Domino retro Diels–Alder/Diels–Alder reaction: an efficient protocol for the synthesis of highly functionalized bicyclo[2.2.2]octenones and bicyclo[2.2.2]octadienones

Santhosh Kumar Chittimalla, Hui-Yi Shiao and Chun-Chen Liao*

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A novel and convenient approach, the domino retro Diels–Alder/Diels–Alder reaction sequence for highly stereo- and regioselective synthesis of various bicyclo[2.2.2]octenone and bicyclo[2.2.2]octadienone derivatives is presented. Thus, the masked *o*-benzoquinones (MOBs) **2a**–**e** generated by the pyrolysis of the respective dimers **3a**–**e** participated in this novel synthetic strategy with a variety of olefinic and acetylenic dienophiles at 220 °C to provide the title compounds in good to excellent yields.

Introduction

The Diels–Alder (DA) reaction is clearly one of the most important and widely used of all processes in organic synthesis. With the potential of forming carbon–carbon, carbon–heteroatom and heteroatom–heteroatom bonds, the reaction is a versatile synthetic tool for constructing simple and complex molecules.[1,2] Aside from the DA reaction, the retro Diels–Alder (rDA) is an important part of the armory of the synthetic chemist seeking to make alkenes or 1,3-dienes.[3,4] The cycloreversion occurs when the diene and/or dienophile are particularly stable molecules (*i.e.* formation of an aromatic ring, nitrogen, carbon dioxide, acetylene, ethylene, nitriles, *etc.*) or when one of them can be easily removed or consumed in a subsequent reaction. Retro DA followed by a DA reaction is one of the examples of a domino reaction. In recent years there has been a great deal of interest in the exploration of new domino reactions due to their various advantages such as formation of several bonds in one operation and obviating the need of isolating the intermediates and changing the reaction conditions.[5] Furthermore, domino reactions proved to be economically and ecologically favorable because of the minimization of solvents, reagents, adsorbents and labor. Domino rDA/DA reactions, while finding limited application compared to simple rDA processes, have been incorporated into numerous synthetic sequences. Recent examples where a domino rDA/DA process was utilized as one of the key steps include the taxane skeleton,[6] the DCB carbon framework of phorbol,[7] and a clever and efficient total synthesis of pseudoptabersonine.[8] Highly reactive selenoaldehydes were regenerated by the rDA process and trapped with 2-methoxyfuran *via* a DA reaction to give new selenium-containing heterocycles which thereby formed penta-2,4-dienoates in high yields with deposition of elemental selenium.[9] A novel [1,3]benzoxazino[2,3-*b*][1,3]benzoxazine was also prepared by a domino cascade of tandem rDA/DA transformation.[10]

Recently, the DA reactions of 6,6-dialkoxycyclohexa-2,4-dienones, generically known as masked *o*-benzoquinones (MOBs), are extensively studied.[11] MOBs are highly reactive and are known for their facile dimerization.[12] However, the bicyclo[2.2.2]octenone derivatives are provided by the *in situ* generated MOBs when trapped with various dienophiles.[12–14] The synthetic potential of these functionally rich bridged cycloadducts as valuable starting materials was demonstrated on several instances by using them as key synthons in the total synthesis of various structurally complex natural products.[11] In the course of our extensive investigations on the DA reactions of MOBs, we found MOBs derived from guaiacol, 5-methyl- and 6-methyl-2-methoxyphenols and 5-carbomethoxy-2-methoxyphenol produced the cycloadducts in low yields along with a considerable amount of dimers.[12–14] To circumvent this problem, we have developed a detour method by introducing an easily removable bromo substitution at C-4 of these 2-methoxyphenols. Though the overall yields of the DA adducts are better by this method, it consists of three synthetic operations[14] (sequential bromination of 2-methoxyphenol, oxidation and cycloaddition, and debromination). In the context of minimizing the number of steps involved in this route and in the view to improve the yield of the cycloadducts, an alternative method, the domino rDA/DA strategy, is sought for the synthesis of these bicyclic compounds.[15] We present herein a full account of our investigations on this novel and convenient approach for highly stereo- and regioselective synthesis of various bicyclo[2.2.2]octenone and bicyclo[2.2.2]octadienone derivatives, employing the dimers **3a**–**e** as starting compounds.

Results and discussion

Dimers **3a**–**e**[12,14b] were synthesized in excellent yields by self-dimerization of two MOBs *via* the DA reaction of a dienophilic MOB and a dienic MOB when 2-methoxyphenols **1a**–**e** in methanol were treated with diacetoxyiodobenzene (DAIB) a hypervalent iodine reagent as oxidizing agent (Scheme 1).

Our previous investigations on DA reactions of MOBs revealed that 6,6-dimethoxycyclohexa-2,4-dienone (MOB **2a**) is the most unstable intermediate towards self-dimerization, leading to low yields of desired DA adducts with concomitant formation of dimer **3a**.[12,13] At the outset, dimer **3a** was of interest to probe

Department of Chemistry, National Tsing Hua University, Hsinchu, Taiwan. E-mail: ccliao@mx.nthu.edu.tw; Fax: +886-3-5728123; Tel: +886-3-5720874

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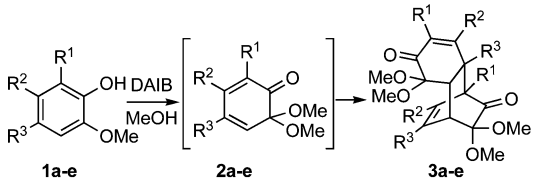
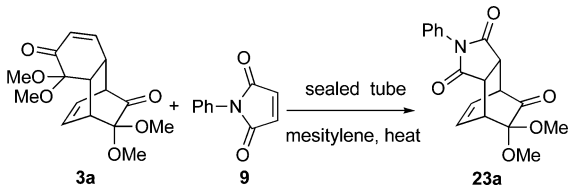


a:$R^1=R^2=R^3=H$ (quantitative)
b:$R^1=R^2=H$, $R^3=Me$ (90%)
c:$R^1=R^3=H$, $R^2=Me$ (90%)
d:$R^2=R^3=H$, $R^1=Me$ (94%)
e:$R^1=R^3=H$, $R^2=CO_2Me$ (93%)

Scheme 1 Preparation of the dimers **3a**–**e**.

Table 1 Standardization of domino rDA/DA reaction condition with *N*-phenylmaleimide (**9**)

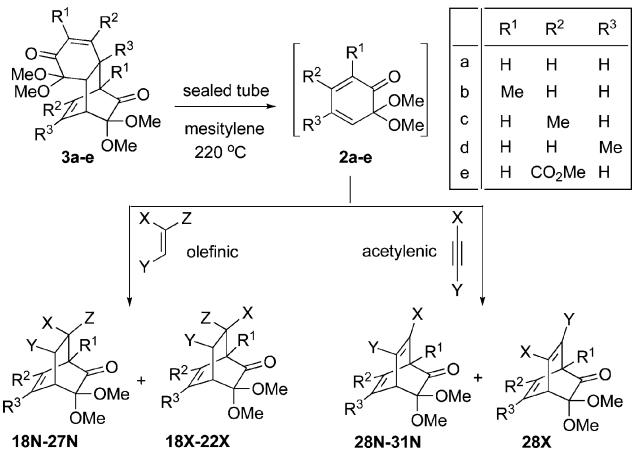


			Yield (%)	
Entry[a]	Temperature/°C	Time/h	**23a**	Recovered **3a**
1	150	24	—	85
2	180	24	25	70
3	200	8	35	60
4	220	2	90	—
5	250	2	88	—

[a] 5 equivalents of dienophile (with respect to the MOB generated) were used.

the proposed reaction. We initiated our study by selecting *N*-phenylmaleimide (NPM, **9**) as the dienophile, an excellent trapping agent in rDA reactions,[3] to optimize the reaction conditions. After much experimentation, entry 4 of Table 1 was found to be the most suitable conditions for the success of this process. Accordingly, MOB **2a** generated *in situ* by the pyrolysis of dimer **3a** in anhydrous mesitylene in the presence of dienophile **9** in a sealed tube at 220 °C furnished the DA adduct **23a** in 90% yield. At this point it should be noted that **23a** could be attained in 45% yield following method A (see the Experimental section) in addition also led to 48% of dimer **3a**.[16] The reaction was very slow at lower temperatures and large amounts of starting material remained unchanged even after longer reaction times (Table 1). The *in situ* generated MOB has two competing reactions, DA dimerization and formation of the expected DA adduct. At low temperatures it appears that the rate of DA dimerization is higher compared to the rate of DA reaction between MOB and the added dienophile and the pre-equilibrium of MOB dimer and MOB is slow.

The dramatic increase in the yield of **23a** encouraged us to apply this strategy to dienophiles, methyl acrylate (**4**, 25 eq.) and styrene (**8**, 25 eq.) separately. Polymerization of these dienophiles took place, making the purification of formed DA adducts from the reaction mixtures difficult. At this instant it was predicted that if lower molar ratios of these dienophiles are used, the reaction might not be complete but purification of the products formed should become easy as the amount of polymer formed would be less. Subsequently 5 eq. of dienophiles **4** and **8** were used in the reaction. To our surprise, DA adducts **18aN** + **18aX** (83% for dienophile **4**); **22aN** + **22aX** (85% for dienophile **8**) were produced in very good yields and easily purified by column chromatography but the stereoisomers formed could not be separated (entry 1 and 5 of Table 2). Though the present strategy gave inseparable mixture of stereoisomers, it became clear that both the electron-rich and electron-poor dienophiles are compatible for this reaction (Scheme 2).



