

General Methods: ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance-300, Varian VRX-300S or Bruker AC-200. NMR spectra were recorded in $CDCl_3$ solutions, except otherwise stated. Chemical shifts are given in ppm relative to TMS (^{1}H, 0.0 ppm), or $CDCl_3$ (^{13}C, 76.9 ppm). Low and high resolution mass spectra were taken on a HP5989A spectrometer using the electronic impact (EI) or electrospray modes (ES) unless otherwise stated. Specific rotation $[\alpha]_D$ is given in 10^{-1} deg cm^2 g^{-1} at 20 °C, and the concentration (*c*) is expressed in grams per 100 mL. All commercially available compounds were used without further purification.

General Procedure for the Preparation of Unsubstituted Terminal α-Allenic Ketones 2a–f: Propargyl bromide (3.0 mmol) was added to a well stirred suspension of the corresponding aldehyde **1** (1.0 mmol) and zinc dust (6.0 mmol) in THF/NH_4Cl (aq. satd.) (1:5, 5 mL) at 0 °C. Then, the mixture was stirred at room temp. After disappearance of the starting material (TLC) the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Then, a solution of the above prepared homopropargylic alcohol (0.64 mmol) in dichloromethane (1 mL) was added to a solution of Dess–Martin periodinane (DMP) (329 mg, 0.77 mmol) in dichloromethane (4 mL) with stirring. After disappearance of the starting material (TLC), the homogeneous reaction mixture was diluted with 5 mL of ethyl acetate and the resulting suspension was added to 2 mL of 1 N sodium hydroxide. The organic extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with ethyl acetate/hexanes or dichloromethane/ethyl acetate mixtures gave analytically pure compounds **2**. Spectroscopic and analytical data for some representative forms of compounds **2** follow.[11]

α-Allenic Ketone (+)-2e: From 355 mg (1.0 mmol) of aldehyde (+)-**1e**, and after chromatography of the residue using dichloromethane/ethyl acetate (36:1) as eluent gave compound (+)-**2e** (224 mg, 57%) as a colorless oil. $[\alpha]_D$ = +59.1 (*c* = 0.5 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.95 and 6.90 (d, *J* = 9.0 Hz, each 2 H), 7.27 and 6.87 (d, *J* = 9.0 Hz, each 2 H), 6.43 (d, *J* = 5.4 Hz, 1 H), 5.87 (t, *J* = 6.5 Hz, 1 H), 5.41 (d, *J* = 5.4 Hz, 1 H), 5.39 (d, *J* = 6.6 Hz, 2 H), 3.86 (s, 3 H), 3.78 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 217.3, 191.9, 164.4, 164.2, 160.4, 156.8, 132.2, 118.5, 118.3, 114.4, 114.0, 113.9, 94.8, 81.1, 74.3, 61.6, 55.5, 55.4 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3030, 1937, 1744, 1732, 1684 cm^{-1}. MS (ES): *m*/*z* (%) = 394 (100) [*M* + H]$^+$, 393 (11) [*M*]. $C_{22}H_{19}NO_6$ (393.4): calcd. C 67.17, H 4.87, N 3.56; found C 67.30, H 4.83, N 3.59.

General Procedure for the Preparation of Substituted Terminal α-Allenic Ketones 3a–l: 1-Bromo-2-butyne or 1-bromo-3-phenyl-2-propyne (3.0 mmol) was added to a well stirred suspension of the corresponding aldehyde **1** (1.0 mmol) and indium powder (6.0 mmol) in THF/NH_4Cl (aq. satd.) (1:5, 5 mL) at 0 °C. Then, the mixture was stirred at room temp. After disappearance of the starting material (TLC) the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Then, a solution of the above prepared allenic alcohol (0.64 mmol) in dichloromethane (1 mL) was added to a solution of DMP (329 mg, 0.77 mmol) in dichloromethane (4 mL) with stirring. After disappearance of the starting material (TLC), the homogeneous reaction mixture was diluted with 5 mL of ethyl acetate and the resulting suspension was added to 2 mL of 1 N sodium hydroxide. The organic extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with ethyl acetate/hexanes or dichloromethane/ethyl acetate mixtures gave analytically pure compounds **3**. Spectroscopic and analytical data for some representative forms of compounds **3** follow.[11]

