192. Novel C_9 and C_{11} Hydrocarbons from the Brown Alga *Cutleria multifida*; Sigmatropic and Electrocyclic Reactions in Nature

Part VI[1])

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In addition to the known $C_{11}H_{16}$ hydrocarbons multifidene (**4**), aucantene (**2**), and ectocarpene (**5**), the marine brown alga *Cutleria multifida* produces trace amounts of the C_9H_{12} hydrocarbon 7-methylcycloocta-1,3,5-triene (**8**) and its valence tautomer 7-methylbicyclo[4.2.0]octa-2,4-diene. A second novel C_9H_{12} hydrocarbon is 6-vinylcyclohepta-1,4-diene (**9**), a lower homologue of ectocarpene (**5**). Among the $C_{11}H_{16}$ hydrocarbons, 7-((1*E*/*Z*)-prop-1-enyl)cycloocta-1,4-diene (**10**/**11**) is found for the first time. The strueture of all new products is confirmed by synthesis and spectroscopic data. The biosynthesis of the new hydrocarbons **8**–**11** is obviously linked to the pathways which lead to the major products giffordene (**7**), (6*S*)-ectocarpene ((6*S*)-**5**), and (4*R*,5*R*)-aucantene ((4*R*,5*R*)-**2**). Consecutive reactions of certain thermolabile primary products proceed *via* electrocyclic ring closure, 3,3-sigmatropic rearrangement, or a 1,7-sigmatropic H-shift.

I. Introduction. – Olefinic C_8 and C_{11} hydrocarbons act as chemical signals during sexual reproduction of marine brown algae [2]. All these pheromones are metabolites of unsaturated C_9- and C_{12}-fatty acids as has been previously shown in a model study with the flowering plant *Senecio isatideus* [3]. (3*Z*,6*Z*,9*Z*)-Dodeca-3,6,9-trienoic acid (**1**) is the precursor for the whole family of $C_{11}H_{16}$ hydrocarbons, while (3*Z*,6*Z*)-dodeca-3,6-dienoic acid furnishes a series of $C_{11}H_{18}$ hydrocarbons. Although still unproven, it is reasonable to assume that the isostructural $C_{11}H_{14}$ pheromones derive from (3*Z*,6*Z*,9*Z*)-dodeca-3,6,9,11-tetraenoic acid in a similar fashion. Thus, each of these fatty-acid precursors is converted by the phytogenic enzymes into a variety of specific acyclic and alicylic olefins.

As depicted in *Scheme 1*, an enzyme-catalyzed loss of one of the two enantiotopic H-atoms of the CH_2 group at C(5) of (3*Z*,6*Z*,9*Z*)-dodeca-3,6,9-trienoic acid (**1**) yields acyclic undeca-1,3,5,8-tetraenes (*e.g.* finavarrene (**6**)), while the same reaction performed onto H–C(8) results in three different series of alicyclic hydrocarbons *via* cyclization and decarboxylation. Typical products are *trans*-1,2-disubstituted cyclopropanes (*e.g.* hormosirene (**3**)), 3,4-disubstituted cyclopentenes (*e.g.* multifidene (**4**)), and 6-alk(en)ylcyclohepta-1,4-dienes like *e.g.* ectocarpene (**5**). Each of these compound classes diversifies further into configurational isomers and, in some instances, enantiomeric mixtures [4]. If the enzymatic reaction affects one of the two enantiotopic H-atoms of the CH_2 group at

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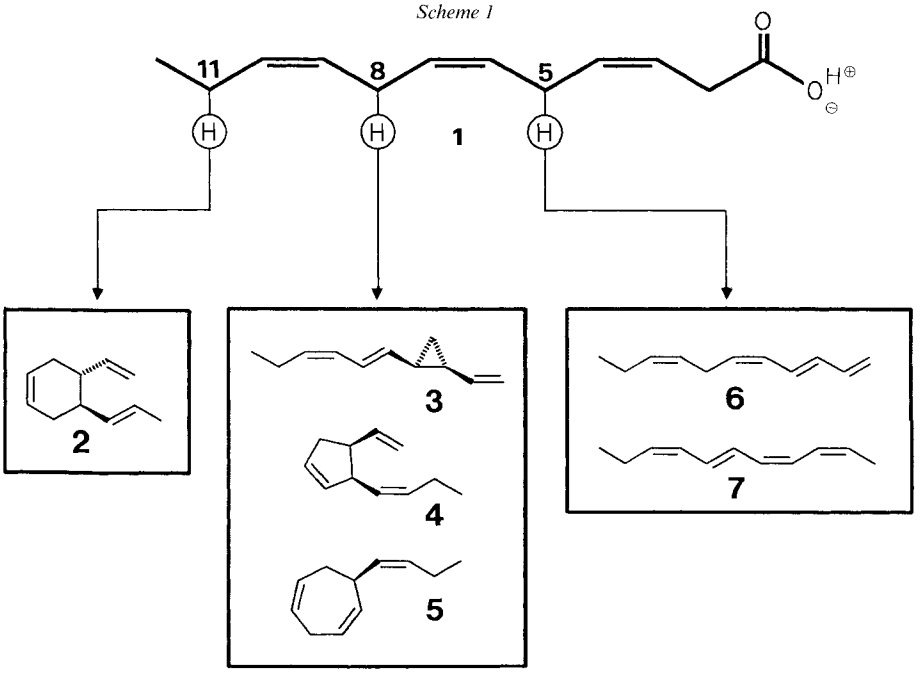
C(11) of **1**, 4,5-disubstituted cyclohexenes (*e.g.* aucantene (**2**)) arise by cyclization between C(9) and C(4) and decarboxylation. Thus, depending on the actual conformation of one and the same substrate at the active center of the enzyme in conjunction with the particular position of the involved CH_2 group, many constitutional isomers of the $C_{11}H_{16}$ hydrocarbons can be formed. Moreover, for each of the above mentioned precursor acids, as well as for epoxy acids derived from them, analogous product genealogies can be drawn. The overall strategy behind this biosynthetic pathway is a highly economic diversification of only a few precursors into a great number of bioactive compounds. In order to explore the biosynthetic potential of this important type of oxidative degradation of fatty acids, the hydrocarbon pattern of the marine brown alga *Cutleria multifida* was reanalyzed with particular emphasis on trace constituents and their possible biosynthetic interrelations to the major $C_{11}H_{16}$ hydrocarbons [5]. This plant offers the unique chance to look onto the whole spectrum of the fatty-acid transformations as shown in *Scheme 1*, since all compounds **2**–**7** are produced. We now report on the occurrence and structure elucidation of novel unsaturated cyclooctatriene and cyclooctadiene hydrocarbons which are obviously linked to the above biosynthetic pathways and which are hitherto not known as natural products.