	R^1	R^2	R^3
a	H	H	H
b	Me	H	H
c	H	Me	H
d	H	H	Me
e	H	CO_2Me	H

Scheme 2 Domino rDA/DA approach for the synthesis of bicyclo[2.2.2]octenones and bicyclo[2.2.2]octadienones.

Recent studies on inverse electron-demand DA reactions, dienophiles benzyl vinyl ether (**6**), vinyl phenyl sulfide (**7**) and dihydrofuran (**12**) gave lower yields of cycloadducts with MOB **2a**, along with substantial amounts of dimer **3a**.[13] We envisaged the possibility of using the present protocol with these dienophiles. The dienophiles **6**, **7** and **12** could afford the DA adducts in 81–87% total yields (entries 3, 4 and 13 of Table 2) with 8% of stereoisomers **20aX** and **21aX** in the cases of dienophiles **6** and **7**, respectively. It is interesting to note entry 15 of Table 2; dimer **3a** and dicyclopentadiene (**13**) provided the DA adduct **27a** in 81% yield *via* the DA reaction of their *in situ* generated monomers (MOB **2a** and cyclopentadiene).

At this stage, we decided to apply this strategy to the dienophiles cyclopentene (**10**) and 2,4-cyclohexadiene (**11**) which failed to undergo DA reaction with MOB **2a** in previous methods.[17] Although a greater number of equivalents of dienophile **10** had to be used, DA adduct **24a** was achieved in considerable yield (35%, entry 10 of Table 2). Dienophile **11** did not give the expected product, instead DA adduct **25** was obtained in acceptable yield (Fig. 2 and entry 10 of Table 2). The diagnostic analytical data shown in Fig. 2 suggest the formation of compound **25**. For an externally added conjugated diene there are two possible reaction pathways; (i) MOB can act as a diene while the added conjugated diene acts as a dienophile or (ii) when added conjugated diene acts as a diene, MOB acts as a dienophile.

Our earlier reports on the DA reactions of MOBs with cyclopentadiene gave a mixture of adducts (following both the reaction pathways) in different ratios, depending on the substitution of MOB.[18] But at higher temperatures a more stable bicyclo[2.2.2] system was obtained as a single product after Cope rearrangement of the initially formed side product.[18] This dual nature of MOB

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Table 2 Domino rDA/DA reactions of MOB dimers **3a**–**e** with selected olefinic dienophiles

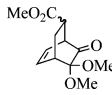
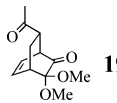
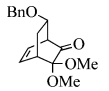
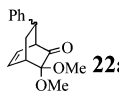
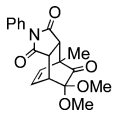
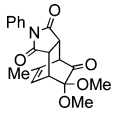
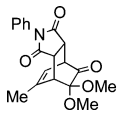
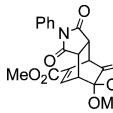
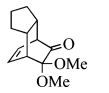
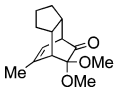
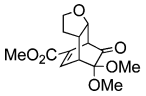
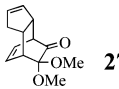
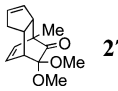
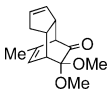
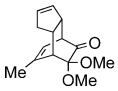
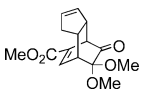
Entry[b]	Dimer	Dienophile/eq.[c]	Reaction time/h	Adduct/yield (%)	Other method[a]		
					Adduct/yield (%)	Equivalents[c]	Reference
1	**3a**	 **4**/5	2	 **18aN** + **18aX** / 83[d]	**18aN**/40[e]	25	12
2	**3a**	 **5**/5	2	 **19aN** (72%)[f]	**19aN**/62[g]	25	12
3	**3a**	 **6**/10	8	  **20aN** / 73 **20aX** / 8	**20aN**/61	25	13
4	**3a**	 **7**/5	2	  **21aN** / 79 **21aX**/ 8	**21aN**/30	50	13*a*
5	**3a**	 **8**/5	2	 **22aN** + **22aX** / 85[d]	**22aN**/45	10	13
6	**3b**	 **9**/5	2	 **23b** / 96	**23b**/45	10	13
7	**3c**	 **9**/5	2	 **23c** / 87	**23c**/68	10	17*a*
8	**3d**	 **9**/5	2	 **23d** / 86	**23d**/81	10	17*a*
9	**3e**	 **9**/5	2	 **23e** / 81	**23e**/60	10	16
10	**3a**	**10**/30	24	 **24a** / 35	**24a**/0[h]	50	17*a*

Table 2 (*Contd.*)

Entry[b]	Dimer	Dienophile/eq.[c]	Reaction time/h	Adduct/yield (%)	Other method[a] Adduct/yield (%)	Equivalents[c]	Reference
11	**3d**	 **10**/30	24	 **24d** / 31	**24d**/0[h]	50	17*b*
12	**3a**	 **11**/20	3	 **25** / 38	**25**/0[h]	50	17*b*
13	**3a**	 **12**/5	2	 **26a** / 87	**26a**/15	50	17*b*
14	**3a**	 **12**/5	3	 **26e** / 50	**26e**/36	20	13
15	**3a**	 **13**/5	2	 **27a** / 81	**27a**/86	25	18
16	**3b**	 **13**/5	2	 **27b** / 60	**27b**/86	25	18
17	**3c**	 **13**/5	2	 **27c** / 100	**27c**/76	25	18
18	**3d**	 **13**/5	2	 **27d** / 100	**27d**/91	25	18
19	**3e**	 **13**/10	3	 **27e** / 60	**27e**/80	25	18

[a] Generation of MOB directly from guaiacol in the presence of dienophile. [b] A 0.25 M solution of dimer in mesitylene was used in the reaction. [c] Number of equivalents of dienophile used is with respect to the MOB generated. [d] A 90:10 ratio (from the ^{1}H NMR of crude sample) of a inseparable mixture of isomers was obtained. [e] 65% of **18aN** was obtained from detour method using 4-bromoguaiacol. [f] < 3% of another isomer was observed from the ^{1}H NMR of crude sample and could not be isolated. [g] 76% of **19aN** was obtained from detour method using 4-bromoguaiacol. [h] Exclusive formation of dimer of the corresponding MOB.

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was observed both in inter- and intramolecular versions of DA reactions.[19,20] The current example, namely cyclohexadiene (**11**), might be following the second reaction pathway or the adduct **25** is more stable than the other possible products under the reaction conditions utilized.

The reaction was further exploited with acetylenic dienophiles **14**–**17** (Fig. 1) which are known to be less reactive in DA reactions with MOBs. Generally, higher temperatures are required to obtain DA adducts with acetylenic dienophiles. Thus, only stable MOBs, which are less prone to self-dimerization, had to be used in these reactions.[21–23] On the other hand, the present strategy could provide an easy access to the bicyclo[2.2.2]octadienones in excellent yields. Initially, dimethylacetylenedicarboxylate (**15**) was used in the reaction to produce **29a** (92%, entry 2 of Table 3). In contrast to phenylacetylene (**16**) and 1-hexyne (**17**), which provided single regioisomers **30aN** and **31aN**, respectively, (entry 7, 8 of Table 3) ethyl propiolate (**14**) gave two regioisomers **28aN** and **28aX** in an almost 1 : 1 ratio (entry 1 of Table 3). This may be attributed to the profound electron-donating effect of phenyl in **16** and alkyl in **17** than the ethoxy carbonyl group in **14**; the observed behavior of these dienophiles is in accord with our previous investigations.[22,23] These results are particularly pertinent since earlier attempts to synthesize these bicyclo[2.2.2]octadienones were unsuccessful. Thus, our new approach looks to be superior to the existing procedures for acetylenic dienophiles.

Having established the efficacy of this methodology with dimer **3a** and a number of olefinic and acetylenic dienophiles, we speculated this reaction could be generalized to other MOB dimers

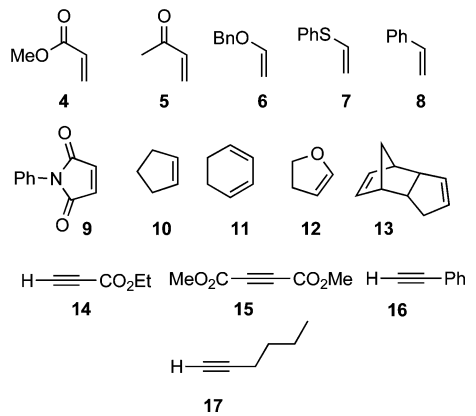


Fig. 1 Dienophiles successfully employed in this study.

