Ring-Fused and Spiro Cyclopentenones by $Ni(CO)_4$-Promoted Intermolecular Carbonylative Cycloaddition of Acetylenes with 3-Halo- and 1-(Halomethyl)cycloalkenes

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Received March 27, 1992

Abstract: The title carbonylative cycloaddition of five- to eight-member ring 3-halo- and 1-(halomethyl)cycloalkenes with different acetylenes was studied. From moderate to good yields of ring-fused and spiro cyclopentenone derivatives were obtained, especially in the reaction with acetylenes bearing electron-withdrawing substituents by proper selection of the reaction conditions to avoid the acetylene polyinsertion and/or other side reactions from the organonickel intermediates. In this context, the beneficial role of acetate ion on the outcome of the reaction is rationalized. This process leading to the formation of bicycloadducts with the concomitant formation of up to six C–C bonds, with high regio- and stereoselectivity, can be useful in the synthesis of natural products as exemplified by the easy preparation of [5-5-5] tricyclic compound **14** from a 1:1 cis and trans isomeric mixture of 6-acetoxy-3-bromocyclooctene (**11**). A plausible general reaction mechanism is proposed that is consistent with all the products obtained.

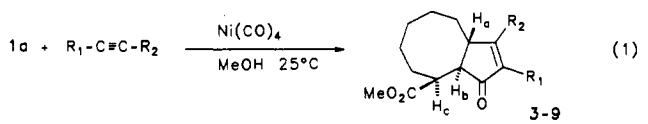
Development of new methodologies for the synthesis of compounds containing five-member rings is currently a subject of broad research interest.[1] Several successful approaches have been designed through free radical intermediates,[2] ring expansion of three-[3] or four-member[4] carbocycles, [3 + 2] cycloadditions,[5] and cyclization methods forming more than one bond in a single step using transition metal complexes.[6,7]

In this context, we have recently reported on the synthesis of 2-cyclopentenone derivatives by inter-[8] and intramolecular[9] carbonylative cycloadditions of allyl halides and acetylenes mediated by $Ni(CO)_4$, a reaction formerly described by Chiusoli.[10] In this ongoing research, we anticipated that the use of cyclic allyl halides in this reaction might lead to the synthesis of 4,5-cyclopentenone-fused bicyclic systems[11] through the corresponding π-allyl nickel[12] complexes that are generally accepted as intermediates in this process. Literature precedents on the reactivity of these putative intermediates were rather scarce and contradictory.[13] However, our first results were quite promising,[14] and this encouraged us to explore the feasibility of this intermolecular carbonylative cycloaddition with different 3-halocycloalkenes **1a–d** (Scheme I).

Likewise, as a logical extension of this methodology, we also investigated the formation of spiro cyclopentenones by using 1-(halomethyl)cycloalkenes **2a–d** as starting allyl halides.[15] In the present paper we give a full account of our results on the preparation of different ring-fused and spiro cyclopentenones by using this $Ni(CO)_4$-promoted intermolecular carbonylative cycloaddition procedure.

Synthesis of Fused Cyclopentenones

Fused [8-5] Bicyclic Systems. Our studies began with the reaction of 2-butyn-1-ol with 3-bromocyclooctene (**1a**). When halide **1a** was added to a methanolic solution of $Ni(CO)_4$ (*Caution*)[16] and the acetylene at 30 °C, a smooth reaction took place, the colorless mixture turning to yellow, red, and finally green. After purification of the crude reaction product by column chromatography, a single compound (**3**, 51% yield) was isolated (eq 1). The presence of a cyclopentenone ring in this compound was inferred from significant spectroscopic data (IR 1705, 1650 cm^{-1}; ^{13}C NMR δ 209.7). Likewise, from its NMR spectra, we established unambiguously the formation of only one of the four possible enantiomeric pairs and only one of the two possible regioisomers resulting from the acetylene insertion. The proton



(1)

3 R_1=Me; R_2=CH_2OH (51%)
4 R_1=Me; R_2=CO_2Me (81%)
5 R_1=Et; R_2=COMe (70%)
6 R_1=CH_2OMe; R_2=H (77%)
7 R_1=Me_3Si; R_2=CH_2OMe (17%)
8 R_1=Me_3Si; R_2=H (57%)
9 R_1=Ph; R_2=H (34%) + 10 (57%)

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[‡] Institut de Ciència de Materials de Barcelona. Authors to whom correspondence on X-Ray structure determination should be addressed.

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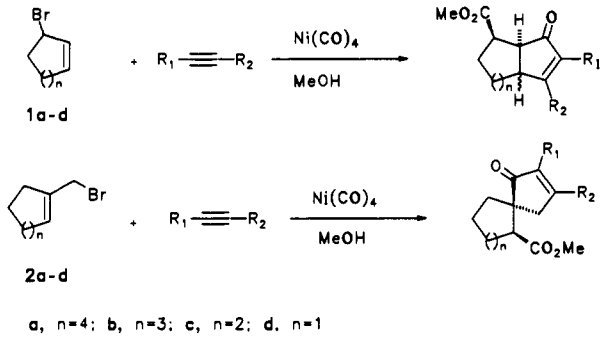
Scheme I

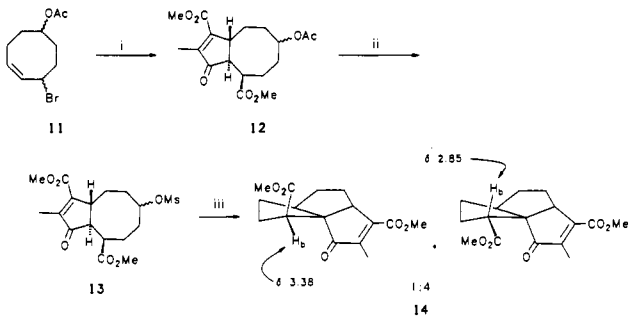


a, n=4; b, n=3; c, n=2; d, n=1

NMR peaks corresponding to H_a (δ 3.1–3.4, m), H_b (δ 2.3, dd), and H_c (δ 3.1–3.4, m), the coupling constants (J_{ab} = 3.0 Hz; J_{bc} = 5.0 Hz), and the methine signals in the ^{13}C NMR suggested a trans ring fusion and a cis mutual arrangement of H_b and H_c in the structure.[17] In an attempt to extend the scope of this reaction, the behavior of several functionalized acetylenes was investigated.

When methyl 2-butynoate was reacted with **1a** under the same conditions, a 68% yield of the bicyclic compound **4** was isolated from the reaction mixture in addition to 8% of dimethyl (*E*)-methylbutene-1,4-dioate. Presumably, this diester was originated by Reppe carbonylation[18] of the alkyne. In order to avoid this side reaction, a methodological modification was introduced, by adding the mixture of the acetylene and the allyl halide onto the $Ni(CO)_4$; therewith the yield of cyclopentenone **4** rose up to 81%. When these conditions were applied to the other acetylenes investigated, the corresponding bicyclic compounds **5–9** were obtained[19] with the yields indicated in eq 1. In general, these yields were good except for compound **7**, where the reaction was sluggish probably due to the steric hindrance inherent in the trimethylsilyl group present in the disubstituted alkyne and a mixture of epimers in a 1:1 ratio was obtained in 17% yield. However, (trimethylsilyl)acetylene rendered quite an acceptable yield of the interesting cycloadduct **8**, which might be regarded as a putative synthon equivalent to that resulting from unsubstituted acetylene after removal of the trimethylsilyl group.

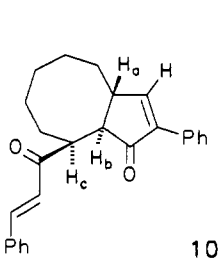
Scheme II. Synthesis of [5-5-5] Tricyclic Compound **14**



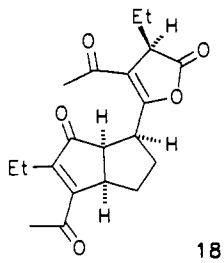
[a] (i) methyl 2-butynoate, $Ni(CO)_4$, MeOH (55%); (ii) KOH, MeOH, room temperature (98%); MsCl, NEt_3, CH_2Cl_2 (76%); (iii) NaOMe, MeOH, reflux (70%).

Structures of compounds **4–9** were assigned as indicated above for compound **3**. Unfortunately, literature data for fused [5-8] bicyclic systems of this type are rather scarce, and hence, the assignment of the relative stereochemical arrangement of rings and methoxycarbonyl groups in these compounds by comparison with related structures was not entirely reliable.[17] Independent confirmation of these tentative structures was brought about by X-ray diffraction analysis of compound **4**.

The formation of compound **10** in the reaction of bromocycloalkene **1a** with phenylacetylene arises from incorporation of two alkyne units in the final structure. Spectral data of **10** were



10



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consistent with the structural assignment. Infrared carbonyl absorptions at 1720 cm^{-1} for the cyclopentenone and at 1695 cm^{-1} for the α,β-unsaturated acyclic ketone and the corresponding ^{13}C NMR peaks at 209 and 202 ppm established clearly the functionalities present. In addition, comparison of the corresponding spectral data with those of the related compound **9** showed the occurrence of very close ^1H and ^{13}C NMR signals for the bridgehead and adjacent methine units that suggested the same stereochemistry for both compounds. The *E* configuration of the double bond at the side chain was assigned from IR absorption at 910 cm^{-1}, the value of the coupling constant of the olefinic hydrogen atoms in the ^1H NMR spectrum (AB system, δ 6.85 and 7.7, J_{ab} = 15.9 Hz), and mechanistic considerations (syn addition of acyl nickel moiety to triple bond, cf. below).

The functional tolerance and the control on the stereochemistry displayed by this process makes it useful for preparation of natural products containing [5-8] fused-ring systems.[17] In addition, this bicyclic system can be easily transformed into a [5-5-5] tricyclic

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(8) Camps, F.; Coll, J.; Moretō, J. M.; Torras, J. *J. Org. Chem.* **1989**, *54*, 1969–1978. Camps, F.; Moretō, J. M.; Pagès, L. M. *Tetrahedron* **1992**, *48*, 3147–3162.

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(10) Chiusoli, G. P.; Cassar, L. *Angew. Chem.* **1967**, *79*, 177–186. Chiusoli, G. P. *Acc. Chem. Res.* **1973**, *6*, 422–427.

(11) For a survey on three-carbon annulation leading to bicyclic fused five-member rings see: Larock, R. C. *Comprehensive Organic Transformations*; VCH Publishers: New York, 1989; pp 661–668.

(12) For a survey of π-allyl nickel complexes in organic syntheses, see: (a) Semmelhack, M. F. *Org. React.* **1972**, *19*, 115–183. (b) Baker, R. *Chem. Rev.* **1973**, *73*, 487–530. (c) Billington, D. C. *Chem. Soc. Rev.* **1985**, 93–120.

(13) The cyclooctenyl complex is reported to give an easy carbonylative coupling and both cyclopentenyl and cyclohexenyl nickel complexes are described to be quite unstable: Wilke, G.; Bogdanovic, B.; Hardt, P.; Heimbach, P.; Keim, W.; Kröner, M.; Oberkirch, W.; Tanaka, K.; Steinrücke, E.; Walter, D.; Zimmermann, H. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 151–164. However, the six-member complex was successfully coupled with aromatic halides: Corey, E. J.; Myers, A. G. *J. Am. Chem. Soc.* **1985**, *107*, 5574–5576.

(14) Camps, F.; Llebaria, A.; Moretō, J. M.; Pagès, Ll. *Tetrahedron Lett.* **1992**, *33*, 109–112.

(15) Camps, F.; Llebaria, A.; Moretō, J. M.; Pagès, Ll. *Tetrahedron Lett.* **1992**, *33*, 113–114.

(16) Caution: Tetracarbonylnickel is an extremely toxic, volatile compound and special precautions have to be taken in its use (see Experimental Section for practical details).

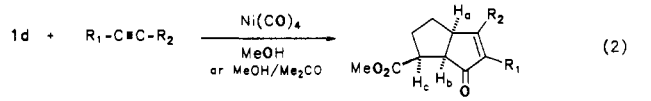
(17) San Feliciano, A.; Barrero, A. F.; Medarde, M.; Miguel del Corral, J. M.; Aramburu, A.; Perales, A.; Fayos, J. *Tetrahedron Lett.* **1985**, *26*, 2369–2372. Mehta, G.; Murty, A. N. *J. Org. Chem.* **1990**, *55*, 3568–3572. Enoki, N.; Fusysaki, A.; Suchiro, K.; Ishida, R.; Matsumoto, T. *Tetrahedron Lett.* **1983**, *24*, 4341–4344.

(18) Falbe, J. *Synthesen mit Kohlenmonoxyd*; Springer-Verlag: Berlin, 1967; pp 73–119.

(19) The efficient formation of cyclopentenone rings from terminal acetylenes in this case is quite remarkable when considering the results previously observed in the corresponding reaction with acyclic allyl halides where no cycloadducts were generally found.[8]

arrangement[20] that is present in several natural bioactive compounds. As an example, we synthesized the tricyclic compound **14** (as a 4:1 mixture of epimers at the methoxycarbonyl-substituted asymmetric center) from 6-acetoxy-3-bromocyclooctene[21] (**11**) and methyl 2-butynoate according to the sequence depicted in Scheme II in 29% overall yield. Although the syn and anti[22] isomers of compound **14** could not be separated, the corresponding stereochemistries at the epimeric center were deduced by considering the chemical shifts of proton H_b at δ 2.85 (major diastereomer) and δ 3.38 (minor diastereomer). The downfield shift might be originated by the proximity of H_b to the cyclopentenone carbonyl group in the anti isomer whereas, in the predominant syn epimer, H_b and the cyclopentenone carbonyl group are bisected by the cyclopentane ring and, hence, the carbonyl group anisotropic effect on H_b should be less effective.

Fused [5-5] Bicyclic Systems. The reaction of 3-bromocyclopentene (**1d**) with acetylenes and $Ni(CO)_4$ gave the expected bicyclo[3.3.0]octane derivatives in modest yields with substantial production of unidentified byproducts (eq 2). Modification of



(2)

15 R_1=Me; R_2=CH_2OH (20%)
16 R_1=Me; R_2=CO_2Me (40%)
17 R_1=Et; R_2=COMe (12%) + 18 (65%)

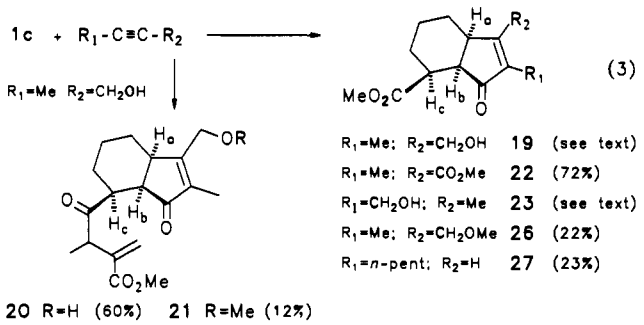
the reaction conditions failed to parallel the high yields obtained with 3-bromocyclooctene (**1a**). Attempts to improve these yields by changing the solvent to acetone (containing 5% methanol) or other variations were ineffective. In this case, we found similar results using 2-butyn-1-ol or methyl 2-butynoate as acetylene partners. Considering the unstability of 3-bromocyclopentene,[23] we decided to carry out the reaction at lower temperatures, but under these conditions, the reaction was completely inhibited. However, portionwise addition of 3-bromocyclopentene (**1d**) to a mixture of acetylenic ester and $Ni(CO)_4$ gave a 40% yield of **16**, corroborating that side reactions of bromoalkene **1** were the main drawbacks.

When 3-hexyn-2-one was reacted with allylic bromide **1d**, we obtained a low yield of the corresponding product **17** whereas tricyclic product **18** was formed in 65% yield by a further insertion of the acetylene. Efforts to increase the **17** to **18** ratio preventing this insertion by addition of acetate anion (cf. below) to the reaction mixture produced a simultaneous reduction in the amounts obtained of both compounds.

Although the yields of bicyclic compounds in the [5-5] series were not outstanding, the process showed high regio- and stereoselectivities and a single isomer was isolated in all cases. The ring fusion is cis as expected for a bicyclo[3.3.0]octane system.[24]

In addition, the relative stereochemistry of H_b and H_c was determined to be cis from comparison of its coupling constant (around 10 Hz), which is coincident with those of closely related structures described in the literature.[20,25] Nuclear Overhauser enhancement difference spectroscopy (NOEDS) of compound **16** confirmed the proposed structure. Irradiation of H_a resulted in a 9% enhancement of the signal at δ 3.0 corresponding to H_b, allowing us to assign a cis relative stereochemistry for both hydrogen atoms. Likewise, when H_b was irradiated, a 10% enhancement of the multiplet centered at δ 2.95 corresponding to H_c was found. Similarly, the structure for compound **18** was assigned from its spectral data and further confirmed by an independent X-Ray diffraction study.

Fused [5-6] Bicyclic Systems. Instead of the expected cyclopentenone ester **19**, the reaction of 3-bromocyclohexene (**1c**) with 2-butyn-1-ol afforded compounds **20** and **21** (eq 3). In contrast, when methyl 2-butynoate was allowed to react with bromocycloalkene **1c**, the cycloadduct **22** was obtained as a single isomer in 72% yield. Several attempts to force the formation of the



(3)

20 R=H (60%) 21 R=Me (12%)

R_1=Me; R_2=CH_2OH **19** (see text)
R_1=Me; R_2=CO_2Me **22** (72%)
R_1=CH_2OH; R_2=Me **23** (see text)
R_1=Me; R_2=CH_2OMe **26** (22%)
R_1=*n*-pent; R_2=H **27** (23%)

bicyclic derivative **19** were made. Since compounds **20** and **21** were presumably originated from insertion of the alkyne on an acyl–Ni intermediate in a competitive reaction with methanol (see Scheme III), we decided to introduce a base in the reaction mixture in order to increase the alcohol nucleophilicity. Alkoxides seemed the obvious choice, but they were discarded due to their capability for promoting elimination side reactions on the starting bromide. Trialkylamines (even as bulky as Hünig's base) and bis(trimethylsilyl)amine inhibited the reaction. However, when an equimolar ratio of KOAc, referred to allyl halide, was added to the reaction mixture and 3-chlorocyclohexene was used instead of the corresponding bromoderivative **1c** to lower the extent of the allylic self-coupling process,[26] we could isolate compound **19** in modest yield (31%) together with its regioisomer **23** (8%), the corresponding elimination product **24** (24%), and another derivative **25** (25%), containing a second acetylene unit in the side chain, structurally related to compounds **20** and **21**. Under similar conditions, modest yields of the adducts **26** and **27** from 2-butynyl methyl ether and 1-heptyne, respectively, were also obtained.