Scheme 1



II. Isolation and Structure Elucidation. – Fertile male and female gametophytes of *Cutleria multifida* (SMITH) GREVILLE were collected in May 1987 in the harbour of Beaulieu, Côte d'Azur, France. The volatiles emitted from the living plants were entrapped on charcoal filters using air circulation in a closed system [2]. Desorption of the carbon filters (1.5 mg) with 30 µl of CH_2Cl_2 resulted in a solution containing *ca.* 5–10 µg

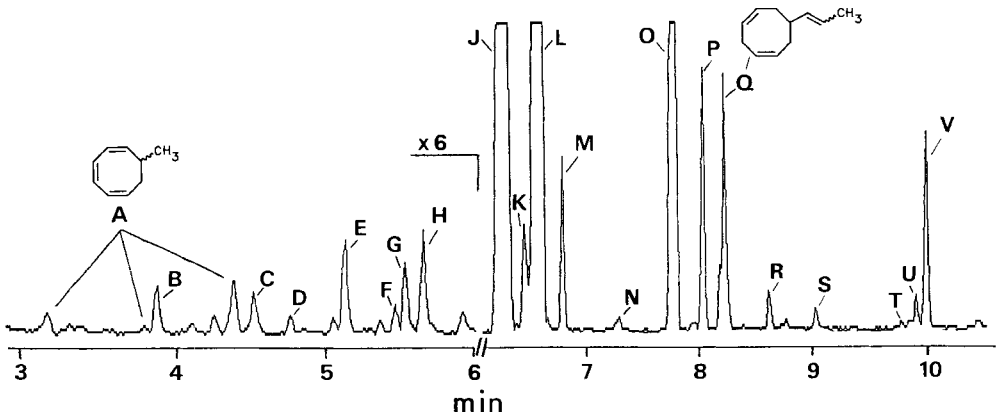
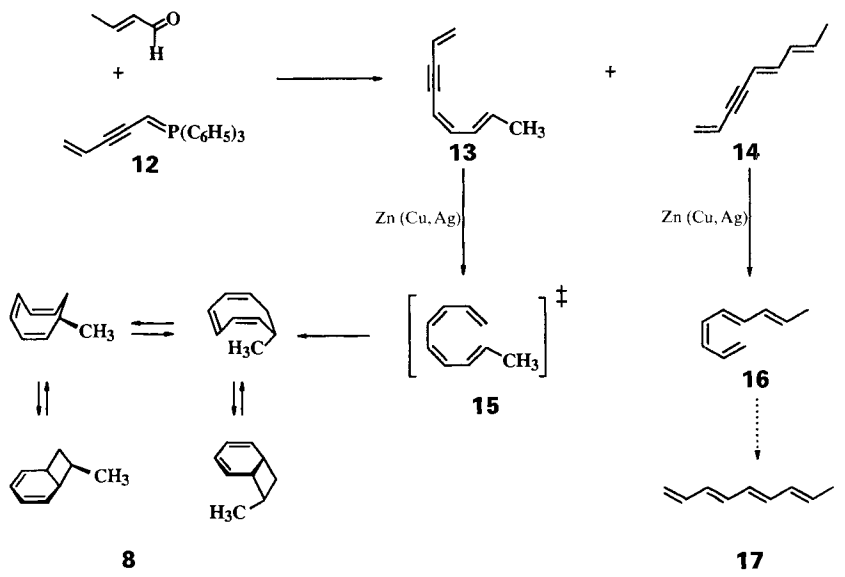


Fig. 1. *GLC Separation of the trapped volatiles from* Cutleria multifida. Conditions: fused-silica column *SE 30* (10 m × 0.32 mm); 40° isotherm for 2 min, then 10°/min to 250°; detector, *Finnigan* ion trap, *ITD 800*; transfer line at 270°; electron impact (70 eV); scan range 35–250 Dalton/s. Due to the very low concentration of the low-boiling compounds, the total ion current is enhanced by a factor of six in the range of 0–6 min. Identification of compounds: **A** = valence tautomers of 7-methylcycloocta-1,3,5-triene (**8**), **B** = 6-vinylcyclohepta-1,4-diene (**9**), **C** = C_9H_{12} (unknown), **D**, **F**, **G** = alkyl- and dialkylbenzenes, **E** = dichlorobenzene, **H** = *trans*-3-((1*Z*)-but-1-enyl)-4-vinylcyclopentene, **J** = (3*S*,4*S*)-3-((1*Z*)-but-1-enyl)-4-vinylcyclopentene (= (3*S*,4*S*)-multifidene; (3*S*,4*S*)-**4**), **K** = *cis*-3-butyl-4-vinylcyclopentene, **L** = (4*R*,5*R*)-4-((1*E*)-prop-1-enyl)-5-vinylcyclohexene (= (4*R*,5*R*)-aucantene; (4R,5*R*)-**2**), **M** = *rac-cis*-4-((1*E*)-prop-1-enyl)-5-vinylcyclohexene, **N** = $C_{11}H_{18}$, **O** = (6*S*)-((1*Z*)-but-1-enyl)cyclohepta-1,4-diene (= ectocarpene; **5**), **P** = 6-butylcyclohepta-1,4-diene (= dictyotene), **Q** = 7-((1*E*/*Z*)-prop-1-enyl)cycloocta-1,4-diene (**10**/**11**), **R**, **S** = $C_{11}H_{16}$ (unknown), **T**, **U** = $C_{11}H_{16}$ (isomers of giffordene (**7**)), **V** = (2*Z*,4*Z*,6*E*,8*Z*)-undeca-2,4,6,8-tetraene (= giffordene; **7**).

of the enriched volatiles per extract. Combined GLC/MS analysis (*Fig. 1*) shows the presence of three major and five minor compounds accompanied by a large number of trace constituents.

Most compounds of *Fig. 1* are readily identified with synthetic references, and their structures are given in the legend of *Fig. 1*. Compounds **A, B,** and **Q** are not identical with any of the hitherto known pheromones or their synthetic isomers. Three of the early eluting trace constituents (= **A**) display virtually identical MS showing M^+ at 120 (C_9H_{12}) and exhibit a characteristic base peak at *m/z* 78. Moreover, the relative peak areas of these compounds are not constant but vary depending on the temperature of the GLC inlet system. Such a behaviour is often indicative for thermal rearrangement. Considering the key fragment *m/z* 78 which is assumed to originate from fragmentative loss of propene yielding benzene, the basic skeleton could be an appropriately substituted cyclohexadiene. The C_3 moiety has to be connected to the ring in such a manner that *i*) thermal rearrangements are possible, and that *ii*) on electron impact, the cleavage of the whole molecule into the two neutral fragments propene and benzene is favoured. In combination of these settings and due to the lack of sufficient material for further spectral characterization, we decided to synthesize (*vide infra*) 7-methylcycloocta-1,3,5-triene (C_9H_{12}; **8**). This hydrocarbon has the correct elemental composition, exhibits a base peak at *m/z* 78, and it exists in a thermal equilibrium between mono and bicyclic '*syn*/*anti*'-isomers [6]. In fact, GLC and GLC/MS analysis confirm the identity of the synthetic reference **8** with the natural product(s). Furthermore, the relative peak areas of the

Scheme 2



'syn/anti'-7-methylbicyclo[4.2.0]hexa-1,4-dienes (*cf. Fig. 1* and *Scheme 2*) and the monocyclic *'syn/anti'*-7-methylcycloocta-1,3,5-trienes of the natural product and the synthetic reference as derived from cool on-column injection and separation at 40° are in complete coincidence.

The second unknown C_9H_{12} hydrocarbon **B** displays a mass fragmentation pattern similar to that of ectocarpene (**5**) or multifidene (**4**). Based on a synthetic reference (*vide infra*), the structure of this compound is readily established as 6-vinylcyclohepta-1,4-diene (**9**). This is the first report on the occurrence of a lower homologue of one of the alicyclic $C_{11}H_{16}$ hydrocarbons of *Scheme 1*.