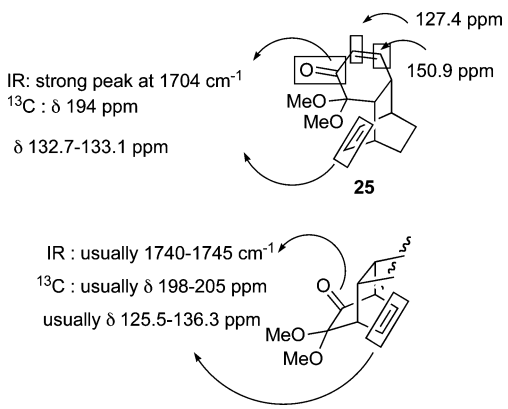
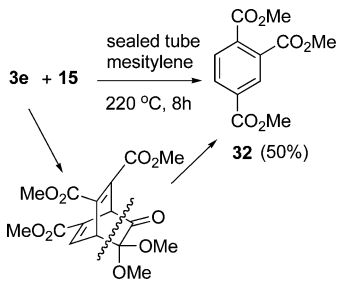


Fig. 2 MOB **3a** acting as dienophile.

bearing electron-donating and electron-withdrawing substituents. Thus, our attention was turned to the dimers **3b**–**e**. The study was performed with a few selected dienophiles, namely **9**, **13** and **15**. When NPM (**9**) was treated separately with the dimers **3b**–**e** under similar conditions as for dimer **3a**, DA adducts **23b**–**e** could be obtained in 81–96% yields (entries 6–9 of Table 2), thus proving the generality of this protocol. Encouraged by this result, when dicyclopentadiene (**13**) was used, DA adducts **27b**–**e** (entries 16–19 of Table 2) could be obtained in good yields *via* DA reaction of *in situ* generated monomers, *i.e.* cyclopentadiene and MOBs **2b**–**2e**. Acetylenic dienophile **15** produced **29b**–**d** in excellent yields as shown in Table 3, whereas in previous methods[21] the reaction led to the exclusive formation of the corresponding self-dimerization products. Dienophile **9**, which gave only 45% of DA adduct with MOB **2e** in method A, provided 81% in this protocol. Similarly, dienophile 2,3-dihydrofuran (**12**) which previously gave a 36% yield of **26e**, could be improved to 50%. Interestingly, when acetylenic dienophile DMAD (**15**) was used in the reaction, no desired bicyclic compound could be isolated, instead compound **32**[24] was obtained in 50% yield whose formation is expected to come from the initially formed DA adduct as depicted in Scheme 3. An uncharacterizable product was also isolated along with compound **32**. Attempts to isolate the DA adduct at lower temperatures 180 °C and 200 °C failed, and the reactions provided the same products, compound **32** and an unknown compound, though the reaction was not complete with large amounts of dimer still present.

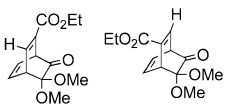
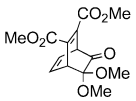
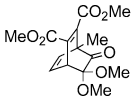
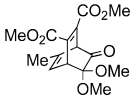
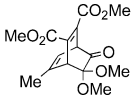
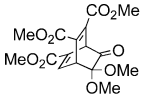
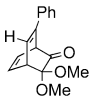
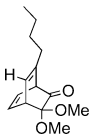


Scheme 3 Domino rDA/DA followed by rDA providing **32**.

The structures of all the new compounds were assigned on the basis of their IR, ^{1}H NMR and ^{13}C NMR, DEPT, and low- and high-resolution mass spectral analyses. For most of the high-resolution mass spectra recorded in electron impact mode (70 eV), the peaks corresponding to the molecular ion (M^+) could not be seen; instead the peaks corresponding to $M^+ - 28$ were observed, indicating that the extrusion of CO resulted from facile fragmentation. The ^{1}H NMR of the known compounds **18aN**–**22aN**, **23a**, **23d**, **26a**, **26e**, **27a**–**e** and **32** were compared with those of the authentic compounds.[12,13,16–18,24] All the cycloadducts exhibited IR absorptions at 1731–1742 cm^{-1} due to the characteristic features of the carbonyl functional group adjacent to α,α-dimethoxyl groups in the functionalized bicyclo[2.2.2]octenone skeleton.[12–14,19] All the compounds showed ^{13}C resonance at about δ 192.1–204.6 and δ 89.2–95.0 revealing the presence of carbonyl and a quarternary carbon bearing two methoxy groups.

The regio- and stereochemistry of the new compounds were confirmed by decoupling and NOE experiments. For instance, in **20aX**, saturation of both the –OMe gave rise to an increase in the signal intensity of H_c (1.9%) while the saturation of H_c

Table 3 Domino rDA/DA reactions of MOB dimers **3a**–**e** with selected acetylenic dienophiles

Entry[a]	Dimer	Dienophile/eq.[b]	Reaction time/h	Adduct/yield (%)	Method A	
					Adduct/yield (%)	Equivalents[b]
1	**3a**	 **14**/10	2	 **28aN** / 45 **28aX** / 38	**28aN** or **28aX**/0[c]	25
2	**3a**	 **15**/5	2	 **29a** / 92	**29a**/0[c]	25
3	**3b**	 **15**/10	8	 **29b** / 95	**29b**/0[c]	10
4	**3c**	 **15**/5	1.5	 **29c** / 95	**29c**/0[c]	10
5	**3d**	 **15**/5	2	 **29d** / 95	**29d**/0[c]	10
6	**3e**	 **15**/5	2	 **29e** / 0	**29e**/0[c]	10
7[d]	**3a**	 **16**/10	2	 **30aN** / 44	**30aN**/0[c]	25
8[d]	**3a**	 **17**/25	8	 **31aN** / 56	**31aN**/0[c]	30

[a] A 0.25 M solution of dimer in mesitylene was used in the reaction. [b] Number of equivalents of dienophile used is with respect to the MOB generated. [c] Exclusive formation of dimer of the corresponding MOB. [d] Reaction was conducted in the absence of solvent.

brought about a significant NOE effect in H_d (1.1%) and H_e (1.4%) thus confirming the assigned regiochemistry. As the structure of **20aN** was already confirmed earlier, **20aX** should be none other than its stereoisomer, hence confirming the regio- and stereochemistry. Similarly, in the case of **21aX**, NOE studies could provide the structure of this bicyclo[2.2.2]octenone (Fig. 2). For **28aN**, the regiochemistry was confirmed by irradiating H_e to find an enhancement in the signal intensity of H_d (1.6%). Likewise, saturation of H_e in compound **28aX** brought about a significant NOE effect on H_d (1.3%), confirming the assigned regiochemistry. The regiochemistry of **30aN** and **31aN** were also assigned in a similar way on the basis of NOE studies. (Fig. 3). On the basis of these analyses, the inseparable products **18aX** and **22aX** are tentatively assigned as *exo* isomers of **18aN** and **22aN**, respectively.

The regioselectivity of these cycloadditions were very high in many cases, and are in accord with our earlier results due to the greater influence of the carbonyl functionality than the two methoxy groups present on the MOB moiety.[12,13] The selectivities observed in the present study have literature precedents.[11] The results illustrated here are particularly notable due to their high regio- and stereoselectivities, even in such harsh conditions. To gain more insight into whether the formation of the stereoisomers **18aX**, **20aX**, **21aX** and **22aX** is a kinetically controlled or thermodynamically controlled process, the following reactions were carried out. We separately subjected **20aN** and **21aN** to the standard rDA/DA reaction conditions (mesitylene, sealed tube, 220 °C) and did not observe any **20aX** and **21aX** as indicated by the ^{1}H NMR of crude reaction mixtures, suggesting that the formation of isomers is a kinetically, rather than thermodynamically, controlled process. Analogous experiments were executed with **18aN** and **22aN**, which were synthesized by following the previously reported procedures. Even in these cases, no **18aX**

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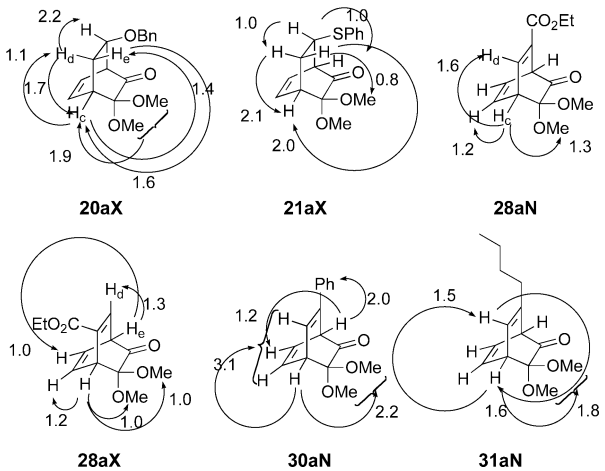

Fig. 3 ^{1}H NMR studies of NOE (%) for **20aX**, **21aX**, **28aN**, **28aX**, **30aN** and **31aN**.

and **22aX** were observed in the ^{1}H NMR of their crude reaction mixtures.

Conclusions

In summary, a detailed investigation of the domino rDA/DA reaction, a novel and efficient approach to synthesize bicyclo[2.2.2]octenones and bicyclo[2.2.2]octadienones, is presented. Though the reaction works well with a series of electronically and sterically distinct olefinic and acetylenic dienophiles (Fig. 1), there were quiet a few dienophiles which could not undergo this tandem rDA/DA reaction to provide the expected DA adducts. The failure of the reaction with dienophiles cyclopentenone and cyclohexenone can be attributed to their fixed *s-trans* configuration; steric factors influence the reactivity of dienophiles like 4,4-dimethylcyclopentene and 2,2-dimethyl-4-cyclopenta-1,3-dione. The reaction of MOBs with monosubstituted acetylenes, compared to the corresponding disubstituted ones [diphenylacetylene, bis(trimethylsilyl)acetylene] may arise basically from the steric effect. However, the effects of substituents on the relative reactivity in the cases of mono- and di-substituted acetylenes is presumably derived from electronic effects which may not be ruled out. Other factors can be ascribed to the side reactions (polymerization, decomposition) which resulted in messy ^{1}H NMR readings.

