C–C versus C–O Anionic Domino Cycloalkylation of Stabilized Carbanions: Facile One-Pot Stereoselective Preparation of Functionalized Bridged Bicycloalkanones and Cyclic Enol Ethers

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Abstract: α,α'-Diactivated cyclic- or acyclic ketones undergo a chemoselective base promoted (K_2CO_3, DBU) one-pot C–C cycloalkylation, with 1,3- and 1,4-dihalides having a *cis*-like fixed configuration. This reaction gives highly functionalized bicyclo[3.2.1]octan-9-one and bicyclo[4.2.1]nonan-9-one derivatives, which are easily transformed to seven- and eight-membered rings through a high yield retro-Dieckmann cleavage. Starting from *trans*-1,4-dibromo-2-butenes, the transformation is governed by stereoelectronic factors and leads, through a chemo- and stereoselective C–O cycloalkylation, to synthetically valuable monocyclic or fused polycyclic functionalized enol ethers of high synthetic value. Semiempirical calculations showed a small difference in energy and the late character of the transition states leading to *cis* and *trans* isomers of the corresponding fused polycyclic enol ethers. These results, although minimizing the influence of a destabilizing 1,3-interaction on the outcome of the reaction, are qualitatively in agreement with the experimental results.

Keywords: carbanions · cycloalkylation · domino reactions · enols

Introduction

Stabilized carbanions such as enolates are well-recognized as very important and versatile synthetic tools in organic synthesis, and they constitute ambident nucleophiles allowing functionalization at either carbon and oxygen.[1] In this family, mono- and dianionic species derived from β-dicarbonyl compounds have been extensively studied over the years,[2] and constitute nowadays the corner-stone of many important and synthetically useful methodologies for the regio-, chemo-, and stereoselective carbon–carbon and carbon–oxygen bonds formation.[3] However, in spite of the synthetic usefulness of these systems, only few reports deal with the reactivity of readily accessible 1,3-diactivated ketones.[4] In the acyclic version, utilization of commercially available dialkyl 1,3-acetonedicarboxylates has led to interesting transformations by reaction with various dielectrophiles such as 1,3-diacetals,[5] 1,2-dicarbonyls,[6] α-bromomethyl acrylates,[7] 1-aza-1,3-butadienes,[8] α,β-unsaturated aldehydes,[9] bisbromomethyl aromatics,[10, 11a] and other α,ω-dihalides.[11b,c] On the other hand, the chemistry of anionic species derived from cyclic 1,3-ketodicarboxylates has found only limited applications. Selective C–C dialkylation of six-membered ring precursors has been used for the preparation of bridged bicyclo[3.3.1]nonanes[7, 12] and good yields of functionalized bicyclo[4.2.1]nonanones,[13] bicyclo[4.3.1]decanones,[11] bicyclo[4.4.1]undecanones,[10b, 11] bicyclo[5.4.1]dodecanones,[11b] and bicyclo[5.5.1]-tridecanones[11b] were reported by condensation of five- to seven-membered ring α,α'-ketodiesters with α,ω-dihalides. In sharp contrast with these results, the chemoselective C–O cycloalkylation of such 1,3-diactivated cycloalkanones resulting in the formation of synthetically valuable functionalized cyclic enol ethers[14] was completely unexplored.[15]

It is the purpose of this paper to describe, in full detail, the scope and limitations of the reactivity of stabilized carbanions derived from acyclic and cyclic 1,3-ketodicarboxylates **1** towards various α,ω-dihalides **2** for the regio-, chemo-, and stereoselective formation of functionalized bridged bicycloalkanones **3** or cyclic enol ethers **4** (Scheme 1). We also present some aspects of the reactivity of these intermediates for the preparation of monocyclic and fused-polycyclic seven- and eight-membered rings.

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[+] Experimental part

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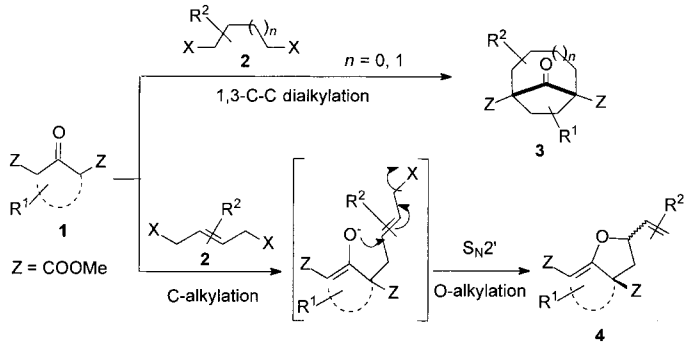


Scheme 1. C–C versus C–O cycloalkylation of acyclic and cyclic ketones **1**.

Results and Discussion

C–C Cycloalkylations of cyclopentanone 1a, b with 1,3- and 1,4-dihalides 2e–m: The results of our study on the one-pot base-promoted C–C versus C–O anionic domino cycloalkylation of 1,3-ketodicarboxylates **1** with α,ω-dihalides **2** are reported in Tables 1, 3, and 7. The presence of α-activating groups allows the enolization of 1,3-ketodicarboxylates under extremely mild conditions: either K_2CO_3 or diazabicycloundecene (DBU) in acetone or THF. While saturated α,ω-dielectrophiles **2a–d** were ineffective in the transformation (Figure 1), more reactive allylic or benzylic conformationally blocked dihalides **2e–m** reacted smoothly with dimethyl 2,5-cyclopentanonedicarboxylate (**1a**)[16] to give, through a chemoselective C–C cycloalkylation, the expected bicyclo[*n*.2.1]alkan-9-ones **3a–h** in very good yields under experimental conditions depending on the nature of the electrophile (Table 1).

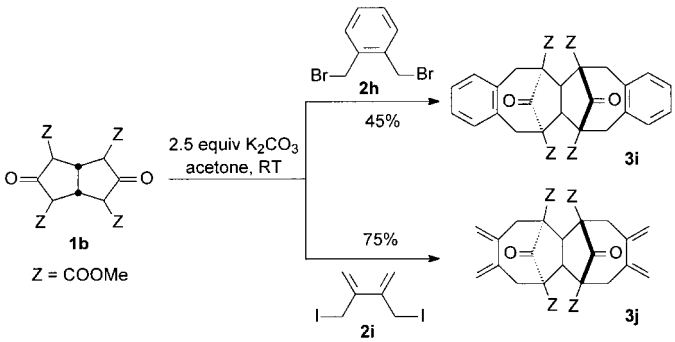
The rate of the transformation was in agreement with the scale of electrophilicity of the halogen atom. For example, DBU in hot toluene was needed to reach a 92% yield in the case of *cis*-1,4-dichlorobutene (**2e**) (entries 1 and 2) while more reactive 1,4-dibromides **2f–h** (entries 3–6) and diiode

Abstract in French: *Nous décrivons une étude détaillée sur la réactivité de cétones α,α′-diactivées, cycliques ou acycliques, vis-à-vis de divers dihalogénures en présence d'une base (K_2CO_3, DBU). Dans un premier temps, l'utilisation de 1,3- ou 1,4-dihalogénures allyliques présentant une configuration cis permet une C–C cycloalkylation totalement chimiosélective conduisant à des squelettes bicyclo[3.2.1]octan-9-one et bicyclo[4.2.1]nonan-9-one fonctionnalisés, précurseurs de noyaux cycloheptaniques ou cyclooctaniques par l'intermédiaire d'une réaction de rétro-Dieckmann. Par ailleurs, lorsque les dihalogénures sont de configuration trans, la réaction est contrôlée par des facteurs stéréoélectroniques et l'on observe alors une C–O cycloalkylation chimio- et stéréosélective qui permet d'obtenir des éthers d'énol fonctionnalisés en série mono- et polycyclique. Des calculs semiempiriques ont montré une faible différence d'énergie entre les états de transition conduisant aux isomères cis et trans des dérivés hydrofuraniques ainsi que leur caractère tardif. Ces résultats, qui tendent à minimiser une interaction-1,3 déstabilisante au niveau des états de transition, reste néanmoins qualitativement en accord avec les résultats expérimentaux.*

Figure 1. Saturated α,ω-dielectrophiles.

2i (entry 7) were cleanly transformed at room temperature with DBU or K_2CO_3 in toluene, acetone or THF. As expected, a double intermolecular 1,3-dialkylation is disfavored compared with an inter–intramolecular C–C bond forming sequence and interestingly, no competitive C–O cycloalkylation was detected regardless of the conditions employed. The method proved to be of general applicability as good yields of functionalized carbocyclic or fused heterocyclic bicyclo[4.2.1]-nonan-9-ones **3a–e** were obtained in a one-pot sequence starting from 1,4-dihalides **2e–i**. Similarly, using 1,3-allylic dihalides **2j–m** (entries 8–10) the overall process gave synthetically useful yields of the corresponding alkylidene bicyclo[3.2.1]octan-9-ones **3f–h**.

Alternatively, more complex bridged tetra- or hexacyclic structures **3i, j** could also be reached selectively starting from readily available Weiss tetraester **1b**[17] (Scheme 2). While **3j**



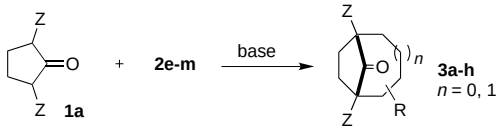
Scheme 2. Chemoselective C–C cycloalkylation of ketone **1b**.

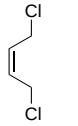
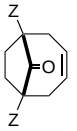
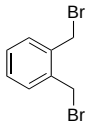
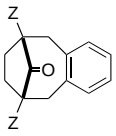
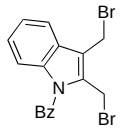
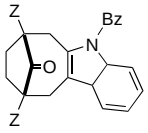
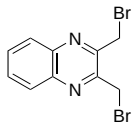
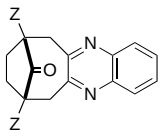
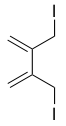
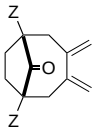
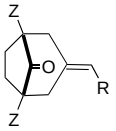
was the only product found starting from diodide **2i**, compound **3i** was obtained as an inseparable mixture (1:1) with an unidentified but symmetric di-C–O cycloalkylation product. From NMR spectra of the crude mixture (see Experimental Section) both structures **A** and **B** can be proposed (Figure 2). First, the crude ^{1}H NMR spectrum shows

Figure 2. Possible polycyclic structures for the C–O cycloalkylation product.

the characteristic AB system expected for the benzylic protons at the α position of the oxygen atom at $\delta = 4.80$ and $\delta = 5.46$, respectively, as two doublets ($J = 11.9$ Hz). Furthermore, the ^{13}C NMR spectrum shows only 16 signals over the

Table 1. C–C Cycloalkylations with **1a** (Z = COOMe).[a]



	Halide	Condition[b]	t [h]	Product[c]	Yield [%][d]
1	 **2e**	**A**	19	 **3a**	30
2		**B**	24[e]		92
3	 **2f**	**B**	1	 **3b**	100
4	 **2g**	**B**	4	 **3c**	89
5		**A**	3		79
	 **2h**			 **3d**	
6		**C**	48		85
7	 **2i**	**A**	15	 **3e**	94
8	R = H **2j**: X = Cl	**B**	24[f]	**3f**	76
9	 R = C_5H_{11} **2k**: X = Cl **2l**: X = Br	**C** **B**	24[f] 18	 **3g** **3g**	66 70
10	R = Ph **2m**: X = Br	**B**	2	**3h**	63

[a] Unless noted otherwise, all reactions were performed at room temperature. [b] **A**: K_2CO_3, acetone; **B**: DBU, toluene; **C**: DBU, THF. [c] Determined by ^{1}H NMR spectra of the crude reaction mixture. [d] Isolated. [e] 70 °C. [f] Reflux.

