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One-Pot Organocatalytic Tandem Aldol/Polycyclization Reactions between 1,3-Dicarbonyl Compounds and α,β,γ,δ-Unsaturated Aldehydes for the Straightforward Assembly of Cyclopenta[*b*]furan-Type Derivatives: New Insight into the Knoevenagel Reaction

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Abstract: A new cascade pathway viable for Knoevenagel chemistry that involves the coupling between 1,3-dicarbonyl systems and α,β,γ,δ-unsaturated aldehydes has been developed. The process comprises the combination of a classic aldol-type condensation and a rare spontaneous metal-free cycloisomerization, representing a convergent and innovative approach for the stereoselective synthesis of cyclopenta[*b*]furan-type derivatives. The scope and limitations with respect to both reaction partners and mechanistic features were investigated. Meaningfully, our study provides valuable guidance concerning the structural and electronic effects controlling the reactivity of conjugated polyene carbonyl systems.

Keywords: aldol reaction · cycloisomerization · cyclopenta[*b*]furans · domino reactions · electrocyclic reactions

Introduction

The construction of carbo- and heteropolycyclic molecular scaffolds has been the focus of extensive research in organic chemistry. Owing to their diverse structural features and interesting properties, promising as scaffolds for drug discovery, and to their potential applications as precursors for the chemical synthesis of natural and natural-like products, the development of innovative and efficient methods for the assembly of multiring frameworks remains an important goal and represents a constant synthetic challenge. In this area, cascade polycyclizations of polyunsaturated precursors have proven to be an extremely useful approach for the rapid and convergent construction of complex systems.[1] Since these processes involve multiple transformations taking place in a minimum number of steps, generally in one-pot, they are intrinsically atom economic with substantial minimization of waste and time.

The conceptual key point in this field is the stereoselective cation–π cyclization of polyolefins containing a repetitive 1,5-diene sequence that has been especially advantageous for the preparation of multicyclic steroid- and terpenoid-like structures,[2] eventually giving rise to specific domains, such as bioorganic chemistry[3] and biomimetic synthesis.[4] As a particular class, conjugated polyenes continue to generate great interest not merely because of their important biological functions in nature, but also because they have been recognized as relevant substrates for a wide variety of chemical applications. From a synthetic point of view they are important intermediates, well suited for intramolecular cascade transformations involving pericyclic reactions, providing efficient and complementary strategies toward polycycle construction.[5]

In this regard, electrocyclic reactions have witnessed extraordinary progress in recent years, demonstrating their ability to participate in sequential processes.[6] Since the spectacular synthesis of endiandric acids establishing the viability and biomimetic characteristics of the 8π–6π electrocyclization cascade to give bicyclo[4.2.0]octadiene structures,[7] the recent discovery of a series of natural products containing this bicyclic-octane moiety has fuelled studies on the pericyclic reactivity of tri- and tetraene-type polyenes ending up in elegant syntheses of several members of this unsaturated polyketide family,[8] providing a deeper understanding of their complex reactivity modes and facilitating, at the same time, the development of novel methodology.[9] Another valuable biomimetic sequence involves the combination of Knoevenagel-type condensation and hetero-6π-electrocyclization between enals and 1,3-dicarbonyl substrates. This process, referred to as formal [3+3] cycloaddition, has become a very useful strategy for the synthesis of natural 2*H*-pyran-containing compounds and derivatives including aza-heterocycles.[10]

A common feature of the mentioned processes is that they proceed easily under mild conditions, frequently with-