The choice in the synthetic strategy of domino rDA/DA methodology served 4 main purposes; (i) improving the yield of DA adducts, (ii) utilization of a dimer which was a side product in the DA reactions of MOBs, (iii) decreasing the number of synthetic steps, (iv) decreasing the number of equivalents of dienophiles, thus making it a cost effective method. Even though the dienophiles **4**–**8** and **14** produced two stereoisomers in this protocol, an increase in the yield of the *endo*-adduct, which is the major reaction product, was observed and the two stereoisomers in the cases of dienophiles **6**, **7** and **14** could be easily separated by column chromatography. Under these conditions **27a**–**e** were achieved in good yields, although previous method still offered the best results. The results showed remarkable selectivity even at that higher temperature. As a new direct and efficient method for the preparation of highly functionalized bicyclo[2.2.2]octenones and bicyclo[2.2.2]octadienones, we have discovered that this methodology should prove to be of value in various synthetic applications.

Experimental section

Unless stated otherwise, reagents were obtained from commercial sources and used without further purification. All reactions were performed under a nitrogen atmosphere in anhydrous solvents which were dried prior to use following standard procedures. Reactions were monitored with thin-layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) using 7% ethanolic phosphomolybdic acid as developing agent. The product composition of each reaction was determined from the ^{1}H NMR (400 MHz) spectrum of the crude reaction mixture. Standard column chromatography was performed using 230–400 mesh silica gel obtained from E. Merck. Melting points are uncorrected. IR spectra were recorded as films on NaCl plates. ^{1}H and ^{13}C spectra were recorded at 400 and 100 MHz, respectively, in $CDCl_3$ and chemical shifts are reported in δ (ppm) using solvent resonance as the internal reference. Mass spectra were recorded by the NSC Instrumentation Center at Hsinchu, Taiwan. Elemental analyses were performed by the NSC Instrumentation Center at Taichung, Taiwan.

General procedure for the preparation of the dimers 3a–e

To a solution of phenol (1 mmol) in dry methanol was added at room temperature DAIB (1.2 mmol) previously dissolved in methanol. The reaction mixture was left overnight to stir at ambient temperature. Solvent was removed with rotary evaporation and then treated with saturated $NaHCO_3$ and then ethylacetate was used for the extraction. The crude product remaining after the removal of solvent was recrystallised from ethyl acetate–hexane to give the corresponding dimer.

General procedure for the domino rDA/DA reaction

To a solution of 0.25 mmol of the dimer in 1 ml of mesitylene in a tube was added a specified equivalents of dienophile. The tube was then sealed after degassing by freeze-thaw purge technique. Reaction mixture was subjected to the appropriate temperature for an appropriate time to give the corresponding products.

General procedure for method A

To a mixture of DAIB (2 mmol) and dienophile in MeOH (6 mL) was added a 2-methoxyphenol (1 mmol) in MeOH (4 mL) during a period of 1 h time with the aid of a syringe pump at rt. The reaction mixture was stirred until the reaction was complete. Then, all the volatiles were removed under reduced pressure and the residue was subjected to purification by column chromatography on silica gel using a mixture of ethyl acetate and hexanes as eluent to obtain the cycloadducts.

The analytical data for compounds **3a**,[14b] **3b**,[14b] **3c**,[14b] **3d**,[12] **3e**,[12] **18aN**,[12] **19aN**,[12] **20aN**,[13] **22aN**,[13] **26a**,[13] **26e**,[13] and **32**[24] are identical with those already reported in the literature.

Methyl (1*R,2*R**,4*S**)-8,8-dimethoxy-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (18aX).** Selected ^{1}H NMR peaks δ_H (400 MHz, $CDCl_3$) (from the mixture) 2.11–2.14 (2 H, m, CH_2), 3.16–3.19 (1 H, m, CHCO$_2$Me), 3.31 (3 H, s, OCH_3), 3.35 (3 H,

s, OCH_3), 3.67 (3 H, s, CO_2CH_3), 6.23 (1 H, ddd, *J* 1.6, 6.4, 8.0, C*H*=CH), 6.29 (1 H, ddd, *J* 1.6, 6.4, 8.0, C*H*=CH). The following data is obtained for the mixture of *endo* and *exo*-isomers, ν_{max}(film)/cm^{-1} of the mixture 2952, 2836, 1744, 1737, 1093, 1061; δ_C(100 MHz, $CDCl_3$) 24.2 (CH_2), 25.9 (CH_2), 37.4 (CH), 38.3 (CH), 38.6 (CH), 41.5 (CH), 47.4 (CH), 49.7 (CH_3), 49.9 (CH), 50.2 (CH_3), 52.1 (CH_3), 93.7 (C), 125.7 (CH), 129.2 (CH), 132.0 (CH), 135.3 (CH), 173.3 (C), 201.0 (C); *m*/*z* (EI) 212.1080 (M^+ − CO, $C_{12}H_{16}O_5$ requires 212.1049) 211 (19), 201 (54), 195 (33), 183 (40), 180 (95), 173 (30), 167 (85), 166 (73).

(1*R,4*S**,7*R**)-7-(Benzyloxy)-3,3-dimethoxybicyclo[2.2.2]oct-5-en-2-one (20aX).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 3102, 3023, 2944, 1742, 1057, 728 and 696; δ_H (400 MHz, $CDCl_3$) 1.85 (1 H, ddd, *J* 3.6, 9.6 and 13.2, CH_2), 1.97 (1 H, ddd, *J* 2.8, 6.4 and 13.2, CH_2), 3.10 (1 H, m, C*H*–C(OMe)$_2$), 3.31 (3 H, s, OCH_3), 3.34 (3 H, s, OCH_3), 3.52 (1 H, ddd, *J* 1.2, 3.6 and 6.8, C*H*–CO), 3.82 (1 H, ddd, *J* 3.6, 6.4 and 9.6, BnO–C*H*), 4.56 (1 H, d, *J* 12.0, Ar–CH_2–O), 4.61 (1 H, d, *J* 12.0, Ar–CH_2–O), 6.02 (1 H, ddd, *J* 1.6, 6.8 and 8.0, C*H*=CH), 6.41 (1 H, ddd, *J* 1.2, 6.4 and 8.0, C*H*=CH), 7.23–7.30 (5 H, m, Ar–*H*); δ_C(100 MHz, $CDCl_3$) 28.6 (CH_2), 38.4 (CH), 49.8 (CH_3), 50.0 (CH_3), 53.2 (CH), 70.3 (CH_2), 75.7 (CH), 94.4 (C), 125.6 (CH), 127.3 (CH), 127.6 (2 × CH), 128.3 (2 × CH), 136.3 (CH), 140.0 (C), 201.3 (C); *m*/*z* (EI) 260.1468 (M^+ − CO, $C_{16}H_{20}O_3$ requires 260.1412) 260 (M^+ − CO, 7), 181(7), 105 (16), 91 (100), 79 (12), 77 (14), 69 (8), 59 (17).

(1*S,4*R**,7*R**)-3,3-Dimethoxy-7-(phenylsulfanyl)bicyclo[2.2.2]-oct-5-en-2-one (21aN).** Obtained as a light brown colored oil; δ_H (400 MHz, $CDCl_3$) 1.22 (1 H, ddd, *J* 2.8, 5.2 and 13.2, CH_2), 2.53 (1 H, ddd, *J* 2.8, 8.0 and 13.2, CH_2), 3.09 (1 H, m, C*H*–C(OMe)$_2$), 3.23 (1 H, ddd, *J* 1.4, 2.4 and 6.2, C*H*–CO), 3.28 (3 H, s, OCH_3), 3.29 (3 H, s, OCH_3), 3.65 (1 H, ddd, *J* 2.4, 6.0 and 8.0, PhS–C*H*), 6.15 (1 H, dddd, *J* 1.2, 1.4, 6.2 and 8.0, C*H*=CH), 6.48 (1 H, ddd, *J* 1.4, 6.2 and 8.0, C*H*=CH), 7.26–7.36 (5 H, m, Ar–*H*); δ_C(100 MHz, $CDCl_3$) 28.3 (CH_2), 38.4 (CH), 41.5(CH), 49.8 (CH_3), 50.0 (CH_3), 52.3 (CH), 93.7 (C), 126.1 (CH), 127.3 (CH), 129.0 (2 × CH), 131.5 (2 × CH), 134.6 (CH), 135.6 (C), 200.9 (C).