The structure elucidation of the unknown $C_{11}H_{16}$ hydrocarbon **Q** is much more difficult. Due to the very low amount of material (*ca.* 50–100 ng per extract), further spectral characterization is, once more, excluded. The only fragment ion at *m/z* 107 (27%) which noticeably differs from the rather uniform MS of the other alicyclic $C_{11}H_{16}$ hydrocarbons may be indicative for the loss of a propenyl group from a ring system. This assumption is supported by hydrogenation of the total extract (PtO_2/H_2). Besides the (cyclo)alkanes derived from **2**, **4**, **5**, and the linear C_{11} polyenes, propylcyclooctane is found. Since the relative amount of this compound is comparable to that of **Q** in the extract, the latter could be a propenylcyclooctadiene. As the natural product reacts only sluggishly with 4-phenyltriazoline-3,5-dione, the presence of a conjugated diene system may be excluded in the first instance. Moreover, since the MS of **Q** does not show even-numbered fragments like *m/z* 54 and 94 (*cf. Fig. 2*) which would be indicative for a 1,5-cyclooctadiene *via* concerted elimination of butadiene, such an arrangement of the endocyclic double bonds can be *a priori* excluded. With respect to these findings and due to biosynthetic considerations (*vide infra*), the ring should be a cycloocta-1,4-diene, and an (1*Z*)-propenyl substituent should be linked to C(7) of the cycloalkene. The position of the double bond is supported by the MS data, since a terminally unsaturated C_3 sub-

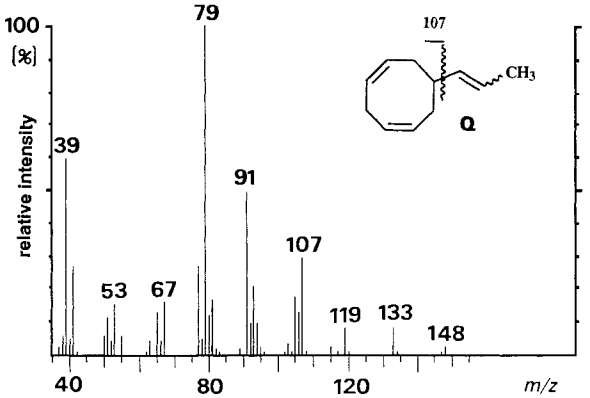
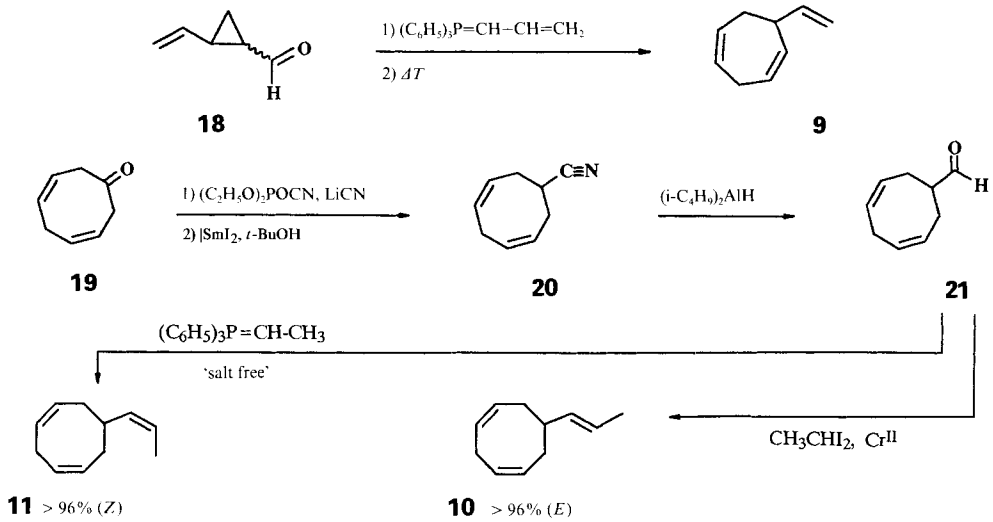


Fig. 2. *Mass spectrum of compound* **Q** (= *7-((1E/Z)-prop-1-enyl)cycloocta-1,4-diene* (**10/11**). Conditions: *Finnigan ITD 800*, see *Exper. Part.*

stituent would readily eliminate propene by β-cleavage leading to a cycloocta-1,3,5-triene radical cation (*m/z* 106) with rather high intensity. This is not the case (see *Fig. 2*). The positive identification is finally achieved by synthesis of some isomeric 6- and 7-((1*E*/*Z*)-prop-1-enyl)cycloocta-1,4-dienes. Out of the various reference substances, only 7-((1*E*)-prop-1-enyl)cycloocta-1,4-diene (**10**) and 7-((1*Z*)-prop-1-enyl)cycloocta-1,4-diene (**11**) match the MS and chromatographic data of the natural product **Q**. As a matter of fact, the (*E*/*Z*)-configuration of the side chain has to be left open, since the two stereoisomers cannot be resolved by GLC. Even, if long polar (50 m × 0.32 mm, *Carbowax*) or unpolar (50 m × 0.32 mm, *Se 30*) high resolution capillaries are employed, the compounds coelute with a perfect symmetrical peak shape. However, since the new hydrocarbon **Q** originates from the same biosynthetic pathway as aucantene (**2**), the (*E*)-configuration is most likely. With respect to the substitution and double-bond pattern, this hydrocarbon is a unique natural product which has no precedent or analogue. Except of 7-vinylcycloocta-1,4-diene, previously reported by *Brudermüller* and *Musso* [7], it is also an unnoticed structure in organic chemistry.

III. Reference Compounds: 7-Methylcycloocta-1,3,5-triene (8), 6-Vinylcyclohepta-1,4-diene (9), and 7-((1*E*)-Prop-1-enyl)- and 7-((1*Z*)-Prop-1-enyl)cycloocta-1,4-diene (10 and 11, resp.). – Although **8** is readily available from simple reagents as described by *Adam et al.* [6], we decided to follow a 'biomimetic' route. As outlined in *Scheme 1*, the algal pheromones are metabolites of unsaturated C_{12}-fatty acids. Thus, **8** could likewise originate from an acyclic precursor like (3*Z*,5*Z*,7*E*/*Z*)-nona-1,3,5,7-tetraene (**15**) *via* a conrotatory electrocyclic ring closure (*Scheme 2*). This interesting aspect prompted us to synthesize not only the postulated acyclic tetraene precursor **15** but also the (3*Z*,5*E*,7*E*)-isomer (**16**) for comparison with the *C. multifida* volatiles. Thus, *Wittig* reaction of (2*E*)-but-2-enal with the acetylenic phosphorane **12** [8] afforded the isomeric enynes **13** and **14** in roughly equal amounts (*Scheme 2*). Both compounds were separated by prep. GLC. Stereospecific reduction of (**13**) with Zn(Cu/Ag) in Me-OH at r.t. [9] gave **8**, which exists in an equilibrium between mono- and bicyclic '*syn*/*anti*'-isomers. Using the same reagent, (**14**) yielded the fairly stable (3*Z*,5*E*,7*E*)-nona-1,3,5,7-tetraene (**16**) which readily isomerized to the more stable (3*E*,5*E*,7*E*)-nona-1,3,5,7-tetraene (**17**). Compound **9** was obtained by *Wittig* reaction between *cis*/*trans*-2-vinylcyclopropanecarbaldehyde (**18**)

