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Dienediolates of Unsaturated Carboxylic Acids in Synthesis. Synthesis of Cyclohexenones and Polycyclic Ketones by Tandem Michael-Dieckmann Decarboxylative Annulation of Unsaturated Carboxylic Acids.

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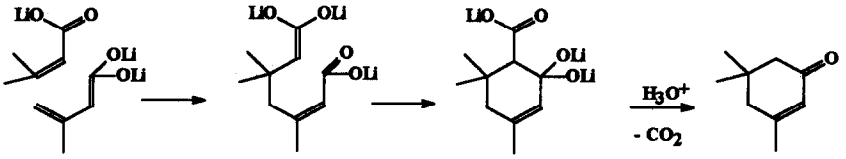
Abstract.- Substituted 2-cyclohexenones **4** to **7** and hexaxydronaphthalenones and hexahydroindenones **13** to **18** are prepared by tandem Michael-Dieckmann addition of lithium dienediolates of acyclic and alicyclic unsaturated carboxylic acids to the lithium salts of the same or other unsaturated carboxylic acids.

Substituted 2-cyclohexenones are important intermediates in organic synthesis. They are usually prepared by condensation reactions of carbonyl and β-dicarbonyl compounds [1]. Other general methods found in the recent Literature are based on reactions of conjugated ylidenephosphoranes with unsaturated ketones [2] or with ketone enolates [3], or on the Diels-Alder reaction of Danishefsky's diene [4] or vinylketene acetals [5]. Some substituted cyclohenenones have been prepared by carbanion additions to anisole chromium complexes [6]. New procedures which improve preparation of cyclohexenones from cyclohexanones have been recently described as well [7]. In contrast with the large array of annulation methods in hand for the synthesis of bicyclic 3-oxo-structures [8], methods for the synthesis of 2-oxo condensed polycyclic compounds are restricted to the photochemical addition of acetylacetone to cycloalkenes and subsequent aldol cyclization by de Mayo and Takeshita [9,10], and few recently described annulations of alicyclic ketones [11,12] or cycloalkenes [13].

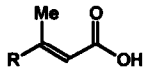
In former studies on the synthetic applications of lithium dienediolates of unsaturated carboxylic acids, isophorone **4a** was found as side product in a number of reactions which had in common the dienediolate of dimethylacrylic acid **1a** as reagent [11]. The most likely origin of this cyclohexenone was decarboxylation of the cyclic β-oxo acid resulting from a tandem addition-cyclization of the dienediolate of dimethylacrylic acid to the lithium salt of the same acid (Scheme 1). Indeed, when dimethylacrylic acid **1a** was deprotonized with 1.5 equivalents of LDE isophorone **4a** was isolated as a neutral compound from the acid fraction of the work-up mixture. The isolated yield for isophorone was not high (32%), but a better yield of 3-methyl-5-phenyl-2-

cyclohexenone **5e** was obtained (65%) when dimethylacrylic acid dienediolate was added to cinnamic acid lithium salt. The reaction could be regarded as a decarboxylative annulation of unsaturated carboxylic acids,

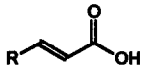


Scheme 1

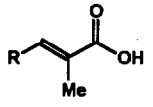
and its application could provide a simple method for the synthesis of some substituted mono- and poly-cyclic six member unsaturated ketones. This finding fostered the study of the scope of the reaction for both acyclic and alicyclic easily available unsaturated carboxylic acids **1** to **3** and **8** to **12**. Some of these acids have been allowed to react either as acceptors or as donors, and others only as acceptors. An account of part of this study has already been the object of a short communication [14].



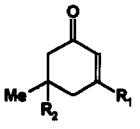
1a; R = Me
1b; R = Ph



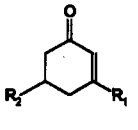
2a; R = Me
2b; R = Et
2c; R = Pr
2d; R = CH=CHMe
2e; R = Ph
2f; R = H



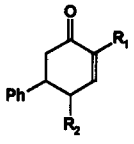
3a; R = Me
3b; R = H



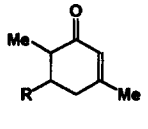
4a; $R_1 = R_2 = Me$
4b; $R_1 = Ph$; $R_2 = Me$
4c; $R_1 = R_2 = Ph$



5a; $R_1 = R_2 = Me$
5b; $R_1 = Me$; $R_2 = Et$
5c; $R_1 = Me$; $R_2 = Pr$
5d; $R_1 = Me$; $R_2 = CH=CHMe$
5e; $R_1 = Me$; $R_2 = Ph$
5f; $R_1 = Me$; $R_2 = H$
5g; $R_1 = Ph$; $R_2 = Me$
5h; $R_1 = Ph$; $R_2 = Et$
5i; $R_1 = Ph$; $R_2 = Pr$
5j; $R_1 = R_2 = Ph$



6a; $R_1 = R_2 = H$
6b; $R_1 = H$; $R_2 = Me$
6c; $R_1 = Me$; $R_2 = H$



7a; R = Me
7b; R = H

The results for the synthesis of substituted 2-cyclohexenones **4** to **7** and polycyclic ketones **13** to **19** are summarized in Tables I and II, respectively. Yields are given for rather standard conditions. Ionization of donor and acceptor acids has been carried out by up to 3 equivalents of LDE. The donor acid has been added first at -70°C, and after completion of its deprotonation at 0°C, the acceptor acid has been added at -70 °C.