32 carbon atoms of the molecule, which indicates the symmetry of the compound. Both, the characteristic deshielded signal of the benzylic carbon atom at the α-position of the oxygen atom at $\delta = 71.5$ and the shielded one of the enol ether function at $\delta = 115.5$ are present together with the conjugate ester function at $\delta = 163.5$.

Interestingly enough, although at least three different C–C dialkylated polycyclic systems **C**–**E** could be formed (Figure 3), only one symmetric structure was obtained as shown by the specific NMR spectra of **3i** and **3j**. The ^{1}H NMR spectra indicated the presence of two distinct methoxy groups as two singlets, at $\delta = 3.61$ and $\delta = 3.80$ for **3i**, and $\delta = 3.44$ and $\delta = 3.65$ for **3j**. On the other hand, the ^{13}C NMR spectra cleary established the presence of one plane of symmetry with the presence of half of the expected signals (14 over 28 carbon atoms, see Experimental Section). On the basis of this analysis the two structures **D** and **E**, both having two planes of symmetry could be excluded.

Retro-Dieckmann fragmentation of bridged bicyclic derivatives 3: Prior to our study, it was known that bridged bicyclic derivatives constituted interesting precusors of fused carbocycles by simple fragmentation reactions.[18] In the case of bicyclo[4.2.1]nonanes, this interesting behavior was first observed by Carruthers[19] in 1973 but found no further development probably due to the lack of general access to functionalized [4.2.1]bicyclic skeletons.[20] On the other hand, the formation and the selective fragmentation of bicyclo[3.2.1]octanes is well-documented and constitutes a powerful method for the stereoselective construction of seven-membered rings.[21]

Since our approach proved to be of general applicability and good yields of functionalized carbocyclic or fused heterocyclic bicyclo[*n*.2.1]alkan-9-ones were obtained in a one-pot sequence we decided to study the reactivity of such highly functionalized bridged intermediaites towards the retro-

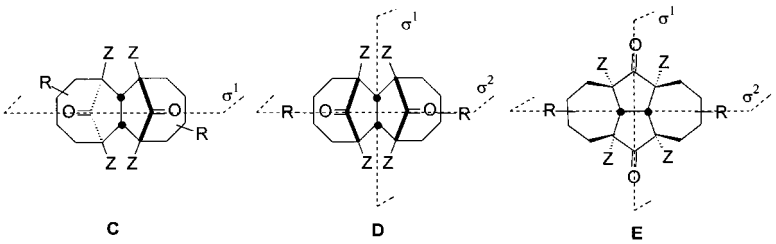


Figure 3. Possible polycyclic structures for **3i** and **3j**.

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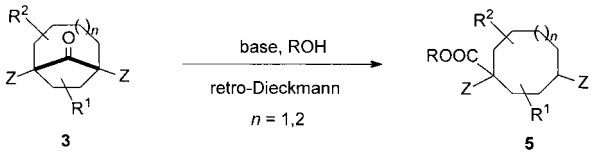
Dieckmann fragmentation leading to the corresponding eight- and seven-membered ring systems (Scheme 3).

Our previous work in this field[22] allowed us to rapidly find optimum experimental conditions for the fragmentation of

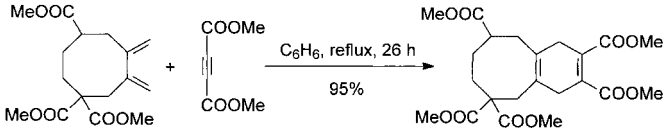


3 5

Scheme 3. Retro-Dieckmann fragmentation of bridged intermediates **3**.

bridged intermediates **3**. This step was achieved by simply heating the substrates in MeOH in the presence of 1.2 equiv DBU (Table 2) excepted in the cases of **3i**, **j** which revealed stable under these conditions or even in the presence of MeO^-Na^+ in refluxing MeOH. The retro-Dieckmann cleavage proved to be general in all the other cases and the corresponding monocyclic eight- and seven-membered rings (entries 1, 4, 6–8) or fused polycyclic compounds including heteroatomic structures (entries 2, 3, 5 and Scheme 6 see below) were obtained with good to excellent yields. For example the bicyclo[6.4.0]dodecane nucleus **5b**, present in many important naturally occurring cyclooctanoids, such as taxane, neolemnanes, and parvifoline,[23] could be obtained easily from **3b** in almost quantitative yield (entry 2). The fragmentation of **3e** (entry 4) is also of interest since the corresponding eight-membered ring **5d** conserves the feature of a synthetically valuable exocyclic *cis*-fixed 1,3-diene.[24] For example, reaction with dimethylacetylenedicarboxylate (**6**) (DMAD) in refluxing benzene for 26 h gave the corresponding [6.4.0] bicyclic compound **7** in 95% yield (Scheme 4).

Alternatively, the same reaction starting from bicyclic intermediate **3e** gave the tricyclic skeleton **3l** bearing a 1,4-diene unit (Scheme 5).



5d 6 7

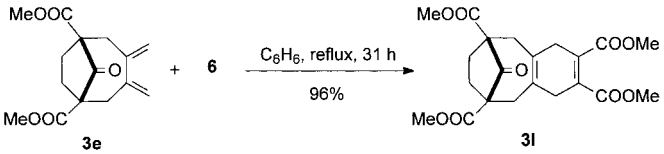
Scheme 4. Diels–Alder cycloaddition of diene **5d** with DMAD **6**.

Cleavage of **3l** under the standard conditions (DBU, MeOH, reflux) gave rise, after 4 h, to a mixture of three bicyclo[6.4.0]dodecanes **5k–m** arising from the isomerization of the 1,4-diene unit and partial aromatization of the resulting 1,3-dienes **5k**, **l**. A prolonged reaction time (41 h) provoked a

Table 2. Seven- and eight-membered rings (Z = COOMe).

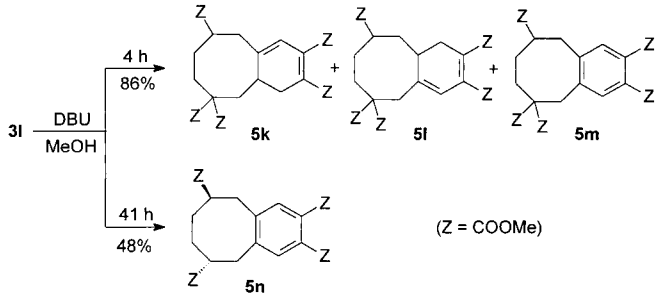
	Bridged Substrate		t [h][a]	Product (isomer ratio)[b]		Yield [%][c]
1		**3a**	5		**5a**	95
2		**3b**	28		**5b**	98
3		**3d**	3		**5c**	100
4		**3e**	6		**5d**	100
					5e (6.5)	
5		**3k**[d]	7	+		97
					5f (1)	
6		**3f**: R = H	12		**5g**	93
7		**3g**: R = C_5H_{11}	18		**5h** (1:1)	62
8		**3h**: R = Ph	20		**5i** (1.8:1)	77

[a] All reactions were performed in refluxing MeOH. [b] Determined by ^{1}H NMR spectra of the crude reaction mixture. [c] Isolated. [d] Obtained by debenzoylation (DBU, MeOH, 5 h, RT) of **3c**.



Scheme 5. Diels–Alder cycloaddition of diene **3e** with DMAD **6**.

total aromatization but also resulted in the partial decarboxylation of the geminal ester functions to give a 48% yield of the C_2 symmetric *trans*-tetraester **5n** as shown by its characteristic NMR spectra (Scheme 6).



Scheme 6. Retro-Dieckmann fragmentation of bridged tricyclic compound **3l**.

Interestingly, in the case of indole **3k**, obtained by debenzoylation of **3c** with DBU in MeOH (Table 2, entry 5), the fragmentation proceeds with good regioselectivity to give the corresponding fused heterocycles **5e** and its regioisomer **5f** in a 6.5:1 ratio determined by ^{1}H NMR spectroscopy. Selective irradiations and HMQC experiments on the major isomer **5e** (Figure 4), allowed for the characterization of each

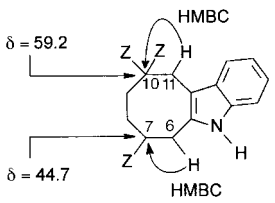
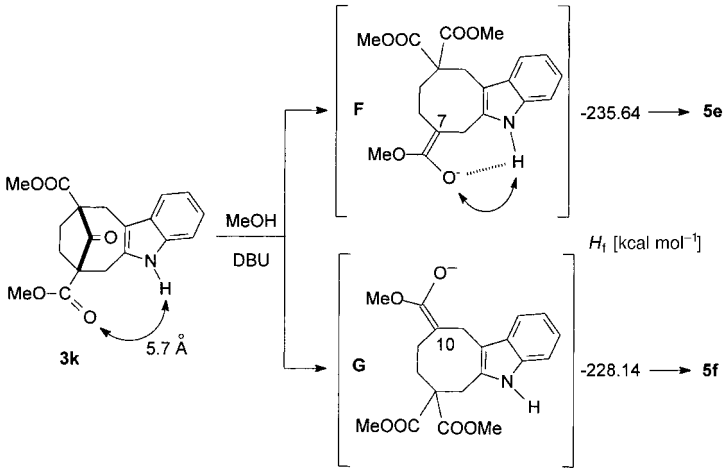


Figure 4. Structure of **5e** (Z = COOMe).

signal and gave the localization of protons at C6 and C11 as characteristic AB systems, at 3.03 (dd, $J = 15.0$, 3.8 Hz) and 3.17 (dd, $J = 15.0$, 7.6 Hz), and 3.43 (d, $J = 15.1$ Hz) and 3.55 (d, $J = 15.1$ Hz), respectively. On the other hand, the HMBC spectrum showed a cross-peak due to a ^2J(C,H) coupling constant between the protons at C6 and the C7 at $\delta = 44.7$, while the quaternary carbon C10 at $\delta = 59.2$ was correlated with the protons at C11.

The observed regioselectivity cannot be explained by an intramolecular activation of the carbomethoxy function at C7 through an intramolecular hydrogen bond since the calculated interatomic distance is larger than 5.7 Å. The stereochemical outcome of this fragmentation can be best rationalized by invoking a thermodynamic stabilization of about 7.5 kcal mol^{-1} for the enolate at C7 in **F** due to the proximity of the N–H bond compared with the enolate at C10 in **G** as shown by the calculated heats of formation (Scheme 7).



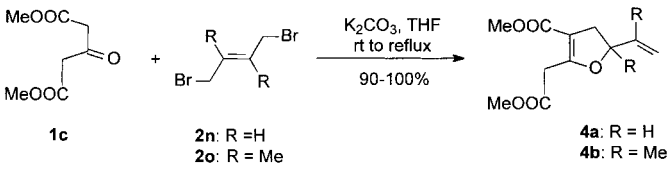
Scheme 7. Regioselective retro-Dieckmann fragmentation of bridged indole **3k**.

Noteworthy this fused indole substructure is found in caulerpin, a naturally occurring plant growth regulator pigment[25] and constitutes also the basic skeleton of the non-natural potent tricyclic antidepressant iprindole.[26] Another example of the synthetic potential of the method is the facile construction of eight-membered ring **5c** (entry 4) present in the biologically important quinoxaline series.[27] Alkylidenecycloheptanes **5g–i** could also be obtained in satisfactory yields starting from bicyclo[3.2.1]octanones **3f–h** (Table 2, entries 6–8) with modest regioselectivity depending upon the bulkiness of the R substituent on the double bond (Table 2, compare entries 7 and 8).