Scheme 3

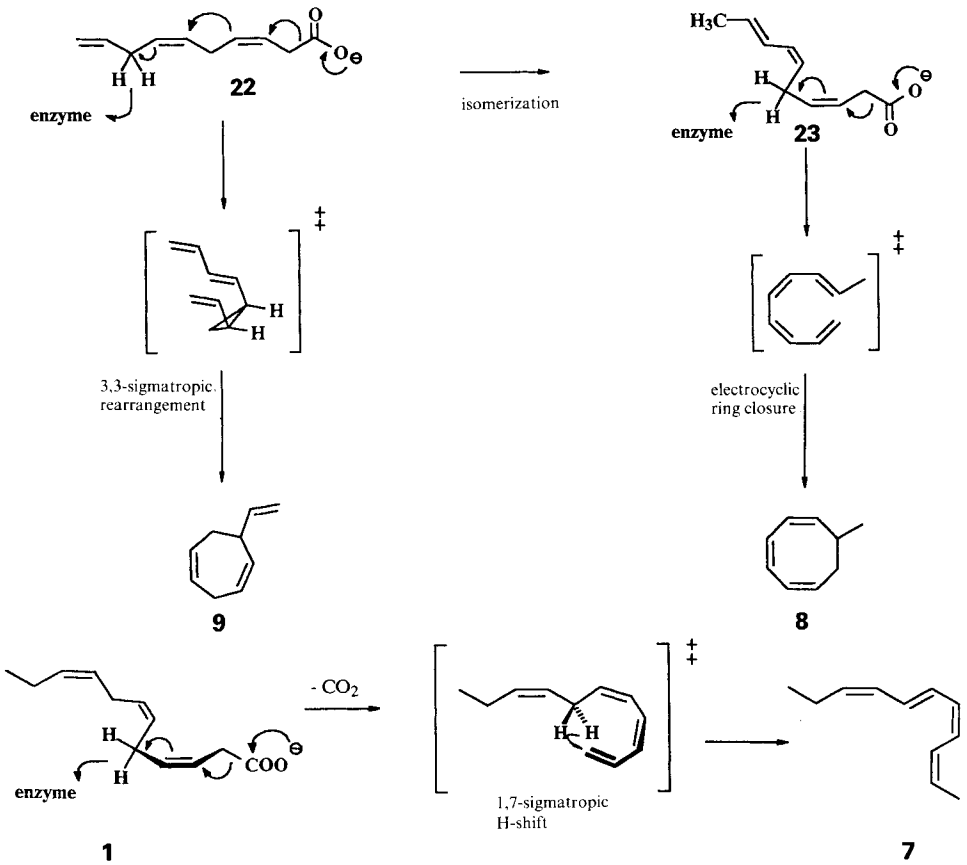


and (prop-2-enylidene)triphenylphosphorane and thermal rearrangement of the product during prep. GLC (*Scheme 3*) [10].

The synthesis of the 7-substituted 1,4-cyclooctadienes **10** and **11** was achieved starting from the known ketone **19** [11]. Treatment of **19** with diethyl phosphocyanidate and LiCN yielded an intermediary cyanohydrin *O,O*-diethyl phosphate which was directly reduced to nitrile **20** by addition of SmI_2/*t*-BuOH [12] (*Scheme 3*). Further reduction with diisobutylaluminium hydride afforded aldehyde **21** which could be elaborated to both isomers **10** and **11**. Thus, *Wittig* reaction of **21** with (ethylidene)triphenylphosphorane, generated under 'salt free' conditions, led mainly to the (*Z*)-olefine **11** (configurational purity $\geq 96\%$ (*Z*) by ^{13}C- and ^1H-NMR). The (*E*)-olefin **10** ($\geq 96\%$ *E*) was obtained from **21** using a bimetallic organochromium reagent, prepared *in situ* from Cr^{II} and 1,1-diiodoethane [13].

IV. Biosynthetic Considerations. – As surveyed in *Scheme 1*, the usual $C_{11}H_{16}$ hydrocarbons are metabolites of unsaturated C_{12} acids. Considering the pheromone of the fucales, namely (3*E*,5*Z*)-octa-1,3,5-triene, derived from (3*Z*,6*Z*)-nona-3,6-dienoic acid [3], together with the novel hydrocarbons described in this work, the number of potential precursors has to be extended to the entire range of unsaturated C_9- to C_{12}-fatty acids having double bonds in adequate positions. Since both of the two novel alicyclic hydrocarbons **8** and **9** are C_9 compounds, the assumption of a common C_{10}-precursor acid seems reasonable. In the case of 6-vinylcyclohepta-1,4-diene (**9**), we can rely on the well established biosynthesis of ectocarpene (**5**) in the flowering plant *Senecio isatideus* [3]. There, this hydrocarbon is formed from (3*Z*,6*Z*,9*Z*)-dodeca-3,6,9-trienoic acid (**1**) with loss of H_{Re}–C(8), cyclization between C(4) and C(6), and decarboxylation. The first product is a thermolabile *cis*-1-((1*E*,2*Z*)-hexa-1,2-dienyl)-2-vinylcyclopropane which at r.t. immediately rearranges to the stable valence isomer **5** [14]. Following this line, the logical precursor of **9** is (3*Z*,6*Z*)-deca-3,6,9-trienoic acid (**22**) as depicted in *Scheme 4*. All other steps are identical to those described for ectocarpene (**5**).

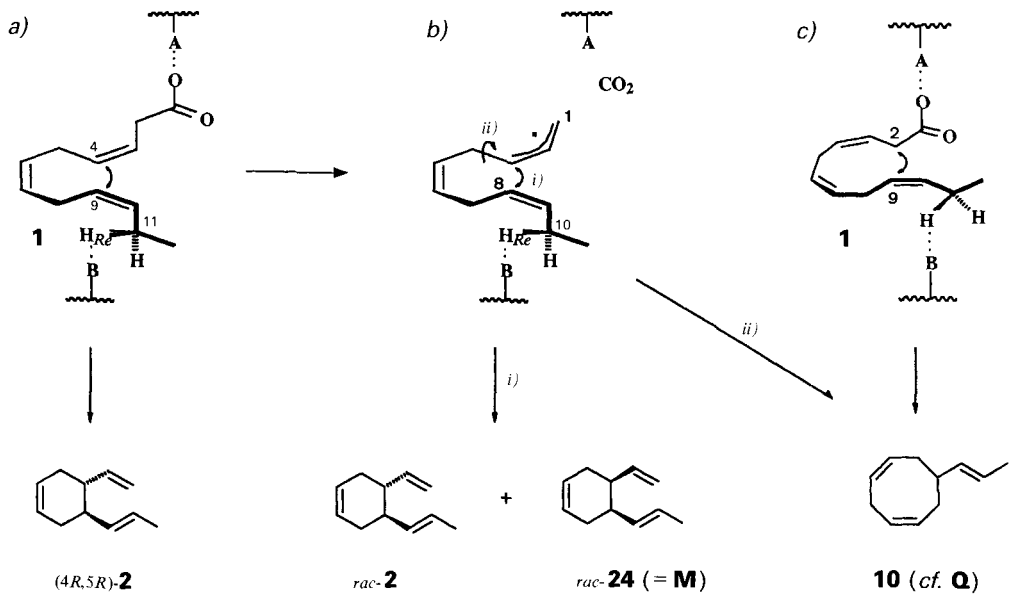
Scheme 4. *Suggestive Biosynthetic Pathways to 6-Vinylcyclohepta-1,4-diene* (**9**) *and 7-Methylcycloocta-1,3,5-triene* (**8**)