(1*S,4*S**,7*R**)-3,3-Dimethoxy-7-(phenylsulfanyl)bicyclo[2.2.2]-oct-5-en-2-one (21aX).** Obtained as a light brown colored oil; ν_{max}(film)/cm^{-1} 3060, 2963, 2944, 2360, 1741, 1057, 740, 691; δ_H (400 MHz, $CDCl_3$) 1.91 (1 H, ddd, *J* 2.4, 7.2 and 14.0, CH_2), 2.04 (1 H, ddd, *J* 3.2, 5.2 and 14.0, CH_2), 3.15 (2 H, ddd, *J* 1.6, 2.8 and 4.4, C*H*–C(OMe)$_2$ and C*H*–CO), 3.31 (3 H, s, OCH_3), 3.34 (1 H, ddd, *J* 3.2, 5.2 and 7.2, PhS–C*H*), 3.40 (3 H, s, OCH_3), 6.08 (1 H, ddd, *J* 1.6, 6.4 and 8.0, C*H*=CH), 6.45 (1 H, ddd, *J* 1.6, 6.4 and 8.0, C*H*=CH) 7.26–7.32 (3 H, m, Ar–*H*), 7.45–7.47 (2 H, m, Ar–*H*); δ_C(100 MHz, $CDCl_3$) 27.5 (CH_2), 38.7 (CH), 43.5 (CH), 49.7 (CH_3), 49.9 (CH_3), 52.4 (CH), 66.1 (C), 94.1 (C), 127.8 (CH), 128.3 (CH), 129.1 (2 × CH), 133.3 (2 × CH), 136.0 (CH), 200.7 (C); *m*/*z* (EI) 262.1069 (M^+ − CO, $C_{15}H_{18}O_2S$ requires 262.1028) 231 (3), 153 (100), 121 (38), 79 (33), 77 (41), 75 (75), 47 (23), 28 (48).

(1*R,4*S**,7*R**)-3,3-Dimethoxy-7-phenylbicyclo[2.2.2]oct-5-en-2-one (22aX).** Selected ^{1}H NMR δ_H (400 MHz, $CDCl_3$) (from the mixture) 2.01 (1 H, dt, *J* 3.6, 12.8 and 12.8, CH_2), 2.15 (1 H, dd, *J* 6.4 and 14.0, CH_2), 6.34 (1 H, t, *J* 7.6, C*H*=CH), 6.44 (1 H, t, *J* 7.2, C*H*=CH). The following data is obtained for the mixture of *endo* and *exo*-isomers, ν_{max}(film)/cm^{-1} 3065, 3031, 2968, 2944, 1737, 1095, 1056, 764 and 691; δ_C(100 MHz, $CDCl_3$) δ 29.6 (CH_2), 29.9 (CH_2), 39.3 (CH), 49.9 (CH_3), 50.2 (CH_3), 55.0 (CH), 93.9 (C), 125.8 (CH), 126. 7(CH), 127.5 (CH), 127.7 (CH), 135.4 (CH), 144.2 (C), 201.7 (C); *m*/*z* (EI) 230.1339 (M^+ − CO, $C_{15}H_{18}O_2$ requires 230.1307) 230 (100), 155 (69), 128 (18), 91 (44), 75 (74), 59 (23), 51 (16).

(1*R,2*R**,6*R**,7*R**)-9,9-Dimethoxy-4-phenyl-4-azatricyclo-[5.2.2.0^{2,6}]undec-10-ene-3,5,8-trione (23a).** Obtained as a white colored solid, mp 227–228 °C; ν_{max}(film)/cm^{-1} 2975, 2839, 1781, 1735, 1718, 1598 and 1498; δ_H (400 MHz, $CDCl_3$) 3.34 (3 H, s, OCH_3), 3.38 (1 H, dd, *J* 3.2, 8.4 Hz, C*H*–CH), 3.40 (3 H, s, OCH_3), 3.56 (1 H, dd, *J* 3.6, 8.4 Hz, C*H*–CH), 3.74 (1 H, ddd, *J* 1.6, 3.2 and 6.4, C*H*–C(OMe)$_2$), 3.79 (1 H, ddd, *J* 1.2, 3.6 and 6.4, C*H*–CO), 6.25 (1 H, ddd, *J* 1.6, 6.4 and 8.0, C*H*=CH), 6.42 (1 H, ddd, *J* 1.2, 6.4 and 8.0, C*H*=CH), 7.16 (2 H, dd, *J* 1.6 and 3.6, Ar–*H*), 7.42 (3 H, m, Ar–*H*); δ_C(100 MHz, $CDCl_3$) 40.0 (CH), 40.7 (2 × CH), 48.8 (CH), 50.3 (2 × CH_3), 92.9 (C), 126.3 (2 × CH), 127.0 (CH), 128.9 (CH), 129.2 (2 × CH), 131.5 (C), 133.1 (CH), 174.9 (C), 176.3 (C), 198.4 (C); *m*/*z* (EI) 299.1156 (M^+ − CO, $C_{17}H_{17}NO_4$ requires 299.1157), 299 (M^+ − CO, 72), 284 (76), 252 (100), 151 (6), 121 (13), 105 (36), 76 (11).

(1*R,2*R**,6*S**,7*R**)-9,9-Dimethoxy-7-methyl-4-phenyl-4-aza-tricyclo[5.2.2.0^{2,6}]undec-10-ene-3,5,8-trione (23b).** ν_{max}(film)/cm^{-1} 3067, 2978, 2944, 2837, 1779, 1741, 1714, 1598, 1498 and 1456; δ_H (400 MHz, $CDCl_3$) 1.57 (3 H, s, CH_3), 2.98 (1 H, d, *J* 8.4, C*H*–CH), 3.34 (3 H, s, OCH_3), 3.40 (3 H, s, OCH_3), 3.57 (1 H, dd, *J* 3.2 and 8.4, C*H*–CH), 3.75–3.78 (1 H, m, C*H*–C(OMe)$_2$), 5.92 (1 H, dd, *J* 0.8 and 8.4, C*H*=CH), 6.38 (1 H, dd, *J* 6.4, 8.0 Hz, C*H*=CH), 7.15–7.43 (5 H, m, Ar–*H*); δ_C(100 MHz, $CDCl_3$) 14.7 (CH_3), 40.2 (CH), 41.5 (CH), 44.7 (CH), 50.3 (2 × CH_3), 51.2 (C), 92.7 (C), 126.4 (2 × CH), 128.9 (CH), 129.2 (2 × CH), 131.6 (C), 132.1 (CH), 132.7 (CH), 174.3 (C), 176.3 (C), 200.2 (C); *m*/*z* (EI) 313.1327 (M^+ − CO, $C_{18}H_{19}NO_4$ requires 313.1314), 313 (24), 298 (28), 266 (19), 264 (100).

(1*R,2*R**,6*R**,7*S**)-9,9-Dimethoxy-11-methyl-4-phenyl-4-aza-tricyclo[5.2.2.0^{2,6}]-undec-10-ene-3,5,8-trione (23c).** ν_{max}(film)/cm^{-1} 2972, 2946, 2837, 1779, 1738, 1713, 1498, 1384, 1189 and 1138; δ_H (400 MHz, $CDCl_3$) 1.85 (3 H, s, CH_3), 3.34 (3 H, s, OCH_3), 3.34 (1 H, m, C*H*–CH), 3.39 (3 H, s, OCH_3), 3.40 (1 H, d, *J* 3.2 Hz, C*H*–CH), 3.60 (1 H, m, C*H*–C(OMe)$_2$), 3.68 (1 H, dd, *J* 1.6, 6.8 Hz, C*H*–CO), 6.00 (1 H, m, C*H*=CCH$_3$), 7.12–7.47 (5 H, m, Ar–*H*); δ_C(100 MHz, $CDCl_3$) 20.8 (CH_3), 40.5 (CH), 40.6 (CH), 40.7 (CH), 50.1 (CH_3), 50.4 (CH_3), 53.9 (CH), 93.3 (C), 124.6 (CH), 126.3 (2 × CH), 129.0 (CH), 129.3 (2 × CH), 131.6 (C), 137.3 (C), 175.0 (C), 176.6 (C), 198.3 (C); *m*/*z* (EI) 313.1331 (M^+ − CO, $C_{18}H_{19}NO_4$ requires 313.1314) 313 (32), 298 (41), 268 (18), 267 (100), 194 (10).

(1*R,2*R**,6*R**,7*R**)-9,9-Dimethoxy-10-methyl-4-phenyl-4-aza-tricyclo[5.2.2.0^{2,6}]-undec-10-ene-3,5,8-trione (23d).** Obtained as a white solid, mp 165–166 °C; (found: C, 66.61; H, 5.91; N, 3.98, $C_{19}H_{19}NO_5$ requires C, 66.85; H, 5.61; N, 4.10%): ν_{max}(film)/cm^{-1} 2945, 2824, 1765, 1742, 1713, 1062 and 754; δ_H (400 MHz, $CDCl_3$) 1.92 (3 H, d, *J* 1.6, CH_3), 3.60 (6 H, s, 2 × OCH_3), 3.36 (1 H, dd, *J* 3.6 and 8.6, C*H*–CH), 3.52 (1 H, dd, *J* 3.4 and 8.6, C*H*–CH), 3.61 (1 H, dd, *J* 1.8 and 3.6, C*H*–C(OMe)$_2$), 3.63 (1 H, dd, *J* 3.4 and 6.0 Hz, C*H*–CO), 5.82 (1 H, ddq, *J* 1.6, 6.0 and 1.8, C*H*=CCH$_3$), 7.12–7.15 (2 H, m, Ar–*H*), 7.38–7.45 (3 H, m, Ar–*H*); δ_C(100 MHz,