C–O Cycloalkylations of ketones 1 with *trans*-1,4-dihalides 2n–q: The chemoselective C–C cycloalkylation giving bicyclo[*n*.2.1]alkanones as precusors of functionalized seven- and eight-membered rings, proved to be general with *cis*-fixed α,ω-dihalides. From these results, and by considering stereoelectronic factors[28] we surmised that the transformation with *trans*-dihalides should evolve through a C-alkylation/intramolecular S_N' O-displacement to form fused functionalized tetrahydrofurans **4** (Scheme 1). Previous work[29] using the reactivity of activated methylene compounds such as acetoacetates and malonic esters have shown the feasibility of the sequence leading to monocyclic vinyl substituted dihydrofurans. This simple pathway, applied to more elaborated substrates, could easily give access to stereodefined and highly functionalized reduced furan structures[30] which abound in nature and have attracted considerable attention.[31] Moreover, related vinyl derivatives have been used as powerful reactive intermediates in many interesting stereoselective synthetic transformations such as thermal[14a, 32] and palladium[33]-catalyzed rearrangements, simple addition reactions[34] and tandem addition–fragmentation sequences.[14b,c,15b]

The overall transformation proved feasible as shown by the model condensation promoted by K_2CO_3 in refluxing THF between commercially available dimethyl 1,3-acetonedicarboxylate (**1c**) and *trans*-1,4-dibromobutenes **2n**, **o** which allowed the one-pot construction of the expected monocyclic vinyldihydrofurans **4a** and **4b** with 90% and 100% isolated yield, respectively (Scheme 8).

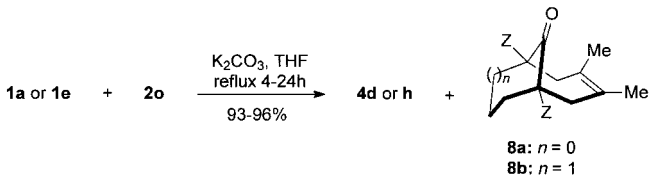
0947-6539/01/0705-1060 $ 17.50+.50/0 *Chem. Eur. J.* **2001**, *7*, No. 5



Scheme 8. Chemoselective C–O cycloalkylation of **1c** with (*E*)-1,4-dibromobutenes **2n**,**o**.

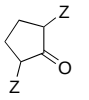
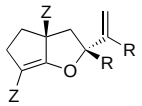
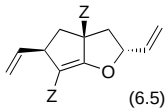
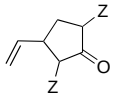
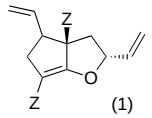
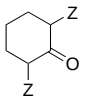
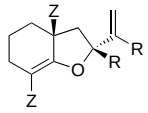
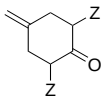
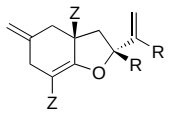
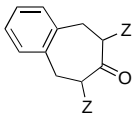
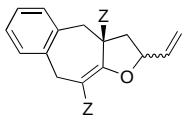
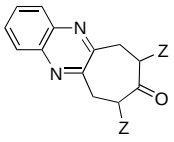
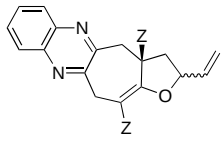
The next step was to check the generality and also to deal with the problem of the regio- and diastereoselectivity. For this purpose, we first prepared a series of functionalized mono- and polycyclic 1,3-diactivated ketones **1d**–**h** from the five- to seven-membered ring series by improvement of the existing experimental procedures.[11] The cyclic version of the selective C–O cycloalkylation was easily accomplished under the standard conditions using K_2CO_3 in refluxing THF with 1,4-dibromobutenes **2n**, **o** (Table 3). In all cases, very good yields of the expected polycyclic enol ethers **4c**–**l** were obtained with generally very high chemical purity after a simple filtration through a short pad of Celite.

In sharp contrast with recent results on the reactivity of 2-substituted cyclohexanone anions,[15b] the olefin geometry has a great influence on the outcome of the overall process when stabilized enolates, derived from cyclic ketones **1a**, **d**–**h**, are concerned. Indeed, while (*Z*)-1,4-dichloro-2-butene (**2e**) gives exclusively a tandem C–C cycloalkylation (Table 1, entries 1, 2), the reaction with its *trans*-isomer **2n** furnishes a clean C–O cycloalkylation (Table 3). A comparable effect was observed during the condensation of ethyl acetoacetate with (*E*)- or (*Z*)-1,4-dibromobutene,[35] while using palladium chemistry, the anions derived from acetoacetates and even from dimethyl 1,3-acetonedicarboxylate (**1c**) condense with either (*Z*)-2-butylene dicarbonates or (*Z*)-1,4-cycloalkenediol derivatives to furnish vinyldihydrofurans.[36] While the condensation of ketoesters **1a**, **e** with (*E*)-1,4-dibromo-2,3-dimethylbut-2-ene (**2o**) at room temperature gave similar results (entries 2, 5), interestingly, when performed in refluxing THF the corresponding bridged bicyclic compounds **8a**, **b** arising from a sigmatropic rearrangement were also isolated as by-products in a 1:6 and 1:5 ratio, respectively (Scheme 9). This interesting skeletal reor-



Scheme 9. Chemoselective C–O cycloalkylation of **1a**,**e** with (*E*)-1,4-dibromo-2,3-dimethyl-but-2-ene (**2o**).

Table 3. Reactions with 1,4-dibromobutenes **2n**,**o** (Z = COOMe).

	Ketone	Halide	*t* [h][a]	Product (isomer ratio)[b]	Yield [%][c]
1	 **1a**	**2n**	5	 **4c**: R = H	87
2		**2o**	24[d]	**4d**: R = Me	95
				 (6.5) **4e**	
3	 **1d**	**2n**	5	+	100
				 (1) **4f**	
4	 **1e**	**2n**	22	 **4g**: R = H	90
5		**2o**	18[d]	**4h**: R = Me	97
6	 **1f**	**2n**	25	 **4i**: R = H	93
7		**2o**	20[d]	**4j**: R = Me	96
8	 **1g**	**2n**	21	 *trans*:*cis* = 17:1 **4k**	92
9	 **1h**	**2n**	9	 *trans*:*cis* = 6.5:1 **4l**	91

[a] Unless noted otherwise, reactions were performed in refluxing THF. [b] Determined by ^{1}H NMR spectra of the crude reaction mixture. [c] Isolated. [d] Room temperature.

ganization has been found general in a series of fused polycyclic tetrahydrofurans allowing an efficient access to functionalized bridged bicyclo[4.2.1] ring systems.[14a]

We observed total 1,3-diastereocontrol with five- and six-membered ring cyloalkanones **1a**, **d**–**f** (entries 1–7, Table 3) leading exclusively to the product bearing the vinyl substituent *trans* to the carbomethoxy group at the ring junction. Moreover, it was found that 3-vinyl substituted cyclopentanone **1d**[37] was alkylated at C5 with complete diastereofacial control and with good regioselectivity to give the expected vinyl regioisomers **4e**, **f** in a 6.5:1 ratio (entry 3).

The structures of compounds **4** based by extensive ^{1}H and ^{13}C NMR studies confirmed by thermal rearrangement leading to the expected bridged bicyclo[4.*n*.1] derivatives.[14a] The following general trends can be observed: In the ^{1}H NMR spectra the signal due to the allylic hydrogen atom of the furan ring appeared between $\delta = 4.73 - 5.95$ for the major *trans* isomers and $\delta = 4.63 - 4.96$ for the *cis* derivatives, both usually presenting characteristic coupling constant patterns. On the other hand, ^{13}C NMR spectra show the allylic methyne of the furan ring from $\delta = 81$ to 94 and the characteristic high field and low field signals of the enol ether function between $\delta = 98 - 103$ and $\delta = 163 - 165$ corresponding to β and α sp^2-C, respectively. Furthermore, selective irradiations and HMQC coupled with NOESY interactions allowed for the characterization of each signal and for the determination of the stereochemistry (Figure 5). For example, *trans* enol ether **4c**,

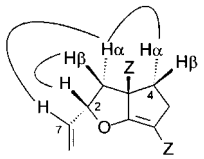


Figure 5. NOESY interactions for compound **4c** (Z = COOMe).

which serves as a model compound, reveals a characteristic signal at $\delta = 5.43$ (dddd, $J = 10.6$, 7.2, 5.0, 1.0 Hz) for the allylic hydrogen atom of the furan ring at C2, which showed a strong interaction with H3β at $\delta = 2.64$ (dd, $J = 12.5$, 5.0 Hz). This allowed the localization of H3α at $\delta = 1.68$ (dd, $J = 12.5$, 10.6 Hz) interacting with both H4α at $\delta = 1.84$ (ddd, $J = 12.5$, 10.4, 8.5 Hz) and the vinylic proton at C7.

In the case of compounds **4e**, **f** (entry 3) a total diastereofacial control was observed and this is probably a consequence of the almost planar structure of the enolate derived from **1d**. By analogy with related systems bearing a stereogenic center at the β position, one can expect that this endocyclic enolate will be attacked exclusively from the face opposite to the vinyl sustituent.[38] This imposes a relative stereochemistry 1,3-*cis* or 1,2-*cis* to the carbomethoxy group at the ring junction and 1,5-*trans* or 1,4-*trans* to the vinyl substituent form by the S_N2' substitution in both isomers **4e** and **4f**, respectively. On the other hand, we observed a good regioselectivity in favor of **4e** (entry 3) arising from a selective C-alkylation at the more accessible C5-position. The expected structure and stereochemistry of **4e**, **f** were detucted from extensive ^{1}H and ^{13}C NMR studies using essentially homonuclear correlations as shown on Figure 6 for compound **4e**.

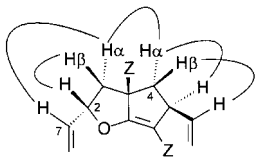


Figure 6. NOESY interactions for compound **4e** (Z = COOMe).

Cycloheptanones **1g**, **h** also give excellent yields of the corresponding tri- and tetracyclic enol ethers **4k**, **l** but surprisingly, a significant loss of the *trans*-selectivity was observed leading to a *trans*/*cis* ratio of 17 and 6.5, respectively (entries 8, 9).

Mechanistic discussion: The overall transformation most likely proceeds under kinetic control since no equilibration was observed under the experimental conditions. Moreover, AM1 calculations,[39] performed on *cis* and *trans* bicyclic vinyl furans **4c**, **g**, **k**, and **l** both in the gas phase and with solvatation (THF),[40] showed no significant differences for their heats of formation (Table 4). In order to verify the accuracy of the

Table 4. Calculated heats of formation for *trans* and *cis* isomers [kcal mol^{-1}].

Vinyl ether	AM1/RHF (gas phase)		AM1/SM (THF)	
	trans	*cis*	*trans*	*cis*
4c	– 160.65	– 160.62	– 175.63	– 175.65
4g	– 177.88	– 177.73	– 192.94	– 192.97
4k	– 141.60	– 140.40	– 158.39	– 158.00
4l	– 96.04	– 94.79	– 116.13	– 115.42

semiempirical calculations in our case, we also run ab initio calculations on both *cis* and *trans* isomers of vinyl furans **4c**. Geometries were optimized at the HF/3-21G* level and energies both at the HF/3-21G* and HF/6-31G* levels since it is known that although the first one is accurate enough for geometries, the latter is more reliable for energies.[41] Energy results at the HF/6-31G* level show a small difference of 1.55 kcal mol^{-1} in favor of the *trans* isomer. Although this value is greater than the one obtained with AM1-RHF, it could not account for the exclusive formation of the *trans* isomer under thermodynamic control (Table 5).

Table 5. Total energies calculated for **4c** [au] and $\Delta E_{[trans-cis]}$ [kcal mol^{-1}].