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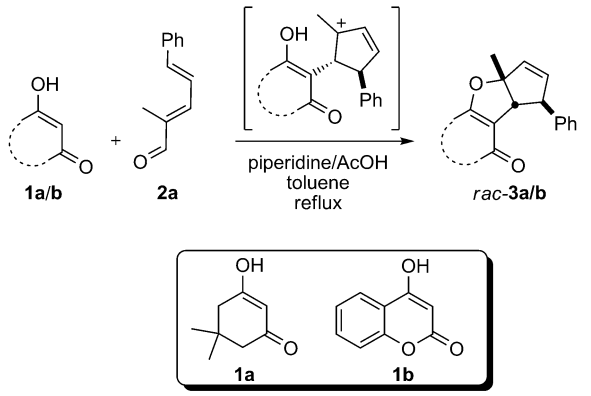
out the isolation of polyene intermediates and in which the formation of a six-membered ring is generally involved. Due to the high architectural control and selectivity displayed, some of these processes are being considered, by analogy to biology, as covalent "self-assembly"[11] events in which polycyclic molecules exhibit an intrinsic capacity to self-construct correlated to an inherent "chemical predisposition"[12] established in the precursors. On the contrary, similar pericyclic cascade reactions for cyclopentanoid-ring-system construction from conjugated polyolefinic skeletons are less common. In this field, the electrocyclization reaction of pentadienyl to cyclopentenyl cations involving 4π-electrons is a central approach, broadly studied in the case of "oxygen stabilized" cross-conjugated cationic species, the Nazarov reaction, for the synthesis of cyclopentenone derivatives.[13] This rearrangement requires the use of either strong Brønsted or Lewis acids, generally in suprastoichiometric amounts. Investigations on rapid and facile cyclizations are of current interest and cascade processes involving the trapping of 2-oxidocyclopentenyl cationic intermediates by nucleophilic species have recently been developed and termed "interrupted Nazarov reactions".[14] The related chemistry concerning unstabilized divinyl cationic systems is far less developed and mainly applied to the synthesis of indenes by electrocyclization/elimination of arylallyl cations, generally requiring harsh reaction conditions.[15] Progress in this regard has been achieved by using alternative arylallenyl precursors allowing the synthesis of benzofulvenes under catalytic conditions.[16] A related catalytic process comprises the acid-promoted cycloisomerization of trienoate moieties to bicyclo[3.1.0]hex-2-enes,[17] for which one possible mechanistic explanation involves a 4π-electrocyclic rearrangement followed by the intramolecular capture of the formed cyclopentenyl cation by an olefinic function,[8d,18] and would formally represent an example of an "interrupted" type process on unstabilized cationic species. Since these cationic pentannulations constitute a useful route to cyclopentene derivatives, improvements in this area, paralleling the Nazarov reaction, would have a significant impact on the design and development of new approaches to the synthesis of polycyclic frameworks containing five-membered rings.

In a preliminary report, we communicated that the Knoevenagel-type condensation between dimedone (**1a**) or 4-hydroxycoumarin (**1b**) and unsaturated aldehyde (*E*,*E*)-2-methyl-5-phenyl-2,4-pentadienal (**2a**) resulted in the formation of unexpected cyclopenta[*b*]furan-type derivatives **3a** and **3b**, respectively, which required consistent structural elucidation and reliable assignment of their relative stereochemistry.[19] Due to the stereoselective nature of this sequence, we have postulated a pentadienyl–cyclopentenyl cationic rearrangement as a key step, uncovering a new type of organocatalytic cascade (Scheme 1). Thus, with the lack of additional information and due to the practical and conceptually important features that emerge from this unexplored domino sequence leading to the covalent "self-assembly" of polycycles **3**, an extensive investigation toward unraveling the substrate requirements was undertaken, aiming



Scheme 1. Aldol/cationic polycyclization cascade for the synthesis of cyclopenta[*b*]furan derivatives.

at understanding the factors governing the particular chemical reactivity displayed and at validating the intermediacy of previously proposed cationic intermediates.