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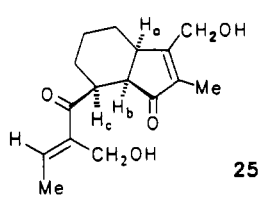

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(20) Geetha, K. Y.; Rajegopalon, K.; Swaminathan, S. *Tetrahedron* **1978**, *34*, 2201–2204. Sheng, M. N. *Synthesis* **1972**, 194–195. Crandall, J. K.; Chong, L. H. *J. Org. Chem.* **1967**, *32*, 532. Nagendrappa, G. *Tetrahedron* **1982**, *38*, 2429–2433. Apparu, M.; Barrelle, M. *Tetrahedron* **1978**, *34*, 1817–1822. Chorlton, A. P.; Morris, G. A.; Sutherland, J. K. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1205–1210. Montaña, A. M.; Moyano, A.; Pericás, M. A.; Serratosa, F. *Tetrahedron* **1985**, *41*, 5995–6003.

(21) Compound **11** was obtained as a mixture of isomers from cyclooctene through a five-step sequence together with 3-acetoxy-6-bromocyclooctene. Separation of these functional isomers could not be accomplished. Therefore the 1:1 mixture of regioisomers (both respectively as a 1:1 mixture of *cis* and *trans* isomers) was employed in the reaction. We took advantage of the fact that allylic acetates do not react with $Ni(CO)_4$, and consequently these compounds were recovered unaltered after the reaction completion.

(22) The terms *syn* and *anti* refer to the relative arrangement of the cyclopentenone carbonyl group and ester group substituents at the adjacent asymmetric centers on the common cyclopentane ring in analogy to the products formed from formal *syn* and *anti* addition in the discussed mechanism.

(23) 3-Halocyclopentenes are thermally unstable, and use of low temperatures in its handling is recommended: Moffett, R. B. *Organic Synthesis*; J. Wiley: New York, 1967; Collect. Vol. IV, pp 238–241.

(24) *cis*-Fusion of cyclopentane rings in [5-5] bicyclic systems is energetically favored relative to the corresponding *trans* geometry by 26.8 kJ mol^{-1}: Chang, S.; McNally, C.; Shary-Tehrany, S.; Hickey, M. J.; Boyd, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 3109–3118.

(25) For [5-5] systems, see: Hudlicky, T.; Koszyk, F. J.; Kutchan, T. M.; Sheth, J. P. *J. Org. Chem.* **1980**, *45*, 5020–5027. Callant, P.; Ongena, M.; Vandewalle, M. *Tetrahedron* **1981**, *37*, 2085–2089. Denmark, S. E.; Jones, T. K. *Helv. Chim. Acta* **1983**, *66*, 2377–2396. Crimmins, M. T.; DeLoach, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 800–806. Paquette, L. A.; Galemmo, R. A., Jr.; Caille, J. C.; Valpey, R. S. *J. Org. Chem.* **1986**, *51*, 686–695. Denmark, S. E.; Habermas, G. A.; Hite, G. A. *Helv. Chim. Acta* **1988**, *71*, 168–194.

(26) Although allyl coupling was also found with the other 3-bromocycloalkenes, this process became very important in the six-member case. The change of bromide by chloride alleviated to some extent this problem. For a discussion on the mechanism of π-allyl nickel complex coupling with organic halides and the role of halide in the process, see: Hegedus, L. S.; Thompson, D. H. P. *J. Am. Chem. Soc.* **1985**, *107*, 5663–5669. See also reference 12.

Table I. Reaction of 3-Bromocycloheptene (**1b**) with Alkynes and $Ni(CO)_4$ in Methanol

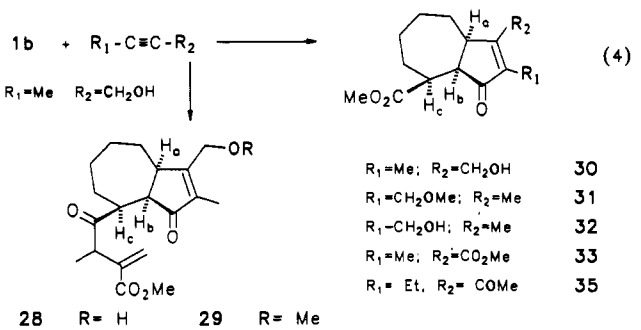
entry	alkyne R_1	alkyne R_2	T (°C)	method[a]	products (% isolated yield)
1	Me	CH_2OH	30	A	**28** (50)
					29 (4)
2	Me	CH_2OH	20	B	**28** (20)
3	Me	CH_2OH	30	B[b]	**30** (10)
					31 (10)
4	Me	CH_2OMe	30	A	**31** (7)
					29 (21)
5	Me	CH_2OH	30	B[c]	**28** (50)
					29 (26)
6[d]	Me	CH_2OH	20	B[c]	**30** (21)
					32 (3)
7	Me	CO_2Me	30	A	**33** (28)
					34 (72)
8	Me	CO_2Me	30	B	**33** (70)
					34 (29)
9[d]	Et	COMe	30	B[c]	**35** (53)

[a] Method A: The allyl halide was dropwise added onto the alkyne and $Ni(CO)_4$ in methanol. Method B: The solution of haloalkene and alkyne was added to the solution of $Ni(CO)_4$ in methanol. [b] In this particular case, the solvent was a 1:1 benzene/methanol mixture. [c] KOAc (equimolar amount with respect to allyl halide) was present in the reaction mixture. [d] 3-Chlorocycloheptene was used.

Structural assignments for compounds **19–27** were inferred from comparison of the corresponding coupling constants J_{ab} and J_{bc} and ^{13}C NMR chemical shifts[27] with those of some related systems described in the literature.[28]

The values of J_{ab} around 6 Hz are consistent with a cis ring fusion, and J_{bc} between 6.0 and 6.7 Hz suggested an equatorial–axial relationship between H_b and H_c with the methoxycarbonyl group located in the most favorable equatorial position. NOEDS for compound **19** confirmed the mutual cis arrangement of H_a, H_b, and H_c. Irradiation of the multiplet corresponding to H_a at δ 3.14 resulted in a 13% enhancement of the signal at δ 3.04 corresponding to H_b, whereas a 17% enhancement of this signal resulted when irradiating the multiplet at δ 2.66 corresponding to H_c. Structures of compounds **20** and **21** were very close to that of **19** in the bicyclic moiety as confirmed by comparison of their spectral data. Additionally, a ketone group (IR 1715 cm^{-1}; ^{13}C NMR δ 210.6), an α,β-unsaturated ester (IR 1750 cm^{-1}; ^{13}C NMR δ 174.7), a $CHCH_3$ moiety, and a terminal methylene (^{13}C NMR δ 126.6) were present at the side chain in agreement with the depicted arrangement of these groups.

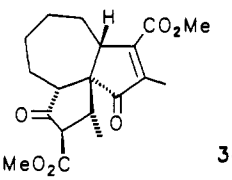
Fused [5-7] Bicyclic Systems. As in the preceding case, preliminary results showed that the reaction of 3-bromocycloheptene (**1b**) with 2-butyn-1-ol afforded products **28** and **29** resulting from the alkyne polyinsertion (eq 4) instead of the expected cyclo-



(4)

pentenone ester **30** (entry 1, Table I). Attempts to induce the formation of this compound by modifying some reaction conditions were unsuccessful or gave low yields (entries 2–6). The addition of KOAc resulted in low yields and/or originated Reppe-type products (entries 5 and 6).

Gratifyingly, the reaction with methyl 2-butynoate by proper choice of experimental conditions (cf. entries 7 and 8) afforded good yields of bicyclic compound **33**. In all cases in which this alkyne was used, this bicyclic product was accompanied by variable amounts of a tricyclic cycloadduct (**34**) coming from an incorporation of a second alkyne moiety. Both compounds **33** and **34** were obtained as a single enantiomeric pair.



34

We assigned the structure of tricyclic compound **34** from the presence in its proton NMR spectrum of signals very close to that of compound **33**. Additionally, two carbonyl groups (IR 1760, 1730 cm^{-1}; ^{13}C NMR δ 212, 206) and a $CHCH_3$ group were also present. While the ring fusion in compound **33** was assigned to be cis from the value of the coupling constant between H_a and H_b (6.6 Hz),[29] the stereochemistry in **34** could not be inferred from spectral data but was established by an X-Ray diffraction study confirming the singular formation of an angular [5-7-5] tricyclic compound in this reaction.

Spiro Systems. The reaction of 1-(bromomethyl)cycloalkenes with 2-butyn-1-ol and methyl 2-butynoate afforded spiro cyclo-

Table II. $Ni(CO)_4$ Promoted Carbonylative Cycloaddition of Alkynes and 1-(Bromomethyl)cycloalkenes

entry	alkyne[a]	allyl halide	method[b]/additive	products (% yield[c])
1	*a*	**2d**	A	**36** (50)
2	*b*	**2d**	B	**37** (45)
3	*a*	**2c**	A	**38** (15)[d]
				43 (37)[d]
4	*b*	**2c**	B	**39** (11)
				44 (32)
				45 (10)
5	*a*	**46**	B	**48** (20)
				49 (29)
6	*a*	**47**	B	**50** (38)[e]
				51 (27)
7	*a*	**52**	B	**53** (12)
8	*b*	**2c**	B/1 equiv of KOAc	**39** (24)
				44 (44)
				54 *E*/*Z* 5:1 (36)
9	*a*	**2c**	B/1 equiv KOAc	**55** *E*/*Z* 9:1 (91)
10	*b*	**2c**	B/0.5 equiv of KOAc	**38** (53)
				43 (10)[f]
11	*a*	**2b**	A	**40** (48)
12	*a*	**2b**	B/1 equiv KOAc	**40** (75)
13	*b*	**2b**	B	**41** (42)
				56 (25)
14	*b*	**2b**	B/1 equiv KOAc	**41** (72)
15	*b*	**2a**	B	**42** (47)
16	*b*	**2a**	B/1 equiv KOAc	**42** (63)

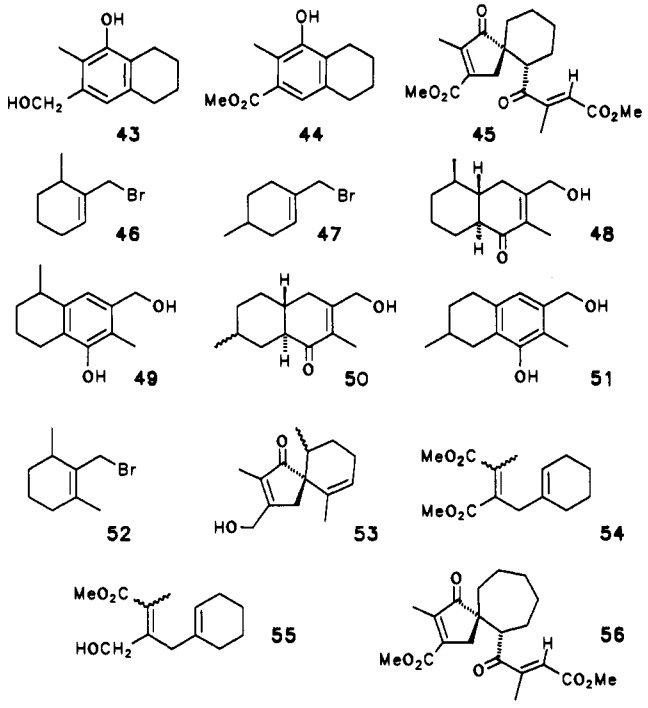
[a] *a*: 2-butyn-1-ol; *b*: methyl 2-butynoate. [b] Method A: The allyl halide was added onto the mixture of nickel carbonyl and alkyne. Method B: The solution of alkyne and the allyl halide was added dropwise onto the solution of the nickel complex. [c] Yields of isolated product. [d] The respective allylic and benzylic hydroxyl groups were acetylated for a better chromatographic separation. [e] 1:1 α-Me/β-Me. [f] Yields were estimated from the ^1H NMR spectrum of the purified reaction mixture.

(27) Whitesell, J. K.; Minton, M. A. *Stereochemical Analysis of Alicyclic Compounds by C-13 NMR Spectroscopy*; Chapman and Hall: London, 1987.

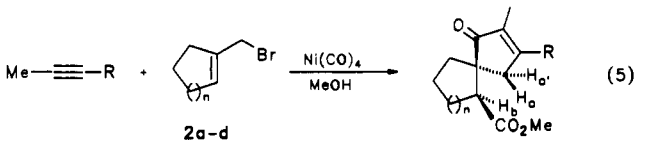
(28) Denmark, S. E.; Habermas, K. L.; Hite, G. A. *Helv. Chem. Acta* **1988**, *71*, 168–194. Denmark, S. E.; Jones, T. K. *Helv. Chim. Acta* **1983**, *66*, 2377–2396. Larock, R. C.; Fried, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 5882–5884. Jones, T. K.; Denmark, S. E. *Helv. Chim. Acta* **1983**, *66*, 2397–2411. Denmark, S. E.; Jones, T. K. *J. Am. Chem. Soc.* **1982**, *104*, 2642–2645. Trost, B. M.; Lynch, J.; Renaut, P.; Steinman, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 284–291 and references 7b and 33.

(29) Tahara, T.; Sakuda, Y.; Kodama, M.; Fukazawa, Y.; Ito, S.; Kawazu, K.; Nakahima, S. *Tetrahedron Lett.* **1980**, *21*, 1861–1862. Herz, W.; Murari, R.; Blount, J. F. *J. Org. Chem.* **1979**, *44*, 1873–1876. Garcia-Granados, A.; Molina, A.; Cabrera, E. *Tetrahedron* **1986**, *42*, 81–87.

Chart I



pentenones according to eq 5. The results obtained are summarized in Table II.



(5)

		R=CH2OH	R=CO2Me
2d	n= 1	36	37
2c	n= 2	38	39
2b	n= 3	40	41
2a	n= 4		42

The reaction of 2-butyn-1-ol with 1-(bromomethyl)cyclopentene (**2d**) was performed in the usual way, by adding the allyl halide to the mixture of the acetylene and $Ni(CO)_4$ in methanol at room temperature. A 50% yield of a pure single product (**36**) was obtained. The structure of this compound was deduced from the general spectroscopic characteristics of the 2-cyclopentenone adducts and the presence of a quaternary carbon atom at δ 55.5 and an AB system of multiplets at δ 2.6–2.9 of H_a and $H_{a'}$ in the corresponding ^{13}C and ^1H NMR spectra, respectively, which strongly supported the presence of a spiro center adjacent to the allylic position in the resulting cyclopentenone. Unfortunately, the overlapping of this AB system with the H_b signal (δ 2.82, t) precluded the performance of NOE experiments on this product to elucidate the relative stereochemistry[30] of the spiro and the adjacent asymmetric centers. However, this assignment was made on the basis of mechanistic considerations and confirmed at a later stage by comparison with the cycloadducts resulting in the six-member series. Analogous results were obtained in the reaction of 1-(bromomethyl)cyclopentene with methyl 2-butynoate (entry 2). The coincidence of the relevant ^{13}C and ^1H NMR signals of compounds **36** and **37** supported the assignment of the same relative geometries.

Next, the reaction of 1-(bromomethyl)cyclohexene (**2c**) with 2-butyn-1-ol was studied (entry 3). In this case, two products were present in the crude reaction mixture that could be separated and characterized only after acetylation of the mixture. The major one **43** was that resulting from carbonylative cycloaddition of the alkyne on both terminal carbons of the allyl moiety and further aromatization. The expected spiro compound **38** was obtained only as the minor component in the product mixture. The change of acetylenic partner led to related compounds **39** and **44** with some acetylene polyinsertion being also detected (formation of **45**, entry 4). To gain further insight on the influence of the steric effects in this process, several reactions of 2-butyn-1-ol with different methyl-substituted 1-(halomethyl)cyclohexenes were tried (entries 5–7). The observed product distributions in the reactions with 4- and 6-methyl-substituted derivatives **46** and **47** suggested that these substitutions were detrimental for the production of spiro compounds, since only dehydrodecalones **48** and **50** (and the corresponding tetralins **49** and **51**) were formed. The trans ring junction in compounds **48** and **50** was established from the ^{13}C NMR chemical shfits for both bridgehead carbon atoms.[27] While dehydrodecalone **50** proved to be a 1:1 mixture of diastereoisomers, compound **48** appeared to be one single isomer. Therefore, substitution at the adjacent position of the allyl group seems to introduce complete stereoselection in the process. When both 2 and 6 positions are substituted as in cyclohexenyl halide **52**, the reaction proceeded very sluggishly but spiro compound **53** was obtained, in 12% yield, as the only isolable product.

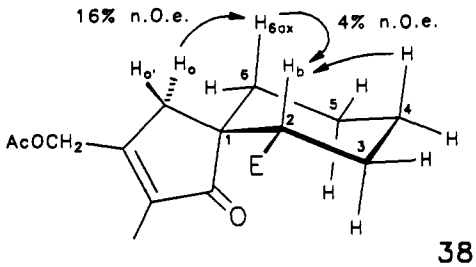
A slight improvement in the yield of spiro cycloadduct **39** was observed after addition of KOAc (in equimolar amount with respect to **2c**) to the reaction mixture (entry 8). Unfortunately, under these conditions, the yield of 1,3-fused cycloadduct **44** was equally increased and, besides, a substantial amount of monocyclic adduct **54** was also formed. Under similar conditions, the reaction of 2-butyn-1-ol resulted in the exclusive formation of the cyclohexenyl acrylate derivative **55** in high yield (entry 9). Nevertheless, by halving the amount of KOAc, the spiro adduct **38** was isolated as the major reaction product together with a minor amount of the aromatic compound **43**, without any evidence of formation of noncyclized carbonylation products (entry 10).

In the seven-member series, although the spiro cycloadduct **40** was produced in a reasonable 48% yield, this could be increased to 75% in the presence of KOAc (entry 12). Again, this additive showed a beneficial role in the reaction with methyl 2-butynoate by suppressing the formation of the side product **56** with a concomitant enhancement in the yield of the spiro adduct **41** (cf. entries 13 and 14).

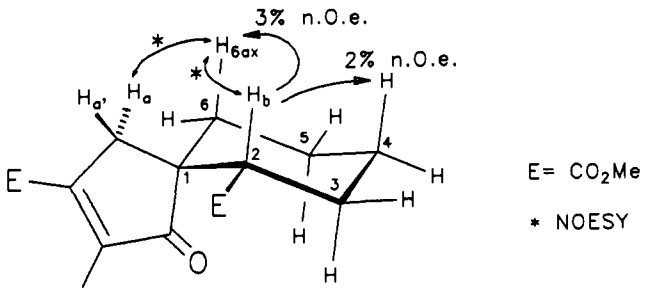
Finally, in the reaction of 1-(bromomethyl)cyclooctene (**2a**) and methyl 2-butynoate, no products from acetylene polyinsertion were detected, nor was there any sign of cycle fusion. Despite that, the yield in spiro adduct **41** was found to benefit from the presence of KOAc (cf. entries 15 and 16).