HF/3-21G*		ΔE	HF/6-31G*//HF/3-21G*		ΔE
trans	*cis*		*trans*	*cis*	
– 871.0265547	– 871.0272253	– 0.42	– 875.8881667	– 875.8856921	1.55

Therefore the stereochemical outcome of the overall transformation could well result from destabilization of transition state **J** by 1,3-interaction between the ring junction carbomethoxy group and the forming vinyl group as postulated by Zhao (Figure 7).[15b]

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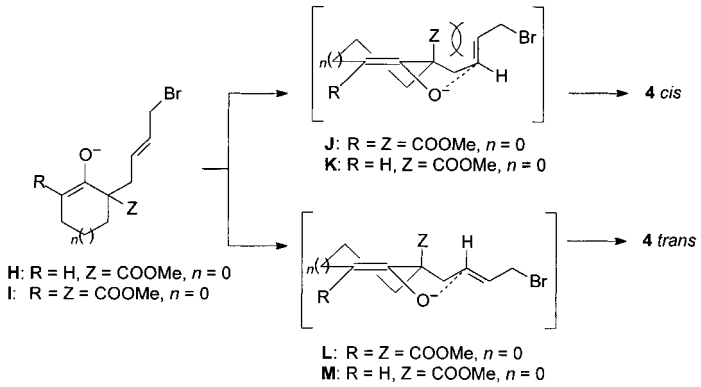


Figure 7. Possible transition states for the C–O cycloalkylation.

In order to verify and quantify this hypothesis, we did also search for the transition states involved in the cyclization of the intermediate cation free enolate to the corresponding *cis* and *trans* [3.3.0] bicyclic vinyl furans. AM1 calculations were performed in the gas phase on model enolate **H**, and with solvatation (THF)[40] on both enolates **H** and **I** which is the precursor of vinyl furan **4c** (Figure 8).

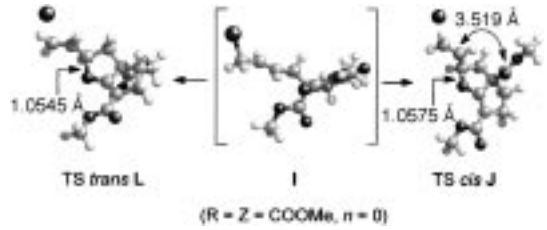


Figure 8. *anti* and *syn* Transition states **J** and **K** from AM1/SM (THF) calculations.

It appears from Table 6 and Figure 8 that in each case the differences between the two transition states leading to the *cis* and *trans* isomers are very small both for the energy and the geometry. This is not too surprising considering the length of

Table 6. Energies of the transition states **J**–**M**.

TS Energy [kcal mol^{-1}]			
AM1 (gas phase)		AM1/SM (THF)	
M *trans*	**K** *cis*	**L** *trans*	**J** *cis*
– 111.08	– 110.28	– 165.95	– 161.49
–	–	– 252.37	– 252.22

the O_1–C_5 bond (1.5045 Å and 1.5075 Å for the *cis* and *trans* isomers, respectively), which is nearly formed completely and accounts for the late character of the transition states. However, although small and unable to account for the exclusive formation of the *trans* isomer under kinetic control, the energy gap between the two transition states leading to the *cis* and *trans* bicyclic isomers, respectively, is always in favor of the *trans* isomer.

In conclusion, these calculations, although minimizing the influence of the 1,3-interaction between the ring junction carbomethoxy group and the forming vinyl group (3.519 Å) on the outcome of the reaction, are qualitatively[42] in agreement with the experimental results (Figure 8).

Interestingly enough, the chemoselective C–O cycloalkylation using K_2CO_3 in THF and 2-substituted 1,4-dibromobutenes **2p**, **q** also proceeded with a total *trans* stereoselectivity, very good chemical yields. A good to excellent regioselectivity was observed depending on the nature of the substituent at the C2-position (Table 7). (*E*)-1,2,4-Tribromobut-2-ene (**2p**) gave 87 to 98 % of the corresponding mono- and bicyclic vinyl ethers **4m**, **p**, **s** bearing a bromine atom at the vinylic position arising from a highly regioselective C-alkylation at the more accessible C4 allylic position (entries 1, 3, 5). The by-products of the reaction are not exceeding 5 %, being furans **9** formed by dehydrobromination of the other regioisomer under the reaction conditions. Utilization of (*E*)-1,4-dibromo-2-methylbut-2-ene (**2q**) also gave good chemical yields in the mono-, bi-, and tricyclic series with a total *trans* stereoselectivity (entries 2, 4, 6, and 7) but a lower regioselectivity in favor of the *trans*-isopropylidene derivatives **4n**, **q**, **t**, and **v** was observed varying from 1:3 to 1:6 depending on the nature of the starting ketodiester (compare entries 2 and 4, 6, 7).

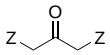
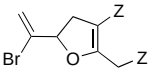
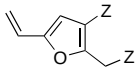
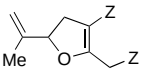
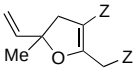
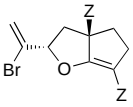
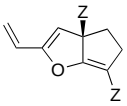
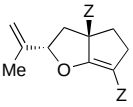
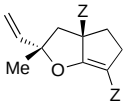
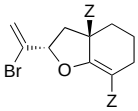
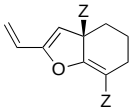
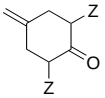
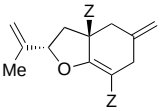
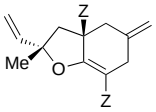
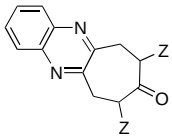
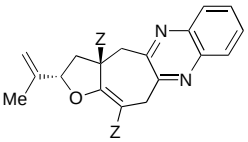
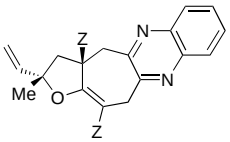
Conclusion

The synthetic versatility of stabilized carbanions derived from easily accessible α,α'-diactivated ketones has been illustrated by several selective anionic domino reactions with various α,ω-dielectrophiles. The overall transformation is governed by the nature of the electrophile. A totally chemoselective C–C cycloalkylation is found when *cis*-fixed-1,3- and 1,4-allylic or benzylic dihalides are used, leading to valuable bridged bicyclic derivatives of the [3.2.1]octane and [4.2.1]nonane series as precursors of the corresponding functionalized seven-and eight-membered rings by a selective retro-Dieckmann fragmentation. Alternatively, a stereoelectronically controlled C–O cycloalkylation leads to highly functionalized and stereochemically defined monocyclic and fused polycyclic enol ethers when *trans*-1,4-dihalides are used. The stereochemical outcome of this heterocyclization has been tentatively rationalized by semiempirical calculations for competing diastereomeric transition states. Since the experimental conditions are extremely simple, inexpensive, and very mild, we hope that extensions of our methodologies would be useful for stereoselective preparation of complex natural and unnatural products.

Experimental Section

General: Melting points were observed in open Pyrex capillary tubes and are uncorrected. FC (flash chromatography) was performed with Merck silica gel 60 (230–240 mesh).[43] TLC was performed on Alugram SIL G/UV 254 silica gel analytical plates with a 250 μm coating. IR spectra were recorded neat or in $CHCl_3$, and NMR spectra were obtained at 200 or 400 MHz in $CDCl_3$ using residual $CHCl_3$ as internal reference. Elemental analyses were determined by the Microanalytical Services at the University of Marseille III.

Table 7. Heterocyclizations with 2-substituted 1,4-dibromobutenes **2p**,**q** (Z = COOMe).

	Ketone	Halide	t [h][a]	Product (ratio)[b]	Yield[%][c]	
1		**2p**	4[d]			98
				4m +	**9a** (< 5%)	
2	**1c**	**2q**	4[d]			100
				4n (6) +	**4o** (1)	
3		**2p**	2[d]			87
				4p +	**9b** (not observed)	
4	**1a**	**2q**	17			96
				4q (4) +	**4r** (1)	
5		**2p**	4[d]			94
	1e			**4s** +	**9c** (< 5%)	
6		**2q**	24			96
	1f			**4t** (4) +	**4u** (1)	
7		**2q**	24			89
	1h			**4v** (3) +	**4w** (1)	

[a] Unless noted otherwise, all reactions were performed at room temperature in THF. [b] Determined by ^{1}H NMR spectra of the crude reaction mixture. [c] Isolated. [d] Reflux.

Calculations methodology: All calculations reported in this work were performed using either the semiempirical AM1 method[39] (RHF/AM1) available in the AMPAC program[44] or the GAUSSIAN 98 package[45] with the 3-21G* and 6-31G* basis sets at the HF level. AM1 calculations were run both in the gas phase phase and in a modeled solvent medium.[40] All transition states reported showed only one negative eigenvalue in their diagonalized force constant matrices and their belonging to the studied reaction path was checked by intrinsic reaction coordinate (IRC) in all semiempirical cases.

Materials: 1,4- and 1,3-Dihalides **2a**, **b**, **e**, **f**, **h**, **j**, **n** are commercially available and were used without further purification. 1,3-Dibromide **2l** was obtained by reaction of the corresponding dichloride **2k**[46] with NaBr in acetone under standard conditions and **2m** was obtained by radical allylic halogenation of 2-methyl-1-phenylprop-1-ene (Fluka) under standard protocol.[47] Finally, 1,3-dibromide **2c**,[48] 1,3-dimesylate **2d**,[49] 1,4-dibromides **2g**, **o**–**q**,[50–52] and diodide **2i**[53] were prepared as previously described. Commercially available anhydrous analytical grade acetone (SDS) was used for the condensations while anhydrous MeOH, toluene, and THF were obtained by distillation from magnesium and sodium/benzophenone under argon, respectively. Unless otherwise specified, all reactions involving air or moisture sensitive compounds were carried out under an atmosphere of dry argon.

General procedure for the preparation of bicyclo[*n*.2.1]alkanones: A solution of the corresponding dihalide (1 mmol) in dry solvent (5 mL) was added with a syringe to a solution of cyclopentanone dicarboxylate **1a** (1 mmol) and the appropriate base (2,5 mmol) in dry solvent (20 mL). The resulting reaction mixture was stirred at room temperature or at reflux under nitrogen for the indicated time (Table 1). After completion, when K_2CO_3 was used, simple filtration through a short pad of Celite and evaporation of the filtrate under reduced pressure gave the crude bicyclic compounds, which were purified by FC. In the case of DBU, the solvent and the volatiles were first eliminated under reduced pressure, the residue was dissolved in Et_2O (25 mL), acidified with 1N HCl (15 mL), and the organic layer was extracted with Et_2O (3×30 mL), washed with H_2O (15 mL), and brine (20 mL) to give, after drying ($MgSO_4$) and evaporation of the solvent, the crude compounds which were purified by FC.

9-Oxobicyclo[4.2.1]non-3-ene-1,6-dicarboxylic dimethyl ester (3a): R_f = 0.33 (diethyl ether/pentane 1:1); IR (neat): $\tilde{\nu}$ = 3410, 2255, 1730, 1440, 1295, 910, 735 cm^{-1}; ^{1}H NMR: δ = 5.65–5.63 (m, 2H), 3.75 (s, 6H), 2.75–2.59 (m, 4H), 2.52–2.35 (m, 2H), 2.01–1.90 (m, 2H); ^{13}C NMR: δ = 211.2, 171.7, 125.3, 57.6, 52.9, 35.0, 30.4; elemental analysis calcd (%) for $C_{13}H_{16}O_5$: C 61.90, H 6.39; found: C 60.87, H 5.98.

13-Oxotricyclo[8.2.1.0^{3,8}]trideca-3(8),4,6-triene-1,10-dicarboxylic dimethyl ester (3b): White crystals; m.p. 49–51 °C; R_f = 0.67 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2255, 1735, 1605, 1440, 1260, 1088 cm^{-1}; ^{1}H NMR: δ = 7.22 (s, 4H), 3.80 (s, 6H), 3.34 (d, J = 15.7 Hz, 2H), 3.09 (d, J = 15.7 Hz, 2H), 2.51–2.42 (m, 2H), 1.56–1.46 (m, 2H); ^{13}C NMR: δ = 212.7, 171.8, 136.3, 133.0, 127.6, 60.2, 52.9, 41.8, 27.3; elemental analysis calcd (%) for $C_{17}H_{18}O_5$: C 67.54, H 6.00; found: C 67.01, H 6.06.