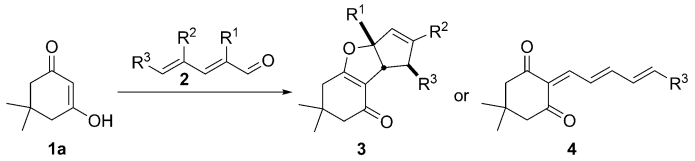
Results and Discussion

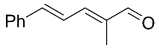
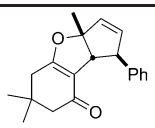
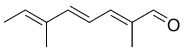
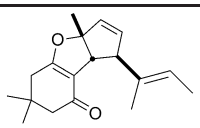
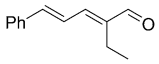
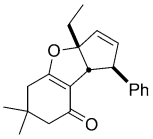
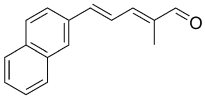
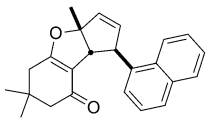
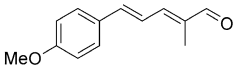
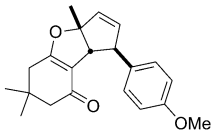
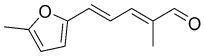
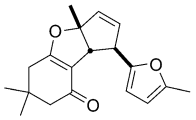
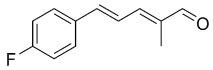
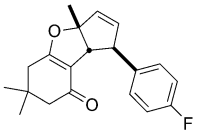
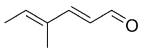
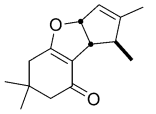
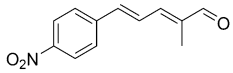
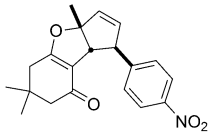
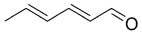
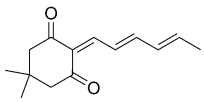
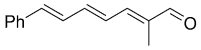
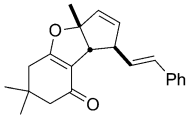
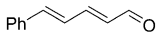
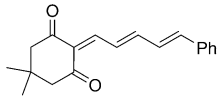
We initiated our studies by evaluating the aldehyde partner's reactivity profile. A variety of α,β,γ,δ-unsaturated aldehydes (**2a–l**), either commercially available or readily synthesized by classical methods, were tested by using dimedone as a model 1,3-dicarbonyl component. Dichloromethane at reflux and ethylenediammonium diacetate (EDDA) as the organocatalyst[20] were chosen as the optimized reaction conditions and the results are summarized in Table 1.

With these data in hand, it became clear that substitution on the aldehyde carbon chain plays a critical role in the condensation pathway. Whereas the reaction of dimedone with unbranched dienals, such as (*E*,*E*)-2,4-hexadienal (**2k**) and (*E*,*E*)-5-phenyl-2,4-pentadienal (**2l**),[21] afforded the trienedione products **4a** and **4b**, respectively, substituted analogues reacted by following a specific divergent pathway leading to the heterocyclic products **3a** and **3c–k** in moderate to good yields. Under these conditions, all successful examples gave a single stereoisomer and a marked influence of substitution pattern was observed; the new domino process becomes more efficient for electrophilic partners bearing α-alkyl groups and terminal phenyl substituents (e.g., **3a** or **3c** vs. **3k**). It has been proposed that the lack of planarity promoted by strain is the origin of the high reactivity of polyene systems prone to undergo rapid and facile transformations.[22] In a similar manner, our results also suggest that steric effects of substituents would destabilize the trienedione open form expected from Knoevenagel condensation for which no stable planar conformations would be available, facilitating in this case the novel tandem process involving a striking "interrupted" pentadienyl–cyclopentenyl cation rearrangement.

Selected substituents that affect the electronic nature of the aromatic nucleus were also examined. For δ-phenyl sub-

Table 1. Impact of aldehyde component substitution on reactivity.[a]



Aldehyde		*t* [h]	Product		Yield [%][b]	Aldehyde		*t* [h]	Product		Yield [%][b]
	**2a**	5		**3a**	82		**2g**	3		**3h**	65
	**2b**	5		**3c**	70		**2h**	4		**3i**	65
	**2c**	5		**3d**	75		**2i**	4		**3j**	30[c]
	**2d**	4		**3e**	63		**2j**	5		**3k**	40
	**2e**	5		**3f**	40		**2k**	4		**4a**	50
	**2f**	4		**3g**	60		**2l**	4		**4b**	90

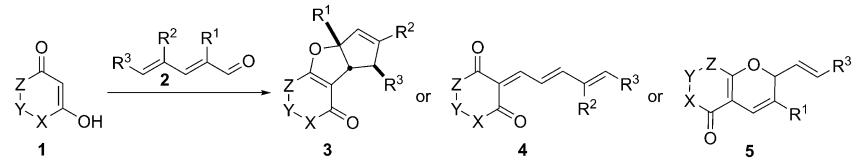
[a] All reactions were run under the following conditions: aldehyde (1 equiv), EDDA (0.2 equiv), dichloromethane (0.2 M), reflux. [b] Isolated yield. [c] 60% of the starting materials were recovered.