The stereochemistry of the spiro cyclopentenones obtained was deduced from NMR studies on cyclohexane derivatives **38** and **39** and inferred to be the same as that of the other spiro compounds by comparison of the corresponding NMR data. Whereas ring conformations in six-member alicyclic compounds are well established and extensively studied by ^1H NMR, they are more difficult to analyze in the other cyclic systems. Unfortunately, in the cyclohexane derivatives **38** and **39**, direct NOEDS experiments involving H_b, H_a, and $H_{a'}$ were again not feasible due to the proximity of the corresponding signals, which prevented selective irradiation. However, after assignation of all the signals in the ^1H NMR spectra of compounds **38** and **39** by means of the corresponding COSY experiments, NOE analysis could be performed to establish the relative stereochemistry between the spiro center and the adjacent stereogenic center. NOESY correlation was found in compound **39** between H_b and H_{6ax} and also between this H_{6ax} and H_a, while that from mutual interaction for $H_{a'}$ and H_b was hampered by signal vicinity in the NOESY map. However, in this compound, by irradiating H_b, 3% and 2% NOE signal enhancements were observed for H_{6ax} and H_{4ax}, respectively, pointing out that all these five protons are located at the same side of the cyclohexane ring. This conclusion was corroborated by NOE experiments on adduct **38**: in this case, the chemical

(30) Indirect evidence for structure **36** was obtained from comparison of the ^1H NMR chemical shift for proton H_b with the corresponding ones in triquinanic compounds **14** (Scheme II). Its value, δ 2.82, is almost identical to that found in the major isomer of **14** (δ 2.85) and significantly different from that of its epimer (δ 3.38). The angularly fused triquinanic bridge can be expected not to introduce any significative additional strain between the two spiranic rings.



38



39

shift of H_a allowed its single irradiation that produced a 16% increase in the signal corresponding to H_{6ax}. Conversely, simultaneous irradiation of H_{6ax} and H_{4ax}, since both protons display very close chemicals shifts, caused a 4% NOE effect on H_b.

Discussion

The results described above are in accordance with the proposed mechanism for this process as exemplified in Scheme III for the corresponding six-member allyl halides.

The first step is the formation of a cyclic π-allyl nickel complex, which, after insertion of the alkyne, would give a vinyl nickel intermediate. This intermediate would suffer a fast CO insertion giving an acyl nickel complex that is ready for stereoselective cyclopentenone ring closure in the case of the 3-bromocyclohexene derivative, whereas, in the other case, it can follow two different paths depending on the Ni atom motion when sliding along the coordinated double bond to give either *5-exo-trig* or *6-endo-trig* ring closures. After ring formation, the resulting cycloalkyl–Ni complexes would preferentially give an acyl complex by a second CO insertion (rather than to suffer a β-elimination) before the final attack by methanol that would complete the sequence. Alternatively, competitive insertion of the alkyne on this acyl–Ni intermediate would lead to the observed polyinsertion products.

Some points deserve further comment. In the fused systems, the stereochemistry found in the ring junction in the compounds obtained with the eight-member cyclic allyl halide is trans, whereas, in the corresponding 5, 6, and 7 cases, only the cis fusion was observed. A possible explanation for these results would lie on the nickel intermediates presumably involved. In fact, careful consideration of the three possible starting π-allyl intermediates (syn–syn, syn–anti, and anti–anti)[13] for these rings confirms that only the anti–anti arrangement (as depicted in the cyclohexenyl series in Scheme IV) seems to be strainless. This relative geometry would also apply to the acyl–Ni complex B prior to ring closure. A trans ring fusion would require coordination of the crotonyl nickel moiety with the cyclic double bond at the opposed face, and that would result in an unacceptable strain. A final syn addition in the ring closure step (through transition state D)[31] would lead to cis ring fusion and to the syn relative arrangement between the bridgehead and the adjacent methine hydrogens.

On the other hand, for the cyclooctenyl halide, only the syn–syn coordination mode on the π-allyl nickel intermediate can be dismissed by strain stereochemical considerations. Therefore, although many conformations may be possible, basically two extreme arrangements have to be considered for the resulting acyl–Ni intermediate: one from a symmetrical disposition of the alicyclic ligand (anti–anti) having a transannular interaction between H_a and $H_{a'}$ and another with no such interaction from a dissymmetrical arrangement of the starting π-allyl complex (syn–anti) as depicted in Scheme V.

Obviously, this second choice seems to be the preferred one from all points of view, in agreement with the results obtained (products with trans ring fusion).[32] As in the other cases, the cis geometry of the ester group referred to the nearby carbonyl reflects a syn addition in the closure of the ring. These stereochemical differences in ring fusions of the resulting 5-8 cycloadducts have precedents in the chemical literature, either in metal-promoted cyclizations or in conventional organic processes.[33]

Likewise, in the spiro series, the preference for either *5-exo-trig* or *6-endo-trig* ring closure is conditioned by the steric and conformational restrictions occurring in the cycloalkenyl moiety. For a nearly planar cyclic allyl moiety, such as the cyclopentenyl derivative, the *5-exo-trig* process would lead the metal center to the less substituted olefin carbon atom with concomitant spiro ring closure. However, this picture may not apply to the higher homologues such as those having a six-member ring, since, in this case, due to conformational effects, steric interactions become important and this may explain that a *6-endo-trig* ring closure would be followed to some extent. As depicted in Scheme VI, considering a four-member transition state for both ring closure pathways, if the acryloyl–Ni chain takes an equatorial arrangement, expected to be preferred for cyclohexane systems, a *6-endo-trig* cyclization becomes the most favored closure and, consequently, ring-fused products are formed. Conversely, if the acyl–Ni chain is located in the axial position, spiro adducts would be formed through a *5-exo-trig* process. For larger rings (cycloheptane and cyclooctane derivatives), the conformational mobility increases, the system becomes less rigid, and coordinating modes of the acyl metal intermediate are allowed that may lead to the corresponding spiro systems. In all cases, the spiro products display the same relative stereochemistry at the stereogenic centers resulting from a syn insertion mode in the ring closure step.

The prevention of further acetylene insertion by the presence of acetate ion in the reaction mixture can be envisioned as resulting from different effects. As a mild base, acetate would probably enhance the nucleophilicity of methanol toward acyl nickel intermediates. As a ligand, acetate might be coordinated in both monohapto or dihapto modes.[34] Consequently, its presence could hamper the necessary coordination of the alkyne to Ni prior to its insertion and facilitate the methanolysis of the acyl–Ni bond. Alternatively, carboxylate anions have been reported to promote the formation of carbalkoxy metal complexes as well as their further reductive elimination to esters in palladium chemistry.[35] Furthermore, acetate might be acting as a nucleophile itself toward the acyl nickel intermediate with the release of a mixed anhydride[36] that could be methanolized to give the corresponding ester.

Conclusions

Ring-fused and spiro cyclopentenones can be efficiently synthesized from easily available compounds by this intermolecular

(31) Arrangement of atoms involved in a four-center planar transition state has been established in related transition metal olefin or acetylene insertion processes: Samsel, E. G.; Norton, J. R. *J. Am. Chem. Soc.* **1984**, *106*, 5505–5512. Thorn, D. L.; Hoffmann, R. *J. Am. Chem. Soc.* **1978**, *100*, 2079–2090. Kawamura-Kuribayashi, H.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1992**, *114*, 2359–2366.

(32) A referee has suggested an alternative explanation for the formation of *trans*-fused products in eight-member ring systems by assuming an equilibration of the possible coordination isomers in the intermediate B (Scheme IV). Whereas the C_5–C_7 rings would not allow a *trans* coordination mode, this would be possible (and might be more favorable) in the C_8 case. Therefore the *anti–anti* intermediate in Scheme V could form the *trans*-fused product if olefin de- and recomplexation is allowed and fast relative to insertion.

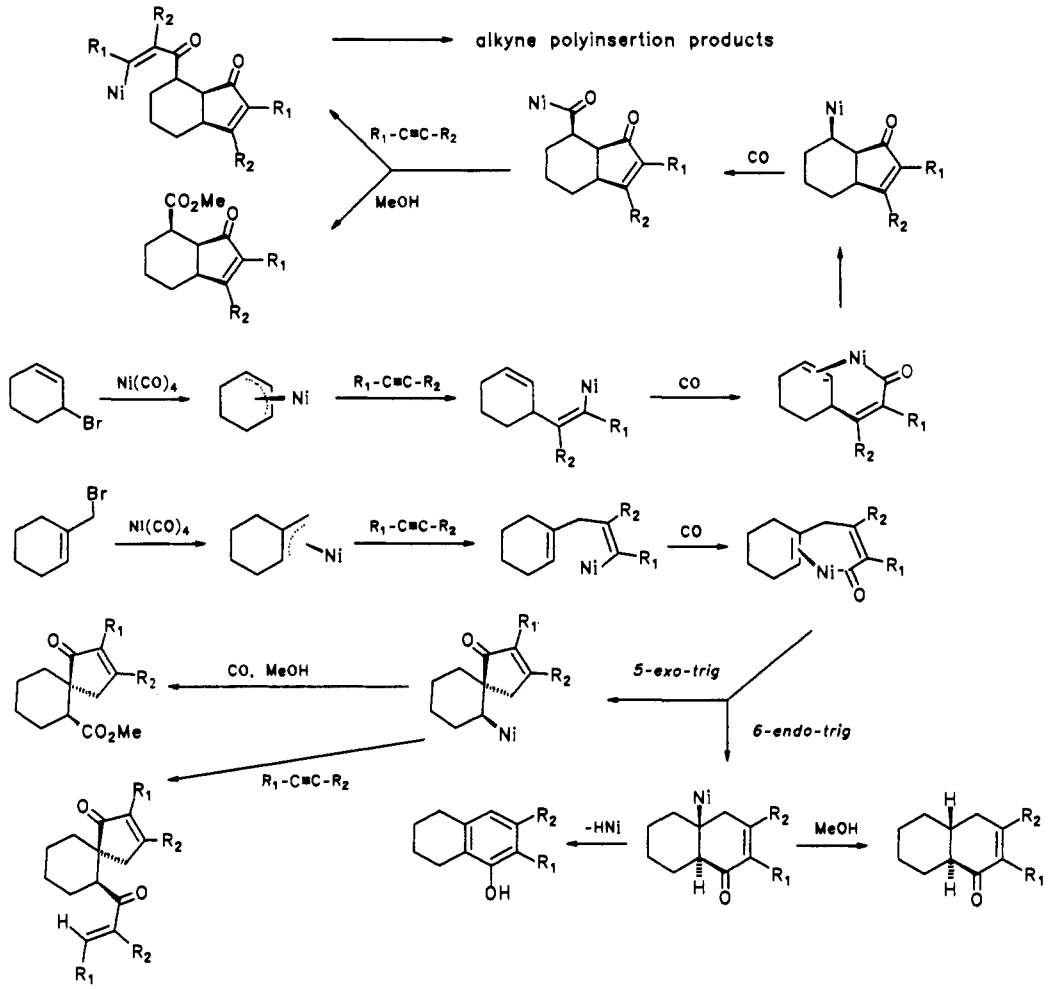
(33) Trost, B. M.; Grese, T. A. *J. Am. Chem. Soc.* **1991**, *113*, 7363–7372 and references therein.

(34) See for example: Crabtree, R. H. *The Organometallic Chemistry of Transition Metals*; J. Wiley: New York, 1988; pp 287–290.

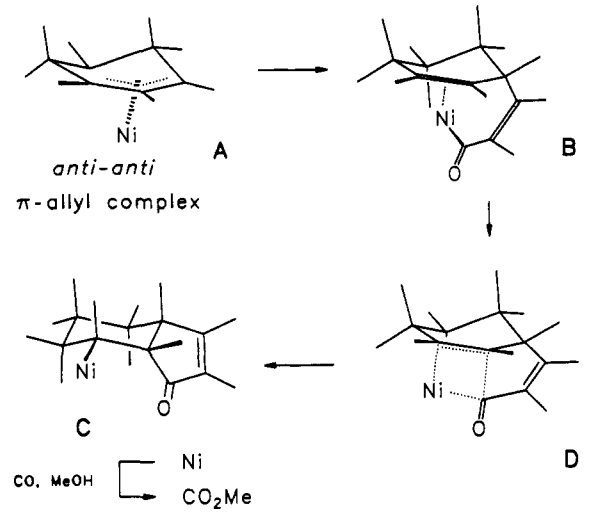
(35) Milstein, D. *Acc. Chem. Res.* **1988**, *21*, 428–434.

(36) Chiusoli, G. P.; Salerno, G.; Foā, M. In *Reactions of Coordinated Ligands*; Braterman, P. S., Ed.; Plenum Press: New York, 1986; pp 460–461.

Scheme III. Proposed Mechanism for Ring-Fused and Spiro Cyclopentenone Formation

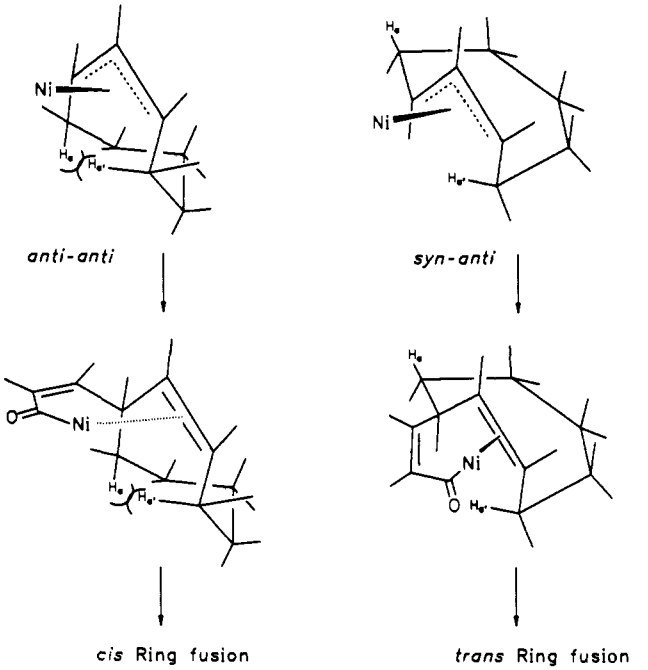


Scheme IV. Stereoselection Origin in the Reactions of Five-, Six-, and Seven-Member 3-Halocycloalkenes, Acetylenes, and $Ni(CO)_4$



carbonylative cycloaddition reaction, in which at least four C–C bonds are built under very mild conditions and remarkable chemo-, regio-, and stereoselective control. The results obtained in all cases agree with the mechanism proposed for this reaction. Detrimental side reactions that may occur can be minimized by simple methodological changes, taking into account this mechanism. In this regard, the beneficial role of the presence of acetate ion in the reaction mixture is discussed. The preparation of [5-5-5] tricyclic compound **14** illustrates the high potential of this cycloaddition in the synthesis of polycyclic natural products.

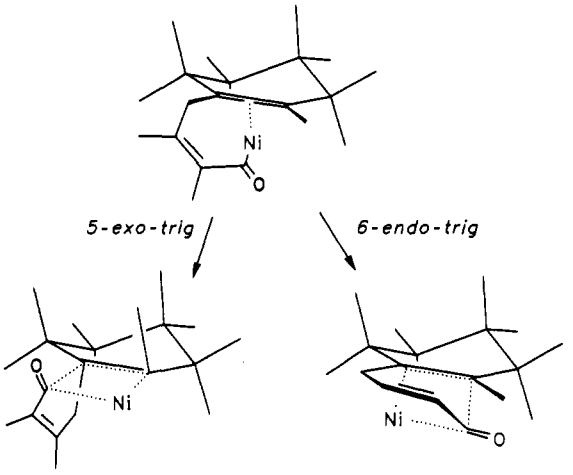
Scheme V. Stereoselection Origin in the Reactions of 3-Bromocyclooctene, Acetylenes, and $Ni(CO)_4$



Experimental Section

Caution: $Ni(CO)_4$ is an extremely harmful chemical, and special precautions have to be taken when using it. All the reactions were carried out inside a glovebox located in a fume cupboard, and any possible

Scheme VI. *5-exo-trig* vs *6-endo-trig* Selectivity in [6-5] Spiro Compounds' Ring Closure



unreacted nickel carbonyl was destroyed by oxidation (see below). IR spectra were recorded with a Perkin-Elmer 399B Spectrometer. ^{1}H NMR and ^{13}C NMR were recorded with WP-80-SY Bruker and Unity 300 Varian machines. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from tetramethylsilane, or in ppm relative to the singlet at 7.26 ppm of chloroform-d_1. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multipleet; b, broad. Coupling constants are reported in hertz (Hz). ^{13}C NMR are reported in ppm relative to the center line of a triplet at 77.0 ppm of chloroform-d_1. Routine ^{13}C NMR spectra were fully broad-band decoupled. Elemental analyses were performed with a Carlo Erba apparatus (1107 and 1500 Models). Mass spectra were taken with a VG-updated AEI MS-902 instrument. GC analyses were performed with a Carlo Erba 4130 instrument, fitted with a 25-m × 0.25-mm capillary column, type SE-54, and a Shimadzu Chromatopac C-R1B recorder and flame ionization detector. TLC were run on Merck 60 F_{254} silica gel plates, with ethyl acetate/hexane mixtures as eluent. Flash chromatography was performed on 230–400-mesh Merck 60 silica gel. $Ni(CO)_4$ was supplied by Merck or Strem. Acetylenes were furnished by Aldrich and Farchan and used as received.

Synthesis of Cycloalkenyl Halides. 3-Bromocycloalkenes **1a–d** were obtained by allylic halogenation of the corresponding cycloalkenes with *N*-bromosuccinimide and benzoyl peroxide according to a described procedure.[37] Similarly, 3-chlorocyclohexene[38] and 3-chlorocycloheptene[39] were synthesized by reaction of the cycloalkenes with Me_3COCl and benzoyl peroxide. Compound **11** (1:1 mixture of cis and trans isomers) was obtained from 1,3-cyclooctadiene in a five-step sequence.[40] Physical constants and spectral data for all these compounds were consistent with those reported in the literature.

5,6-Epoxycyclooctene.[41] Bp: 83–85 °C/25 Torr. Yield: 87%. IR ($CHCl_3$) cm^{-1}: 1660, 1490, 1450, 1220, 930, 860. ^{1}H NMR ($CDCl_3$) δ: 1.9–2.8 (8 H, m, 4 CH_2), 2.9–3.2 (2 H, m, 2 CH-O), 5.4–5.7 (2 H, m, 2 HC=). ^{13}C NMR ($CDCl_3$) δ: 23.1 (t), 27.6 (t), 55.9 (d), 128.3 (d).