4-Benzoyltetracyclo[11.2.1.0^{3,11}.0^{5,10}]hexadeca-3(11),5(10),6,8-tetraen-16-one-1,3-dicarboxylic dimethyl ester (3c): White crystals; m.p. 108–110 °C; R_f = 0.50 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 3070, 2955, 1760, 1460, 1245, 1060, 910 cm^{-1}; ^{1}H NMR: δ = 7.75 (d, J = 7.5 Hz, 2H), 7.66 (tt, J = 7.5, 1.3, 1.2 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.48 (t, J = 7.5 Hz, 2H), 7.17 (td, J = 7.9, 0.8 Hz, 1H), 7.07 (td, J = 8.3, 1.1 Hz, 1H), 6.86 (d, J = 8.3 Hz, 1H), 3.84 (s, 3H), 3.76 (s, 3H), 3.50 (d, J = 17.1 Hz, 1H), 3.33 (d, J = 16.1 Hz, 1H), 3.25 (dd, J = 17.1, 1.8 Hz, 1H), 3.18 (dd, J = 16.1, 0.8 Hz, 1H), 2.72–2.66 (m, 2H), 1.94–1.86 (m, 2H); ^{13}C NMR: δ = 212.0, 171.8, 171.3, 169.4, 136.4, 135.1, 133.7, 133.1, 130.3, 130.2 (2CH), 129.1 (2CH), 124.1, 122.6, 118.5, 115.6, 113.8, 60.1, 59.2, 53.1 (2CH$_3$), 35.3, 31.8, 30.2, 29.8; elemental analysis calcd (%) for $C_{26}H_{23}NO_6$: C 70.10, H 5.20, N 3.14; found: C 70.13, H 5.33, N 3.13.

Bicyclo[8.2.1][b]quinoxalin-17-one-1,10-dicarboxylic dimethyl ester (3d): White crystals; m.p. 141–143 °C; R_f = 0.34 (diethyl ether/pentane 9:1); IR (neat): $\tilde{\nu}$ = 3155, 2850, 2255, 1740, 1465, 735 cm^{-1}; ^{1}H NMR: δ = 8.09–8.01

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(m, 2H), 7.99–7.74 (m, 2H), 3.97 (d, $J = 16.0$ Hz, 2H), 3.84 (s, 6H), 3.52 (d, $J = 16.0$ Hz, 2H), 2.71–2.62 (m, 2H), 1.58–1.48 (m, 2H); ^{13}C NMR: $\delta =$ 211.7, 170.8, 152.4, 141.3, 130.2, 128.8, 59.0, 53.2, 44.5, 27.3; elemental analysis calcd (%) for $C_{19}H_{18}N_2O_5$: C 64.40, H 5.12, N 7.91; found: C 65.10, H 5.98, N 8.06.

3,4-Dimethylene bicyclo[4.2.1]nonan-9-one-1,6-dicarboxylic dimethyl ester (3e): white crystals, m.p. 121–123 °C; $R_f = 0.45$ (diethyl ether/pentane 1:1); IR (neat): $\tilde{\nu} = 3080$, 2925, 1760, 1440, 1250, 1110, 910 cm^{-1}; ^{1}H NMR: $\delta = 4.97$ (s, 4H), 3.73 (s, 6H), 2.88 (d, $J = 14.4$, 1.0 Hz, 2H), 2.67–2.57 (m, 2H), 2.50 (d, $J = 14.4$ Hz, 2H), 2.11–2.02 (m, 2H); ^{13}C NMR: $\delta = 209.7$, 171.6, 146.2, 117.3, 59.1, 52.9, 41.8, 30.5; elemental analysis calcd (%) for $C_{15}H_{18}O_5$: C 64.74, H 6.52; found: C 64.92, H 6.98.

Tetracyclo[8.8.1.0^{3,8}.0^{12,17}]nonadeca-3,5,7,12,14,16-hexaen-19-one-1,10-dicarboxylic dimethyl ester (3f): $R_f = 0.55$ (diethyl ether/pentane 1:1); IR (neat): $\tilde{\nu} = 2955$, 1730, 1440, 1240, 1120, 730 cm^{-1}; ^{1}H NMR: $\delta = 5.08$–5.06 (m, 2H), 3.75 (s, 6H), 3.00 (br d, $J = 14.0$ Hz, 2H), 2.63 (br d, $J = 14.0$ Hz, 2H), 2.54 (m, 2H), 1.91 (m, 2H); ^{13}C NMR: $\delta = 208.7$, 170.6, 139.1, 117.2, 58.4, 52.7, 46.3, 26.5; elemental analysis calcd (%) for $C_{13}H_{16}O_5$: C 61.9, H 6.39; found: C 62.12, H 6.08.

3-Hexylidene bicyclo[3.2.1]octan-8-one-1,5-dicarboxylic dimethyl ester (3g): $R_f = 0.64$ (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu} = 1735$, 1435, 1240, 980 cm^{-1}; ^{1}H NMR: $\delta = 5.50$ (t, $J = 7.2$ Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.02–2.90 (m, 2H), 2.60–2.43 (m, 4H), 2.20–1.43 (m, 4H), 1.39–1.20 (m, 6H), 0.87 (t, $J = 6.4$ Hz, 3H); ^{13}C NMR: $\delta = 207.8$, 170.5, 170.0, 131.6, 128.2, 58.0, 57.8, 51.9, 51.8, 39.3, 37.4, 31.0, 27.6, 26.9, 26.0, 25.7, 22.0, 13.5; elemental analysis calcd (%) for $C_{18}H_{26}O_5$: C 67.06, H 8.13; found: C 66.73, H 8.14.

3-Benzylidene bicyclo[3.2.1]octan-8-one-1,5-dicarboxylic dimethyl ester (3h): $R_f = 0.51$ (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu} = 2950$, 2360, 1735, 1435, 910 cm^{-1}; ^{1}H NMR: $\delta = 7.40$–7.20 (m, 5H), 6.67 (s, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 3.22–3.18 (m, 2H), 2.96–2.89 (m, 1H), 2.80–2.70 (m, 1H), 2.57–2.46 (m, 2H), 1.76–1.70 (m, 2H); ^{13}C NMR: $\delta = 208.3$, 170.5, 136.5, 131.7, 131.6 (2CH), 128.4, 127.1, 120.0 (2CH), 58.6, 58.4, 52.6 (2CH$_3$), 48.4, 40.7, 26.5, 26.1; elemental analysis calcd (%) for $C_{19}H_{20}O_5$: C 69.50, H 6.14; found: C 70.01, H 6.18.

Mixture of symmetric di-C–C and di-C–O cycloalkylation products (1:1): $R_f = 0.63$ (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu} = 3075$, 2945, 1765, 1260, 910 cm^{-1}; compound **3i**: ^{1}H NMR: $\delta = 7.28$–6.99 (m, 8H), 4.30 (d, $J =$ 15.1 Hz, 2H), 3.80 (s, 6H), 3.61 (s, 6H), 3.13–3.01 (m, 4H), 2.81 (d, $J =$ 10.0 Hz, 2H), 2.59 (d, $J = 10.0$ Hz, 2H); ^{13}C NMR (only 16 signals for 32 carbon atoms): $\delta = 208.1$, 170.3, 170.0, 137.9, 137.2, 129.4 (2CH), 127.3 (2CH), 62.0, 61.9, 52.1 (2OCH$_3$), 46.3, 44.3, 41.8.

Di-C–O cycloalkylation product A or B: Characteristic signals: ^{1}H NMR: $\delta = 7.40$–7.30 (m, 8H), 5.46 (d, $J = 11.9$ Hz, 2H), 4.80 (d, $J = 11.9$ Hz, 2H), 3.51 (s, 6H), 3.49 (s, 6H); ^{13}C NMR (only 16 signals for 32 carbon atoms) $\delta = 169.6$, 163.5, 161.5, 134.6, 134.2, 132.3, 131.9, 129.2, 128.4, 115.5, 71.5, 64.2, 50.9, 50.8, 46.6, 45.9; compound **3j**: white crystals; m.p. 164–166 °C; $R_f = 0.66$ ($CHCl_3$/MeOH 4:1); IR (neat): $\tilde{\nu} = 3084$, 2955, 1776, 1624, 1434, 1260, 913 cm^{-1}; ^{1}H NMR: $\delta = 5.08$–5.01 (m, 4H), 3.65 (s, 3H), 3.44 (s, 3H), 3.29 (s, 1H), 3.32 (dd, $J = 13.5$ Hz, 1H), 2.93 (d, $J = 16.2$ Hz, 1H), 2.66 (d, $J = 12.8$ Hz, 1H), 2.49 (d, $J = 12.8$ Hz, 1H); ^{13}C NMR (only 14 signals for 28 carbon atoms): $\delta = 203.4$, 169.9, 168.7, 148.6, 145.1, 118.5, 117.8, 63.0, 62.5, 52.1, 51.5, 50.3, 48.4, 41.2; elemental analysis calcd (%) for $C_{28}H_{30}O_{10}$: C 63.87, H 5.74; found: C 63.04, H 5.86.

1,13-Dimethylcarboxylate-tetracyclo[11.2.0^{3,11}.0^{5,10}]hexadeca-3(11),5(10),6,8-tetraen-4H-6-one (3k): Obtained by debenzoylation (DBU, MeOH, RT, 5 h of **3c**); white crystals; m.p. 177–179 °C; $R_f = 0.38$ (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu} = 3070$, 1760, 1460, 1245, 1055, 910 cm^{-1}; ^{1}H NMR: $\delta = 7.92$ (br s, 1H), 7.52–7.04 (m, 4H), 3.83 (s, 3H), 3.81 (s, 3H), 3.52–3.33 (m, 2H), 3.20–3.08 (m, 2H), 2.71–2.59 (m, 2H), 1.90–1.82 (m, 2H); ^{13}C NMR: $\delta = 212.6$, 172.0, 171.9, 135.2, 130.2, 129.5, 122.3, 119.7, 118.4, 110.4, 107.6, 60.4, 59.3, 53.1, 53.0, 34.8, 32.2, 30.3, 30.1; elemental analysis calcd (%) for $C_{19}H_{19}NO_5$: C 66.85, H 5.61; found: C 65.09, H 5.86.

General procedure for the Diels–Alder reaction with DMAD: A stirrered solution of the exocyclic 1,3-diene **3e** or **5d** (0.5 mmol) and DMAD (1.5 mmol) in benzene (10 mL) was refluxed under argon for the indicated time (Schemes 4 and 5). After completion (TLC), evaporation of the volatiles under reduced pressure gave the crude adducts **3l** and **7**, which were purified by FC.

1,5,6,10-Tetramethylcarboxylate-tricyclo[8,2,1,0^{3,8}]trideca-3(8),5-dien-13-one (3l): White crystals; m.p. 129–131 °C; $R_f = 0.51$ (CH_2Cl_2/MeOH 98:2); IR (neat): $\tilde{\nu} = 2955$, 1730, 1435, 1275, 910 cm^{-1}; ^{1}H NMR: $\delta = 3.75$ (s, 6H), 3.74 (s, 6H), 3.02 (s, 4H), 2.65–2.57 (m, 4H), 2.38 (d, $J = 16.1$ Hz, 2H), 1.86–1.77 (m, 2H); ^{13}C NMR: $\delta = 211.6$, 171.5, 167.7, 132.0, 124.5, 59.3, 52.9, 52.4, 40.7, 36.2, 29.2; elemental analysis calcd (%) for $C_{21}H_{24}O_9$: C 60.00, H 5.75; found: C 60.54, H 5.84.