α-Allenic Ketone (+)-3i: From 178 mg (0.5 mmol) of aldehyde (+)-**1e**, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent gave compound (+)-**3i** (130 mg, 64%) as a colorless oil. $[a]_D$ = +125.9 (*c* = 0.6 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.74 and 6.72 (d, *J* = 9.0 Hz, each 2 H), 7.08 and 6.68 (d, *J* = 9.0 Hz, each 2 H), 6.25 (d, *J* = 5.5 Hz, 1 H), 5.38 (d, *J* = 5.5 Hz, 1 H), 5.15 (m, 2 H), 3.67 (s, 3 H), 3.60 (s, 3 H), 1.47 (t, *J* = 2.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 216.5, 192.5, 164.3, 164.1, 160.5, 156.7, 132.1, 130.4, 120.3, 118.6, 114.3, 113.8, 102.5, 80.8, 74.3, 61.4, 55.4, 12.6 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3028, 1935, 1747, 1730, 1686 cm^{-1}. MS (ES): *m*/*z* (%) = 408 (100) $[M + H]^+$, 407 (7) $[M]^+$. $C_{23}H_{21}NO_6$ (407.4): calcd. C 67.80, H 5.20, N 3.44; found C 67.93, H 5.16, N 3.41.

α-Allenic Ketone (+)-3j: From 178 mg (0.5 mmol) of aldehyde (+)-**1e**, and after chromatography of the residue using dichloromethane/ethyl acetate (40:1) as eluent gave compound (+)-**3j** (249 mg, 53%) as a colorless oil. $[a]_D$ = +28.3 (*c* = 0.3 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.89 and 6.88 (d, *J* = 9.0 Hz, each 2 H), 7.33 and 6.82 (d, *J* = 9.0 Hz, each 2 H), 7.21 (m, 5 H), 6.53 (d, *J* = 5.4 Hz, 1 H), 5.70 (d, *J* = 5.4 Hz, 1 H), 5.68 (br. s, 2 H), 3.83 (s, 3 H), 3.80 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 218.0, 190.8, 164.6, 164.1, 159.5, 156.9, 132.3, 130.4, 130.0, 128.6, 128.2, 128.0, 120.2, 118.8, 114.4, 113.8, 109.0, 82.8, 74.6, 62.2, 55.5 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3033, 1937, 1745, 1732, 1685 cm^{-1}. MS (ES): *m*/*z* (%) = 470 (100) $[M + H]^+$, 469 (11) $[M]^+$. $C_{28}H_{23}NO_6$ (469.5): calcd. C 71.63, H 4.94, N 2.98; found C 71.49, H 4.90, N 3.02.

General procedure for the substrate-controlled switching of dimerization to cycloisomerization in the Pd^{II}-catalyzed reaction of terminal α-allenones. $[PdCl_2(MeCN)_2]$ (0.005 mmol) and K_2CO_3 (0.10 mmol) were sequentially added to a stirred solution of the corresponding α-allenone 2 or 3 (0.10 mmol) in acetonitrile (1.0 mL). The reaction was stirred under argon atmosphere until disappearance of the starting material (TLC). Water (0.5 mL) was added before being extracted with ethyl acetate (3 × 4 mL). The organic phase was washed with water (2 × 2 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure 3-furanyl-2-butenones 4 or furans 5. Spectroscopic and analytical data for some representative forms of compounds 4 and 5 follow.[11]

3-Furanyl-2-butenone (–)-4h: From 68 mg (0.17 mmol) of α-allenone (+)-**2e**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (–)-**4h** (42 mg, 64%) as a colorless oil. $[a]_D$ = –290.0 (*c* = 0.6 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.97 and 7.65 (d, *J* = 9.0 Hz, each 2 H), 7.54 and 7.32 (d, *J* = 8.8 Hz, each 2 H), 7.45 (br. s, 1 H), 6.87 (m, 4 H), 6.72 and 6.63 (d, *J* = 9.0 Hz, each 2 H), 6.46 (br. s, 1 H), 6.28 (d, *J* = 5.0 Hz, 1 H), 6.21 (d, *J* = 5.5 Hz, 1 H), 5.43 (d, *J* = 5.0 Hz, 1 H), 5.41 (d, *J* = 5.5 Hz, 1 H), 5.21 (br. s, 1 H), 3.82 (s, 3 H), 3.77 (s, 3 H), 3.72 (s, 3 H), 3.45 (s, 3 H), 1.58 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 195.6, 164.8, 164.7, 164.5, 164.1, 157.0, 156.9, 153.7, 144.7, 133.1, 132.4, 131.8, 130.0, 129.9, 120.0, 118.7, 118.3, 117.3, 114.2, 122.8, 118.6, 118.5, 114.7, 114.6, 114.0, 77.6, 76.9, 63.9, 55.6, 55.5, 55.4, 55.3, 51.2, 23.0 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1766, 1720, 1672 cm^{-1}. MS (ES): *m*/*z* (%) = 787 (100) $[M + H]^+$, 786 (25) $[M]^+$; $C_{44}H_{38}N_2O_{12}$ (786.8): calcd. C 67.17, H 4.87, N 3.56; found C 67.30, H 4.83, N 3.59.