The same C_{10} acid may also serve as the ultimate precursor for 7-methylcycloocta-1,3,5-triene (**8**), if the isomeric (3*Z*,6*Z*,8*Z*/*E*)-deca-3,6,8-trienoic acid (**23**) is also present in the plant. Starting from **23**, the biosynthesis of **8** can be rationalized by analogy to that of giffordene (**7**) [15] (*Scheme 4*). Typical for all linear hydrocarbons is the loss of one of the two enantiotopic H-atoms from C(5) of the precursor acid, reorganization of the π-system, and decarboxylation. If acid **23** adopts the same conformation as acid **1** (see *Scheme 4*), the resulting olefin will be the (3*Z*,5*Z*,7*E*)-nona-1,3,5,7-tetraene (**15**). This compound is unstable and cyclizes immediately to an equilibrium mixture of '*syn*/*anti*'-isomers of 7-methylcycloocta-1,3,5-triene (**8**) and its bicyclic valence tautomer (*cf. Scheme 2*). Following this concept, the plant must not possess a great number of highly specialized enzymes, but instead some rare or uncommon precursor acids can be transformed by a limited set of enzymes into lower homologues of the anyhow present major or minor constituents. Due to the particular location and configuration of the double bonds in the intermediates, the subsequent electrocyclic ring closure or the 3,3-sigmatropic rearrangement are inevitable events, which, of course, need not to be catalyzed by enzymes.

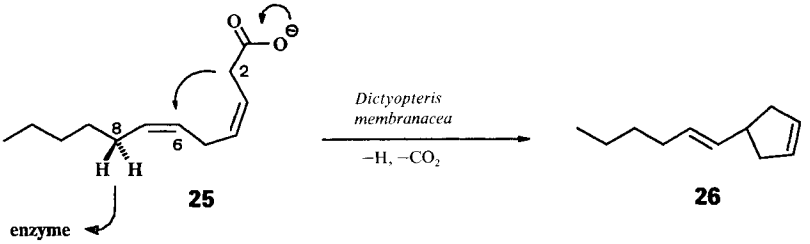
From a mechanistic point of view, the simultaneous occurrence of the cyclooctadiene **10**/**11** (= **Q**, *Fig. 1*) and the two 'aucantenes' **2** and **24** in the extracts of *Cutleria multifida* [5] is of great importance. With respect to (3*Z*,6*Z*,9*Z*)-dodeca-3,6,9-trienoic acid (**1**) both types of $C_{11}H_{16}$ hydrocarbons belong to the same category of fatty-acid transformation (*Scheme 1*; involvement of C(11)). In the case of the cyclooctadiene **Q**, the new σ-bond is formed between C(2) and C(9) of the precursor **1**, while the major product, (3*R*,4*R*)-aucantene ((3*R*,4*R*)-**2**) is consistent with an enzyme-catalyzed loss of H_{Re}–C(11), σ-bond formation between C(9) and C(4) of the acid, and decarboxylation [16] (*cf. Scheme 5*).

Scheme 5. *Biosynthesis of the 'Aucantenes' (4*R,5R*)-***2***, rac-***2***, rac-***24***, and of Compound* **Q**. *a*) Controlled transformation of **1** into (4*R*,5*R*)-**2**. *b*) After decarboxylation of **1**, the primarily generated radical may escape the control of the active center A of the enzyme. Random cyclization of the radical between C(1) and C(8) may be responsible for the production of *rac*-**24** and the small amount of *rac*-**2** [16] (*Path i*)). After rotation around C(3)–C(4), the allylic radical may effect σ-bond formation between C(1) and C(8) leading to **Q** (*Path ii*)). *c*) Controlled transformation of **1** into **Q**. Both pathways are indistinguishable on configurational grounds.



Up to here, this description reflects only the configurational implications of the fatty-acid transformations, but does not describe the sequence of events between the activation of the fatty acid and the termination of the sequence. Considering the new compound **10**, for the first time, far-reaching statements can be made. A formal 'hydride' mechanism (fatty-acid activation at a CH_2 group, followed by decarboxylation), which is implicitely used as a rationale for the biosynthesis of all previously known pheromones, can not adequately describe the origin of this compound. The fact that in **10** the new σ-bond develops between C(9) and C(2) of acid **1** strictly demands for the decarboxylation as the initializing step in a sequence of further reactions. Only if the acid first decarboxylates, the resulting mesomeric intermediate (radical?) can provide the required C(1)→C(8) interaction leading to the cyclooctadienyl framework **Q** (*Scheme 5b*, *Path ii*).

Scheme 6



In a final reaction, a H-atom (radical?) has to be transferred from C(10) of the intermediate to the enzyme. Note, that the same cyclization could be also the product of a diradical intermediate. This more detailed sequence of events cannot be deduced from the previously known pheromones since their particular connectivity pattern is consistent with both, the 'hydride' and the 'decarboxylation' approach.

The decarboxylation/cyclization sequence also matches the biosynthesis of **26** from (3*Z*,6*Z*)-dodeca-3,6-dienoic acid (**25**; *Scheme 6*). Cyclopentene **26** is found among the volatiles emitted by the Mediterranean phaeophyte *Dictyopteris membranacea* [17]. Once again, the peculiar C-framework of **26** can only arise, if the precursor acid **25** is first decarboxylated, yielding a mesomeric intermediate (radical?) which in turn executes the necessary C(2)→C(6) σ-bond formation. The termination may be achieved by transfer of a H-atom (radical?) from C(8) to the enzyme. Again, a diradical intermediate cannot be ignored.

However, the problem is even more complex as described by now. As already mentioned, the new cyclooctadiene **Q**, (4*R*,5*R*)-aucantene ((4*R*,5*R*)-**2**), and the *cis*-isomer **24** (compound **M** in *Fig. 1*) obviously belong to one and the same type of fatty-acid transformation as depicted in *Scheme 1* (involvement of C(11)). We have recently shown that **24** is racemic [16]. Such a finding is clearly not compatible with the usual course of an enzyme-catalyzed reaction. However, if we assume that the reactive intermediate escapes the control of the active center after decarboxylation (see *Scheme 5b*), small amounts of *rac*-**2** and of *cis*-isomer *rac*-**24** may be formed by random interaction between C(3) and C(8) of the decarboxylated fatty acid. After rotation around the C(3)–C(4)-bond, probably also the cyclooctadiene **Q** is nothing but the result of a random cyclization of the primarily generated allyl intermediate. Due to the symmetry of this molecule, no further information on the nature of this interaction (random or controlled) between C(1) and C(8) of the intermediate is available. Thus, at least at present, the above sequence of reactions, namely *1*) decarboxylation, *2*) σ-bond formation, and *3*) H-transfer, should be not generalized, since *rac*-**2** and **Q** may represent structures derived from an atypical mechanistic course, and there is the formation of other $C_{11}H_{16}$ hydrocarbons, *e.g.* multifidene (**4**), which is not compatible with this view.