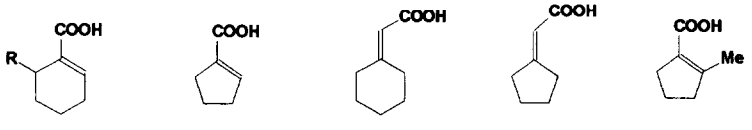
The resulting mixtures have then been allowed to react at room temperature for 2 to 20 h. Lower temperatures gave lower yields, and heating at 50°C has a deleterious effect, more complex mixtures being then obtained. On work-up the ketones have been obtained as neutral products from the acid fraction of the reaction mixture. The main acid constituents of these mixtures are the unreacted starting acids and their deconjugated isomers. Michael adducts have been generally observed only as minor components, except for addition of the dianion of methylcyclopentene carboxylic acid **12** to the cyclic acids **8** and **9**. Thus, the dianion of acid **12** failed to afford the tricyclic ketones **18b** and **19**, the Michael adducts **20b** and **21** being isolated and spectroscopically observed, respectively. The methylcyclopentenecarboxylic acid **12** and cyclohexenecarboxylic acid **8a** gave both expected Michael adduct **20a** and the ketone **18a**.

Table I. Synthesis of 2-Cyclohexenones

Donor Acid	Acceptor Acid	Ketone	Yield[a] (%)	Donor Acid	Acceptor Acid	Ketone	Yield[a] (%)
1a	**1a**	**4a**	32	**1a**	**3a**	**7a**	20[c]
1b	**1a**	**4b**	54	**1a**	**3b**	**7b**	0
1b	**1b**	**4c**	59	**1b**	**2a**	**5g**	24
1a	**2a**	**5a**	14[b]	**1b**	**2b**	**5h**	48
1a	**2b**	**5b**	41	**1b**	**2c**	**5i**	57
1a	**2c**	**5c**	42	**1b**	**2e**	**5j**	64
1a	**2d**	**5d**	38	**2a**	**2e**	**6a**	14[b]
1a	**2e**	**5e**	65	**2b**	**2e**	**6b**	11[c]
1a	**2f**	**5f**	0	**3a**	**2e**	**6c**	32[bc]

a.- Chromatographically and spectroscopically pure substance; b.- Not entirely pure compound; c.- Isolated as a *cis/trans* mixture.

Longer reaction times tend to enhance the amount of isophorone observed as side product whenever dimethylacrylic acid is used as either acceptor or donor acid. A similar behaviour has been found for β-methylcinnamic acid **1b**, and the self-condensation ketone **4c** has been obtained as minor component, along with the corresponding cyclohexenones **5**, on reaction with crotonic and pentenoic acids **2a** and **2b**. This feature shows that proton interchange between the dianion of the donor acid and the lithium salt of the

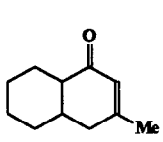


8a; R = H
8b; R = Me

9 **10** **11** **12**

acceptor acid or any other proton source is occurring, with the result of partial interchange between the acids in their roles as donors or acceptors. Proton interchange is probably as well the main side process responsible for low yields of runs where dimethylacrylic acid or other butenoic acids are employed as acceptors. Not

surprisingly, cinnamic acid is the best acceptor acid here examined. Unfortunately acrylic and methacrylic acids **2f** and **3b** did not afford the corresponding cyclohexenones when allowed to react as acceptors with dimethylacrylic acid. Only the unconjugated acid of the donor acid, isophorone, and occasionally polymeric materials were recovered.



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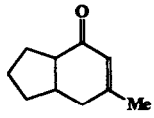

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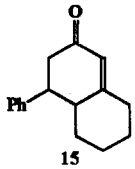

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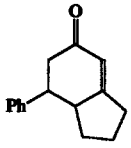

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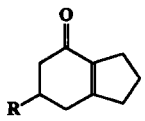
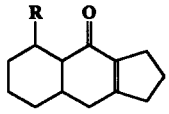
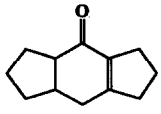


17a; R = Ph
17b; R = Et
17c; R = Pr



18a; R = H
18b; R = Me



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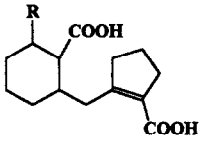

20a; R = H
20b; R = Me

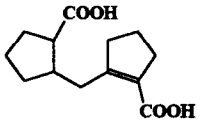

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Table II. Synthesis of Polycyclic Ketones

Donor Acid	Acceptor Acid	Ketone (%)	Yield[a]	Michael Adduct	Yield[a] (%)
1a	**8a**	**13**[b]	45		
1a	**9**	**14**[b]	29		
10	**2e**	**15**[b]	16		
11	**2e**	**16**	13		
12	**2e**	**17a**	60		
12	**2b**	**17b**	43		
12	**2c**	**17c**	43		
12	**8a**	**18a**[b]	45	**20a**	17
12	**8b**	**18b**	-	**20b**	31
12	**9**	**19**	-	**21**	40

a.- Chromatogrphically and spectroscopically pure substance; b.- Isolated as a *cis/trans* mixture; c.- Not isolated in pure form. Yield estimated spectroscopically.