4-Cyclooctenol.[42] Bp: 109–110 °C/25 Torr. Yield: 87%. IR ($CHCl_3$) cm^{-1}: 3625–3400, 3020, 1645, 1470, 1225, 1050, 990. ^{1}H NMR ($CDCl_3$) δ: 1.2–2.4 (11 H, m, OH, 5 CH_2), 3.7–3.9 (1 H, m, CH-O), 5.5–5.8 (2 H, m, 2 HC=). ^{13}C NMR ($CDCl_3$) δ: 22.4 (t), 24.5 (t), 25.2 (t), 35.9 (t), 36.9 (t), 71.9 (d), 128.8 (d), 129.6 (d).

2-Bromo-9-oxabicyclo[4.2.1]nonane.[43] Bp: 65–66 °C/0.7 Torr. Yield: 90%. IR ($CHCl_3$) cm^{-1}: 1470, 1450, 1440, 1100, 1060, 1030, 980. ^{1}H NMR ($CDCl_3$) δ: 1.2–1.4 (1 H, m, CH), 1.5–1.7 (3 H, m, 3 CH), 1.75–1.9 (1 H, m, CH), 1.95–2.3 (5 H, m, CH, 2 CH_2), 4.15 (1 H, dt, J = 4.8, 11.1 Hz, CHBr), 4.4–4.6 (2 H, m, 2 CH-O). ^{13}C NMR ($CDCl_3$) δ: 22.8 (t), 24.3 (t), 34.6 (t), 34.9 (t), 35.3 (t), 54.2 (d), 76.5 (d), 81.9 (d).

9-Oxabicyclo[4.2.1]non-2-ene.[44] Bp: 75–77 °C/30 Torr. Yield: 87%. IR ($CHCl_3$) cm^{-1}: 3005, 1475, 1450, 1055, 1030, 905, 860, 690. ^{1}H NMR ($CDCl_3$) δ: 1.4–2.5 (8 H, m, 4 CH_2), 4.4–4.7 (2 H, m, 2 CH-O), 5.5–6.0 (2 H, m, 2 HC=). ^{13}C NMR ($CDCl_3$) δ: 24.0 (t), 28.5 (t), 32.7 (t), 35.4 (t), 76.6 (d), 77.1 (d), 129.9 (d), 135.2 (d).

6-Acetoxy-3-bromocyclooctene[45] **(11).** Obtained as a mixture with 3-acetoxy-5-bromocyclooctene. Bp: 90–92 °C/0.5 Torr. Yield: 73%. GC (isothermal 100 °C): 8.43 min (46%), 11.25 min (46%). IR (CCl_4, mixture of isomers) cm^{-1}: 1740, 1650, 1240, 1060, 1030, 900, 695. ^{1}H NMR ($CDCl_3$, mixture of both isomers) δ: 1.4–1.9 (8 H, m, 2 CH_2), 2.0 (3 H, s, Me), 2.05 (3 H, s, Me), 2.1–2.5 (8 H, m, 2 CH_2), 3.9–4.2 (2 H, m, CHBr), 4.4–4.6 (2 H, m, CH-O), 5.5–6.1 (4 H, m, 2 HC=). ^{13}C NMR ($CDCl_3$, mixture of isomers) δ: 21.2 (q), 21.3 (q), 29.0 (t), 31.3 (t), 32.2 (t), 33.2 (t), 33.9 (t), 34.1 (t), 35.7 (t), 37.2 (t), 46.3 (d), 48.2 (d), 72.8 (d), 74.6 (d), 128.8 (d), 129.6 (d), 132.3 (d), 134.0 (d), 170.0 (s), 170.1 (s). MS (CI, mixture of both isomers): 204/206 (M^+ – 43, 9), 162/160 (10), 134/132 (1), 125 (13), 107 (100), 79/81 (37), 54/56 (21), 43/41 (35). Anal. Calcd for $C_{10}H_{15}BrO_2$ (mixture of isomers): C, 48.59; H, 6.13. Found: C, 48.24; H, 6.14.

Synthesis of 1-(Halomethyl)cycloalkenes: General Procedure. The corresponding cycloalkenyllithium was prepared in 0.1–0.25-mol scale as described in the literature by reaction of the 1-chlorocycloalkene (prepared from the cycloalkanone by treatment with PCl_5) with lithium in ether.[46] The organolithium solution was transferred (via cannula under Ar) to a dry, three-necked flask equipped with a thermometer and a reflux condenser to separate out unreacted lithium and lithium chloride. Paraformaldehyde (solid, 1.2 equiv with respect to the vinylic chloride) was added in small portions to keep a gentle reflux of the ether, with occasional external warming if necessary (although the reaction of paraformaldehyde with lithium compounds does not start below room temperature, it is moderately exothermic; care should be taken to avoid adding the solid in too large portions). Once the addition was over, the solution was refluxed for 1–1.5 h. The reaction flask was cooled down to −10 °C, and a precooled saturated solution of ammonium chloride (100 mL) was carefully added. After the reaction mixture was warmed to room temperature, both phases were separated and the aqueous one was repeatedly extracted with ether (6 × 20 mL). This organic phase was dried and the solvent evaporated to yield the corresponding allylic alcohol. The crude alcohol was treated with PBr_3 and distilled to render the corresponding allyl halide as described.[47]

The following allyl halides were prepared under the general procedure reported above.

1-(Bromomethyl)cyclopentene (2d). Yield: 76%, with respect to the alcohol (23–25% from cyclopentanone). Bp: 59–60 °C/15 Torr. IR (CCl_4) cm^{-1}: 3026, 2950, 2840, 1640, 1440, 1210, 1035, 910, 600. ^{1}H NMR ($CDCl_3$) δ: 1.7–2.6 (6 H, m, 3 CH_2), 4.0–4.1 (2 H, b s, CH_2Br), 5.7–5.9 (1 H, b s, HC=). ^{13}C NMR ($CDCl_3$) δ: 23.3 (t), 31.3 (t), 32.7 (t), 33.1 (t), 130.6 (d), 140.3 (s).

1-(Bromomethyl)cyclohexene (2c). Yield: 83%, with respect to the

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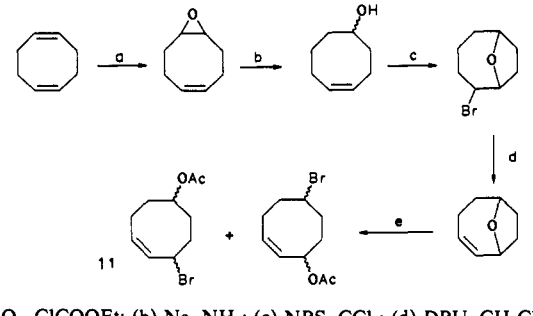
(40) The five-step sequence for formation of compound **11** is shown below.



(a) H_2O_2, ClCOOEt; (b) Na, NH_3; (c) NBS, CCl_4; (d) DBU, CH_2Cl_2; (e) $MgBr_2$, Ac_2O, Et_2O. Formation of **11** from its precursor afforded also 3-acetoxy-6-bromocyclooctene (also as a 1:1 mixture of *cis* and *trans* isomers) in a 1:1 ratio. Although several other methods were tried for the transformation depicted in step e, formation of **11** was always accompanied by equimolar amounts of allylic acetate isomers. All attempts aimed to separate allylic acetates from allylic bromides were also unsuccessful.

(41) Bach, R. D.; Klein, M. N.; Ryntz, R. A.; Holubka, J. W. *J. Org. Chem.* **1979**, *44*, 2569–2571.

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(45) Goldsmith, D. J.; Kennedy, E.; Campbell, R. G. *J. Org. Chem.* **1975**, *40*, 3571–3574.

(46) Brandsma, L.; Verkruijsse, H. D. *Preparative Polar Organometallic Chemistry 1*; Springer Verlag: Berlin, Heidelberg, 1987; pp 50–51.

(47) Hwa, J. C. H.; Sims, H. *Organic Synthesis*; J. Wiley: New York, 1973; Collect. Vol. V, pp 609.

alcohol (33% from cyclohexanone). Bp: 70–72 °C/20 Torr. IR (CCl_4) cm^{-1}: 1660, 1430, 1205, 955, 600. ^1H NMR ($CDCl_3$) δ: 1.4–2.3 (8 H, m, 4 CH_2), 3.9 (2 H, b s, CH_2Br), 5.9 (1 H, b s, HC=). ^{13}C NMR ($CDCl_3$) δ: 21.7 (t), 22.2 (t), 25.3 (t), 26.2 (t), 39.5 (t), 127.8 (d), 134.5 (s).

1-(Bromomethyl)cycloheptene (2b). Yield: 77%, with respect to the alcohol (27% from cycloheptanone). Bp: 30–32 °C/0.1 Torr. IR (CCl_4) cm^{-1}: 1650, 1440, 1230, 1200, 950, 905, 855, 625. ^1H NMR ($CDCl_3$) δ: 1.4–1.9 (6 H, m, 3 CH_2), 2.0–2.4 (4 H, m, 2 CH_2), 3.95 (2 H, s, CH_2Br), 6.0 (1 H, t, J = 13.0, 7.0 Hz, HC=). ^{13}C NMR ($CDCl_3$) δ: 26.7 (t), 26.8 (t), 28.6 (t), 31.7 (t), 32.3 (t), 42.0 (t), 132.7 (d), 140.9 (s).

1-(Bromomethyl)cyclooctene (2a). Yield: 70% with respect to the alcohol (9% from cyclooctanone). Bp: 66–68 °C/2.5 Torr. IR (CCl_4) cm^{-1}: 1650, 1435, 1100, 990. ^1H NMR ($CDCl_3$) δ: 1.0–1.9 (8 H, m, 4 CH_2), 2.4 (4 H, m, 2 CH_2), 3.85 (1 H, d, J = 1.1 Hz, CHBr), 3.95 (1 H, d, J = 1.1 Hz, CHBr), 5.8 (1 H, tt, J = 8.0, 2.3 Hz, HC=). ^{13}C NMR ($CDCl_3$) δ: 24.1 (t), 26.2 (t), 26.4 (t), 27.7 (t), 28.9 (t), 29.3 (t), 38.4 (t), 131.3 (d), 137.3 (s).

1-(Bromomethyl)-4-methylcyclohexene (47). Yield: 89%, with respect to the alcohol (45% from 4-methylcyclohexanone). Bp: 50–52 °C/2.5 Torr. IR (CCl_4) cm^{-1}: 1655, 1430, 1375, 1205, 950, 900, 665, 600. ^1H NMR ($CDCl_3$) δ: 0.85 (3 H, d, J = 5 Hz, Me), 1.2–2.3 (7 H, m, CH, 3 CH_2), 3.95 (2 H, s, CH_2Br), 5.8–5.9 (1 H, b s, HC=). ^{13}C NMR ($CDCl_3$) δ: 21.4 (q), 26.2 (t), 27.8 (d), 30.5 (t), 33.8 (t), 39.2 (t), 127.5 (d), 134.2 (s).

1-(Bromomethyl)-6-methylcyclohexene (46). Prepared from (6-methylcyclohex-1-enyl)methanol with PBr_3. The alcohol was synthesized by reacting (6-methylcyclohex-1-enyl)lithium (obtained from 2-methylcyclohexanone *p*-(tolylsulfonyl)hydrazone[48]) with paraformaldehyde in refluxing ether. Yield: 72%, with respect to the alcohol (34% from the ketone). Bp: 28–30 °C/0.15 Torr. IR (CCl_4) cm^{-1}: 1655, 1460, 1450, 1435, 1210, 905, 645, 635, 625. ^1H NMR ($CDCl_3$) δ: 1.05 (3 H, d, J = 8.0 Hz, Me), 1.3–2.2 (6 H, m, 3 CH_2), 2.5 (1 H, q, J = 8.0 Hz, CH), 4.16 (2 H, dd, J = 11.4, 0.6 Hz, CH_2Br), 5.84 (1 H, t, J = 3.9 Hz, HC=). ^{13}C NMR ($CDCl_3$) δ: 19.0 (q), 19.6 (t), 26.0 (t), 29.4 (d), 31.1 (t), 37.8 (t), 128.7 (d), 138.8 (s).

1-(Bromomethyl)-2,6-dimethylcyclohexene (52). Prepared from (2,6-dimethylcyclohex-1-enyl)methanol and PBr_3. The allylic alcohol was prepared from the *p*-(tolylsulfonyl)hydrazone of the 2,6-dimethylcyclohexanone as described in the literature.[49] Yield: 68% (18% from the ketone). Bp: 64–66 °C/2.0 Torr. IR (CCl_4) cm^{-1}: 1650, 1440, 1380, 1250. ^1H NMR ($CDCl_3$) δ: 1.06 (3 H, d, J = 6.3 Hz, Me), 1.2–2.0 (6 H, m, 3 CH_2), 1.85 (3 H, s, Me), 3.14 (2 H, dd, J = 11.4, 3.6 Hz, CH_2Br). ^{13}C NMR ($CDCl_3$) δ: 20.0 (q), 22.7 (t), 32.2 (t), 33.5 (q), 35.1 (t), 35.4 (d), 44.1 (t), 122.4 (s), 131.5 (s).

Cyclization Reactions. Method A. General Procedure. To 0.6 mL (4.6 mmol) of $Ni(CO)_4$ and 2.3 mmol of the acetylene in 15 mL of methanol was added dropwise a solution of 4.6 mmol of the allyl halide in 2 mL of methanol while the mixture was magnetically stirred for 6–12 h in a thermostatic flask under an inert atmosphere closed by a Hg valve. After this time, the solution was heated at 40 °C for 1 h while an inert gas (Ar) was passed through the flask to remove most of the solvent and any unreacted nickel carbonyl, which was condensed and oxidized in a cold trap containing iodine connected at the outlet of the reaction flask. The remaining solvent was evaporated under vacuum, and the residue treated with 40 mL of water and extracted three to four times with dichloromethane (10 mL each portion) until there was evidence of no further product extraction. The organic phase was dried over $MgSO_4$, the solvent evaporated, and the residue passed through a flash chromatography column using hexane/EtOAc as eluent.

Method B. The mixture of allyl halide and the acetylene was added onto the suspension of $Ni(CO)_4$ in methanol. When KOAc was used, an equimolar amount (1 equiv) with respect to allyl halide (unless otherwise stated) was dissolved in methanol in the flask before the introduction of $Ni(CO)_4$. In this case, a solid precipitate appeared shortly after the addition of allyl halide and the alkyne mixture and reaction times were shortened to 3–6 h. Workup and isolation were performed as in method A.

9-(Hydroxymethyl)-2-(methoxycarbonyl)-10-methylbicyclo[6.3.0]undec-9-en-11-one (3). Method A yield: 51%. R_f: 0.24 (hexane/EtOAc 1:1). IR (CCl_4) cm^{-1}: 3500, 2925, 1740, 1705, 1650, 1230. ^1H NMR ($CDCl_3$) δ: 1.5–1.9 (11 H, m, OH, CH_2), 1.75 (3 H, b s, Me), 2.3 (1 H, H_b; dd, J_{ab} = 3.0, J_{bc} = 5.0 Hz, CH), 3.1–3.4 (2 H, H_a, H_c; m, CH), 3.55 (3 H, s, OMe), 4.55 (2 H, AB sys, m, δ_A = 4.67, δ_B = 4.43, J_{AB} = 13 Hz, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 7.7 (q), 24.0 (t), 24.6 (t), 25.0 (t), 26.2 (t), 26.5 (t), 32.3 (d), 42.1 (d), 43.6 (d), 51.0 (q), 58.0 (t), 134.4 (s), 171.8 (s), 174.4 (s), 209.7 (s). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.62; H, 8.34. Found: C, 67.64; H, 8.34.

2,9-Bis(methoxycarbonyl)-10-methylbicyclo[6.3.0]undec-9-en-11-one (4). Method B yield: 81%. Method A yield: 68%. R_f: 0.36 (hexane/EtOAc 4:1). Mp: 76–77 °C (hexane/ether). IR ($CHCl_3$) cm^{-1}: 1720, 1710, 1440, 1230, 1160. ^1H NMR ($CDCl_3$) δ: 1.0–1.1 (1 H, m, CH_2), 1.4–1.6 (4 H, m, CH_2), 1.7–1.9 (4 H, m, CH_2), 1.95 (3 H, d, J = 2 Hz, Me), 2.0–2.25 (1 H, m, CH_2), 2.37 (1 H, H_b; dd, J_{ab} = 3.6, J_{bc} = 4.5 Hz, CH), 3.2–3.25 (1 H, H_a; m, CH), 3.3 (1 H, H_c; ddd, J = 3.9, 8.4, 12.3 Hz, CH), 3.55 (3 H, s, OMe), 3.85 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 9.4 (q), 24.1 (t), 24.4 (t), 26.2 (t), 26.5 (t), 32.9 (t), 41.9 (d), 44.3 (d), 51.0 (q), 51.3 (q), 51.5 (d), 144.0 (s), 157.3 (s), 165.8 (s), 173.7 (s), 209.2 (s). MS (EI): 294 (M^+, 54), 262 (100), 234 (52), 202 (57), 175 (81), 147 (35), 105 (30), 91 (40), 77 (28), 79 (29), 59 (34). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.28; H, 7.55. Found: C, 65.31; H, 7.57.

9-Acetyl-10-ethyl-2-(methoxycarbonyl)bicyclo[6.3.0]undec-9-en-11-one (5). Method B yield: 70%. R_f: 0.20 (hexane/EtOAc 4:1). IR (CCl_4) cm^{-1}: 1770, 1735, 1710, 1200, 910. ^1H NMR ($CDCl_3$) δ: 1.0 (3 H, t, J = 7.5 Hz, Me), 1.4–2.1 (10 H, m, CH_2), 2.3 (2 H, b q, J = 7.5 Hz, CH_2), 2.4 (3 H, s, MeCO), 3.2–3.3 (3 H, H_a, H_b, H_c; m, CH), 3.55 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 13.1 (q), 17.3 (t) 24.5 (q), 24.8 (t), 26.4 (t), 27.0 (t), 30.2 (t), 33.3 (t), 42.6 (d), 44.4 (d), 51.3 (q), 51.6 (d), 144.0 (s), 166.5 (s), 174.1 (s), 202.1 (s), 209.2 (s). MS (EI): 292 (M^+, 76), 260 (100), 232 (62), 217 (62), 203 (26), 189 (90), 175 (36), 161 (45), 135 (18), 105 (24), 91 (43), 79 (37), 67 (36), 55 (50). Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.82; H, 8.29. Found: C, 69.84; H, 8.40.