If we summarize all hitherto known facets of algal pheromone biosynthesis, the following picture emerges: *i*) unsaturated C_9- to C_{12}-fatty acids are the precursors for the C_8 to C_{11} hydrocarbons of marine brown algae. *ii*) Each precursor acid can adopt a number of well defined, enzyme-induced conformations which in conjunction with the involved CH_2 group at C(5), C(8), or C(11) are responsible for individual product families. *iii*) In some instances, the developing mesomeric intermediates are insufficiently controlled by the active center of the enzymes and give rise to uncommon products at a

trace or minor-product level. Insufficient control may be also anticipated for the formation of uncommon (*E*/*Z*)-combinations of linear polyenes or the sometimes observed plant-specific mixtures of enantiomers [4]. *iv*) The plant-specific set of enzymes is probably limited to a few major types which also transform rare and uncommon fatty acids having at least two double bonds in adequate positions. *v*) Some of the primary products of the enzymes are unstable and undergo subsequent sigmatropic rearrangements or an electrocyclic ring closure. The biosynthesis of the most common pheromone type, namely the 6-alk(en)ylcyclohepta-1,4-dienes always proceeds *via* a 3,3-sigmatropic rearrangement of appropriately substituted cyclopropanes. In addition, the peculiar configuration of giffordene (**7**), which has to be formed from an intermediary (3*Z*,5*Z*,8*Z*)-undeca-1,3,5,8-tetraene, is obviously the result of an antarafacial 1,7-sigmatropic H-shift.

In summary, the new hydrocarbons found in the pheromone blend of the Mediterranean phaeophyte *Cutleria multifida* provide further insight into the sequence of reactions leading from free fatty acids to a series of highly bioactive messenger molecules. However, it still remains an open question whether or not decarboxylation is always the initiating step in algal pheromone biosynthesis. At least in the case of multifidene (**4**), the connectivity pattern requires a preceding activation of the CH_2 group at C(8) of **1**, followed by orbital overlap of the developing intermediate with the first double bond of the acid, and decarboxylation. Further work on this question, the nature of the intermediates involved (radicals or ions?), and the origin of plant-specific enantiomeric mixtures is necessary to understand this important biotransformation of fatty acids in detail.

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Experimental Part

General. Reactions are performed under Ar. Solvents and reagents are purified and dried prior to use. Anh. $MgSO_4$ is used for drying operations. Solns. are usually concentrated by flash evaporation under reduced pressure. Anal. GLC: *Carlo-Erba* gaschromatograph, *HRGC 5300*, *Mega* series, equipped with fused-silica capillaries, *SE30* (10 m × 0.31 mm); carrier gas, H_2 at 30 cm^3/s. Prep. GLC: *Varian 920*; stainless-steel column: 3 m × 6.5 mm, filled with *Chromosorb P AW/DMCS* treated, 80–100 mesh, coated with 20% *SE30*. IR (cm^{-1}): *Perkin-Elmer-882* IR spectrophotometer. ^{1}H-NMR (250 MHz or 400 MHz, $CDCl_3$, TMS as internal standard): *Bruker Cryospec WM 250* and *Bruker WM 400*, MS (*m*/*z*): *Finnigan MAT 90* GLC/MS system and *Finnigan ITD 800* combined with a *Carlo-Erba* gas chromatograph, model *Vega*, equipped with a fused-silica capillary *OV 101* (10 m × 0.32 mm); carrier gas, He at 30 cm^3/s; scan range: 35–249 Daltons/s.

(5E,7E)-Nona-1,3,5-triene-3-yne (**14**) *and (5Z,6E)-Nona-1,3,5-triene-3-yne* (**13**). To a chilled suspension of **12** (4.0 g, 9.8 mmol) in Et_2O (75 ml) is slowly added with stirring BuLi (4 ml, 9.8 mmol; 2.5M in hexane). After stirring for 30 min at 0°, (*E*)-but-2-enal (0.8 ml, 9.8 mmol) is added and stirring continued for 30 min. Then, the suspension is poured onto ice/HCl and the aq. phase extracted with Et_2O (3 × 30 ml). The org. layer is washed with brine, dried, and evaporated. The residue is purified by CC on silica gel (pentane): **13**/**14** (0.65 g, 56.2%). The separation is readily achieved by prep. GLC.

(5Z)-Isomer (**13**) (peak 1; *ca.* 43%): IR ($CDCl_3$): 3031, 2971, 2918, 2336, 2249, 1846, 1680, 1639, 1605, 1448, 1415, 1375, 1303, 1171, 1121, 982, 927, 818, 706. ^{1}H-NMR ($CDCl_3$, 400 MHz): 6.59–6.63 (*m*, H–C(7)); 6.35 (*t*, *J* = 10.8, H–C(6)); 5.96 (*ddd*, *J* = 8.8, 8.7, 2.3, H–C(2)); 5.87–5.94 (*m*, H–C(8)); 5.65 (*dd*, *J* = 15.5, 2.02, 1 H–C(1)); 5.48 (*dd*, *J* = 9.1, 2.03, 1 H–C(1)); 5.43 (br., *d*, *J* = 10.5, H–C(5)); 1.90 (*d*, 3 H–C(9)). ^{13}C-NMR ($CDCl_3$): 140.3 (C(6)); 133.8 (C(8)); 129.2 (C(7)); 126.2 (C(1)); 117.4 (C(2)); 106.3 (C(5)); 93.6 (C(4)); 87.5 (C(3)); 18.4 (C(9)). MS (70 eV): 118 (23, $M^{+\cdot}$), 117 (100), 116 (15), 115 (82), 103 (20), 102 (9), 91 (65), 89 (17), 86 (5), 78 (19), 77 (46), 74 (10), 65 (28), 63 (39), 51 (40), 39 (73). HR-MS: 118.0779 (C_9H_{10}, $M^{+\cdot}$, calc. 118.0782).

(5E)-Isomer (**14**) (peak 2: *ca.* 57%): IR ($CDCl_3$): 3705, 3160, 3030, 2916, 2337, 2254, 2182, 1793, 1639, 1610, 1471, 1381, 1290, 1214, 1189, 1165, 1096, 985, 914, 724, 651. ^{1}H-NMR ($CDCl_3$, 400 MHz): 6.56 (*dd*, J = 15.6, 4.8, H–C(6)); 6.08–6.15 (*m*, H–C(7)); 5.92 (*ddd*, J = 8.8, 8.5, 2.3, H–C(2)); 5.83 (*m*, H–C(8)); 5.59, 5.63 (*dd*, J = 15.4, 2.07, 1 H–C(1)); 5.57, 5.61 (*d*, J = 15.9, H–C(5)); 5.44 (*dd*, J = 9.05, 2.07, 1 H–C(1)); 1.75 (*d*, 3 H–C(9)). ^{13}C-NMR: 142.22 (C(6)); 132.91 (C(8)); 131.11 (C(7)); 126.10 (C(1)); 117.35 (C(2)); 108.38 (C(5)); 89.94 (C(4)); 89.79 (C(3)); 18.34 (C(9)). MS (70 eV): 118 (60, M^+), 117 (100), 116 (20), 115 (97), 103 (29), 102 (11), 91 (83), 89 (16), 86 (10), 84 (10), 78 (22), 77 (56), 65 (33), 63 (50), 51 (52), 44 (33), 39 (85). HR-MS: 118.0762 (C_9H_{10}, M^+, calc. 118.0782).