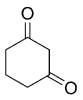
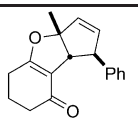
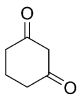
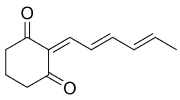
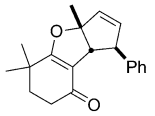
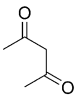
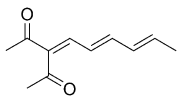
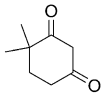
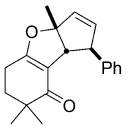
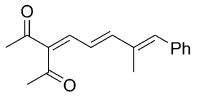
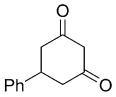
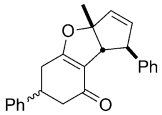
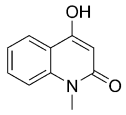
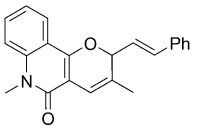
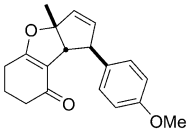
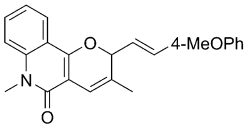
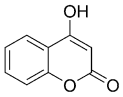
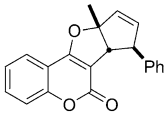
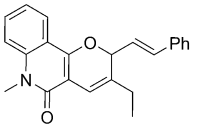
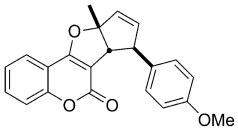
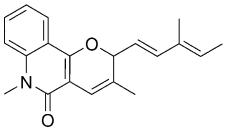
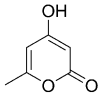
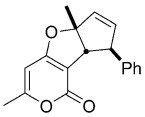
stituted dienals, although both electron-withdrawing and -donating groups were tolerated on the ring, as the electron-withdrawing strength of the substituent increases the yield decreases, an effect that is consistent with the cationic nature of the proposed intermediate (e.g., **3d** vs. **3e** vs. **3f**). On the other hand, aldehyde substrates with even more extended conjugation did not stabilize the conjugated polyene carbonyl system open form, as expected from enhancement of mesomeric effects, nor did they give alternative reaction routes, affording in all cases the same heterocyclic framework with an extra double bond (e.g., **3a** vs. **3g** or **3h** vs. **3k**).

To define the scope of the reaction as regards the nucleophilic component and to gain a reasonable overview of the extent of the process, diverse functionalized variants of 1,3-dicarbonyl structures were screened. As shown in Table 2, among the numerous reaction pathways available, again only characteristic Knoevenagel-type condensation and electrocyclization reactions, enriched by the newly discovered cycloisomerization process, were observed. Nonetheless, the 1,3-dicarbonyl partner showed a stronger impact on reactivity.

Nucleophilic components different from dimedone but keeping the cyclohexane-1,3-dione skeleton displayed low reactivity toward α-substituted aldehydes. The heterocyclic compounds of interest (**3**) were indeed the only products isolated albeit in poor yields due to modest conversion (e.g., **3l–p**). Unfortunately, this problem could not be circumvented by either using an excess of reagents or catalyst, nor by prolonging the reaction time. However, for cyclic β-keto esters 4-hydroxycoumarin (**1b**) and 4-hydroxy-6-methyl-2-pyrone (**1f**), we found good reactivity and moderate yields of the cyclized products were obtained. Nevertheless, although yields were low, the process still remains useful for practical purposes due to the degree of molecular complexity that is furnished in a single step with remarkable stereoselectivity from readily available precursors. To our surprise, whereas reactions using 4-hydroxycoumarin afforded the de-