2-(Methoxycarbonyl)-10-(methoxymethyl)bicyclo[6.3.0]undec-9-en-11-one (6). Method B yield: 77%. R_f: 0.32 (hexane/EtOAc 7:2). IR ($CHCl_3$) cm^{-1}: 3010, 2960, 1725, 1700, 1640, 1450, 1230, 1200, 1110, 1050, 990. ^1H NMR ($CDCl_3$) δ: 0.9–2.2 (10 H, m, CH_2), 2.4 (1 H, H_b; dd, J_{ab} = 3.0, J_{bc} = 5.0 Hz, CH), 2.9–3.4 (2 H, H_a, H_c; m, 2 CH), 3.4 (3 H, s, OMe), 3.6 (3 H, s, OMe), 4.12 (2 H, dd, J = 1.8, 2.2 Hz, CH_2O), 7.36 (1 H, m, HC=). ^{13}C NMR ($CDCl_3$) δ: 24.7 (t), 24.9 (t), 26.5 (t), 27.0 (t), 34.5 (t), 42.6 (d), 43.7 (d), 51.5 (q), 52.9 (d), 58.7 (q), 66.2 (t), 140.7 (s), 162.5 (s), 174.4 (s), 208.7 (s). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.32. Found: C, 67.86; H, 8.47.

2-(Methoxycarbonyl)-9-(methoxymethyl)-10-(trimethylsilyl)bicyclo[6.3.0]undec-9-en-11-one (7). Method B yield: 17%. R_f: 0.36 (hexane/EtOAc 4:1), mixture of two diastereoisomers 1:1 by capillary GC. IR ($CHCl_3$, mixture) cm^{-1}: 1725, 1685, 1590, 1250, 845. ^1H NMR ($CDCl_3$, mixture of both diastereoisomers) δ: 0.2 (9 H, s, $SiMe_3$), 0.22 (9 H, s, $SiMe_3$), 0.8–2.2 (10 H, m, CH_2), 2.78 (1 H, H_b; dd, J_{ab} = 3.8, J_{bc} = 4.7 Hz, CH), 3.0–3.2 (2 H, H_a, H_c; m, CH), 3.35 (3 H, s, OMe), 3.4 (3 H, s, OMe), 3.5 (3 H, s, OMe), 3.55 (3 H, s, OMe), 4.35 (2 H, b s, CH_2O), 4.4 (2 H, b s, CH_2O). ^{13}C NMR ($CDCl_3$, mixture of both diastereoisomers) δ: −0.36 (q), −0.45 (q), 24.6 (t), 24.8 (t), 24.9 (t), 25.1 (t), 26.6 (t), 27.1 (t), 27.8 (t), 31.1 (t), 32.8 (t), 44.0 (d), 45.3 (d), 45.6 (d), 47.7 (d), 49.2 (d), 51.2 (q), 51.4 (q), 52.5 (q), 58.4 (q), 58.9 (q), 69.4 (t), 70.4 (t), 140.0 (s), 140.6 (s), 174.3 (s), 174.4 (s), 182.5 (s), 185.3 (s), 213.3 (s), 214.0 (s). Anal. Calcd for $C_{18}H_{30}O_4Si$ (mixture of both diastereoisomers): C, 63.87; H, 8.93. Found: C, 63.96; H, 8.93.

2-(Methoxycarbonyl)-10-(trimethylsilyl)bicyclo[6.3.0]undec-9-en-11-one (8). Method B yield: 57%. R_f: 0.22 (hexane/EtOAc 8:1). IR ($CHCl_3$) cm^{-1}: 3030, 2960, 2920, 1730, 1695, 1580, 1270, 1250, 1220, 850. ^1H NMR ($CDCl_3$) δ: 0.18 (9 H, s, $SiMe_3$), 1.1–2.0 (10 H, m, CH_2); 2.25 (1 H, H_b; dd, J_{ab} = 3.5, J_{bc} = 5.3 Hz, CH), 2.9–3.4 (2 H, H_a, H_b; m, 2 CH), 3.55 (3 H, s, OMe), 7.54 (1 H, d, J = 1 Hz, HC=). ^{13}C NMR ($CDCl_3$) δ: −1.9 (q), 25.0 (t), 26.6 (t), 27.6 (t), 34.5 (t), 43.8 (d), 45.8 (d), 51.3 (q), 53.2 (d), 144.2 (s), 174.5 (s), 174.9 (s), 213.7 (s). Anal. Calcd for $C_{16}H_{26}O_3Si$: C, 65.25; H, 8.90. Found: C, 65.22; H, 8.93.

2-(Methoxycarbonyl)-10-phenylbicyclo[6.3.0]undec-9-en-11-one (9). Method B yield: 34%. R_f: 0.13 (hexane/EtOAc 10:1). IR ($CDCl_3$) cm^{-1}: 1725, 1705, 1610, 1230, 1175, 910. ^1H NMR ($CDCl_3$) δ: 0.8–1.0 (2 H, m, CH_2), 1.2–2.2 (8 H, m, CH_2), 2.48 (1 H, H_b; t, J_{ab} = J_{bc} = 4.2 Hz, CH), 3.11 (1 H, H_a; dq, J = 3.0, 12.6 Hz, CH), 3.35 (1 H, H_c; ddd, J = 4.5, 9.0, 13.5 Hz, CH), 3.6 (3 H, s, OMe), 7.5 (5 H, m, Ph), 7.63 (1 H, d, J = 2.4 Hz, HC=). ^{13}C NMR ($CDCl_3$) δ: 24.7 (t), 25.1 (t), 26.5 (t), 27.1 (t), 34.7 (t), 41.9 (d), 44.1 (d), 51.6 (q), 53.7 (d), 127.1 (d), 161.8 (s), 174.6 (s), 208.1 (s). Anal. Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.73; H, 7.50.

11-Oxo-10-phenylbicyclo[6.3.0]undec-9-en-2-yl Styryl Ketone (10). Method B yield: 57%. R_f: 0.11 (hexane/EtOAc 10:1). IR ($CHCl_3$) cm^{-1}: 3020, 1720, 1695, 1620, 910. ^1H NMR ($CDCl_3$) δ: 0.8–1.0 (2 H, m, CH_2), 1.15–2.3 (8 H, m, CH_2), 2.62 (1 H, H_b; dd, J_{ab} = 3.0, J_{bc} = 5.7 Hz, CH), 3.34 (1 H, H_a; dq, J = 3.0, 12.6 Hz, CH), 3.67 (1 H, H_c; dt, J = 5.7, 7.2 Hz, CH), 6.85 (1 H, d, J = 15.9 Hz, HC=), 7.2–7.8 (11 H, m, 2 Ph, HC=), 7.7 (1 H, d, J = 8.2 Hz, HC=). ^{13}C NMR ($CDCl_3$) δ: 24.1 (t), 25.7 (t), 26.0 (t), 26.2 (t), 35.0 (t), 42.0 (d), 49.6

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(d), 54.5 (d), 124.9 (d), 127.1 (d), 127.2 (d), 128.2 (d), 128.3 (d), 128.4 (d), 128.9 (d), 130.4 (d), 141.2 (s), 143.0 (d), 161.8 (d), 161.9 (s), 201.9 (s), 208.9 (s). Anal. Calcd for $C_{26}H_{26}O_2$: C, 84.29; H, 7.07. Found: C, 84.30; H, 7.06.

5-Acetoxy-2,9-bis(methoxycarbonyl)-10-methylbicyclo[6.3.0]undec-9-en-11-one (12). Method B yield: 55%. R_f: 0.20 (hexane/EtOAc 3:1, mixture of two diastereoisomers in a 1.5:1 ratio as detected by ^{1}H NMR). IR (CCl_4, mixture of both stereoisomers) cm^{-1}: 1740, 1720, 1645, 1435, 1225, 1020, 900. ^{1}H NMR ($CDCl_3$, major stereoisomer) δ: 1.1–1.4 (2 H, m, CH_2), 1.5–1.7 (4 H, m, CH_2), 1.8–2.0 (2 H, m, CH_2), 2.02 (3 H, s, MeCO), 2.03 (3 H, d, J = 1.8 Hz, Me), 2.3 (1 H, t, J = 3.6 Hz, CH), 3.2–3.3 (1 H, m, CH), 3.35 (1 H, m, CH), 3.5 (1 H, m, CH), 3.59 (3 H, s, OMe), 3.85 (3 H, s, OMe). ^{1}H NMR ($CDCl_3$, minor stereoisomer) δ: 1.1–1.4 (2 H, m, CH_2), 1.5–1.7 (4 H, m, CH_2), 1.8–2.0 (2 H, m, CH_2), 2.01 (3 H, d, J = 2.1 Hz, Me), 2.02 (3 H, s, MeCO), 2.2 (1 H, t, J = 3.6 Hz, CH), 3.2–3.3 (1 H, m, CH), 3.35 (1 H, m, CH), 3.5 (1 H, m, CH), 3.58 (3 H, s, OMe), 3.87 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$, major stereoisomer) δ: 9.6 (q), 21.0 (q), 22.2 (t), 26.4 (t), 29.2 (t), 30.7 (t), 40.6 (d), 43.5 (d), 50.0 (d), 51.6 (q), 51.7 (q), 72.4 (d), 144.4 (s), 156.6 (s), 165.5 (s), 169.7 (s), 173.1 (s), 208.1 (s). ^{13}C NMR ($CDCl_3$, minor stereoisomer) δ: 13.9 (q), 20.7 (q), 21.0 (t), 25.2 (t), 28.2 (t), 29.3 (t), 41.8 (d), 44.0 (d), 51.1 (d), 51.6 (q), 51.7 (q), 74.0 (d), 144.5 (s), 156.5 (s), 165.6 (s), 169.2 (s), 173.3 (s), 208.3 (s). MS (EI, mixture of both stereoisomers): 352 (M^+, 21), 321 (35), 292 (23), 278 (69), 260 (100), 246 (24), 232 (92), 218 (28), 201 (60), 189 (25), 173 (64), 166 (48), 145 (47), 117 (18), 105 (30), 91 (47), 77 (34), 59 (33). Anal. Calcd for $C_{18}H_{24}O_7$ (mixture of both stereoisomers): C, 61.34; H, 6.88. Found: C, 61.19; H, 6.90.

2,9-Bis(methoxycarbonyl)-10-methyl-5-(mesyloxy)bicyclo[6.3.0]undec-9-en-11-one (13). 0.33 g (9.4×10^{-4} mol) of **12** (mixture of stereoisomers) in 20 mL of methanol was stirred with 40 mg (9.4×10^{-4} mol) of KOH at 50 °C. The reaction was complete in 30 min. Column chromatography of the crude (silica, hexane/EtOAc 1:1) afforded 0.28 g of the desired alcohol 2,9-bis(methoxycarbonyl)-5-hydroxy-10-methylbicyclo[6.3.0]undec-9-en-11-one. Yield: 98%. R_f: 0.1 (hexane/EtOAc 1:1). IR (CCl_4) cm^{-1}: 3650, 3500, 1720, 1435, 1220. ^{1}H NMR ($CDCl_3$) δ: 1.1–1.4 (2 H, m, CH_2), 1.6–2.0 (4 H, m, CH_2), 2.01 (3 H, d, J = 2.1 Hz, Me), 2.1–2.3 (3 H, m, OH, CH_2), 2.31 (1 H, t, J = 3.6 Hz, CH), 3.1–3.3 (2 H, m, 2 CH), 3.5 (3 H, s, OMe), 3.85 (3 H, s, OMe), 4.0 (1 H, m, CH). ^{13}C NMR ($CDCl_3$) δ: 9.9 (q), 21.7 (t), 26.6 (t), 31.8 (t), 32.4 (t), 40.6 (d), 43.9 (d), 50.3 (d), 51.91 (q), 51.94 (q), 69.9 (d), 144.6 (s), 157.0 (s), 166.0 (s), 173.6 (s), 208.8 (s). MS (EI): 310 (M^+, 16), 308 (15), 278 (100), 260 (19), 246 (62), 232 (30), 218 (33), 173 (36), 166 (33), 145 (34), 105 (36), 91 (55), 77 (45), 55 (62). Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.91; H, 7.16. Found: C, 62.03; H, 7.20. This alcohol (0.1 g, 3.2×10^{-4} mol) in 2 mL of dichloromethane and 67 μL (4.8×10^{-4} mol) of triethylamine was cooled to 0 °C; to this solution was added 28 μL (3.5×10^{-4} mol) of mesyl chloride, and after 15 min at 0 °C and 30 min at room temperature, the reaction mixture was poured onto ice. Usual workup and flash chromatography of the crude (hexane/EtOAc 2:1) afforded 91 mg of **13** as a mixture of stereoisomers in a 2:1 ratio. Yield: 76%. R_f: 0.1 (hexane/EtOAc 2:1, mixture of two stereoisomers in a 2:1 ratio as detected by ^{1}H NMR). IR ($CHCl_3$) cm^{-1}: 3030, 1720, 1435, 1355, 1330, 1210, 1170, 900. ^{1}H NMR ($CDCl_3$, major stereoisomer) δ: 1.0–2.0 (4 H, m, CH_2), 1.96 (3 H, d, J = 1.8 Hz, Me), 2.1–2.2 (4 H, m, CH_2), 2.2 (1 H, t, J = 3.6 Hz, CH), 2.94 (3 H, s, $MeSO_3$), 3.1–3.2 (2 H, m, 2 CH), 3.53 (3 H, s, OMe), 3.71 (1 H, m, CH), 3.79 (3 H, s, OMe). ^{1}H NMR ($CDCl_3$, minor stereoisomer) δ: 1.0–2.0 (4 H, m, CH_2), 1.94 (3 H, d, J = 1.8 Hz, Me), 2.1–2.2 (4 H, m, CH_2), 2.1 (1 H, t, J = 3.6 Hz, CH), 2.96 (3 H, s, $MeSO_3$), 3.1–3.2 (2 H, m, 2 CH), 3.53 (3 H, s, OMe), 3.70 (1 H, m, CH), 3.81 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$, major stereoisomer) δ: 9.8 (q), 20.0 (t), 24.8 (t), 29.9 (t), 31.5 (t), 38.5 (t), 40.5 (d), 43.4 (d), 50.3 (d), 51.89 (q), 51.9 (q), 81.7 (d), 145.0 (s), 156.4 (s), 165.7 (s), 173.1 (s) 207.9 (s). ^{13}C NMR ($CDCl_3$, minor stereoisomer) δ: 9.9 (q), 21.9 (t), 26.2 (t), 30.6 (t), 31.6 (t), 38.7 (q), 41.6 (d), 43.9 (d), 51.1 (d), 51.9 (q), 52.0 (q), 82.1 (d), 145.1 (s), 156.5 (s), 165.8 (s), 173.1 (s), 208.1 (s).

4,11-Bis(methoxycarbonyl)-3-methyltricyclo[6.3.0.0^{1,5}]undec-3-en-2-one (14). A sample of 75 mg (1.9×10^{-4} mol) of **13** was dissolved in 5 mL of anhydrous THF. To this solution was added 21 mg (3.8×10^{-4} mol) of sodium methoxide, and the reaction mixture was refluxed gently for 7 h. After evaporation of the solvent, conventional chromatography of the crude (hexane/EtOAc 2:1) afforded a 71% yield of **14** as a mixture of two diastereoisomers in a 4:1 ratio. R_f: 0.7 (hexane/EtOAc 2:1). IR (CCl_4, mixture of stereoisomers) cm^{-1}: 1743, 1730, 1718, 1435, 1220. ^{1}H NMR ($CDCl_3$, major stereoisomer) δ: 1.1–1.95 (8 H, m, CH_2), 1.9 (3 H, d, J = 2.1 Hz, Me), 2.4–2.5 (1 H, m, CH), 3.17 (1 H, ddq, J = 2.1, 4.2, 8.7 Hz, CH), 3.37 (1 H, dd, J = 6.6, 11.7 Hz, CH), 3.5 (3 H, s, OMe), 3.8 (3 H, s, OMe). ^{1}H NMR ($CDCl_3$, minor stereoisomer) δ: 1.1–1.95 (8 H, m, CH_2), 2.0 (3 H, d, J = 2.1 Hz, Me), 2.4–2.5 (1 H, m, CH), 2.85 (1 H, dd, J = 7.8, 9.9 Hz, CH), 3.3 (1 H, ddq, J = 2.1, 4.2, 8.7 Hz, CH), 3.5 (3 H, s, OMe), 3.8 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$, major stereoisomer) δ: 10.2 (q), 29.0 (t), 29.6 (t), 31.2 (t), 31.3 (t), 49.3 (d), 49.5 (d), 51.6 (q), 52.0 (q), 52.4 (d), 67.5 (s), 146.7 (s), 155.0 (s), 165.7 (s), 173.0 (s), 211.7 (s). MS (EI, mixture of stereoisomers): 292 (M^+, 26), 260 (100), 232 (70), 204 (38), 173 (30), 145 (31), 117 (13), 105 (13), 91 (17), 77 (15), 59 (13). Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.73; H, 6.91. Found: C, 65.89; H, 7.09.

4-(Hydroxymethyl)-8-(methoxycarbonyl)-3-methylbicyclo[3.3.0]oct-3-en-2-one (15). Method A yield: 20%. R_f: 0.36 (hexane/EtOAc 4:1). IR ($CHCl_3$) cm^{-1}: 3650, 3500, 1750, 1710, 1655, 1170, 910. ^{1}H NMR ($CDCl_3$) δ: 1.1–1.3 (4 H, m, CH_2), 1.6 (3 H, b s, Me), 1.8 (1 H, m, OH), 2.9 (1 H, H_c; ddd, J = 6.7, 10.0, 13.5 Hz, CH), 3.0 (1 H, H_b; dd, J_{ab} = 6.7, J_{bc} = 10.1 Hz, CH), 3.45 (1 H, H_a; m, CH), 3.75 (3 H, s, OMe), 4.58 (2 H, AB sys, m, δ_A = 4.65, δ_B = 4.51, J_{AB} = 15 Hz, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 8.1 (q), 26.4 (t), 27.6 (t), 44.3 (d), 46.7 (d), 51.4 (q), 51.9 (d), 59.8 (t), 137.5 (s), 170.4 (s), 173.2 (s), 208.6 (s). MS (EI): 224 (M^+, 6), 205 (6), 192 (70), 164 (91), 149 (49), 135 (68), 119 (59), 105 (49), 91 (82), 79 (60), 67 (100). Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.26; H, 7.21. Found: C, 64.36; H, 7.14.

4,8-Bis(methoxycarbonyl)-3-methylbicyclo[3.3.0]oct-3-en-2-one (16). Method A yield: 40%. Method B yield: 30%. R_f: 0.21 (hexane/EtOAc 7:2). IR ($CHCl_3$) cm^{-1}: 1740, 1710, 1440, 1230, 910. ^{1}H NMR ($CDCl_3$) δ: 1.6–1.9 (4 H, m, CH_2), 2.05 (3 H, d, J = 2 Hz, Me), 2.96 (1 H, H_c; ddd, J = 5.7, 9.6, 11.4 Hz, CH), 3.11 (1 H, H_b; dd, J_{ab} = 6.0, J_{bc} = 9.6 Hz, CH), 3.61 (1 H, H_a; m, CH), 3.75 (3 H, s, OMe), 3.85 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 9.4 (q), 26.3 (t), 28.4 (t), 43.6 (d), 46.8 (d), 51.0 (q), 51.1 (q), 51.6 (d), 147.4 (s), 155.1 (s), 165.2 (s), 172.3 (s), 208.5 (s). MS (EI): 252 (M^+, 31) 219 (100), 192 (72), 161 (29), 133 (50), 105 (71), 91 (24), 59 (30). Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.89; H, 6.41. Found: C, 61.35; H, 6.24.