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$CDCl_3$) 21.8 (CH_3), 39.9 (CH), 41.1 (CH), 45.4 (CH), 48.8 (CH), 50.1 (CH_3), 50.7 (CH_3), 93.1 (C), 118.1 (CH), 126.2 (2 × CH), 128.8 (CH), 129.2 (2 × CH), 131.6 (C), 144.1 (C), 175.2 (C), 176.2 (C), 198.5 (C); *m/z* (EI) 313.1314 ($M^+ - CO$, $C_{18}H_{19}NO_4$ requires 313.1314) 313 ($M^+ - CO$, 85), 298 (33), 266 (100), 135 (10), 119 (21), 91 (20), 59 (9)

Methyl (1*R,2*R**,6*R**,7*S**)-10,10-dimethoxy-3,5,11-trioxo-4-phenyl-4-azatricyclo[5.2.2.0^{2,6}]undec-8-ene-8-carboxylate (23e).** ν_{max}(film)/cm^{-1} 1716 and 1748; δ_H (400 MHz, $CDCl_3$) 3.33 (3 H, s, OC*H*$_3$), 3.42 (3 H, s, OC*H*$_3$), 3.47 (1 H, dd, *J* 3.2 and 8.0, C*H*–CH), 3.58 (1 H, dd, *J* 3.2 and 8.0, C*H*–CH), 3.76 (3 H, s, CO_2CH_3), 3.98 (1 H, dd, *J* 3.2 and 8.0, C*H*–C(OMe)$_2$), 4.33 (1 H, dd, *J* 2.0 and 1.6, C*H*–CO), 7.07 (1 H, dd, *J* 1.6 and 8.0, C*H*=CCO_2CH_3), 7.30–7.44 (5 H, m, Ar–*H*); δ_C(100 MHz, $CDCl_3$) 39.6 (CH), 40.6 (CH), 41.5 (CH), 48.1 (CH), 50.2 (CH_3), 50.2 (CH_3), 52.5 (CH_3), 92.4 (C), 126.2 (2 × CH), 128.9 (CH), 129.2 (2 × CH), 130.9 (C), 131.2 (C), 140.9 (CH), 162.6 (C), 173.7 (C), 175.5 (C), 197.2 (C); *m/z* (EI) 385.1172 (M^+, $C_{20}H_{19}O_7N$ requires 385.1162), 357 ($M^+ - 28$, 29), 311 (19), 310 (100), 179 (11), 163 (38).

(1*R,2*R**,6*S**,7*R**)-9,9-Dimethoxytricyclo[5.2.2.0^{2,6}]undeca-10-en-8-one (24a).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 2918, 1731 and 1415; δ_H (400 MHz, $CDCl_3$) 1.20 (3 H, m), 1.64 (1 H, broad dd, *J* 6.0), 1.82 (2 H, m), 2.46 (1 H, ddd, *J* 2.4, 8.0 and 9.6), 2.57 (1 H, ddd, *J* 2.8, 9.6 and 10.0), 3.08 (2 H, m), 3.28 (3 H, s, OC*H*$_3$), 3.30 (3 H, s, OC*H*$_3$), 6.09 (1 H, dddd, *J* 1.2, 2.4, 6.0 and 8.0, C*H*=CH), 6.32 (1 H, ddd, *J* 0.8, 5.2 and 8.0, C*H*=CH); δ_C(100 MHz, $CDCl_3$) 26.8 (CH_2), 31.4 (CH_2), 31.7 (CH_2), 38.3 (CH), 41.2 (CH), 42.8 (CH), 49.6 (CH_3), 50.3 (CH_3), 52.9 (CH), 94.1 (C), 127.7 (CH), 134.5 (CH), 203.8 (C); *m/z* (EI) 194.1341 ($M^+ - CO$, $C_{12}H_{18}O_2$ requires 194.1307) 194 (87), 163 (35), 147 (25), 119 (81), 91 (100), 77 (39), 59 (30), 51 (21).

(1*R,2*R**,6*S**,7*R**)-9,9-Dimethoxytricyclo[5.2.2.0^{2,6}]undec-10-en-8-one (24d).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 2952 (m), 2861 (w), 1733 (s), 1642 (w), 1050 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.95–1.05 (1 H, m), 1.12–1.34 (2 H, m), 1.58–1.67 (1 H, m), 1.74–1.84 (2 H, m), 1.87 (3 H, s, C*H*$_3$), 2.39 (1 H, dd, *J* 9.6, 18.8 Hz), 2.51 (1 H, ddd, *J* 2.8, 10.0, 12.8 Hz), 2.83 (1 H, t, *J* 2.0 Hz), 2.93 (1 H, dd, *J* 2.4, 6.4 Hz), 3.28 (3 H, s, OC*H*$_3$), 3.29 (3 H, s, OC*H*$_3$), 5.64 (1 H, d, *J* 6.0 Hz, =C*H*); δ_C(100 MHz, $CDCl_3$) 23.5 (CH_3), 27.0 (CH_2), 30.9 (CH_2), 31.4 (CH_2), 38.2 (CH), 39.9 (CH), 47.7 (CH), 49.5 (CH_3), 50.5 (CH_3), 52.1 (CH), 94.3 (C), 118.7 (CH), 144.3 (C), 204.2 (C); *m/z* (EI) 236.1425 (M^+, $C_{14}H_{20}O_3$ requires 236.1412) 236 (98), 208 (20), 176 (43), 151 (61).

(1*R,2*S**,7*R**,8*R**)-3,3-Dimethoxytricyclo[6.2.2.0^{2,7}]dodeca-5,9-dien-4-one (25).** Obtained as a white solid; (found: C, 71.93; H, 7.92, $C_{14}H_{18}O_3$ requires C, 71.77; H, 7.74%): ν_{max}(film)/cm^{-1} 3021, 2937, 2866 and 1704; δ_H (400 MHz, $CDCl_3$) 1.36–1.43 (1 H, m), 1.51–1.65 (3 H, m), 2.49 (2 H, t, *J* 7.2), 2.64 (1 H, br m), 2.85–2.90 (1 H, br m), 2.97 (3 H, s, OC*H*$_3$), 3.25 (3 H, s, OC*H*$_3$), 5.80 (1 H, t, *J* 7.6, C*H*=CH), 5.84 (1 H, dd, *J* 1.2 and 10.0, C*H*=CH), 6.04 (1 H, t, *J* 7.2, CH=C*H*CO), 6.44 (1 H, dd, *J* 4.0 and 10.0 Hz, C*H*=CHCO); δ_C(100 MHz, $CDCl_3$) 23.6 (CH_2), 27.6 (CH_2), 30.7 (CH), 35.7 (CH), 42.7 (CH), 44.8 (CH), 48.4 (CH_3), 49.9 (CH_3), 99.4 (C), 127.4 (CH), 132.7 (CH), 133.1 (CH), 150.9 (CH), 194.6 (C); *m/z* (EI) 234.1241 (M^+, $C_{14}H_{18}O_3$ requires 234.1256), 234 (73), 206 (28), 154 (100), 131.0 (45), 127 (21), 123 (45), 111 (45).

(1*R,2*R**,6*S**,7*R**)-9,9-Dimethoxytricyclo[5.2.2.0^{2,6}]undeca-4,10-dien-8-one (27a).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 3052, 2841, 1737, 1094 and 1052; δ_H (400 MHz, $CDCl_3$) 1.97 (1 H, dm, *J* 17.2, CH_2–CH=CH), 2.54 (1 H, dm, *J* 17.2, CH_2–CH=CH), 2.90 (1 H, m, C*H*–CH), 2.97 (1 H, m, C*H*–C(OMe)$_2$), 3.12 (1 H, ddd, *J* 1.6, 2.8 and 6.0, C*H*–CO), 3.19 (1 H, m, C*H*–CH), 3.30 (s, 3 H, –OCH_3), 3.35 (3 H, s, –OCH_3), 5.41 (1 H, m, CH_2–C*H*=CH), 5.65 (1 H, ddd, *J* 2.4, 6.0 and 3.6, CH_2–C*H*=CH), 6.04 (1 H, m, C*H*=CH), 6.24 (1 H, m, C*H*=CH); δ_C(100 MHz, $CDCl_3$) 33.7 (CH), 38.4 (CH_2), 43.7 (CH), 49.4 (CH), 49.6 (CH_3), 50.2 (CH_3), 52.0 (CH), 94.7 (C), 127.7 (CH), 130.0 (CH), 131.8 (CH), 133.1 (CH), 203.4 (C); *m/z* (EI) 220.1100 (M^+, $C_{13}H_{16}O_3$ requires 220.1099), 192 ($M^+ - CO$, 100), 177 (7), 161 (78), 127 (9), 117 (39), 96 (8), 75 (20).