2,3,6,6,9-Pentamethylcarboxylate-1,5,7,8,9,10-hexahydro-4*H*-benzocyclooctane (7): $R_f = 0.50$ (CH_2Cl_2/MeOH 98:2); IR (neat): $\tilde{\nu} = 3000$, 2960, 1730, 1435, 1200, 915 cm^{-1}; ^{1}H NMR: $\delta = 3.74$ (s, 3H), 3.73 (s, 3H), 3.70 (s, 6H), 3.64 (s, 3H), 3.11–2.96 (m, 3H), 2.83–2.77 (m, 2H), 2.50–2.38 (m, 1H), 2.77–2.55 (m, 2H), 2.39–2.12 (m, 2H), 1.98–1.87 (m, 2H), 1.63–1.58 (m, 1H); ^{13}C NMR: $\delta = 175.4$, 172.2, 171.8, 168.0, 167.9, 152.2, 132.3, 129.1, 125.2, 58.4, 53.4, 52.8, 52.7, 52.2, 51.8, 44.3, 35.3, 34.9, 33.6, 33.1, 29.0, 25.7; elemental analysis calcd (%) for $C_{22}H_{28}O_{10}$: C 58.40, H 6.24; found: C 59.11, H 6.48.

General procedure for the retro-Dieckmann fragmentation of bicyclic compounds: A solution of bridged bicyclic compounds **3** (1 mmol) and DBU (1 mmol) in MeOH (15 mL) was stirred under argon at reflux for the time indicated in Table 2. After completion (TLC), evaporation of the volatiles under reduced pressure gave the corresponding crude seven- or eight-membered rings **5a–n**, which were purified by FC. Compounds **5a–d** and **5g–i** have been fully characterized and described by us, previously.[54]

Cyclooctane[*b*]indole-7,10,10(11*H*)-tricarboxylic methyl ester (5e) (major isomer): White crystals; m.p. 137–139 °C; $R_f = 0.44$ (diethyl ether/pentane 9:1); IR (neat): $\tilde{\nu} = 3390$, 2995, 1725, 1460, 1435, 1270, 1245, 910, 735 cm^{-1}; ^{1}H NMR: $\delta = 8.15$ (br s, 1H), 7.38 (d, $J = 7.6$ Hz, 1H), 7.24 (d, $J = 1.8$ Hz, 1H), 7.07 (td, $J = 7.0$, 0.8, 1H), 7.02 (td, $J = 7.3$, 0.8 Hz, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 3.66 (s, 3H), 3.55 (d, $J = 15.1$ Hz, 1H), 3.43 (d, $J = 15.1$ Hz, 1H), 3.17 (d, $J = 15.0$ Hz, 1H), 3.03 (dd, $J = 15.0$, 3.8 Hz, 1H), 2.84 (m, 1H), 2.08–1.77 (m, 4H); ^{13}C NMR: $\delta = 175.2$, 172.3, 171.9, 135.0, 134.3, 128.2, 121.2, 119.3, 118.1, 110.8, 107.4, 59.2, 52.7, 52.6, 52.0, 44.7, 29.0, 27.9, 27.6, 24.7; elemental analysis calcd (%) for $C_{20}H_{23}NO_6$: C 64.33, H 6.21, N 3.25; found: C 63.98, H 6.19, N 3.68.

Cyclooctane[*b*]indole-7,7,10(6*H*)-tricarboxylic methyl ester (5f) (minor isomer): not isolated; ^{13}C NMR: $\delta = 175.2$, 172.3, 171.9, 135.0, 134.3, 128.2, 121.2, 119.3, 118.1, 110.8, 107.4, 59.6, 53.0, 52.9, 51.8, 45.9, 29.0, 28.8, 25.7, 22.5.

Inseparable mixture of 5k–m: Characteristic NMR signals of the mixture; ^{1}H NMR: $\delta = 7.44$–6.83 (m, 4H), 3.75 (s, 3H), 3.69 (s, 3H), 3.65 (s, 3H), 3.64 (s, 3H), 3.62 (s, 3H); ^{13}C NMR: $\delta = 175.3$, 173.4, 171.8, 170.8, 166.7, 141.4, 138.5, 127.6, 123.6, 58.9, 52.8, 52.5, 52.3, 52.2, 51.8, 43.7, 37.1, 35.4, 34.8, 31.6, 28.7, 25.2.

5,6,7,8,9,10-Hexahydrobenzocyclooctene-2,3,6,9-tetramethylcarboxylate (5n): IR (neat): $\tilde{\nu} = 2950$, 1730, 1440, 1200, 1035, 980, 790 cm^{-1}; ^{1}H NMR: $\delta = 7.52$ (s, 1H), 7.49 (s, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.71 (s, 3H), 3.69 (s, 3H), 3.20–2.96 (m, 4H), 2.76–2.48 (m, 2H), 2.23–1.49 (m, 4H); ^{13}C NMR: $\delta = 175.0$ (2CO), 174.7 (2CO), 141.8, 142.5, 130.8 (2CH), 130.4, 130.0, 52.7 (2OCH$_3$), 52.0, 51.9, 47.2, 46.4, 34.8, 34.1, 25.9, 25.6; elemental analysis calcd (%) for $C_{20}H_{24}O_8$: C 61.22, H 6.16; found: C 61.52, H 6.63.

General procedure for the preparation of cyclic enol ethers: Powdered K_2CO_3 (2.5 mmol) was added to a solution of keto dicarboxylate **1** (1 mmol) in dry THF (15 mL) and the mixture was stirred under nitrogen for 15 min at room temperature. The selected 1,4-dihalide **2** (1 mmol) in dry THF (10 mL) was then added through a syringe and the resulting reaction mixture was stirred under reflux for the time indicated in Table 3. After completion (TLC), filtration through a short pad of celite and evaporation of the volatiles under reduced pressure gave crude enol ethers **4** with very high chemical purety. Analytical samples were obtained by rapid flash chromatography on SiO_2.

4,5-Dihydro-2-methoxycarbonylmethyl-3-methylcarboxylate-5-vinylfuran (4a): $R_f = 0.59$ (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu} = 3060$, 1745, 1700, 1655, 1000, 940 cm^{-1}; ^{1}H NMR: $\delta = 5.92$ (ddd, $J = 17.1$, 10.3, 6.6 Hz, 1H), 5.30 (dt, $J = 17.1$, 1.1 Hz, 1H), 5.19 (dt, $J = 10.3$, 1.1 Hz, 1H), 5.13–5.04 (m, 1H), 3.73 (s, 2H), 3.70 (s, 3H), 3.68 (s, 3H), 3.10 (ddt, $J = 14.7$, 10.5, 1.0 Hz, 1H), 2.69 (ddt, $J = 14.7$, 7.7, 1.0 Hz, 1H); ^{13}C NMR: $\delta = 168.3$, 165.4, 162.4, 136.3, 116.5, 103.8, 82.9, 52.0, 50.8, 35.1, 33.4; elemental analysis calcd (%) for $C_{11}H_{14}O_5$: C 58.40, H 6.24; found: C 58.39, H 6.26.

4,5-Dihydro-5-isopropenyl-2-methoxycarbonylmethyl-5-methyl-3-methylcarboxylate furan (4b): $R_f = 0.35$ (diethyl ether/pentane 7:3); IR (neat):

$\tilde{\nu}$ = 2955, 1750, 1700, 1650, 1440, 1245, 1050, 910, 760 cm^{-1}; ^{1}H NMR: δ = 5.00 – 4.98 (m, 1H), 4.81 (t, J = 1.4 Hz, 1H), 3.74 (s, 2H), 3.69 (s, 3H), 3.67 (s, 3H), 2.93 (dt, J = 14.7, 1.0 Hz, 1H), 2.68 (dt, J = 14.7, 1.0 Hz, 1H), 1.76 (s, 3H), 1.46 (s, 3H); ^{13}C NMR: δ = 168.5, 165.8, 161.5, 146.7, 109.9, 103.3, 90.1, 52.0, 50.8, 40.8, 33.7, 25.8, 18.2; elemental analysis calcd (%) for $C_{13}H_{18}O_5$: C 61.41, H 7.13; found: C 61.45, H 7.11.

3a,6-Dimethylcarboxylate-2,3,4,5-tetrahydro-2-vinyl-cyclopenta[b]furan (4c): White crystals; m.p. 42 – 44 °C; R_f = 0.39 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 3060, 1730, 1720, 1700, 1670, 1000, 940 cm^{-1}; ^{1}H NMR: δ = 5.92 (ddd, J = 17.1, 10.4, 7.2 Hz, 1H), 5.43 (dddd, J = 10.6, 7.2, 5.0, 1.0 Hz, 1H), 5.36 (dt, J = 17.1, 1.0 Hz, 1H), 5.24 (dt, J = 10.4, 1.0 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.02 (ddd, J = 14.5, 10.4, 6.0 Hz, 1H), 2.75 (dd, J = 14.5, 8.5 Hz, 1H), 2.64 (dd, J = 12.5, 5.0 Hz, 1H), 2.35 (dd, J = 12.5, 6.0 Hz, 1H), 1.84 (ddd, J = 12.5, 10.4, 8.5 Hz, 1H), 1.68 (dd, J = 12.5, 10.6 Hz, 1H); ^{13}C NMR: δ = 172.8, 170.6, 165.0, 135.7, 118.9, 98.8, 94.2, 64.7, 52.8, 51.3, 40.9, 34.2, 33.9; elemental analysis calcd (%) for $C_{13}H_{16}O_5$: C 61.90, H 6.39; found: C 61.80, H 6.35.

3a,6-Dimethylcarboxylate-2-isopropenyl-2-methyl-2,3,4,5-tetrahydro-cyclopenta[b]furan (4d): R_f = 0.45 (diethyl ether/pentane 7:3); IR (neat) δ = 2950, 1730, 1700, 1670, 1440, 1230, 1060, 910 cm^{-1}; ^{1}H NMR: δ = 5.07 (s, 1H), 4.76 (t, J = 1.4 Hz, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 2.95 (ddd, J = 14.3, 10.4, 5.7 Hz, 1H), 2.73 (dd, J = 14.1, 7.7 Hz, 1H), 2.69 (d, J = 12.7 Hz, 1H), 2.21 (dd, J = 12.3, 5.7 Hz, 1H), 1.97 – 1.83 (m, 1H), 1.89 (d, J = 12.7 Hz, 1H), 1.76 (t, J = 0.6 Hz, 3H), 1.45 (s, 3H); ^{13}C NMR: δ = 173.8, 170.0, 165.1, 148.1, 109.4, 100.4, 100.2, 64.1, 52.7, 51.1, 44.1, 36.5, 33.0, 25.3, 18.5; elemental analysis calcd (%) for $C_{15}H_{20}O_5$: C 64.27, H 7.19; found: C 64.21, H 7.21.

3a,6-Dimethylcarboxylate-2,5-divinyl-2,3,4,5-tetrahydro-cyclopenta[b]furan (4e): R_f = 0.47 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 3080, 1740, 1730, 1700, 1665, 990, 935 cm^{-1}; ^{1}H NMR: δ = 5.92 (ddd, J = 16.2, 10.3, 7.1 Hz, 1H), 5.90 (ddd, J = 17.1, 11.6, 6.1 Hz, 1H), 5.42 – 5.37 (m, 1H), 5.37 (dt, J = 16.2, 1.0 Hz, 1H), 5.27 (dt, J = 10.3, 1.0 Hz, 1H), 5.00 (dt, J = 17.1, 1.5 Hz, 1H), 4.96 (dt, J = 11.6, 1.5 Hz, 1H), 3.79 – 3.67 (m, 1H), 3.69 (s, 3H), 3.71 (s, 3H), 2.44 (dd, J = 12.7, 4.8 Hz, 1H), 2.38 (d, J = 12.8 Hz, 1H), 2.14 (dd, J = 12.8, 8.5 Hz, 1H), 171.5, 1.78 (dd, J = 12.7, 10.8 Hz, 1H); ^{13}C NMR: δ = 173.5, 164.6, 139.1, 135.3, 119.2, 114.1, 100.0, 93.1, 63.3, 52.7, 51.3, 50.0, 41.8, 39.5; elemental analysis calcd (%) for $C_{15}H_{18}O_5$: C 64.74, H 6.52; found: C 64.86, H 6.36.