4-Acetyl-3-ethyl-8-(methoxycarbonyl)bicyclo[3.3.0]oct-3-en-2-one (17). Method A yield: 12%. Method B/1 equiv KOAc yield: 8%. R_f: 0.3 (hexane/EtOAc 2:1). IR ($CHCl_3$) cm^{-1}: 1740, 1705, 1660, 1360, 1190. ^{1}H NMR ($CDCl_3$) δ: 1.07 (3 H, t, J = 8 Hz, Me), 1.4–1.9 (4 H, m, CH_2), 2.25 (2 H, q, J = 8 Hz, CH_2), 2.45 (3 H, s, MeCO), 2.95 (1 H, H_c; m, CH), 3.07 (1 H, H_b; dd, J_{ab} = 5.7, J_{bc} = 9.6 Hz, CH), 3.6 (1 H, H_a; t, J = 5.7 Hz, CH), 3.75 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 13.1 (q), 17.7 (t), 26.8 (q), 28.7 (t), 30.4 (t), 44.0 (d), 47.2 (d), 51.5 (d), 51.8 (d), 149.1 (s), 162.4 (s), 172.7 (s), 199.8 (s), 209.1 (s). MS (EI): 219 (M^+ – OMe, 62), 191 (100), 179 (28), 163 (40), 149 (49), 91 (37), 67 (61). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.17; H, 7.26. Found: C, 67.48; H, 7.08.

5-(4-Acetyl-3-ethyl-2-oxobicyclo[3.3.0]oct-3-en-8-yl)-4-acetyl-3-ethyl-2(3*H*)furanone (18). Method A yield: 65%. Method B/1 equiv KOAc yield: 24%. R_f: 0.14 (hexane/EtOAc 2:1). Mp: 108–109 °C (hexane/ether). IR ($CHCl_3$) cm^{-1}: 1810, 1705, 1680, 1660, 1360, 1190, 910. ^{1}H NMR ($CDCl_3$) δ: 0.83 (3 H, t, J = 7.5 Hz, Me), 1.02 (3 H, t, J = 7.8 Hz, Me), 1.7–1.9 (4 H, m, CH_2), 1.96 (2 H, q, J = 7.8 Hz, CH_2), 2.14 (2 H, q, J = 7.5 Hz, CH_2), 2.3 (3 H, s, MeCO), 2.4 (3 H, s, MeCO), 3.08 (1 H, dd, J = 6, 10.2 Hz, CH), 3.6 (1 H, m, CH), 3.65 (1 H, dd, J = 3.9, 6.3 Hz, CH), 4.04 (1 H, td, J = 6.3, 10.8 Hz, CH). ^{13}C NMR ($CDCl_3$) δ: 9.1 (q), 13.0 (q), 17.8 (q), 23.2 (q), 26.5 (t), 29.3 (t), 29.8 (t), 30.5 (t), 40.6 (d), 44.3 (d), 45.7 (d), 50.9 (d), 118.7 (s), 149.5 (s), 162.8 (s), 163.2 (s), 175.1 (s), 193.8 (s), 199.9 (s), 208.7 (s). MS (EI): 344 (M^+, 89), 316 (11), 301 (38), 274 (58), 219 (38), 191 (89), 125 (100), 91 (55). Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.74; H, 7.04. Found: C, 69.72; H, 6.84.

7-(Hydroxymethyl)-2-(methoxycarbonyl)-8-methylbicyclo[4.3.0]non-7-en-9-one (19). Method B/1 equiv KOAc yield: 31%. R_f: 0.1 (hexane/EtOAc 2:1). IR ($CHCl_3$) cm^{-1}: 3500, 3420, 3000, 2940, 1730, 1700, 1640, 1430, 1240, 1160, 1020, 925. ^{1}H NMR ($CDCl_3$) δ: 0.9–1.1 (1 H, m, CH), 1.2–1.4 (2 H, m, CH_2), 1.5–1.6 (1 H, m, CH), 1.76 (3 H, b s, Me), 1.8–2.0 (1 H, m, CH), 2.0–2.2 (1 H, m, CH), 2.4–2.6 (1 H, m, OH), 2.66 (1 H, H_c; ddd, J = 6.0, 8.4, 17.1 Hz, CH), 3.04 (1 H, H_b; dd, J_{ab} = 6.0, J_{bc} = 6.6 Hz, CH), 3.14 (1 H, H_a; m, J = 6.6, 14.1 Hz, CH), 3.76 (3 H, s, OMe), 4.54 (2 H, AB sys, m, δ_A = 4.63, δ_B = 4.45, J_{AB} = 15 Hz, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 7.9 (q), 21.1 (t), 23.1 (t), 29.3 (t), 39.2 (d), 40.2 (d), 47.7 (d), 51.7 (q), 59.3 (t), 133.7 (s), 171.9 (s), 174.8 (s), 208.1 (s). MS (EI): 238 (M^+, 5), 206 (41), 176 (54), 147 (100), 133 (36), 119 (42), 105 (51), 91 (89), 79 (69), 67 (33), 53 (46).

Methyl 4-(7-(Hydroxymethyl)-8-methyl-9-oxobicyclo[4.3.0]non-7-en-2-yl)-3-methyl-2-methylene-4-oxobutanoate (20). Method A yield: 60%. R_f: 0.16 (hexane/EtOAc 1:1). IR (CCl_4) cm^{-1}: 3650, 3500, 1750, 1715, 1655, 910, 730. ^{1}H NMR ($CDCl_3$) δ: 1.35 (3 H, d, J = 6 Hz, Me), 1.69 (3 H, b s, Me), 1.8–2.4 (7 H, m, CH_2, OH), 2.92 (1 H, H_c; m, CH), 3.0 (1 H, t, H_b; J_{ab} = J_{bc} = 6.3 Hz, CH), 3.15 (1 H, H_a; m, CH), 3.72 (3 H, s, OMe), 4.08 (1 H, q, J = 6 Hz, CH), 4.56 (2 H, AB sys, m, δ_A =

4.65, δ_B = 4.47, J_{AB} = 15 Hz, CH_2O), 5.7 (1 H, b s, HC=), 6.3 (1 H, b s, HC=). ^{13}C NMR ($CDCl_3$) δ: 7.6 (q), 16.5 (q), 20.8 (t), 22.9 (t), 28.9 (t), 39.0 (d), 39.9 (d), 43.8 (d), 47.5 (d), 51.4 (q), 58.9 (t), 126.6 (t), 133.1 (s), 140.7 (s), 172.7 (s), 174.7 (s), 208.1 (s), 210.6 (s). MS (EI): 302 (M^+ − 18, 1), 288 (2), 270 (6), 238 (8), 207 (80), 178 (46), 161 (68), 147 (78), 117 (100), 91 (73), 81 (60), 55 (51). Anal. Calcd for $C_{18}H_{24}O_5$: C, 67.47; H, 7.57. Found: C, 67.88; H, 7.86.

Methyl 4-(7-(Methoxymethyl)-8-methyl-9-oxobicyclo[4.3.0]non-7-en-2-yl)-3-methyl-2-methylene-4-oxobutanoate (21). Method A yield: 12%. R_f: 0.4 (hexane/EtOAc 1:1). IR cm^{-1}: (CCl_4) 1740, 1710, 1690, 1650, 910, 730. ^1H NMR ($CDCl_3$) δ: 1.3 (3 H, d, J = 7 Hz, Me), 1.65 (3 H, b s, Me), 1.5–2.2 (6 H, m, CH_2), 2.9 (1 H, m, CH), 3.0 (1 H, t, J = 6.3 Hz, CH), 3.15 (1 H, m, CH), 3.4 (3 H, s, OMe), 3.7 (3 H, s, OMe), 4.0 (1 H, q, J = 7 Hz, CH), 4.25 (2 H, AB sys, J = 15 Hz, CH_2O), 5.8 (1 H, b s, HC=), 5.95 (1 H, b s, HC=). ^{13}C NMR ($CDCl_3$) δ: 7.9 (q), 16.3 (q), 20.9 (t), 22.9 (t), 28.5 (t), 39.5 (t), 39.8 (t), 42.7 (d), 48.7 (d), 51.8 (q), 58.9 (d), 68.6 (t), 121.4 (t), 134.7 (s), 147.5 (s), 169.6 (s), 175.4 (s), 202.2 (s), 207.3 (s). MS (EI): 334 (M^+, 2), 319 (4), 302 (5), 247 (7), 221 (9), 193 (14), 161 (23), 141 (94), 113 (100), 81 (38), 58 (35). Anal. Calcd for $C_{19}H_{26}O_5$: C, 68.17; H, 7.85. Found: C, 67.95; H, 7.99.

2,7-Bis(methoxycarbonyl)-8-methylbicyclo[4.3.0]non-7-en-9-one (22). Method A yield: 72%. R_f: 0.4 (hexane/EtOAc 2:1). IR (CCl_4) cm^{-1}: 2950, 1740, 1735, 1635, 1440, 1220. ^1H NMR ($CDCl_3$) δ 0.8–1.0 (2 H, m, CH_2), 1.2–1.4 (4 H, m, CH_2), 2.05 (3 H, s, Me), 2.68 (1 H, H_c; ddd, J = 6.0, 11.1, 16.8 Hz, CH), 3.16 (1 H, H_b; dd, J_{ab} = 6.0, J_{bc} = 6.3 Hz, CH), 3.2–3.3 (1 H, H_a; m, CH), 3.75 (3 H, s, Me), 3.85 (3 H, s, Me). ^{13}C NMR ($CDCl_3$) δ: 9.1 (q), 20.9 (t), 22.9 (t), 30.1 (t), 38.8 (d), 39.4 (d), 48.2 (d), 50.8 (q), 51.2 (q), 144.7 (s), 155.8 (s), 164.7 (s), 173.2 (s), 206.5 (s). MS (FAB): 266 (M^+, 39), 234 (78), 207 (98), 175 (79), 147 (98), 127 (100). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.13; H, 6.83. Found: C, 63.24; H, 6.75.

8-(Hydroxymethyl)-2-(methoxycarbonyl)-7-methylbicyclo[4.3.0]non-7-en-9-one (23). Method B/1 equiv KOAc yield: 8%. R_f: 0.05 (hexane/EtOAc 2:1). IR ($CHCl_3$) cm^{-1}: 3500, 3420, 3000, 2940, 1730, 1700, 1640, 1430, 1240, 1160, 1020, 925. ^1H NMR ($CDCl_3$) δ: 1.0–1.9 (6 H, m, CH_2), 2.05 (3 H, b s, Me), 2.4–2.6 (1 H, m, OH), 2.66 (1 H, H_c; m, J = 6.6, 8.4, 17.1 Hz, CH), 3.0 (1 H, H_b; dd, J_{ab} = 6.0, J_{bc} = 6.6 Hz, CH), 3.14 (1 H, H_a; ddm, J = 6.0, 12.6 Hz, CH), 3.76 (3 H, s, OMe), 4.3 (2 H, b s, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 15.2 (q), 20.4 (t), 22.9 (t), 29.1 (t), 39.7 (d), 42.0 (d), 47.6 (d), 51.7 (q), 55.2 (t), 136.5 (s), 171.4 (s), 174.4 (s), 208.3 (s). HRMS Calcd for $C_{13}H_{18}O_4$: 238.12050, (M^+). Found: 238.12032.

7-(Hydroxymethyl)-8-methylbicyclo[4.3.0]nona-2,7-dien-9-one (24). Method B/1 equiv KOAc yield: 24%. R_f: 0.16 (hexane/EtOAc 2:1). IR (CCl_4) cm^{-1}: 3500, 3400, 1710, 1685, 1640. ^1H NMR ($CDCl_3$) δ: 1.2–1.6 (2 H, m, CH_2), 1.7 (3 H, b s, Me), 1.8–2.5 (2 H, m, CH_2), 2.8–3.3 (3 H, m, CH, OH), 4.59 (2 H, AB sys, m, δ_A = 4.68, δ_B = 4.50, J_{AB} = 14.4 Hz, CH_2O), 5.9 (2 H, b s, HC=). ^{13}C NMR ($CDCl_3$) δ: 8.2 (q), 23.6 (t), 26.5 (t), 39.0 (d), 46.8 (d), 59.0 (t), 123.6 (d), 129.5 (d), 134.6 (s), 172.5 (s), 208.6 (s). MS (EI): 178 (M^+, 22), 159 (53), 149 (81), 129 (36), 117 (59), 105 (43), 91 (100), 79 (82), 67 (44), 53 (53). HRMS Calcd for $C_{11}H_{14}O_2$: 178.09938 (M^+). Found: 178.09866.

7-(Hydroxymethyl)-8-methyl-9-oxobicyclo[4.3.0]non-7-en-2-yl (*Z*)-1-Hydroxybut-2-en-2-yl Ketone (25). Method B/1 equiv KOAc yield: 25%. R_f: 0.02 (hexane/EtOAc 1:1). IR ($CHCl_3$) cm^{-1}: 3600, 3500, 1710, 1690, 1645, 910. ^1H NMR ($CDCl_3$) δ: 0.9–1.6 (6 H, m, CH_2), 1.65 (3 H, b s, Me), 1.9 (3 H, d, J = 8 Hz, Me), 2.4–2.8 (2 H, m, CH, OH), 2.9–3.5 (3 H, m, 2 CH, OH), 4.38 (2 H, AB sys, m, δ_A = 4.49, δ_B = 4.27, J_{AB} = 12 Hz, CH_2O), 4.48 (2 H, AB sys, m, δ_A = 4.55, δ_B = 4.42, J_{AB} = 15.6 Hz, CH_2O), 6.5 (1 H, q, J = 8 Hz, HC=). ^{13}C NMR ($CDCl_3$) δ: 7.9 (q), 14.3 (q), 21.1 (t), 22.7 (t), 29.3 (t), 39.6 (d), 43.1 (d), 49.1 (d), 56.9 (t), 59.2 (t), 133.8 (s), 136.1 (d), 140.7 (s), 173.4 (s), 204.6 (s), 208.8 (s).

2-(Methoxycarbonyl)-7-(methoxymethyl)-8-methylbicyclo[4.3.0]non-7-en-9-one (26). Method B/1 equiv KOAc yield: 22%. R_f: 0.24 (hexane/EtOAc 7:1). IR ($CHCl_3$) cm^{-1}: 1725, 1700, 1645, 1085. ^1H NMR ($CDCl_3$) δ: 1.1–1.6 (4 H, m, CH_2), 1.72 (3 H, b s, Me), 1.8–2.2 (2 H, m, CH_2), 2.7 (1 H, H_b; dd, J_{ab} = 6.0, J_{bc} = 6.3 Hz, CH), 2.9–3.2 (2 H, H_a, H_c; m, 2 CH), 3.4 (3 H, s, OMe), 3.75 (3 H, s, OMe), 4.25 (2 H, b s, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 6.1 (q), 19.2 (t), 21.2 (t), 27.3 (t), 37.6 (d), 38.2 (d), 45.7 (d), 49.8 (q), 57.1 (q), 66.8 (t), 132.9 (s), 167.4 (s), 172.7 (s), 205.8 (s). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.63; H, 8.01. Found: C, 66.83; H, 8.04.

2-(Methoxycarbonyl)-8-pentylbicyclo[4.3.0]non-7-en-9-one (27). Method B/1 equiv KOAc yield: 23%. R_f: 0.3 (hexane/EtOAc 10:1). IR ($CHCl_3$) cm^{-1}: 1735, 1700, 1625. ^1H NMR ($CDCl_3$) δ: 0.9 (3 H, t, J = 8 Hz, Me), 1.0–1.8 (12 H, m, CH_2), 2.15 (2 H, b t, J = 8 Hz, CH_2), 2.9–3.2 (3 H, H_a, H_b, H_c; m, CH), 3.75 (3 H, s, OMe), 7.1–7.2 (1 H, m, HC=). ^{13}C NMR ($CDCl_3$) δ: 14.0 (q), 20.0 (t), 22.4 (t), 22.5 (t), 24.7 (t), 27.4 (t), 28.6 (t), 31.6 (t), 38.7 (d), 39.9 (d), 47.9 (d), 51.7 (q), 144.6 (s), 159.3 (s), 174.7 (s), 208.3 (s). Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.28; H, 9.17. Found: C, 72.46; H, 9.24.

Methyl 4-(8-(Hydroxymethyl)-9-methyl-10-oxobicyclo[5.3.0]dec-8-en-2-yl)-3-methyl-2-methylene-4-oxobutanoate (28). Method A yield: 50%. Method B yield: 20%. Method B/1 equiv KOAc yield: 50%. E_t = 12.5 min (semipreparative HPLC; column Spherisorb ODS-2 30 × 0.7 cm, methanol/water 40:60, λ = 233 nm). IR ($CHCl_3$) cm^{-1}: 3550–3400, 1740, 1710, 1645, 1450. ^1H NMR ($CDCl_3$) δ: 1.0–1.9 (8 H, m, CH_2), 1.3 (3 H, d, J = 10 Hz, Me), 1.75 (3 H, b s, Me), 2.0 (1 H, H_a; m, CH), 2.3–2.4 (1 H, m, OH), 2.79 (1 H, H_b; dd, J_{bc} = 4.2, J_{ab} = 7.8 Hz, CHCO), 3.2 (1 H, H_c; m, CH), 3.65 (3 H, s, OMe), 4.05 (1 H, q, J = 10 Hz, CH), 4.58 (2 H, AB sys, m, δ_A = 4.68, δ_B = 4.48, J_{AB} = 14.1 Hz, CH_2O), 5.92 (1 H, b s, HC=), 6.17 (1 H, b s, HC=). ^{13}C NMR ($CDCl_3$) δ: 8.2 (q), 16.2 (q), 27.3 (t), 28.57 (t), 28.6 (t), 29.6 (t), 29.7 (d), 39.9 (d), 46.7 (d), 51.3 (q), 51.9 (d), 59.0 (t), 116.9 (t), 124.0 (s), 146.7 (s), 169.6 (s), 174.7 (s), 202.4 (s), 209.5 (s). MS (EI): 334 (M^+, 1), 316 (1), 303 (2), 274 (3), 252 (9), 221 (100), 193 (53), 175 (53), 161 (45), 141 (60), 113 (58), 105 (45), 91 (60), 67 (39), 55 (58).