(1*S,2*R**,3*S**,7*R**)-9,9-Dimethoxy-7-methyltricyclo-[5.2.2.0^{2,6}]-undeca-4,10-dien-8-one (27b).** ν_{max}(film)/cm^{-1} 3050, 2945, 2908, 1733, 1454, 1241, 1158, 1145, 1056 and 988; δ_H (400 MHz, $CDCl_3$) 1.20 (3 H, s, C*H*$_3$), 1.97–2.02 (1 H, m, CH_2–CH=CH), 2.49–2.56 (1 H, m, CH_2–CH=CH), 2.81–2.85 (1 H, m, C*H*–CH), 2.89–2.96 (1 H, m, C*H*–CH), 3.10–3.13 (1 H, m, C*H*–C(OMe)$_2$), 3.29 (3 H, s, OC*H*$_3$), 3.34 (3 H, s, –OC*H*$_3$), 5.49–5.52 (1 H, m, C*H*=CH), 5.68–5.70 (2 H, m, C*H*=C*H*), 6.18–6.22 (1 H, t, *J* 6.4, C*H*=CH); δ_C(100 MHz, $CDCl_3$) 15.5 (CH_3), 35.2 (CH), 38.7 (CH_2), 43.2 (CH), 49.7 (CH_3), 50.3 (CH_3), 52.3 (C), 54.7 (CH), 94.5 (C), 128.7 (CH), 131.3 (CH), 133.2 (CH), 134.0 (CH), 204.6 (C); *m/z* (EI) 234.1243 (M^+, $C_{14}H_{18}O_3$ requires 234.1256), 234 (5), 225 (14), 208 (15), 207 (15), 206 (100).

(1*S,2*R**,6*S**,7*R**)-9,9-Dimethoxy-11-methyltricyclo[5.2.2.0^{2,6}]-undeca-4,10-dien-8-one (27c).** Obtained as a white solid; (found: C, 70.84, H, 7.76, $C_{14}H_{18}O_4$ requires C, 71.15, H, 7.74%): ν_{max}(film)/cm^{-1} 3046, 2951, 2842, 1734, 1442, 1148, 1095, 1055, 978, 833, 790 and 698; δ_H (400 MHz, $CDCl_3$) 1.74 (3 H, d, *J* 1.6 Hz, C*H*$_3$), 2.04 (1 H, dm, *J* 17.2 Hz, CH_2–CH=CH), 2.54 (1 H, dm, *J* 17.2 Hz, CH_2–CH=CH), 2.89 (1 H, m, C*H*–CH), 2.94 (1 H, t, *J* 2.4 Hz, C*H*–CO), 3.03 (1 H, dd, *J* 2.8, 6.4 Hz, C*H*–C(OMe)$_2$), 3.25 (1 H, m, C*H*–CH), 3.33 (3 H, s, –OC*H*$_3$), 3.37 (3 H, s, –OC*H*$_3$), 5.40 (1 H, m, C*H*=CH), 5.67 (1 H, ddd, *J* 2.0, 4.4 and 5.6 Hz, C*H*=CH), 5.85 (1 H, dm, *J* 6.4 Hz, C*H*=C–CH_3); δ_C(100 MHz, $CDCl_3$) 21.4 (CH_3), 33.5 (CH), 38.2 (CH_2), 43.0 (CH), 49.0 (CH), 49.6 (CH_3), 49.9 (CH_3), 57.4 (CH), 94.8 (C), 123.3 (CH), 129.3 (CH), 132.9 (CH), 136.6 (C), 203.2 (C); *m/z* (EI) 234.1255 (M^+, $C_{14}H_{18}O_3$ requires 234.1256), 206 ($M^+ - 28$, 99), 191 (13), 175 (100), 159 (6), 153 (10), 131 (30), 117 (14), 91 (5), 75 (33).

(1*S,2*R**,6*S**,7*R**)-9,9-Dimethoxy-10-methyltricyclo[5.2.2.0^{2,6}]-undeca-4,10-dien-8-one (27d).** ν_{max}(film)/cm^{-1} 3048, 2949, 2842, 1735, 1444, 1230, 1139, 1087, 1051, 979, 824 and 719; δ_H (400 MHz, $CDCl_3$) 1.91 (3 H, d, *J* 1.6, C*H*$_3$), 1.92 (1 H, dm, *J* 16.8, CH_2–CH=CH), 2.55 (1 H, dm, *J* 16.8, CH_2–CH=CH), 2.89 (1 H, m, C*H*–CH), 2.96 (1 H, t, *J* 2.4, C*H*–C(OMe)$_2$), 3.04 (1 H, dd, *J* 6.8 and 2.4, C*H*–CO), 3.20 (1 H, m, C*H*–CH), 3.35 (3 H, s, –OC*H*$_3$), 3.36 (3 H, s, –OC*H*$_3$), 5.39 (1 H, m, C*H*=CH), 5.60 (1 H, dm, *J* 6.8, C*H*=CCH_3), 5.68 (1 H, ddd, *J* 6.0, 4.4 and 2.4 Hz, C*H*=CH); δ_C(100 MHz, $CDCl_3$) 23.6 (CH_3), 33.7 (CH), 37.6 (CH_2), 48.2 (CH), 48.6 (CH), 49.6 (CH_3), 50.5 (CH_3), 51.9 (CH), 94.9 (C), 118.4 (CH), 129.9 (CH), 132.9 (CH), 141.7 (C), 203.7 (C); *m/z* (EI) 234.1260 (M^+, $C_{14}H_{18}O_3$ requires 234.1256),

206 (M^+-28, 100), 191 (19), 175 (42), 153 (12), 131 (95), 117 (30), 105 (8), 91 (26), 75 (30).

(1*R,2*R**,6*S**,7*R**)-9,9-dimethoxy-11-methyoxy-carbonyltricyclo[5.2.2.0^{2,6}]undeca-4,10-dien-8-one (27e).** ν_{max}(film)/cm^{-1} 2947, 1740, 1719, 1630, 1441, 1283, 1235, 1136 and 1099; δ_H (400 MHz, CD_3COCD_3) 2.02 (1 H, d, *J* 17.6, CH_2–CH=CH), 2.57 (1 H, d, *J* 17.6, CH_2–CH=CH), 2.96 (1 H, d, *J* 0.8, C*H*–CH), 3.24 (3 H, s, –OCH_3), 3.28 (1 H, m, C*H*–CH), 3.36 (3 H, s, –OCH_3), 3.50 (1 H,dd, *J* 6.8 and 2.8, C*H*–C(OMe)$_2$), 3.63 (1 H, dd, *J* 2.8 and 2.0, C*H*–CO), 3.70 (3 H, s, CO_2CH_3), 5.42 (1 H, m, C*H*=CH), 5.64 (1 H, m, C*H*=CH), 7.26 (1 H, ddd, *J* 6.8, 2.0 and 0.8, C*H*=C(CO_2Me)); δ_C(100 MHz, CD_3COCD_3) 34.4 (CH), 38.9 (CH_2), 45.6 (CH), 49.9 (CH_3), 50.2 (CH), 50.4 (CH_3), 52.1 (CH_3), 52.3 (CH), 95.0 (C), 130.4 (CH), 131.9 (C), 134.0 (CH), 142.8 (CH), 164.8 (C), 202.2 (C); *m*/*z* (EI) 278.1151 (M^+, $C_{15}H_{18}O_5$ requires 278.1154), 250 (M^+ − CO, 100), 219 (84), 203 (16), 191 (26), 185 (12), 159 (17), 127 (17), 115 (42).

Ethyl (1*R,4*R**)-8,8-dimethoxy-8-oxobicyclo[2.2.2]octa-2,5-diene-2-carboxylate (28aN).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 3016, 2901, 1737, 1710 and 1050; δ_H (400 MHz, $CDCl_3$) 1.27 (3 H, t, *J* 7.2, $CO_2CH_2CH_3$), 3.27 (3 H, s, OCH_3), 3.30 (3 H, s, OCH_3), 4.11 (2 H, dt, *J* 6.8 and 1.6, $CO_2CH_2CH_3$), 4.20 (1 H, ddd, *J* 1.2, 7.2 and 8.4, C*H*–C(OMe)$_2$), 4.53 (1 H, td, *J* 6.8 and 2.0, C*H*–CO), 6.41 (1 H, dt, *J* 6.0 and 1.6, C*H*=CH), 6.50 (1 H, dt, *J* 7.2 and 1.6, C*H*=CH), 7.30 (1 H, dd, *J* 1.6 and 7.2, C*H*=CCO_2Et); δ_C(100 MHz, $CDCl_3$) 14.1 (CH_3), 44.8 (CH), 49.9 (CH_3), 50.4 (CH_3), 53.6 (CH), 61.1 (CH_2), 89.8 (C), 129.9 (CH), 132.2 (CH), 134.5 (C), 142.1 (CH), 163.5 (C), 193.8 (C); *m*/*z* (EI) 224.1082 (M^+ − CO, $C_{12}H_{16}O_4$ requires 224.1049), 224 (7), 193 (10), 151 (6), 105 (69), 91 (9), 77 (27), 74 (44), 59 (100).

Ethyl (1*R,4*R**)-7,7-dimethoxy-8-oxobicyclo[2.2.2]octa-2,5-diene-2-carboxylate (28aX).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 3018, 2905, 1737, 1713 and 1052; δ_H (400 MHz, $CDCl_3$) 1.29 (3 H, t, *J* 6.8, $CO_2CH_2CH_3$), 3.29 (3 H, s, OCH_3), 3.32 (3 H, s, OCH_3), 4.11 (1 H, dt, *J* 1.6, 6.0 and 7.6, C*H*–CO), 4.22 (2 H, ddd, *J* 2.8, 6.8 and 10.0, $CO_2CH_2CH_3$), 4.56 (1 H, td, *J* 2.0 and 4.0, C*H*–C(OMe)$_2$), 6.40 (1 H, dt, *J* 1.6, 5.6 and 7.2 Hz, C*H*=CH), 6.53 (1 H, dt, *J* 1.6, 7.2 and 8.0, C*H*=CH), 7.30 (1 H, dd, *J* 2.0 and 6.0, C*H*=CCO_2Et); δ_C(100 MHz, $CDCl_3$) 14.1 (CH_3), 43.9 (CH), 50.4 (2 × CH_3), 55.2 (CH), 61.0 (CH_2), 89.8 (C), 128.1 (CH), 133.8 (CH), 137.4 (C), 138.3 (CH), 163.9 (C), 193.9 (C); *m*/*z* (EI) 224.1044 (M^+ − CO, $C_{12}H_{16}O_4$ requires 224.1049), 224 (8), 151.1 (8), 105 (77), 91 (10), 77 (34), 74 (42), 59 (100), 51 (9).