Table 2. Impact of 1,3-dicarbonyl component on reactivity.[a]



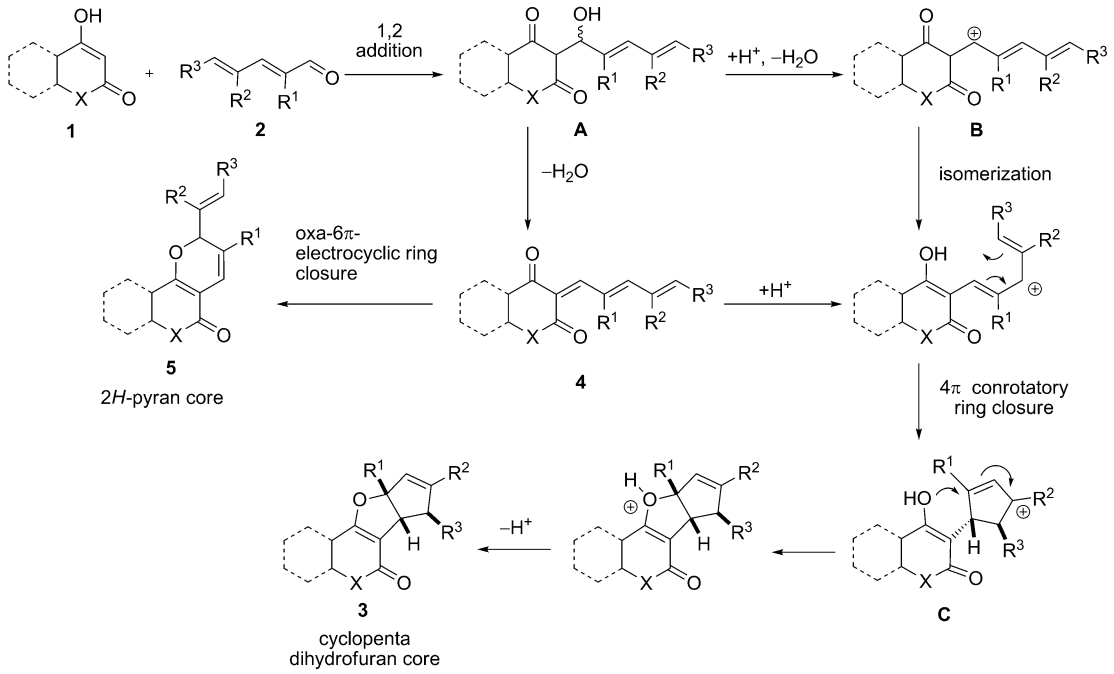
Dicarbonyl substrate		Aldehyde	t [h]	Product		Yield [%][b]	Dicarbonyl substrate		Aldehyde	t [h]	Product		Yield [%][b]
	**1c**	**2a**	6		**3l**	30[c]		**1c**	**2k**	4		**4c**	65
					**3m**			**1g**	**2k**	4		**4d**	60
	**1d**	**2a**	9			34[c,d]							
					3n			**1g**	**2m**[f]	4		**4e**	70
	**1e**	**2a**	7		**3o**	25[c,e]		**1h**	**2a**	4		**5a**	85
	**1c**	**2c**	5		**3p**	30[c]		**1h**	**2c**	3		**5b**	65
	**1b**	**2a**	6		**3b**	48		**1h**	**2b**	5		**5c**	60
	1b	**2c**	4		**3q**	52		**1h**	**2g**	3		**5d**	60
	**1f**	**2a**	9		**3r**	40							

[a] All reactions were run under the following conditions: aldehyde (1 equiv), EDDA (0.2 equiv), dichloromethane (0.2 M), reflux. [b] Isolated yields. [c] 60% of the starting materials were recovered. [d] **3m** and **3n** were obtained as an 1:1 mixture of separable regioisomers when 4,4-dimethyl-1,3-cyclohexanedione (**1d**) was used as the dicarbonyl component. [e] Mixture of diasteroisomers (see the Supporting Information for details). [f] See Scheme 3 for the chemical structure of aldehyde **2m**.

sired cyclopenta[*b*]dihydrofuran derivatives **3b** and **3q**, the use of the nitrogen counterpart 4-hydroxy-1-methyl-2-(1*H*)quinolone (**1h**) gave 2*H*-pyran derivatives **5a–d** exclusively, arising from a formal [3+3] cycloaddition. The chemical behavior of acyclic partners was also studied finding no evidence for the newly described cationic chemistry. In spite of all efforts made, we could not find conditions to promote the condensation between acyclic dicarbonyl substrates, such as acetylacetone (**1g**) or ethyl acetoacetate and α-substituted dienals recovering in all cases only starting materials.