Methyl 4-(8-(Methoxymethyl)-9-methyl-10-oxobicyclo[5.3.0]dec-8-en-2-yl)-3-methyl-2-methylene-4-oxobutanoate (29). Method A yield: 7%. Method B/1 equiv KOAc yield: 26%. R_f: 0.56 (hexane/ EtOAc 1:1). IR (CCl_4) cm^{-1}: 1745, 1710, 1655, 1210, 1190. ^1H NMR ($CDCl_3$) δ: 1.25 (3 H, d, J = 6.6 Hz, Me), 1.4–1.6 (6 H, m, CH_2), 1.75 (3 H, b s, Me), 1.9–2.0 (2 H, m, CH_2), 2.3 (1 H, H_a; m, CH), 2.8 (1 H, H_b; dd, J_{bc} = 5.3, J_{ab} = 9.0 Hz, CHCO), 3.2 (1 H, H_c; m, CH), 3.4 (3 H, s, OMe), 3.6 (3 H, s, OMe), 4.15 (1 H, q, J = 6.6 Hz, CH), 4.25 (2 H, b s, CH_2O), 5.85 (1 H, b s, HC=), 6.15 (1 H, b s, HC=). ^{13}C NMR ($CDCl_3$) δ: 8.2 (q), 16.3 (q), 27.8 (t), 28.2 (t), 28.5 (t), 28.6 (t), 39.9 (d), 46.6 (d), 46.7 (d), 51.8 (q), 51.9 (d), 59.0 (q), 68.3 (t), 123.6 (t), 137.1 (s), 147.0 (s), 167.6 (s), 174.7 (s), 202.3 (s), 208.2 (s). Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.93; H, 8.12. Found: C, 68.81; H, 7.99.

8-(Hydroxymethyl)-2-(methoxycarbonyl)-9-methylbicyclo[5.3.0]dec-8-en-10-one (30). Method B/1 equiv KOAc yield: 21%. R_f: 0.12 (hexane/EtOAc 1:1). IR ($CHCl_3$) cm^{-1}: 3650, 3400, 1735, 1700, 1655. ^1H NMR ($CDCl_3$) δ: 1.3–1.6 (4 H, m, CH_2), 1.76 (3 H, b s, Me), 1.8–2.0 (5 H, m, OH, CH_2), 2.95–3.0 (1 H, H_b; m, CH), 3.1–3.2 (1 H, H_a; m, CH), 3.25–3.35 (1 H, H_c; m, CH), 3.75 (3 H, s, OMe), 4.56 (2 H, AB sys, m, δ_A = 4.68, δ_B = 4.44, J_{AB} = 14.1 Hz, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 8.2 (q), 26.8 (t), 28.36 (t), 28.43 (t), 29.1 (t), 44.3 (d), 48.3 (d), 50.5 (d), 51.9 (q), 65.9 (t), 136.8 (s), 170.3 (s), 174.8 (s), 209.9 (s). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.63; H, 8.01. Found: C, 66.83; H, 8.04.

2-(Methoxycarbonyl)-9-(methoxymethyl)-8-methylbicyclo[5.3.0]dec-8-en-10-one (31). Method A yield: 7%. Method B/1 equiv KOAc yield: 10%. R_f: 0.26 (hexane/EtOAc 2:1). IR ($CHCl_3$) cm^{-1}: 1730, 1700, 1650, 1090. ^1H NMR ($CDCl_3$) δ: 1.3–1.5 (6 H, m, CH_2), 1.75 (3 H, b s, Me), 1.8–1.9 (3 H, m, OH, CH_2), 2.3–2.5 (1 H, H_a; m, CH), 2.75 (1 H, H_b; dd, J_{bc} = 2.2, J_{ab} = 6.0 Hz, CH), 2.8–3.2 (1 H, H_c; m, CH), 3.4 (3 H, s, OMe), 3.65 (3 H, s, OMe), 4.25 (2 H, b s, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 8.2 (q), 23.9 (t), 24.4 (t), 28.3 (t), 28.5 (t), 44.3 (d), 48.4 (d), 50.5 (d), 51.9 (q), 58.9 (q), 68.3 (t), 137.6 (s), 168.3 (s), 174.7 (s), 209.7 (s). MS (EI): 266 (M^+, 58), 234 (54), 206 (31), 189 (41), 161 (100), 105 (58), 91 (97).

9-(Hydroxymethyl)-2-(methoxycarbonyl)-8-methylbicyclo[5.3.0]dec-8-en-10-one (32). Method B/1 equiv KOAc yield: 3%. R_f: 0.08 (hexane/EtOAc 1:1). IR ($CHCl_3$) cm^{-1}: 3650, 3400, 1735, 1700, 1655. ^1H NMR ($CDCl_3$) δ: 1.3–1.65 (4 H, m, CH_2), 2.05 (3 H, b s, Me), 1.8–2.0 (5 H, m, OH, CH_2), 2.4–2.8 (1 H, m, CH), 2.9–3.2 (2 H, m, 2 CH), 3.7 (3 H, s, OMe), 4.35 (2 H, b s, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 15.0 (q), 28.2 (t), 28.5 (t), 28.9 (t), 31.6 (t), 44.2 (d), 48.5 (d), 50.8 (d), 51.9 (q), 55.8 (t), 138.8 (s), 174.1 (s), 174.6 (s), 210.4 (s). MS (EI): 252 (M^+, 11), 234 (8), 218 (11), 190 (48), 175 (29), 161 (95), 147 (36), 134 (46), 121 (46), 105 (60), 91 (100), 79 (75), 67 (64), 55 (79). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.63; H, 8.01. Found: C, 66.88; H, 7.67.

2,8-Bis(methoxycarbonyl)-9-methylbicyclo[5.3.0]dec-8-en-10-one (33). Method B yield: 70%. Method A yield: 28%. R_f: 0.36 (hexane/EtOAc 3:1). IR ($CHCl_3$) cm^{-1}: 1740, 1710, 1440, 1230. ^1H NMR ($CDCl_3$) δ: 1.3–1.9 (8 H, m, CH_2), 2.0 (3 H, d, J = 2.5 Hz, Me), 3.0 (1 H, H_b; dd, J_{bc} = 4.5, J_{ab} = 6.6 Hz, CH), 3.19 (1 H, H_a; m, CH), 3.42 (1 H, H_c; m, CH), 3.7 (3 H, s, OMe), 3.85 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 9.4 (q), 26.4 (t), 27.9 (t), 28.5 (t), 28.7 (t), 43.8 (d), 44.2 (d), 50.7 (d), 51.5 (q), 51.6 (q), 145.3 (s), 156.6 (s), 165.7 (s), 173.9 (s), 209.1 (s). MS (EI): 280 (M^+, 20), 248 (74), 220 (64), 189 (52), 161 (100), 133 (28), 105 (38), 84 (54), 59 (27). Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.26; H, 7.21. Found: C, 64.02; H, 7.14.

4,12-Bis(methoxycarbonyl)-3,13-dimethyltricyclo[8.3.0.0^{1,5}]tridec-3-ene-2,11-dione (34). Method A yield: 72%. Method B yield: 29%. R_f: 0.28 (hexane/EtOAc 3:1). Mp: 122–123 °C (hexane/ether). IR ($CHCl_3$) cm^{-1}: 3010, 1760, 1730, 1705, 1210. ^1H NMR ($CDCl_3$) δ: 0.86

(3 H, d, J = 6.3 Hz, Me), 0.9–1.2 (4 H, m, CH_2), 1.5–1.8 (4 H, m, CH_2), 1.99 (3 H, d, J = 1.2 Hz, Me), 2.16–2.3 (2 H, m, 2 CH), 2.36 (1 H, dd, J = 1.8, 10.5 Hz, CH), 2.61 (1 H, dq, J = 1.2, 6.3 Hz, CH), 3.8 (3 H, s, OMe), 3.9 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 8.9 (q), 12.9 (q), 23.1 (t), 25.1 (t), 28.7 (t), 28.9 (t), 43.0 (d), 47.1 (d), 51.9 (d), 52.2 (d), 57.2 (q), 57.8 (q), 60.1 (s), 146.2 (s), 157.9 (s), 165.2 (s), 169.5 (s), 206.2 (s), 212.2 (s). MS (EI): 348 (M^+, 16), 317 (19), 248 (76), 221 (79), 161 (100), 91 (25), 69 (60). Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.49; H, 6.96. Found: C, 65.39; H, 6.90.

8-Acetyl-9-ethyl-2-(methoxycarbonyl)bicyclo[5.3.0]dec-8-en-10-one (35). Method B/1 equiv KOAc yield: 53%. R_f: 0.16 (hexane/EtOAc 3:1). IR (CCl_4) cm^{-1}: 1735, 1710, 1670, 1195, 1170. ^1H NMR ($CDCl_3$) δ: 1.09 (3 H, t, J = 7 Hz, Me), 1.3–2.1 (8 H, m, CH_2), 2.35 (2 H, dq, J = 1.0, 7.0 Hz, CH_2), 2.42 (3 H, s, MeCO), 2.95 (1 H, H_b; dd, J_{bc} = 4.5, J_{ab} = 6.3 Hz, CH), 3.1–3.2 (1 H, H_a; m, CH), 3.44 (1 H, H_c; ddd, J = 4.5, 7.8, 11.7 Hz, CH), 3.7 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 13.2 (q), 17.5 (t), 26.8 (t), 28.1 (t), 28.8 (t), 29.2 (t), 30.5 (q), 44.2 (d), 44.8 (d), 50.9 (d), 51.9 (q), 145.5 (s), 165.7 (s), 174.3 (s), 202.0 (s), 209.4 (s). Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.03; H, 7.98. Found: C, 69.20; H, 8.08.

3-(Hydroxymethyl)-6-(methoxycarbonyl)-2-methylspiro[4.4]non-2-en-1-one (36). Method A yield: 50%. Method B/1 equiv KOAc yield: 46%. R_f: 0.1 (hexane/EtOAc 1:1). IR ($CHCl_3$) cm^{-1}: 3630, 3500, 1735, 1700, 1655. ^1H NMR ($CDCl_3$) δ: 1.55–1.68 (2 H, m, CH_2), 1.70 (3 H, b s, Me), 1.9–2.1 (4 H, m, CH_2), 2.4 (1 H, b s, OH), 2.74 (2 H, H_a, $H_{a'}$; m, AB sys, δ_A = 2.83, δ_B = 2.65, J_{AB} = 18.0 Hz, CH_2), 2.82 (1 H, H_b; dd, J = 8.4, 8.7 Hz, $CHCO_2$), 3.57 (3 H, s, OMe), 4.55 (2 H, b s, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 8.2 (q), 23.5 (t), 28.4 (t), 37.9 (t), 43.4 (t), 51.6 (q), 53.4 (d), 55.5 (s), 60.6 (t), 134.2 (s), 166.9 (s), 173.9 (s), 211.5 (s). MS (EI): 238 (M^+, 17), 206 (33), 197 (60), 178 (30), 165 (74), 147 (38), 139 (100), 105 (22), 91 (36), 79 (27), 67 (21), 55 (21). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.52; H, 7.63. Found: C, 65.50; H, 7.66.

3,6-Bis(methoxycarbonyl)-2-methylspiro[4.4]non-2-en-1-one (37). Method B yield: 45%. Method B/1 equiv KOAc yield: 38%. R_f: 0.24 (hexane/EtOAc 4:1). IR (CCl_4) cm^{-1}: 1730, 1720, 1645, 1435, 1220. ^1H NMR ($CDCl_3$) δ: 1.5–2.0 (4 H, m, CH_2), 2.05 (3 H, t, J = 2.1 Hz, Me), 2.1–2.4 (2 H, m, CH_2), 2.85 (1 H, H_b; t, J = 9 Hz, $CHCO_2$), 2.86 (2 H, H_a, $H_{a'}$; AB sys, q, δ_A = 2.96, δ_B = 2.76, J_q = 2.1 Hz, J_{AB} = 18.3 Hz, CH_2), 3.55 (3 H, s, OMe), 3.85 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 9.8 (q), 11.4 (t), 28.1 (t), 37.8 (t), 42.3 (t), 51.4 (q), 51.8 (q), 53.5 (d), 55.3 (s), 145.8 (s), 150.5 (s), 165.6 (s), 173.1 (s), 211.4 (s). MS (EI): 266 (M^+, 6), 235 (22), 225 (76), 206 (27), 193 (81), 174 (19), 167 (100), 147 (45), 119 (42), 91 (49), 77 (35). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.13; H, 6.83. Found: C, 63.26; H, 7.05.

3-(Hydroxymethyl)-6-(methoxycarbonyl)-2-methylspiro[4.5]dec-2-en-1-one (38) and 7-(Hydroxymethyl)-5-hydroxy-6-methyl-1,2,3,4-tetrahydronaphthalene (43). The reaction was carried out according to methods A and B followed by acetylation for better separation of compounds **38** and **43**, giving the following yields of the corresponding allylic and benzylic acetates of **38** and **43**.

Acetate of 38. Method A yield: 15%. Method B/0.5 equiv KOAc yield: 53%. R_f: 0.2 (hexane/EtOAc 2:1). IR ($CHCl_3$) cm^{-1}: 1741, 1708, 1664, 1445, 1370, 1224, 1170, 1026. ^1H NMR ($CDCl_3$) δ 1.0–1.5 (4 H, m, CH_2), 1.73 (3 H, m, Me), 1.75–2.0 (3 H, m, CH, CH_2), 2.1 (3 H, s, Me), 2.33 (1 H, ddd, J = 3.6, 12.0, 24.9 Hz, CH), 2.38 (2 H, H_a, $H_{a'}$; AB sys, m, δ_A = 2.52, δ_B = 2.24, J_{AB} = 18.0 Hz, CH_2), 2.53 (1 H, H_b; dd, J = 4.2, 12.0 Hz, $CHCO_2$), 3.57 (3 H, s, OMe), 4.88 (2 H, b s, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 8.2 (q), 20.6 (t), 20.7 (q), 24.9 (t), 25.3 (t), 35.3 (t), 43.9 (t), 46.3 (s), 50.6 (d), 51.6 (q), 61.5 (t), 136.1 (s), 159.1 (s), 170.6 (s), 174.2 (s), 210.4 (s). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.28; H, 7.55. Found: C, 65.17; H, 7.53.

Acetate of 43. Method A yield: 37%. Method B/0.5 equiv KOAc yield: 10%. R_f: 0.38 (hexane/EtOAc 2:1). IR ($CHCl_3$) cm^{-1}: 1743, 1370, 1220, 1199. ^1H NMR ($CDCl_3$) δ: 1.75 (6 H, m, CH_2), 2.1 (3 H, s, Me), 2.35 (3 H, s, Me), 2.4–2.5 (1 H, m, OH), 2.75 (2 H, m, CH_2), 5.07 (2 H, b s, CH_2O), 6.99 (1 H, s, H-Ar). ^{13}C NMR (MeOH-d_4) 11.7 (q), 20.5 (q), 22.4 (t), 22.6 (t), 23.5 (t), 20.9 (t), 64.7 (t), 126.3 (s), 128.3 (d), 129.9 (s), 132.0 (s), 136.1 (s), 147.9 (s), 168.9 (s). HRMS (EI). Calcd for $C_{16}H_{22}O_5$: 234.12559. Found: 234.12466.

3,6-Bis(methoxycarbonyl)-2-methylspiro[4.5]dec-2-en-1-one (39). Method B yield: 11%. Method B/1 equiv KOAc yield: 24%. R_f: 0.38 (hexane/EtOAc 4:1). IR (CCl_4) cm^{-1}: 1740, 1730, 1720, 1650, 1440, 1220. ^1H NMR ($CDCl_3$) δ: 1.3–2.0 (8 H, m, CH_2), 2.05 (3 H, t, J = 2.1 Hz, Me), 2.57 (2 H, H_a, $H_{a'}$; q, AB sys, δ_A = 2.68, δ_B = 2.46, J_q = 2.1 Hz, J_{AB} = 18.3 Hz, CH_2), 2.60 (1 H, dd, J = 3.9, 12.3 Hz, $CHCO_2$), 3.6 (3 H, s, OMe), 3.8 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 9.9 (q), 20.2 (t), 25.0 (t), 25.4 (t), 35.0 (t), 37.0 (t), 43.2 (d), 50.7 (q), 51.6 (q), 51.8 (s), 146.1 (s), 148.8 (s), 165.8 (s), 174.1 (s), 210.8 (s). MS (FAB, Magic Bullet): 281 (M^+ + 1, 81), 249 (100), 221 (94), 189 (24), 161 (25), 133 (29), 105 (37). Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.26; H, 7.21. Found: C, 64.45; H, 7.42.

5-Hydroxy-7-(methoxycarbonyl)-6-methyl-1,2,3,4-tetrahydronaphthalene (44). Method B yield: 32%. Method B/1 equiv KOAc yield: 44%. R_f: 0.32 (hexane/EtOAc 4:1). IR (CCl_4) cm^{-1}: 3640, 3510, 1730, 1440, 1340, 1295, 1270, 1210, 1200, 1050. ^1H NMR ($CDCl_3$) δ: 1.3–2.1 (8 H, m, CH_2), 2.4 (3 H, b s, Me), 2.7 (1 H, b s, OH), 3.85 (3 H, s, OMe), 7.2 (1 H, b s, H-Ar). ^{13}C NMR (MeOH-d_4) δ: 13.2 (q), 23.7 (t), 23.8 (t), 24.8 (t), 30.2 (t), 52.1 (q), 123.6 (s), 123.7 (s), 128.9 (s), 129.8 (s), 136.1 (d), 154.2 (s), 170.4 (s). MS (FAB, Magic Bullet): 221 (M^+ + 1, 100), 189 (62), 161 (23), 135 (23), 115 (12), 105 (11). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.87; H, 7.34. Found: C, 70.95; H, 7.32.

Methyl 4-(3-(Methoxycarbonyl)-2-methyl-1-oxospiro[4.5]dec-2-en-6-yl)-3-methyl-4-oxobut-2-enoate (45). Method B yield: 10%. R_f: 0.22 (hexane/EtOAc 4:1). IR (CCl_4) cm^{-1}: 1720, 1660, 1625, 1435, 1215. ^1H NMR ($CDCl_3$) δ: 1.3–1.9 (8 H, m, CH_2), 1.95 (3 H, d, J = 7.1 Hz, Me), 2.05 (3 H, t, J = 2.7 Hz, Me), 2.2–2.5 (2 H, m, CH_2), 3.2–3.3 (1 H, m, $CHCO_2$), 3.75 (3 H, s, OMe), 3.80 (3 H, s, OMe), 6.9 (1 H, q, J = 7.1 Hz, HC=). ^{13}C NMR ($CDCl_3$) δ: 10.1 (q), 15.9 (q), 20.2 (t), 25.7 (t), 25.8 (t), 35.6 (t), 43.5 (t), 45.6 (s), 51.7 (q), 52.0 (q), 56.0 (d), 136 (s), 145.3 (d), 146.6 (s), 148.1 (s), 166.1 (s), 167.0 (s), 198.5 (s), 210.9 (s). MS (EI): 316 (M^+ – 32, 10), 249 (38), 221 (100), 189 (33), 161 (35), 127 (38), 91 (34), 67 (42), 58 (76).