Dimethyl (1*R,4*R**)-7,7-dimethoxy-8-oxobicyclo[2.2.2]octa-2,5-diene-2,3-dicarboxylate (29a).** Obtained as a light yellow colored oil; ν_{max}(film)/cm^{-1} 2953, 2846, 1737, 1718, 1645 and 1071; δ_H (400 MHz, $CDCl_3$) 3.31 (6 H, s, 2 X–OCH_3), 3.78 (3 H, s,CO_2CH_3), 3.80 (3 H, s, CO_2CH_3), 4.32 (1 H, dd, *J* 1.6 and 5.2, C*H*–C(OMe)$_2$), 4.41 (1 H, dd, *J* 2.4 and 6.0, C*H*–CO), 6.51 (2 H, m, C*H*=C*H*); δ_C(100 MHz, $CDCl_3$) 46.2 (CH), 50.0 (CH_3), 50.6 (CH_3), 52.2 (CH_3), 52.5 (CH_3), 53.0 (CH), 58.6 (C), 89.2 (C), 128.7 (CH), 133.0 (CH), 137.1 (C), 139.0 (C), 164.9 (C), 192.1 (C); *m*/*z* (EI) 268.0940 (M^+ − CO, $C_{13}H_{16}O_6$ requires 268.0947), 268 (57), 221 (68), 210 (89), 178 (92), 135 (70), 105 (81), 92 (82), 76 (61).

Dimethyl (1*R,4*R**)-8,8-dimethoxy-1-methyl-7-oxobicyclo[2.2.2]octa-2,5-diene-2,3-dicarboxylate (29b).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 2978, 2946, 2836, 1735, 1703, 1646, 1455, 1159 and 1056; δ_H (400 MHz, $CDCl_3$) 1.41 (3 H, s, CH_3), 3.27 (3 H, s, OCH_3), 3.29 (3 H, s, OCH_3), 3.74 (3 H, s, CO_2CH_3), 3.77 (3 H, s, CO_2CH_3), 4.52 (1 H, dd, *J* 1.6 and 6.8, C*H*–C(OMe)$_2$), 6.04 (1 H, dd, J 2.0, 6.8 Hz, C*H*=CHCH$_3$), 6.50 (1 H, t, *J* 6.8 Hz, CH=C*H*CH$_3$); δ_C(100 MHz, $CDCl_3$) 12.0 (CH_3), 43.6 (CH), 49.9 (CH_3), 50.6 (CH_3), 52.3 (CH_3), 52.5 (CH_3), 57.0 (C), 89.7 (C), 133.5 (CH), 133.6 (CH), 146.0 (2 × C), 162.9 (C), 166.0 (C), 193.5 (C); *m*/*z* (EI) 310.1050 (M^+, $C_{15}H_{18}O_7$ requires 310.1053), 310 (5), 283 (8), 282 (19), 280 (5), 279 (22).

Dimethyl (1*R,4*R**)-7,7-dimethoxy-5-methyl-8-oxobicyclo[2.2.2]octa-2,5-diene-2,3-dicarboxylate (29c).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 2999, 2954, 2915, 2840, 1738, 1731, 1725, 1659, 1632, 1435 and 1266; δ_H (400 MHz, $CDCl_3$) 1.93 (3 H, s, CH_3), 3.28 (3 H, s, OCH_3), 3.31 (3 H, s, OCH_3), 3.78 (3 H, s, CO_2CH_3), 3.79 (3 H, s, CO_2CH_3), 4.06 (1 H, d, *J* 1.6, C*H*–C(OMe)$_2$), 4.24 (1 H, d, *J* 6.4, C*H*–CO), 6.04–6.07 (1 H, m, C*H*=CCH$_3$); δ_C(100 MHz, $CDCl_3$) 19.1 (CH_3), 45.8 (CH), 49.9 (CH_3), 50.9 (CH_3), 52.6 (2 × CH_3), 60.8 (CH), 89.7 (C), 125.1 (CH), 136.6 (C), 139.5 (C), 139.8 (C), 165.0 (C), 165.2 (C), 192.5 (C); *m*/*z* (EI) 310.1035 (M^+, $C_{15}H_{18}O_7$ requires 310.1053), 310 (5), 282 (23), 279 (4).

Dimethyl (1*R,4*R**)-8,8-dimethoxy-5-methyl-7-oxobicyclo[2.2.2]octa-2,5-diene-2,3-dicarboxylate (29d).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 3050, 2945, 2910, 1740, 1734, 1721, 1654, 1615, 1422 and 1272; δ_H (400 MHz, $CDCl_3$) 1.91 (3 H, s, CH_3), 3.19 (3 H, s, OCH_3), 3.26 (3 H, s, OCH_3), 3.70 (3 H, s, CO_2CH_3), 3.71 (3 H, s, CO_2CH_3), 4.06 (1 H, d, *J* 5.6, C*H*–C(OMe)$_2$)), 4.08 (1 H, d, *J* 2.4, C*H*–CO), 5.93–5.95 (1 H, m, C*H*=CCH$_3$); δ_C(100 MHz, $CDCl_3$) 20.1 (CH_3), 50.2 (CH_3), 50.5 (CH_3), 50.9 (CH), 52.3 (CH_3 × 2), 54.9 (CH), 89.4 (C), 120.2 (CH), 138.0 (C), 138.4 (C), 144.4 (C), 164.6 (C), 165.0 (C), 192.2 (C); *m*/*z* (EI) 310.1049 (M^+, $C_{15}H_{18}O_7$ requires 310.1053) 310 (10), 283 (18), 279 (25).

(1*R,4*R**)-3,3-Dimethoxy-6-phenylbicyclo[2.2.2]octa-5,7-dien-2-one (30aN).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 3100, 3022, 2944, 1737 and 1071; δ_H (400 MHz, $CDCl_3$) 3.34 (3 H, s, OCH_3), 3.36 (3 H, s, OCH_3), 4.20 (1 H, m, C*H*–C(OMe)$_2$)), 4.47 (1 H, m, C*H*–CO), 6.56 (3 H, m, C*H*=C*H* and C*H*=CPh), 7.27 (1 H, td, *J* 7.2 and 1.2, Ar–*H*), 7.33 (3 H, m, 3 × Ar–*H*), 7.47 (1 H, t, *J* 3.6, Ar–*H*); δ_C(100 MHz, $CDCl_3$) 44.3 (CH), 50.1 (CH_3), 50.2 (CH_3), 57.2 (CH), 90.8 (C), 118.9 (CH), 125.4 (2 × CH), 127.9 (CH), 128.3 (2 × CH), 128.6 (CH), 133.3 (C), 133.4 (CH), 134.9 (C), 195.3 (C); *m*/*z* (EI) 228.1181 (M^+ − CO, $C_{15}H_{16}O_2$ requires 228.1150), 228 (5), 197 (35), 154 (49), 153 (32), 115 (7.16), 77 (17), 74 (71), 59 (100).

(1*R,4*R**)-6-Butyl-3,3-dimethoxybicyclo[2.2.2]octa-5,7-dien-2-one (31aN).** Obtained as a colorless oil; ν_{max}(film)/cm^{-1} 3069, 2965, 2930 and 1738; δ_H (400 MHz, $CDCl_3$) 0.86 (3 H, t, *J* 7.2, CH_3), 1.25 (2 H, dd, *J* 6.8 and 14.4, ^{n}Bu), 1.38 (2 H, dd, *J* 7.2 and 14.4, ^{n}Bu), 2.20 (2 H, apparent tt, *J* 1.6 and 6.8 Hz, ^{n}Bu), 3.29 (3 H, s, OCH_3), 3.30 (3 H, s, OCH_3), 3.78 (1 H, td, *J* 2.0 and 5.6, C*H*–CO), 3.85 (1 H, m, C*H*–C(OMe)$_2$)), 5.94 (1 H, ddd, *J* 1.2, 3.2 and 4.8, C*H*=C-^{n}Bu), 6.41 (2 H, m, C*H*=C*H*); δ_C(100 MHz, $CDCl_3$) 13.8 (CH_3), 22.0 (CH_2), 29.2 (CH_2), 33.2 (CH_2), 43.6

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(CH), 49.9 (CH_3), 50.1 (CH_3), 58.8 (CH), 91.0 (C), 124.4 (CH), 130.1 (CH), 133.3 (CH), 143.7 (C), 195.5 (C); *m/z* (EI) 236.1408 (M^+, $C_{14}H_{20}O_3$ requires 236.1412), 236 (2), 208 (20), 178 (13), 151 (65), 119 (4), 105 (8), 102 (11).

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