Preparation of 3-Furanyl-2-butenone (+)-4i and Furan (+)-5k: From 40 mg (0.098 mmol) of α-allenone (+)-**3i**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent, 20 mg (50%) of the less polar compound (+)-**5k** and 13 mg (32%) of the more polar compound (+)-**4i** were obtained.

3-Furanyl-2-butenone (+)-4i: Colorless oil. $[a]_D$ = +86.5 (*c* = 0.5 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.92 and 7.28 (d, *J* = 9.0 Hz, each 2 H), 7.81 and 7.27 (d, *J* = 9.0 Hz, each 2 H), 6.86 (m, 8 H), 6.71 (br. s, 1 H), 6.39 (d, *J* = 5.5 Hz, 1 H), 6.11 (d, *J* = 5.0 Hz, 1 H), 5.39 (d, *J* = 5.0 Hz, 1 H), 5.28 (d, *J* = 5.5 Hz, 1 H), 3.87 (s, 3 H), 3.86 (s, 3 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 1.71 (d, *J* = 1.5 Hz, 3 H), 1.64 (s, 3 H), 1.45 (d, *J* = 1.7 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 195.0, 164.3, 164.0, 161.3, 161.2, 156.8, 142.2, 140.5, 132.3, 131.9, 131.8, 130.5, 130.3, 129.1, 121.0, 120.4, 119.7, 118.8, 118.4, 114.6, 114.5, 114.4, 113.9, 113.7, 113.6, 76.5, 67.4, 62.7, 55.6, 55.5, 55.4, 55.3, 54.9, 23.4, 23.3, 16.4 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1746, 1731, 1670 cm^{-1}. MS (ES): *m*/*z* (%) = 815 (100) $[M + H]^+$, 814 (17) $[M]^+$; $C_{46}H_{42}N_2O_{12}$ (814.8): calcd. C 67.80, H 5.20, N 3.44; found C 67.94, H 5.15, N 3.40.

Furan (+)-5k: Colorless oil. $[a]_D$ = +161.7 (*c* = 0.3 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.87 and 6.86 (d, *J* = 8.8 Hz, each 2 H), 7.29 and 6.84 (d, *J* = 8.8 Hz, each 2 H), 7.24 (d, *J* = 2.0 Hz, 1 H), 6.18 (d, *J* = 4.8 Hz, 1 H), 6.08 (d, *J* = 2.0 Hz, 1 H), 5.45 (d, *J* = 4.8 Hz, 1 H), 3.85 (s, 3 H), 3.78 (s, 3 H), 2.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 164.7, 163.8, 161.5, 156.7, 142.7, 141.1, 132.0, 130.7, 121.1, 120.7, 118.5, 114.5, 113.6, 113.5, 76.6, 55.5, 55.4, 54.6, 9.7 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1745, 1732 cm^{-1}. MS (ES): *m*/*z* (%) = 408 (100) $[M + H]^+$, 407 (19) $[M]^+$; $C_{23}H_{21}NO_6$ (407.4): calcd. C 67.80, H 5.20, N 3.44; found C 67.78, H 5.15, N 3.47.

Furan (+)-5l: From 55 mg (0.12 mmol) of α-allenone (+)-**3j**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (+)-**5l** (40 mg, 72%) as a colorless oil. $[a]_D$ = +109.7 (*c* = 0.2 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.91 and 6.86 (d, *J* = 9.0 Hz, each 2 H), 7.47 (m, 5 H), 7.38 (d, *J* = 1.7 Hz, 1 H), 7.17 and 6.78 (d, *J* = 9.0 Hz, each 2 H), 6.45 (d, *J* = 1.7 Hz, 1 H), 6.34 (d, *J* = 4.9 Hz, 1 H), 5.58 (d, *J* = 4.9 Hz, 1 H), 3.84 (s, 3 H), 3.75 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 164.8, 163.9, 161.4, 156.6, 155.4, 143.4, 141.5, 139.9, 132.1, 130.6, 128.9, 128.4, 128.3, 127.7, 118.5, 114.4, 113.6, 111.9, 76.7, 55.4, 54.4 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1747, 1734 cm^{-1}. MS (ES): *m*/*z* (%) = 470 (100) $[M + H]^+$, 469 (11) $[M]^+$; $C_{28}H_{23}NO_6$ (469.5): calcd. C 71.63, H 4.94, N 2.98; found C 71.76, H 4.90, N 2.90.

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