3,7-Dimethyl-4-(hydroxymethyl)bicyclo[4.4.0]dec-3-en-2-one (48). Method B yield: 20%. R_f: 0.36 (hexane/EtOAc 2:1). IR (CCl_4) cm^{-1}: 3640, 3470, 1710, 1670, 1380, 1140, 1010. ^1H NMR ($CDCl_3$) δ: 1.0 (3 H, d, J = 8 Hz, Me), 1.2–1.6 (5 H, m, CH, CH_2), 1.70 (3 H, b s, Me), 1.8–2.0 (3 H, m, CH_2, OH), 2.05–2.2 (2 H, m, CH_2), 2.25–2.4 (2 H, m, CH), 4.35 (2 H, b s, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 10.4 (q), 13.3 (q), 19.5 (t), 26.7 (t), 31.3 (t), 31.6 (t), 32.8 (d), 41.9 (d), 43.7 (d), 63.1 (t), 129.7 (s), 154.4 (s), 202.1 (s). MS (EI): 208 (M^+, 70), 179 (100), 161 (41), 121 (55), 112 (93), 95 (52), 81 (41), 67 (43), 55 (57). Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.94; H, 9.70. Found: C, 74.62; H, 9.76.

1,6-Dimethyl-5-hydroxy-7-(hydroxymethyl)-1,2,3,4-tetrahydronaphthalene (49). Method B yield: 29%. R_f: 0.26 (hexane/EtOAc 2:1). IR (CCl_4) cm^{-1}: 3400, 1670, 1630, 1580, 1460, 1335, 1200, 1110, 1075. ^1H NMR ($CDCl_3$) δ: 1.25 (3 H, d, J = 6.3 Hz, Me), 1.3–2.1 (6 H, m, CH_2), 2.2 (3 H, s, Me), 2.86 (1 H, q, J = 6.3 Hz, CH), 3.6 (1 H, s, OH), 4.65 (2 H, s, CH_2O), 5.1 (1 H, m, OH), 6.85 (1 H, s, H-Ar). ^{13}C NMR ($CDCl_3$) δ: 10.8 (q), 19.7 (q), 22.7 (t), 23.5 (t), 30.8 (t), 32.3 (d), 64.1 (t), 118.5 (s), 120.1 (d), 122.4 (s), 136.8 (s), 140.7 (s), 151.7 (s). MS (EI): 206 (M^+, 95), 191 (100), 188 (52), 175 (85), 161 (63), 121 (21), 91 (22), 77 (17). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.68; H, 8.81. Found: C, 75.61; H, 8.93.

3,9-Dimethyl-4-(hydroxymethyl)bicyclo[4.4.0]dec-3-en-2-one (50). Method B yield: 38%. R_f: 0.22 (hexane/EtOAc 2:1, mixture of two stereoisomers in a 1:1 ratio as detected by ^1H NMR). IR ($CHCl_3$, mixture of both stereoisomers) cm^{-1}: 3620, 3500, 1665, 1640. ^1H NMR ($CDCl_3$, mixture of both stereoisomers) δ: 0.90 (3 H, d, J = 5.5 Hz, Me), 0.95 (3 H, d, J = 5.5 Hz, Me), 1.2–1.7 (8 H, m, CH_2), 1.75 (6 H, b s, 2 Me), 1.8–2.4 (12 H, m, 4 CH_2, 2 CH, 2 OH), 2.55 (2 H, dd, J = 2.7, 5.5 Hz, 2 CH), 2.65 (2 H, dd, J = 2.7, 5.5 Hz, 2 CH), 4.35 (4 H, b s, CH_2O). ^{13}C NMR ($CDCl_3$, mixture of both stereoisomers) δ: 10.4 (q), 10.5 (q), 17.5 (q), 22.7 (q), 27.0 (d), 27.6 (t), 30.5 (t), 31.4 (t), 32.1 (t), 33.6 (t), 34.0 (t), 34.3 (t), 34.5 (t), 34.6 (t), 38.8 (d), 39.5 (d), 44.6 (d), 50.1 (d), 62.8 (t), 62.9 (t), 130.0 (s), 130.2 (s), 154.0 (s), 154.1 (s), 201.3 (s), 202.1 (s). MS (EI, mixture of both stereoisomers): 208 (M^+, 41), 190 (13), 179 (69), 161 (20), 149 (17), 135 (17), 121 (35), 112 (100), 95 (38), 81 (40), 67 (33), 55 (50). Anal. Calcd for $C_{13}H_{20}O_2$ (mixture of both stereoisomers): C, 74.94; H, 9.70. Found: C, 74.58; H, 9.39.

2,7-Dimethyl-8-hydroxy-6-(hydroxymethyl)-1,2,3,4-tetrahydronaphthalene (51). Method B yield: 27%. R_f: 0.46 (hexane/EtOAc 2:1). IR (CCl_4) cm^{-1}: 3400, 1670, 1630, 1580, 1460, 1335, 1200, 1110, 1075. ^1H NMR ($CDCl_3$) δ: 1.1 (3 H, d, J = 5.7 Hz, Me), 1.2–2.0 (7 H, m, CH_2CH), 2.2 (3 H, b s, Me), 3.45 (3 H, s, OMe), 4.7 (2 H, b s, CH_2O), 6.45 (1 H, b s, H-Ar), 7.9 (1 H, b s, HO-Ar). ^{13}C NMR ($CDCl_3$) δ: 19.1 (q), 22.2 (q), 29.0 (t), 29.4 (t), 31.2 (t), 31.4 (d), 58.2 (q), 70.7 (t), 116.4 (s), 121.9 (d), 122.7 (s), 132.4 (s), 137.6 (s), 154.3 (s). MS (EI): 220 (M^+, 8), 188 (91), 173 (100), 159 (41), 145 (31), 118 (21), 105 (12), 91 (22), 77 (14), 58 (23). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.31; H, 9.17. Found: C, 76.64; H, 8.95.

3-(Hydroxymethyl)-2,6,10-trimethylspiro[4.5]deca-2,6-dien-1-one (53). Method B yield: 12%. R_f: 0.20 (hexane/EtOAc 5:1). IR (CCl_4) cm^{-1}: 3650, 3450, 1745, 1720, 1700, 1660, 1455, 1450, 1380, 1020. ^1H NMR ($CDCl_3$) δ: 0.84 (3 H, d, J = 8.1 Hz, Me), 1.0–1.3 (5 H, m, CH, CH_2), 1.4 (1 H, s, OH), 1.8 (3 H, t, J = 1.2 Hz, Me), 2.1 (3 H, s, Me), 2.29 (2 H, q, J = 1.2 Hz, CH_2), 4.22 (2 H, dq, J = 1.2, 6.3 Hz, CH_2O), 5.89 (1 H, tq, J = 1.2 Hz, 6.3 Hz, HC=). ^{13}C NMR ($CDCl_3$) δ: 11.4 (q), 14.1 (q), 21.0 (q), 22.6 (t), 28.8 (t), 30.9 (d), 31.6 (t), 41.3 (s), 62.4 (t),

124.1 (s), 124.8 (s), 128.2 (d), 171.2 (s), 207.1 (s).

Methyl 4-(1-Cyclohexenyl)-3-(methoxycarbonyl)-2-methylbut-2-enoate (54). Method B/1 equiv KOAc yield: 36%. R_f: 0.6 (hexane/EtOAc 4:1, mixture of isomers *E* (83) and *Z* (17) as detected by ^{1}H NMR). IR (CCl_4) cm^{-1}: 1740, 1730, 1690, 1650, 1435, 1250, 1200, 1150, 1130, 1075, 1050. ^{1}H NMR ($CDCl_3$, major isomer *E*) δ: 1.4–1.6 (4 H, m, CH_2), 1.8–1.9 (4 H, m, CH_2), 1.99 (3 H, b s, Me), 3.11 (2 H, b s, CH_2), 3.71 (3 H, s, OMe), 3.74 (3 H, s, Me), 5.4 (1 H, b s, HC=). ^{1}H NMR ($CDCl_3$, minor isomer *Z*) δ: 1.4–1.6 (4 H, m, CH_2), 1.8–1.9 (4 H, m, CH_2), 1.98 (3 H, b s, Me), 2.91 (2 H, b s, CH_2), 3.70 (3 H, s, OMe), 3.73 (3 H, s, Me), 5.5 (1 H, b s, HC=). ^{13}C NMR ($CDCl_3$, major isomer *E*) δ: 17.7 (q), 22.2 (t), 22.9 (t), 25.3 (t), 28.1 (t), 39.2 (t), 51.7 (q), 51.9 (q), 123.6 (d), 132.5 (s), 134.2 (s), 137.3 (s), 169.1 (s), 169.3 (s). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.63; H, 8.01. Found: C, 66.98; H, 8.00.

Methyl 4-(1-Cyclohexenyl)-3-(hydroxymethyl)-2-methylbut-2-enoate (55). Method B/1 equiv KOAc yield: 91%. R_f: 0.51 (hexane/EtOAc 2:1; mixture of isomers *E* (89) and *Z* (11) as detected by ^{1}H NMR). IR (CCl_4) cm^{-1}: 3650, 3400, 1725, 1650, 1435, 1230, 1190, 1130. ^{1}H NMR ($CDCl_3$, major isomer *E*) δ: 1.48–1.66 (4 H, m, CH_2), 1.94 (3 H, b s, Me), 1.96–2.6 (4 H, m, CH_2), 3.11 (2 H, b s, CH_2), 3.70 (3 H, s, OMe), 4.2 (2 H, b s, CH_2O), 5.48 (1 H, m, HC=). ^{1}H NMR ($CDCl_3$, minor isomer *Z*) δ: 1.48–1.66 (4 H, m, CH_2), 1.75 (3 H, b s, Me), 1.96–2.6 (4 H, m, CH_2), 3.24 (2 H, b s, CH_2), 3.71 (3 H, s, Me), 4.0 (2 H, b s, CH_2O), 5.68 (1 H, b s, HC=). ^{13}C NMR ($CDCl_3$, major isomer *E*) δ: 15.4 (q), 22.4 (t), 22.9 (t), 25.4 (t), 28.4 (t), 40.0 (t), 51.6 (q), 62.2 (t), 123.3 (d), 127.0 (s), 136.2 (s), 143.5 (s), 170.2 (s). Anal. Calcd for $C_{13}H_{20}O_3$ (mixture of isomers *E* and *Z*): C, 69.60; H, 9.00. Found: C, 69.52; H, 9.00.

3-(Hydroxymethyl)-6-(methoxycarbonyl)-2-methylspiro[4.6]undec-2-en-1-one (40). Method A yield: 48%. Method B/1 equiv KOAc yield: 75%. R_f: 0.2 (hexane/EtOAc 2:1). IR (CCl_4) cm^{-1}: 3500, 3380, 1725, 1700, 1650, 1435, 1195, 1150, 1020, 910. ^{1}H NMR ($CDCl_3$) δ: 1.3–1.44 (4 H, m, CH_2), 1.64 (3 H, b s, Me), 1.71–1.78 (2 H, m, CH_2), 1.86–1.98 (4 H, m, CH_2), 2.55 (2 H, H_a, $H_{a'}$; q, J = 1.2 Hz, CH_2), 2.66 (1 H, H_b; d, J = 9.0 Hz, $CHCO_2$), 3.0–3.1 (1 H, m, OH), 3.55 (3 H, s, OMe), 4.51 (2 H, q, AB sys, δ_A = 4.53, δ_B = 4.49, J_q = 1.2 Hz, J_{AB} = 14.4 Hz, CH_2O). ^{13}C NMR ($CDCl_3$) δ: 8.1 (q), 23.7 (t), 26.7 (t), 30.4 (t), 30.6 (t), 38.8 (t), 44.2 (t), 50.5 (s), 51.6 (q), 53.5 (d), 60.4 (t), 134.2 (s), 166.2 (s), 174.9 (s), 212.9 (s). MS (FAB, Magic Bullet): 267 (M^+ + 1, 46), 235 (61), 207 (70), 189 (29), 175 (20), 161 (30), 133 (38), 119 (45), 109 (60), 105 (100). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.63; H, 8.34. Found: C, 67.56; H, 8.51.

3,6-Bis(methoxycarbonyl)-2-methylspiro[4.6]undec-2-en-1-one (41). Method B yield: 42%. Method B/1 equiv KOAc yield: 72%. R_f: 0.54 (hexane/EtOAc 4:1). IR (CCl_4) cm^{-1}: 1740, 1720, 1640, 1440, 1225. ^{1}H NMR ($CDCl_3$) δ: 1.2–1.9 (10 H, m, CH_2), 2.0 (3 H, t, J = 2.1 Hz, Me), 2.60 (2 H, H_a, $H_{a'}$; AB sys, q, δ_A = 2.65, δ_B = 2.55, J_q = 2.1 Hz, J_{AB} = 18.0 Hz, CH_2), 2.64 (1 H, H_b; d, J = 9.3 Hz, $CHCO_2$), 3.5 (3 H, s, OMe), 3.8 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 10.0 (q), 23.5 (t), 26.9 (t), 30.3 (t), 30.7 (t), 38.9 (t), 43.7 (t), 50.5 (s), 51.8 (q), 51.9 (q), 53.9 (d), 146.6 (s), 149.1 (s), 166.0 (s), 174.6 (s), 213.0 (s). MS (FAB, Magic Bullet): 295 (M^+ + 1, 86), 263 (100), 235 (78), 203 (25), 167 (24). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.28; H, 7.55. Found: C, 65.12; H, 7.71.

Methyl 4-(3-(Methoxycarbonyl)-2-methyl-1-oxospiro[4.6]undec-2-en-6-yl)-3-methyl-4-oxobut-2-enoate (56). Method B yield: 25%. R_f: 0.24 (hexane/EtOAc 4:1). IR (CCl_4) cm^{-1}: 1720, 1620, 1435, 1220. ^{1}H NMR ($CDCl_3$) δ: 1.1–1.9 (10 H, m, CH_2), 1.97 (3 H, d, J = 2.3 Hz, Me), 2.1 (3 H, b s, Me), 2.2–2.4 (1 H, m, $CHCO_2$), 2.5–2.8 (2 H, m, CH_2), 3.8 (3 H, s, OMe), 3.83 (3 H, s, OMe), 6.95 (1 H, q, J = 2.3 Hz, HC=). ^{13}C NMR ($CDCl_3$) δ: 10.3 (q), 16.0 (q), 23.3 (t), 25.8 (t), 30.4 (t), 30.5 (t), 39.7 (t), 43.7 (t), 49.2 (s), 51.9 (q), 52.2 (q), 58.9 (d), 135.6 (s), 145.4 (d), 147.4 (s), 147.9 (s), 166.1 (s), 166.8 (s), 197.8 (s), 213.6 (s). MS (FAB, Magic Bullet): 363 (M^+ + 1, 61), 345 (30), 337 (43), 263 (45), 235 (59), 167 (19), 91 (13).

3,6-Bis(methoxycarbonyl)-2-methylspiro[4.7]dodec-2-en-1-one (42). Method B yield: 47%. Method B/1 equiv KOAc yield: 63%. R_f: 0.3 (hexane/EtOAc 5:1). IR (CCl_4) cm^{-1}: 1740, 1715, 1650, 1435, 1370, 1220. ^{1}H NMR ($CDCl_3$) δ: 1.3–1.9 (12 H, m, 6 CH_2), 2.05 (3 H, t, J = 2.1 Hz, Me), 2.53 (2 H, H_a, $H_{a'}$; AB sys, q, δ_A = 2.67, δ_B = 2.40, J_q = 2.1, J_{AB} = 18.3 Hz, CH_2), 2.95 (1 H, H_b; dd, J = 2.7, 7.5 Hz, $CHCO_2$), 3.55 (3 H, s, OMe), 3.83 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ: 10.0 (q), 23.9 (t), 25.4 (t), 26.4 (t), 27.9 (t), 28.1 (t), 33.4 (t), 41.1 (t), 49.2 (d), 49.9 (s), 51.8 (q), 51.9 (q), 146.7 (s), 148.9 (s), 166.0 (s), 175.6 (s), 212.4 (s). MS (FAB, glycerol): 309 (M^+ + 1, 19), 277 (47), 249 (36), 217 (12), 167 (22), 115 (23), 105 (27). Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.20; H, 7.86. Found: C, 65.90; H, 7.78.

Acknowledgment. Financial support from DGICYT (Project PB87-0201-C-03-03) is gratefully acknowledged. Two of us thank the MEC (Ll.P.) and the CSIC and SEDEQ (A.Ll.) for respective fellowships. We are also kindly indebted to Dr. A. Echavarren for his assistance in stereochemical studies.

Supplementary Material Available: Full X-ray data for structure determination of compounds **4**, **18**, and **34** (34 pages); tables of observed and calculated structure factors for **4**, **18**, and **34** (56 pages). Ordering information is given on any current masthead page.

ESR Study of the Photochemistry of Benzoic Acid Derivatives

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Abstract: Electron spin resonance (ESR) has been used to study radical intermediates in the photochemistry of a number of aromatic carboxylic acids, esters, anhydrides, amides, imides, and nitriles. Continuous photolysis was used to produce the radicals in either aqueous or alcoholic media. The triplet states of the compounds undergo two reactions in the presence of a hydrogen donor such as 2-propanol. A hydrogen atom is transferred to certain carbon atoms of the aromatic ring forming cyclohexadienyl radicals. In most cases, addition occurs at or opposite the carboxyl (or cyano) group. The pattern of addition is attributed to the higher spin density in the triplet at those positions. This pattern also correlates with the positions of higher hyperfine splitting in the corresponding anion radicals. In a parallel reaction, a hydrogen atom is also transferred to an oxygen of the carboxyl group (for acids, anhydrides, and esters) to form the one-electron-reduction product. The cyclohexadienyl radicals are not formed by protonation on a carbon of an anion radical. The ESR spectra of most of the cyclohexadienyl radicals are highly polarized to the extent that the low-field lines appear in emission. This effect is believed to be normal chemically induced dynamic spin polarization (CIDEP) as a result of cross reactions with the other radicals present.

Introduction

The present work began with an attempt to use continuous photolysis to produce the anion radical of terephthalic acid for study of its ^{13}C hyperfine constants (hfc's) in conjunction with Qin et al.[1] Photolysis of acetone in the presence of 2-propanol was used to form $(CH_3)_2\dot{C}O^-$ in basic aqueous solution, and that radical reduced the terephthalate. In addition to the desired anion radical, $[^-O_2CC_6H_4CO_2^-]^{\bullet-}$, lines were observed from a cyclo-

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(1) Qin, L.; Madden, K. P.; Schuler, R. H. *J. Phys. Chem.* **1988**, *92*, 3790.

0002-7863/92/1514-10461$03.00/0