Once again, for α-unsubstituted aldehydes, trienedione products were obtained (e.g., **4c–e**). As illustrated, the isolated products depend on the nature of the system, which demonstrates a diverse and mechanistically complex behavior and exemplifies the manifold of the Knoevenagel chemistry.

The selective formation of each individual class of products can be rationalized by considering a common synthetic intermediate (Scheme 2). Aldol **A**, resulting from initial 1,2-addition, may dehydrate to α,β,γ,δ,ε,ζ-unsaturated com-

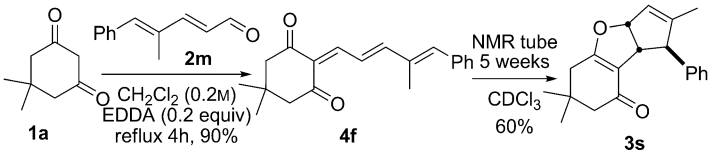


Scheme 2. Mechanism and evolution of possible intermediates.

pounds **4**, which if stable, can be isolated. When 4-hydroxy-1-methyl-2(1*H*)quinolone is used as the dicarbonyl component, these intermediates were not stable probably due to steric destabilization and an oxa-6π-electrocyclization would then follow to afford 2*H*-pyrans **5**. On the other hand, if the formation of aldol **A** results in the generation of a cationic dienyl structure **B** through protonation and loss of water, then isomerization and conformational changes to the "*U*-form" would set the stage for a 4π-electrocyclization to occur. The latter ring closure would proceed in a conrotatory manner to form brand new cyclopentenyl cation **C**, which would then be consistently trapped by the enolic oxygen to provide cyclopenta[*b*]furan derivatives **3** after deprotonation. Although both cascade processes (the aldol/oxa-6π-electrocyclization and the aldol/pentadienyl–cyclopentenyl rearrangement/intramolecular cation trapping) are based on the destabilization of the initially generated π-bond system we have not observed the formation of both product types from any reaction.

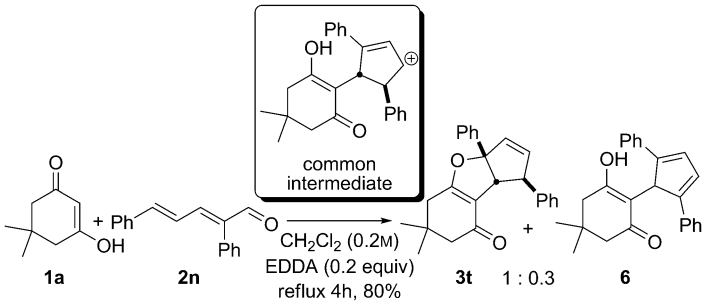
As is evident from our results, a balance of steric and electronic factors is needed for the tandem Knoevenagel/cationic cyclization process to take place, avoiding the characteristic well known chemistry of the dienone moiety. Due to a steric destabilization of the trienedione open form concomitant with a stabilization of the developing positive charge (presumably reached in the case of the β-keto ester but not for β-keto amide nucleophiles), a match combination of dienal and dicarbonyl partners evolves into a direct precursor of the proposed pentadienyl cation, which is generated in situ and unusually easily formed without the need for harsh acidic conditions. These specific structures could be considered to be a new type of polyene system capable of a previously unknown mode of reactivity.