3a,6-Dimethylcarboxylate-2,4-divinyl-2,3,4,5-tetrahydro-cyclopenta[b]furan (4f): R_f = 0.73 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 3080, 1760, 1745, 1715, 1665, 1645, 995, 930 cm^{-1}; ^{1}H NMR: δ = 5.93 (ddd, J = 16.2, 10.3, 7.1 Hz, 1H), 5.73 (ddd, J = 17.1, 10.4, 6.6 Hz, 1H), 5.34 (d, J = 16.2, 1H), 5.23 (d, J = 10.3 Hz, 1H), 5.20 – 5.16 (m, 1H), 5.08 (dt, J = 17.1, 1.1 Hz, 1H), 5.05 (dt, J = 10.4, 1.1 Hz, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 3.08 (dd, J = 13.0, 9.3 Hz, 1H), 2.95 – 2.91 (m, 1H), 2.86 (dd, J = 12.2, 4.8 Hz, 1H), 2.84 (dd, J = 13.0, 7.5 Hz, 1H), 1.64 (dd, J = 12.2, 10.9 Hz, 1H); ^{13}C NMR: δ = 170.8, 170.0, 164.4, 141.1, 135.2, 119.0, 117.4, 98.8, 93.0, 68.2, 52.3, 51.8, 50.9, 39.8, 38.8; elemental analysis calcd (%) for $C_{15}H_{18}O_5$: C 64.74, H 6.52; found: C 64.66, H 6.41.

3a,7-Dimethylcarboxylate-2,3,5,6-tetrahydro-2-vinyl-4*H*-benzofuran (4g): R_f = 0.40 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 3070, 1730, 1685, 1650 cm^{-1}; ^{1}H NMR: δ = 5.83 (dddd, J = 17.1, 10.3, 6.5, 1.0 Hz, 1H), 5.37 (dt, J = 17.1, 1.0 Hz, 1H), 5.21 (dt, J = 10.3, 1.0 Hz, 1H), 4.86 – 4.75 (m, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 2.57 (ddt, J = 12.7, 4.8, 1.0 Hz, 1H), 2.46 – 2.40 (m, 1H), 2.44 (dd, J = 8.4, 3.9 Hz, 1H), 1.85 – 1.78 (m, 1H), 1.70 – 1.58 (m, 1H), 1.38 – 1.31 (m, 3H); ^{13}C NMR: δ = 173.5, 167.4, 163.5, 135.7, 118.1, 99.5, 82.1, 55.2, 52.8, 51.2, 42.3, 31.8, 23.7, 19.6; elemental analysis calcd (%) for $C_{14}H_{18}O_5$: C 63.15, H 6.81; found: C 63.05, H 6.78.

3a,7-Dimethyl-2-isopropenyl-2-methyl-2,3,5,6-tetrahydro-4*H*-benzofuran (4h): White crystals; m.p. 92 – 94 °C; R_f = 0.55 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2950, 1730, 1700, 1670, 1440, 1380, 1230, 1055, 910, 770 cm^{-1}; ^{1}H NMR: δ = 5.13 (m, 1H), 4.73 (t, J = 1.4 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 2.64 (d, J = 12.9 Hz, 1H), 2.30 – 2.39 (m, 3H), 1.89 (d, J = 12.9 Hz, 1H), 1.74 (m, 3H), 1.52 – 1.40 (m, 3H), 1.37 (s, 3H); ^{13}C NMR: δ = 174.8, 167.2, 163.1, 148.5, 109.1, 99.4, 89.0, 54.7, 52.6, 51.0, 45.8, 33.1, 25.2, 23.3, 19.0, 18.5; elemental analysis calcd (%) for $C_{16}H_{22}O_5$: C 65.29, H 7.53; found: C 65.88, H 7.58.

3a,7-Dimethylcarboxylate-5-methylene-2-vinyl-2,3,5,6-tetrahydro-4*H*-benzofuran (4i): R_f = 0.41 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 3080, 1785, 1730, 1690, 1010, 865 cm^{-1}; ^{1}H NMR: δ = 5.88 (ddd, J = 17.0, 10.3, 6.3 Hz, 1H), 5.41 (dt, J = 17.0, 1.2 Hz, 1H), 5.25 (dt, J = 10.3, 1.1 Hz, 1H), 4.92 – 4.80 (m, 3H), 3.74 (s, 3H), 3.66 (s, 3H), 3.20 (dm, J = 19.5 Hz, 1H), 3.03 (d, overlapping, J = 19.5 Hz, 1H), 3.00 (d, J = 12.7 Hz, 1H), 2.98 (d, J = 12.7 Hz, 1H), 2.66 (dd, J = 12.6, 4.9 Hz, 1H), 2.19 (br d, J = 12.7 Hz, 1H), 1.75 (dd, J = 12.6, 11.3 Hz, 1H); ^{13}C NMR: δ = 172.3, 166.6, 163.8, 139.9, 135.2, 118.5, 112.3, 98.3, 83.0, 56.9, 52.6, 51.2, 41.6, 40.9, 31.3; elemental analysis calcd (%) for $C_{15}H_{18}O_5$: C 64.74, H 6.52; found: C 64.83, H 6.36.

3a,7-Dimethylcarboxylate-2-isopropenyl-2-methyl-5-methylene-2-vinyl-2,3,5,6-tetrahydro-4*H*-benzofuran (4j): R_f = 0.40 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 3155, 3080, 1790, 1730, 1680, 1650, 1215, 890 cm^{-1}; ^{1}H NMR: δ = 5.15 (m, 1H), 4.90 (m, 1H), 4.77 (m, 2H), 3.74 (s, 3H), 3.65 (s, 3H), 3.21 (dm, J = 19.7 Hz, 1H), 3.03 (dm, J = 19.7 Hz, 1H), 2.85 (d, J = 12.6 Hz, 1H), 2.68 (d, J = 12.9 Hz, 1H), 2.21 (br d, J = 12.6 Hz, 1H), 1.97 (d, J = 12.9 Hz, 1H), 1.76 (br s, 3H), 1.37 (s, 3H); ^{13}C NMR: δ = 173.9, 166.9, 163.7, 148.3, 140.2, 112.0, 109.5, 98.5, 90.3, 56.8, 52.6, 51.3, 45.3, 42.8, 31.2, 25.4, 18.7; elemental analysis calcd (%) for $C_{17}H_{22}O_5$: C 66.65, H 7.24; found: C 67.02, H 7.38.

3a,10-Dimethylcarboxylate-1-oxa-2,3,4,9-tetrahydro-2-vinyl-benzo[f]azulene (4k): Two isomers (*trans*/*cis* = 17:1): White crystals; m.p. 126 – 128 °C; R_f = 0.54 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 3080, 1730, 1685, 1640, 975, 940, 920 cm^{-1}; elemental analysis calcd (%) for $C_{19}H_{20}O_5$: C 69.50, H 6.14; found: C 68.37, H 5.96.

***trans* Isomer**: ^{1}H NMR: δ = 7.01 – 7.22 (m, 4H), 5.77 (ddd, J = 17.0, 10.3, 6.3 Hz, 1H), 5.35 (dt, J = 17.0, 1.0 Hz, 1H), 5.19 (dt, J = 10.3, 1.0 Hz, 1H), 4.73 (dddd, J = 11.0, 6.3, 5.0, 1.0 Hz, 1H), 3.76 (s, 3H), 3.71 (d, J = 2.2 Hz, 2H), 3.46 (s, 3H), 3.31 (d, J = 14.0 Hz, 1H), 3.12 (d, J = 14.0 Hz, 1H), 2.74 (dd, J = 12.4, 5.0 Hz, 1H), 1.83 (dd, J = 12.4, 11.0 Hz, 1H); ^{13}C NMR: δ = 172.8, 168.0, 163.2, 141.1, 135.7, 135.0, 129.5, 129.0, 127.4, 126.6, 118.1, 103.3, 80.8, 58.0, 52.8, 51.7, 41.8, 39.0, 31.5.

***cis* Isomer**: ^{1}H NMR: δ = 7.22 – 7.10 (m, 4H), 5.76 (ddd, J = 17.1, 10.4, 6.3 Hz, 1H), 5.28 (dt, J = 17.1, 1.5 Hz, 1H), 5.11 (dt, J = 10.4, 1.5 Hz, 1H), 4.86 – 4.87 (m, 1H), 3.71 (s, 3H), 3.71 (d, J = 2.2 Hz, 2H), 3.38 (s, 3H), 3.27 (d, J = 14.5 Hz, 1H), 3.14 (d, J = 14.5 Hz, 1H), 2.60 (dd, J = 12.7, 3.2 Hz, 1H), 2.28 (dd, J = 12.7, 8.4 Hz, 1H).

3a,12-Dimethyldicarboxylate-2,3,4,11,12,12a-hexahydro-1-oxa-2-vinyl-5,10-diazanaphtho[2,3-f]azulene (4l): Two isomers (*trans*/*cis* = 6.5:1): White crystals; m.p. 152 – 154 °C; R_f = 0.54 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 3080, 1735, 1690, 1640, 965, 915 cm^{-1}; elemental analysis calcd (%) for $C_{21}H_{20}N_2O_5$: C 66.31, H 5.30, N 7.36; found: C 67.01, H 5.66, N 7.57.

***trans* Isomer**: ^{1}H NMR: δ = 8.05 – 7.91 (m, 3H), 7.73 – 7.63 (m, 1H), 5.66 (ddd, J = 17.0, 10.3, 6.2 Hz, 1H), 5.25 (d, J = 17.0 Hz, 1H), 5.07 (d, J = 10.3 Hz, 1H), 4.96 – 4.80 (m, 1H), 4.10 (d, J = 15.9 Hz, 1H), 3.95 (d, J = 15.9 Hz, 1H), 3.76 (s, 3H), 3.63 (s, 3H), 3.72 (d, J = 14.9 Hz, 1H), 3.37 (d, J = 14.9 Hz, 1H), 2.81 (dd, J = 12.7, 5.4 Hz, 1H), 1.83 (dd, J = 12.7, 10.3 Hz, 1H); ^{13}C NMR: δ = 171.5, 166.3, 163.5, 155.0, 151.2, 140.8, 140.6, 135.0, 129.2, 128.8, 128.4, 128.0, 118.0, 100.8, 81.9, 56.5, 53.0, 51.4, 41.4, 41.2, 33.2.

***cis* Isomer**: ^{1}H NMR: δ = 8.05 – 7.91 (m, 3H), 7.73 – 7.63 (m, 1H), 5.90 (ddd, J = 17.0, 10.4, 6.0 Hz, 1H), 5.27 (d, J = 17.0 Hz, 1H), 5.13 (d, J = 10.4 Hz, 1H), 4.96 – 4.63 (m, 1H), 4.10 (d, J = 15.9 Hz, 1H), 3.95 (d, J = 15.9 Hz, 1H), 3.75 (s, 3H), 3.72 (d, J = 14.9 Hz, 1H), 3.62 (s, 3H), 3.37 (d, J = 14.9 Hz, 1H), 2.81 (dd, J = 12.8, 6.6 Hz, 1H), 2.40 (dd, J = 12.8, 7.3 Hz, 1H); ^{13}C NMR: δ = 172.0, 166.2, 165.9, 152.6, 151.3, 140.6, 140.4, 134.9, 129.1, 129.0, 128.3, 127.8, 117.8, 99.6, 82.6, 58.7, 55.4, 51.9, 41.4, 41.2, 33.8.

5-(1-Bromovinyl)-2-methoxycarbonylmethyl-3-methylcarboxylate-4,5-dihydrofuran (4m): R_f = 0.53 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2955, 1745, 1710, 1630, 1440, 1240, 1070, 915 cm^{-1}; ^{1}H NMR: δ = 6.00 (dd, J = 2.1, 1.0 Hz, 1H), 5.58 (dd, J = 2.1, 1.0 Hz, 1H), 5.16 (ddt, J = 10.9, 7.4, 1.0 Hz, 1H), 3.81 (dd, J = 16.4, 8.1 Hz, 1H), 3.75 – 3.65 (m, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.15 (ddt, J = 15.2, 10.9, 1.0 Hz, 1H), 2.93 (ddt, J = 15.2, 7.4, 1.0 Hz, 1H); ^{13}C NMR: δ = 168.6, 164.3, 162.1, 131.2, 117.9, 104.3, 83.9, 52.4, 51.3, 35.4, 33.6; elemental analysis calcd (%) for $C_{11}H_{13}BrO_3$: C 43.30, H 4.29; found: C 42.92, H 4.03.