7-Methylcycloocta-1,3,5-triene and Its Valence Tautomers (**8**). As described [9], **13** (47 mg, 0.4 mmol) is reduced with freshly prepared Zn(Cu,Ag) in MeOH/H_2O 1:1 (5.0 ml). Following complete conversion (GLC control), the metal is removed by filtration, washed with MeOH (*ca.* 2 ml), and the products are extracted with pentane (3 × 10 ml). After drying, evaporation, and CC on silica gel (pentane), **8** (12 mg, 25%) is obtained as a colorless oil. GLC shows the presence of one major (60%) and two minor components (29 and 11%; *cf.* also *Fig. 1*). For IR, ^{1}H- and ^{13}C-NMR, see [6]. MS (70 eV, identical for all three isomers): 120 (5, M^+), 105 (25), 103 (9), 93 (5), 92 (20), 91 (33), 79 (23), 78 (100), 77 (26), 65 (11), 51 (20).

(3Z,5E,7E)-Nonatetra-1,3,5,7-ene (**16**). From **14** (68 mg, 0.58 mmol) and freshly prepared Zn(Cu,Zn) in MeOH/H_2O 1:1 (5 ml) as described above: **16** (20 mg, 29%). IR ($CHCl_3$): 3024, 2966, 1260, 1197, 1100, 1018, 794, 716, 664. ^{1}H-NMR (CD_2Cl_2, 400 MHz): 6.78–6.88 (*dt*, J = 10.4, 6.5, H–C(2)); 6.53–6.59 (*dd*, J = 10.5, 3.8, H–C(5)); 6.20–6.27 (*dd*, J = 14.4, 3.7, H–C(6)); 6.12–6.19 (*m*, H–C(7)); 5.93–6.04 (*quint. d*, J = 10.5, 0.9, H–C(3), H–C(4)); 5.75–5.83 (*sept.*, H–C(8)); 5.13 (*d*, J = 9.6, 1 H–C(1)); 5.22 (*dd*, J = 16.8, 1.9, 1 H–C(1)); 1.8 (*d*, 3 H–C(9)). ^{13}C-NMR (CD_2Cl_2): 134.72 (C(6)); 132.54 (C(2)); 131.99 (C(7)); 131.37 (C(8)); 130.45 (C(4)); 129.35 (C(3)); 125.62 (C(5)); 117.72 (C(1)); 18.40 (C(9)). MS (70 eV): 120 (65, M^+), 119 (5), 105 (98), 104 (9), 103 (22), 93 (18), 92 (23), 91 (100), 79 (62), 78 (42), 77 (49), 66 (8), 65 (23), 63 (16), 55 (16), 53 (12), 52 (11), 51 (27), 50 (22), 41 (20), 40 (8), 39 (86). HR-MS: 120.0922 (C_9H_{12}, M^+, calc. 120.0939).

6-Vinylcyclohepta-1,4-diene (**9**). A chilled and well stirred suspension of (allyl)triphenylphosphonium bromide (17.8 g, 46.5 mmol) in Et_2O (150 ml) is gradually treated with BuLi (18.6 ml, 46.5 mmol; 2.5M in hexane). After stirring for 30 min at 0°, **18** (3.0 g, 31 mmol) is added and stirring continued for 2.5 h. Then, the suspension is poured onto ice/HCl and the aq. phase extracted with Et_2O (4 × 100 ml). The org. layer is washed with brine, dried, and evaporated. The residue is purified by CC on silica gel (pentane): **19** *trans*-disubstituted intermediate (1.15 g, 31%; 84% purity). Final purification and rearrangement of the *trans*-disubstituted intermediate to **9** is achieved by prep. GLC (inject. port and detector cell: 200°). IR ($CDCl_3$): 3158, 3086, 3017, 2979, 2933, 2872, 1697, 1638, 1603, 1444, 1383, 1249, 1107, 993, 926, 871, 763, 646. ^{1}H-NMR ($CDCl_3$): 5.82–5.90 (*m*, 1 H–C(1′)); 5.69–5.76 (*m*, H–C(1), H–C(2)); 5.59–5.69 (*m*, H–C(5), H–C(4)); 5.01–5.06 (*dt*, J = 17.2, 1.5, 1 H–C(2′)); 4.96–4.99 (*dt*, J = 10.25, 1.2, 1 H–C(2′)); 3.12–3.17 (br. *s*, H–C(6)); 2.89–2.96 (*d*, J = 19, 1 H–C(3)); 2.73–2.81 (*d*, J = 19, 1 H–C(3)); 2.24–2.38 (*m*, 2 H–C(7)). ^{13}C-NMR ($CDCl_3$, 400 MHz): 142.05 (C(1′)); 133.69 (C(5)); 129.34 (C(2)); 129.02 (C(1)); 127.67 (C(4)); 113.34 (C(2′)); 41.54 (C(6)); 32.68 (C(7)); 28.32 (C(3)). MS (70 eV): 120 (3, M^+), 119 (3), 117 (3), 115 (5), 106 (3), 105 (40), 103 (12), 93 (5), 92 (30), 91 (85), 80 (7), 79 (100), 78 (40), 77 (64), 67 (7), 66 (70), 65 (32), 63 (15), 62 (7), 61 (5), 58 (4), 55 (7), 53 (13), 52 (11), 51 (29), 50 (18), 43 (4), 41 (21), 39 (93). HR-MS: 120.0923 (C_9H_{12}, M^+, calc. 120.0939).

Cycloocta-3,6-dienecarbonitrile (**20**). A soln. of cycloocta-3,6-dienone (**19**; 1.22 g, 10 mmol), diethyl phosphocyanidate (4.89 g, 30 mmol), and LiCN (989 mg, 30 mmol) in THF (200 ml) is stirred for 30 min at r.t. Following the addition of H_2O (400 ml), the mixture is extracted with AcOEt/hexane 1:1 (3 × 150 ml), and the combined org. layers are washed with brine (2 × 50 ml). After drying and evaporation, the crude residue is redissolved in THF (200 ml) containing *t*-BuOH (740 mg, 10 mmol). The soln. is added to a soln. of SmI_2 (30 mmol) in THF (300 ml) and stirring continued for 3 h at r.t. Then, 3N HCl (200 ml) is added and the product extracted with Et_2O (3 × 100 ml). The combined extracts are washed with 5% $Na_2S_2O_3$ soln. (100 ml), brine (2 × 50 ml), dried, and evaporated. CC (silica gel, hexane/Et_2O 12:1) yields 720 mg **20** (54%). Colorless oil. IR (film): 3024, 2945, 2874, 2819, 2239, 1646, 1454, 1421, 913, 733, 673. ^{1}H-NMR ($CDCl_3$, 250 MHz): 5.89 (br. *td*, J = 11.3, 5.4, H–C(4), H–C(6)); 5.50–5.38 (*m*, H–C(3), H–C(7)); 2.90 (*m*, 2 H–C(5)); 2.64–2.54 (*m*, H–C(1), 2 H–C(2), 2 H–C(8)). ^{13}C-NMR ($CDCl_3$, 400 MHz): 134.26 (C(4), C(6)); 124.55 (C(3), C(7)); 123.09 (CN); 30.63 (C(5)); 27.82 (C(2), C(8)); 26.14 (C(1)). MS (70 eV): 134 (4), 133 (56, M^+), 132 (69), 118 (53), 105 (41), 104 (36), 92 (32), 91 (84), 80 (40), 79 (100), 78 (38), 77 (47), 67 (17), 65 (21). HR-MS: 133.0842 ($C_9H_{11}N$, M^+, calc. 133.0891).