Further experimental evidence supported our current mechanistic understanding of this scenario. Of particular interest was the condensation between dimedone and (*E*,*E*)-4-methyl-5-phenyl-2,4-pentadienal (**2m**, Scheme 3). The outcome of the reaction was the formation of trienedione **4f** in good yield as a stable product characterized by NMR spectroscopy. Unexpectedly, upon standing in deuterated chloroform, the conjugated system is not stable enough and rearranges to cyclopenta[*b*]furan heterocycle **3s** (see the Supporting Information for ^{1}H NMR spectroscopic monitoring). This phenomenon undoubtedly validates trienediones **4** as possible intermediates toward heterocycles **3** and is probably induced by acid traces contained in the deuterated solvent. Unfortunately, this has not been observed for the other trienone products obtained.



Scheme 3. Synthesis of trienedione **4f** and further isomerization to cyclopenta[*b*]dihydrofuran **3s**.

To obtain additional support for the cationic nature of the proposed intermediate involved, the reactivity of (*E*,*E*)-2,5-diphenyl-2,4-pentadienal (**2n**) was examined by using dime-



Scheme 4. Evidence for the cationic nature of the intermediate involved.

done as the dicarbonyl component (Scheme 4). We originally hypothesized that the yield of the expected tricyclic product would benefit from cationic intermediate stabilization provided by a phenyl substituent at the α-position where the charge would be partially located. To our surprise, heterocycle **3t** was indeed obtained in fair yield but contaminated with cyclopentadiene **6**. The formation of compound **6** can be explained to arise from the same cationic intermediate that gives products **3**. Although **3t** is produced, as stated before, through intramolecular trapping of the cyclopentenyl cation moiety (intermediate **C**, Scheme 2), **6** could result from β-elimitation of the same intermediate and therefore be considered as the "normal" not interrupted product of a 4π-cationic electrocyclization.

Conclusion

A new reaction pathway has been investigated in which, as a result of a Knoevenagel reaction type between 1,3-dicarbonyl substrates and α,β,γ,δ-unsaturated aldehydes, cyclopenta[*b*]furan derivatives are obtained. The development of this chemistry is based on the specific ability of appropriate substrates that react under classic condensation conditions leading to the formation of conjugated polyene carbonyl systems as reactive intermediates for which electronic and structural features permit an unusual reaction pathway. Our study also provides new fundamental insights into factors that control the reactivity of polyenic systems, identifying key elements concerning product distribution and structure–selectivity trends, offering opportunities for the development of new strategies based on easily formed cationic intermediates.

The developed protocol represents a useful approach to cyclopenta[*b*]dihydrofuran heterocycles[23] that combines atom, step, and pot economy,[24] validating a new type of spontaneous cascade reaction that expands the scope and versatility of one of the most traditional reactions, the aldol condensation. Further investigations will focus on related transformations and the development of an enantioselective version of this tandem process.

Experimental Section

Example procedure for the preparation of aldehydes 2a–d and 2n through aldol condensation and aldehydes 2e–i through vinylogous aldol condensation:

*(2*E*,4*E*,6*E*)-2-Methyl-7-phenyl-2,4,6-heptatrienal (**2f**)*: NaOH (10% w/v aq., 0.12 mL) was added to a stirred solution of cinnamaldehyde (0.38 mL, 3.00 mmol) and *trans*-2-methyl-2-butenal (0.29 mL, 3.00 mmol) in absolute ethanol (3.0 mL) at 0°C. The resulting mixture was warmed to room temperature and stirred for 72 h. HCl (0.6 N, 0.25 mL) was then added. Ethanol was evaporated under reduced pressure and the resulting crude mixture was extracted twice with ethyl acetate (10 mL). The combined organic layers were washed with brine (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Flash column chromatography on silica gel (hexanes/ethyl acetate) afforded aldehyde **2f** as an orange solid (0.355 g, 60% yield). M.p.: 89.5–90.5°C; ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ=9.46 (s, 1H), 7.47–7.43 (m, 2H), 7.37–7.25 (m, 3H), 6.99–6.70 (m, 5H), 1.89 ppm (d, J=1.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=194.4, 148.2, 141.3, 137.3, 136.3, 128.6, 128.55, 128.48, 128.0, 127.4, 126.8, 9.4 ppm; IR (KBr): $\tilde{\nu}$=3080, 3025, 3014, 2921, 2840, 2728, 1679, 1602, 1229, 1186, 1003 cm^{-1}; HRMS: m/z calcd for $C_{14}H_{14}O+H^+$: 199.1117 [M+H$^+$]; found: 199.1115.