2-Methoxycarbonylmethyl-3-methylcarboxylate-5-vinylfuran (9a): R_f = 0.55 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2960, 1750, 1720, 1440, 1410, 1260, 1075, 790 cm^{-1}; ^{1}H NMR: δ = 6.51 (s, 1H), 6.41 (dd, J = 17.5, 11.3 Hz, 1H), 5.67 (dd, J = 17.5, 1.0 Hz, 1H), 5.21 (dd, J = 11.3, 1.0 Hz, 1H), 4.05 (s, 2H), 3.80 (s, 3H), 3.71 (s, 3H); ^{13}C NMR: δ = 169.0, 163.8, 153.5, 153.4, 124.3, 116.9, 114.1, 108.2, 52.5, 51.6, 33.7.

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Methyl-substituted 4,5-dihydrofurans 4n and 4o: Two isomers (6:1); R_f = 0.72 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2960, 2905, 1750, 1710, 1655, 1410, 1260, 1070, 800 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{16}O_5$: C 59.99, H 6.71; found: C 59.82, H 6.56.

5-Isopropenyl-2-methoxycarbonylmethyl-3-methylcarboxylate-4,5-dihydrofuran (4n) (major isomer): ^{1}H NMR: δ = 5.95 (dd, J = 17.3, 10.8 Hz, 1H), 5.00 (m, 1H), 4.87 (t, J = 1.4 Hz, 1H), 3.73 (s, 2H), 3.70 (s, 3H), 3.68 (s, 3H), 3.07 (ddt, J = 14.8, 11.6, 1.0 Hz, 1H), 2.73 (ddt, J = 14.8, 8.3, 1.0 Hz, 1H), 1.73 (s, 3H); ^{13}C NMR: δ = 168.4, 165.5, 162.6, 143.1, 112.2, 103.9, 85.3, 52.0, 50.8, 34.1, 33.5, 16.5.

5-Methyl-2-methoxycarbonylmethyl-3-methylcarboxylate-5-vinyl-4,5-dihydrofuran (4o) (minor isomer): ^{1}H NMR: δ = 5.29–5.11 (m, 1H), 5.11 (d, J = 8.4 Hz, 1H), 5.05 (d, J = 8.4 Hz, 1H), 3.78 (s, 2H), 3.71 (s, 3H), 3.67 (s, 3H), 2.89 (dt, J = 14.7, 1.0 Hz, 1H), 2.73 (dt, J = 14.7, 1.0 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR: δ = 168.5, 165.7, 161.5, 140.8, 112.8, 103.2, 87.9, 52.0, 50.8, 41.3, 33.6, 26.0.

2-(1-Bromovinyl)-3a,6-dimethylcarboxylate-2,3,4,5-tetrahydrocyclopenta[b]furan (4p): R_f = 0.51 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2950, 2870, 1730, 1670, 1440, 1290, 1195, 1020, 915 cm^{-1}; ^{1}H NMR: δ = 6.08 (dd, J = 2.0, 1.0 Hz, 1H), 5.63 (dd, J = 2.0, 1.0 Hz, 1H), 5.51 (ddt, J = 10.0, 5.6, 1.0 Hz, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.07 (ddd, J = 14.4, 10.0, 6.0 Hz, 1H), 2.85–2.73 (m, 1H), 2.76 (dd, J = 12.5, 5.6 Hz, 1H), 2.42 (dd, J = 12.5, 6.0 Hz, 1H), 1.91 (dd, J = 12.5, 10.0 Hz, 1H), 1.86 (dd, J = 12.5, 10.0 Hz, 1H); ^{13}C NMR: δ = 172.3, 169.4, 164.5, 130.4, 118.9, 99.9, 93.8, 63.9, 52.8, 51.4, 40.0, 33.8 (2CH_2); elemental analysis calcd (%) for $C_{13}H_{15}BrO_5$: C 47.15, H 5.57; found: C 48.01, H 6.22.

Methyl-substituted 4,5-dihydrofurans 4q and 4r: Two isomers (4:1); R_f = 0.48 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2950, 1730, 1700, 1440, 1200, 905 cm^{-1}; elemental analysis calcd (%) for $C_{14}H_{18}O_5$: C 63.15, H 6.81; found: C 63.18, H 6.86.

3a,6-Dimethylcarboxylate-2-methyl-2-vinyl-2,3,4,5-tetrahydrocyclopenta[b]furan (4q) (major isomer): ^{1}H NMR: δ = 5.44 (dd, J = 10.5, 5.0 Hz, 1H), 5.09 (s, 1H), 4.92 (s, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.05 (ddd, J = 14.4, 9.8, 5.9 Hz, 1H), 2.77 (dd, J = 14.4, 8.5 Hz, 1H), 2.64 (dd, J = 12.5, 5.4 Hz, 1H), 2.38 (dd, J = 12.5, 5.9 Hz, 1H), 1.74 (s, 3H), 1.93–1.67 (m, 2H); ^{13}C NMR: δ = 172.8, 170.7, 165.0, 142.2, 113.1, 98.7, 95.6, 64.5, 52.7, 51.2, 39.4, 34.2, 33.7, 17.1.

3a,6-Dimethylcarboxylate-2-isopropenyl-2,3,4,5-tetrahydrocyclopenta[b]-furan (4r) (minor isomer): ^{13}C NMR: δ = 172.8, 170.0, 165.0, 142.2, 113.1, 98.7, 95.6, 64.5, 52.7, 51.2, 39.4, 34.2, 33.7, 17.1.

2-(1-Bromovinyl)-3a,7-dimethylcarboxylate-2,3,5,6-tetrahydro-4*H*-benzofuran (4s): White crystals; m.p. 61–63 °C; R_f = 0.59 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2950, 1735, 1695, 1435, 1270, 1150, 910 cm^{-1}; ^{1}H NMR: δ = 6.14 (dd, J = 2.0, 1.0 Hz, 1H), 5.57 (dd, J = 2.0, 1.0 Hz, 1H), 4.90 (ddt, J = 10.5, 5.5, 1.0 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 2.76 (dd, J = 12.8, 5.5 Hz, 1H), 2.55–2.21 (m, 3H), 1.91–1.75 (m, 2H), 1.55–1.27 (m, 2H); ^{13}C NMR: δ = 173.0, 166.9, 162.4, 130.1, 117.6, 100.6, 82.9, 54.3, 52.8, 51.2, 41.7, 31.4, 23.5, 19.3; elemental analysis calcd (%) for $C_{14}H_{17}BrO_5$: C 48.71, H 4.96; found: C 49.43, H 5.47.

5,6-Dihydro-3a,7-dimethylcarboxylate-2-vinyl-4*H*-benzofuran (9c): R_f = 0.63 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2950, 1730, 1680, 1435, 1130, 1015, 930 cm^{-1}; ^{1}H NMR: δ = 6.23 (dd, J = 17.3, 11.0 Hz, 1H), 5.84 (dd, J = 17.3, 0.7 Hz, 1H), 5.42 (dd, J = 11.0, 1.2 Hz, 1H), 5.28 (s, 1H), 3.78 (s, 3H), 3.67 (s, 3H), 2.66–2.50 (m, 2H), 2.30–2.16 (m, 1H), 1.82–1.68 (m, 1H), 1.61–1.40 (m, 2H); ^{13}C NMR: δ = 166.5, 163.5, 156.0, 123.9, 119.7, 105.4, 102.9, 59.1, 53.0, 51.6, 29.7, 22.7, 17.9; elemental analysis calcd (%) for $C_{14}H_{16}O_5$: C 63.63, H 6.10; found: C 63.76, H 6.22.

Methyl-substituted 4,5-dihydrofurans 4t and 4u: Two isomers (4:1); R_f = 0.47 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2980, 1670, 1443, 1265, 1150, 1005, 905 cm^{-1}.

3a,7-Dimethylcarboxylate-2-methyl-5-methylene-2-vinyl-2,3,5,6-tetrahydro-4*H*-benzofuran (4t) (major isomer): ^{1}H NMR: δ = 5.13 (m, 1H), 4.91 (m, 1H), 4.83 (m, 2H), 4.87–4.79 (m, 1H), 3.74 (s, 3H), 3.66 (s, 3H), 3.21 (dq, J = 19.5, 1.7 Hz, 1H), 3.02 (d, J = 19.5 Hz, 1H), 2.97 (d, J = 12.5 Hz, 1H), 2.66 (dd, J = 12.6, 5.1 Hz, 1H), 2.18 (d, J = 12.5 Hz, 1H), 1.77 (dd, J = 12.6, 11.2 Hz, 1H), 1.73 (s, 3H); ^{13}C NMR: δ = 172.6, 166.9, 163.9, 142.0, 140.0, 112.4 (2CH_2), 98.4, 84.7, 57.0, 52.7, 51.4, 41.1, 40.6, 31.4, 17.7.

3a,6-Dimethylcarboxylate-2-methyl-2-vinyl-2,3,4,5-tetrahydrocyclopenta[b]furan (4u) (minor isomer): ^{1}H NMR (characteristic signals): δ = 5.96 (dd, J = 17.2, 10.7 Hz, 1H), 5.36 (dd, J = 16.2, 1.1 Hz, 1H), 5.05 (dd, J = 10.7, 1.1 Hz, 1H), 3.73 (s, 3H), 3.64 (s, 3H), 2.85 (d, J = 12.7 Hz, 1H), 2.64 (d, J = 13.0 Hz, 1H), 1.95 (d, J = 13.0 Hz, 1H).

Methyl-substituted 4,5-dihydrofurans 4v and 4w: Two isomers (3:1); R_f = 0.45 (diethyl ether/pentane 7:3); IR (neat): $\tilde{\nu}$ = 2950, 1735, 1690, 1435, 1260, 1135, 910, 730 cm^{-1}; elemental analysis calcd (%) for $C_{22}H_{22}N_2O_5$: C 66.99, H 5.62, N 7.10; found: C 67.23, H 5.46, N 7.37.

3a,12-Dimethylcarboxylate-2-isopropenyl-2,3,4,11-tetrahydro-1-oxa-5,10-diazanaphtho-[2,3-f]azulene (4v) (major isomer): ^{1}H NMR: δ = 8.06–7.64 (m, 4H), 5.06 (s, 1H), 5.02–4.87 (m, 1H), 4.84 (d, J = 1.2 Hz, 1H), 4.22 (d, J = 15.9 Hz, 1H), 4.10 (d, J = 15.9 Hz, 1H), 3.77 (s, 3H), 3.67–3.04 (m, 2H), 3.60 (s, 3H), 2.93 (dd, J = 12.6, 5.6 Hz, 1H), 2.06–1.94 (m, 1H), 1.64 (s, 3H); ^{13}C NMR: δ = 171.9, 166.9, 163.8, 155.5, 151.6, 141.9, 141.2, 140.9, 130.3, 129.8, 129.5, 128.2, 112.3, 101.0, 83.9, 56.9, 53.4, 51.9, 41.3, 40.1, 33.4, 17.7.

3a,12-Dimethyl-2-methyl-1-oxa-2,3,4,11-tetrahydro-2-vinyl-5,10-diazanaphtho[2,3-f]azulene (4w) (minor isomer): ^{13}C NMR: δ = 172.4, 170.2, 166.8, 152.2, 151.9, 141.9, 141.3, 140.8, 130.4, 129.8, 129.1, 128.2, 113.1, 101.0, 84.8, 58.7, 53.2, 52.0, 40.4, 39.8, 34.0, 18.1.

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