Cycloocta-3,6-dienecarbaldehyde (**21**). Diisobutylaluminiumhydride (1.43 ml, 8.0 mmol) is added slowly to a cold (−78°) soln. of **20** (532 mg, 4.0 mmol) in hexane (50 ml). Stirring is continued for 30 min at −78° and then for 5 h at r.t. MeOH (0.2 ml) is added and the mixture poured into a sat. NH_4Cl soln. (50 ml). Following acidification with 2N H_2SO_4 (20 ml), the org. layer is separated and the aq. phase extracted with Et_2O (3 × 50 ml). Neutralization

($NaHCO_3$) of the combined extracts, washing (sat. NaCl soln.), drying, and evaporation of the solvents leaves crude **21** which is purified by CC (silica gel, hexane/AcOEt 3:1): **21** (380 mg, 70%). Colorless, sourish smelling liquid. IR (film): 3020, 2957, 2931, 2873, 2817, 2715, 1726, 1664, 1647, 1453, 1111, 1075, 1038, 672. ^{1}H-NMR ($CDCl_3$, 250 MHz): 9.71 (*d*, J = 0.6, CHO); 5.77 (br. *dt*, J = 11.3, 5.3, H–C(4), H–C(6)); 5.46–5.41 (*m*, H–C(3), H–C(7)); 2.87 (*m*, 2 H–C(5)); 2.55–2.44 (*m*, H–C(1), 2 H–C(2), 2 H–C(8)). MS (70 eV): 136 (8, M^+), 135 (2), 117 (20), 108 (15), 105 (17), 93 (17), 91 (44), 80 (32), 79 (100), 77 (44), 67 (35), 65 (17). HR-MS: 136.0890 ($C_9H_{12}O$, M^+, calc. 136.0888).

7-((1Z)-Prop-1-enyl)cycloocta-1,4-diene (**11**). A freshly prepared soln. of (ethylidene)triphenylphosphorane (1.0 mmol; $NaNH_2$ as base) in benzene (5 ml) is added to a well stirred, cold (−78°) soln. of **21** (53 mg, 0.39 mmol) in THF (5 ml). The mixture is allowed to come to 0°, and after 1 h, 2N HCl (10 ml) is added. The org. layer is separated and the aq. phase extracted with pentane (3 × 20 ml). The combined org. phases are washed with H_2O and $NaHCO_3$. After drying and evaporation of the solvents, the residue is treated with cold pentane to precipitate the triphenylphosphine oxide. The filtrate is concentrated and the crude product purified by CC (silica gel, pentane). Due to losses during workup and evaporation of the solvents, 8 mg (14%) **11** are obtained. Colorless oil. IR (film): 3016, 2933, 2871, 2818, 1646, 1451, 909, 735, 669. ^{1}H-NMR ($CDCl_3$, 250 MHz): 5.77–5.69 (br. *dt*, J = 11.3, 5.4, H–C(2), H–C(4)); 5.51–5.27 (*m*, H–C(1), H–C(5), H–C(1′), H–C(2′)); 2.86 (*m*, 2 H–C(3)); 2.62–2.51 (*m*, H–C(7)); 2.40–2.30 (*m*, 1 H–C(6), 1 H–C(8)); 2.20–2.08 (*m*, 1 H–C(6), 1 H–C(8)); 1.64 (br. *d*, J = 5.1, 3 H–C(3′)). ^{13}C-NMR ($CDCl_3$, 400 MHz): 134.87 (C(1′)); 130.51 (C(2), C(4)); 127.05 (C(1), C(5)); 122.40 (C(2′)); 32.25 (C(7)); 30.24 (C(6), C(8)); 29.91 (C(3)); 12.84 (C(3′)). MS (70 eV): 148 (11, M^+), 133 (4), 119 (4), 107 (45), 106 (6), 105 (14), 94 (10), 93 (17), 92 (12), 91 (59), 80 (14), 79 (100), 78 (13), 77 (45), 67 (12), 65 (14). HR-MS: 148.1285 ($C_{11}H_{16}$, M^+, calc. 148.1252).

7-((1E)-Prop-1-enyl)cycloocta-1,4-diene (**10**). A soln. of **21** (56 mg, 0.41 mmol) and 1,1-diiodoethane (231 mg, 0.82 mmol) in THF (2 ml) is added to a well stirred suspension of anh. $CrCl_2$ (404 mg, 3.29 mmol) at r.t. After 15 h, the mixture is diluted with pentane (20 ml), poured into H_2O (40 ml), and extracted with pentane (3 × 20 ml). The combined extracts are successively washed with 10% $NaHSO_3$ soln. (20 ml) and H_2O (20 ml), dried, and evaporated. CC (silica gel) gives **10** along with some diiodoethane which is readily decomposed on stirring with 10% with aq. $AgNO_3$ soln. (30 ml) and pentane (30 ml) for 30 min. After filtration, the aq. phase is extracted with pentane (2 × 20 ml). The combined org. layers are dried and evaporated: **10** (7 mg, 12% due to losses during workup and solvent evaporation). Colorless oil. IR (film): 3018, 2935, 2875, 2734, 1646, 1451, 966, 909, 734, 674. ^{1}H-NMR ($CDCl_3$, 250 MHz): 5.74–5.66 (br. *dt*, J = 11.3, 5.4, H–C(2), H–C(4)); 5.50–5.38 (*m*, H–C(1), H–C(5), H–C(1′), H–C(2′)); 2.85 (*m*, 2 H–C(3)); 2.39–2.33 (*m*, 1 H–C(6), 1 H–C(8)); 2.21–2.11 (*m*, 1 H–C(6), H–C(7), 1 H–C(8)); 1.65 (br. *d*, J = 4.4, 3 H–C(3′)). ^{13}C-NMR ($CDCl_3$, 400 MHz): 135.59 (C(1′)); 130.23 (C(2), C(4)); 127.21 (C(1), C(5)); 123.17 (C(2′)); 37.46 (C(7)); 30.28 (C(6), C(8)); 29.91 (C(3)); 17.97 (C(3′)). MS (70 eV): 148 (10, M^+), 133 (4), 119 (4), 107 (46), 106 (7), 94 (13), 93 (19), 92 (13), 91 (61), 80 (14), 79 (100), 78 (14), 77 (45), 67 (11), 65 (14). HR-MS: 148.1255 ($C_{11}H_{16}$, M^+, calc. 148.1252).

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