General procedure for the condensation of 1,3-dicarbonyl substrates and unsaturated aldehydes: A mixture of 1,3-dicarbonyl substrate (1 mmol), unsaturated aldehyde (1 mmol), and EDDA (36.0 mg, 0.2 mmol) in dichloromethane (5.0 mL) was heated at reflux for the time indicated in Tables 1 or 2. The solvent was then evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexanes/ethyl acetate) to afford the corresponding products.

Compound rac-**3c**: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ=7.38–7.27 (m, 4H), 7.22–7.16 (m, 1H), 6.07 (dd, J=5.6, 2.4 Hz, 1H), 5.96 (dd, J=5.7, 2.2 Hz, 1H), 4.02 (q, J=2.0 Hz, 1H), 3.20 (q, J=1.6 Hz, 1H), 2.27 (brs, 2H), 2.24 (d, J=1.3 Hz, 2H), 1.89 (dq, J=14.9, 7.5 Hz, 1H), 1.76 (dq, J=14.5, 7.3 Hz, 1H), 1.11 (s, 3H), 1.08 (s, 3H), 0.87 ppm (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=194.3, 173.8, 143.5, 137.7, 132.4, 128.2, 127.2, 126.2, 115.6, 107.9, 56.8, 54.1, 50.9, 37.8, 33.8, 30.8, 28.7, 28.1, 7.9 ppm; IR (film): $\tilde{\nu}$=3059, 3028, 2963, 2927, 1630, 1401 cm^{-1}; HRMS: m/z calcd for $C_{21}H_{24}O_2+H^+$: 309.1849 [M+H$^+$]; found: 309.1848.

Compound **4b**: Orange/red crystals; m.p.: 118.0–119.0°C; ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ=7.89 (dd, J=13.5, 12.4 Hz, 1H), 7.70 (d, J=12.4 Hz, 1H), 7.50–7.45 (m, 2H), 7.39–7.28 (m, 3H), 7.20–7.01 (m, 2H), 6.92 (d, J=14.8 Hz, 1H), 2.52 (brs, 2H), 2.51 (brs, 2H), 1.07 ppm (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=198.6, 197.6, 153.4, 150.4, 141.7, 135.8, 129.7, 129.3, 128.7, 128.2, 128.0, 127.3, 53.7, 52.1, 29.8, 28.3 ppm; IR (KBr): $\tilde{\nu}$=3055, 3026, 2947, 2922, 1645, 1533, 1379, 1234, 1175, 1005 cm^{-1}; HRMS: m/z calcd for $C_{19}H_{20}O_2+H^+$: 281.1536 [M+H$^+$]; found: 281.1530.

Compound rac-**5a**: Colorless crystals; m.p.: 149.0–150.0°C; ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ=7.92 (brd, J=7.3 Hz, 1H), 7.46 (t, J=7.4 Hz, 1H), 7.35–7.30 (m, 2H), 7.27–7.13 (m, 5H), 6.69 (brs, 1H), 6.66 (d, J=16.0 Hz, 1H), 6.29 (dd, J=15.8, 7.4 Hz, 1H), 5.40 (d, J=7.5 Hz, 1H), 3.65 (s, 3H), 1.89 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=160.5, 152.8, 138.6, 135.5, 133.1, 130.2, 128.3, 128.2, 128.0, 126.6, 124.2, 122.6, 121.5, 115.5, 114.9, 113.7, 106.8, 80.1, 29.0, 19.3 ppm; IR (KBr): $\tilde{\nu}$=3060, 3022, 2976, 2910, 1667, 1626, 1590, 1498, 1411, 1183, 1120 cm^{-1}; HRMS: m/z calcd for $C_{22}H_{19}NO_2+Na^+$: 352.1308 [M+Na$^+$]; found: 352.1302.

Acknowledgements

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