The study of donor acids for the synthesis of monocyclic ketones has been almost restricted to

dimethylacrylic and β-methylcinnamic acids **1a** and **1b**. *Z*-Configuration for the Michael addition enolate intermediate resulting from γ-attack of the donor acid to the conjugated double bond of the acceptor acid is required in order to enable Dieckmann cyclization. It is well known that *Z*-configuration of γ-adducts is found on reaction of the lithium dianions of β-substituted acids **1** with electrophiles, in contrast with the *E*-γ-adducts usually obtained from dianions of unsaturated carboxylic acids **2**, with no second methyl substituent at the β-carbon [15,16]. The dienolates of acids **1a** and **1b** were expected then to lead to *Z*-Michael addition enolate intermediates, and hence to Dieckmann ketoacids, whereas crotonic and tiglic acids **2a** and **3a** should give *E*-Michael adducts, not ready for cyclization. This assumption has been confirmed, and some experiments with crotonic or tiglic acids **2a** and **3a** as donor acids and cinnamic acid as acceptor have led to the corresponding 5-phenylcyclohexenones **6** in low yields (14 and 32 %, respectively, of not entirely purified materials).

For polycyclic ketones best results are observed again for cinnamic acid **2e** as acceptor, and 2-methylcyclopentenyl carboxylic acid **12** as donor, observations which are in keeping with the above comments on proton interchange and configuration of the dianion. Poor yields found for additions of cyclohexylidene and cyclopentylidene acetic acids **10** and **11** to cinnamic acid were disappointing and discouraged further study on their addition to cyclic acids, which should lead to structures related to the steroid B-C-D rings.

Along the present discussion the reaction has been referred to as a tandem Michael-Dieckmann addition. An alternative Diels Alder cycloaddition mechanism might not seem unlikely when the dianions of the unsaturated carboxylic acids are formulated as dienediolates. Diels Alder cycloaddtitions of related vinylketeneacetals have been cited in the introduction of this study among the known procedures for synthesis of cyclohexenones [6], whereas vinylketene acetals afford dihydropyrans by cycloaddition to carbonyl groups [17] and cycloaddition of alkoxy substituted vinylketene acetals to quinones have recently been described [18]. However, a cycloaddition mechanism would not be consistent with isolation of Michael adducts. Furthermore, a Diels Alder cycloaddition should occur not only with the lithium salt of an unsaturated carboxylic acid, but also with other dienophiles, such as unsaturated ketones, esters or nitriles. However earlier findings showed that Michael addition of dienediolates of unsaturated carboxylic acids to enones occurs satisfactorily [19], and some experiments have shown now that additions to the unsaturated esters or nitriles fail, no Michael adducts or cyclic β-keto esters or nitriles being observed. Michael addition prevailed as well when the dianion of dimethylacrylic acid was allowed to react with a good dienophile as N-phenylmaleimide under the usual addition conditions. No other neutral product was obtained but isophorone. Practically all material was a highly insoluble acid, whose esterification led to an apparently polymeric material. Finally, the observation of stereoisomeric mixtures for ketones **13**, **14**, and **18a** is not indicative of a stereochemically unselective cyclization, as the ketones result from decarboxylation of a β-oxo carboxylic acids through enolic intermediates, but this is not the case for additions leading to the phenyl octalone **15** and the hexahydroindenone **16**. The first of them is obtained as a *cis/trans* mixture, whereas for the hexahydroindenone a single isomer has been isolated in pure form, but the presence of a second isomer in the crude mixture is not unlikely. The mechanism for these annulations most probably consists then of a Michael addition of the *s-cis* conformer of the dienediolate of the donor acid to the lithium salt of the acceptor acid, followed by cyclization by aldol like addition of the resulting enediolate to the lithium carboxylate, as shown in Scheme 1. The resulting trilithium derivative converts into the cyclic β-oxo carboxylic acid in the work-up, which decarboxylates when acidified.

As a conclusion, we think that the present decarboxylative annulation of unsaturated carboxylic acids provides a simple procedure for preparation of 3,5-disubstituted, and 3,5,5- trisubstituted cyclohexenones and 2-oxo-polycyclic ketones. Although yields are not high, starting materials are commercial or conveniently prepared by conventional or well described procedures, and the target ketones are easily isolated by a simple work-up and purified by common chromatographic methods.

EXPERIMENTAL PART

M.p.s were determined with a Reichert apparatus and are uncorrected. IR spectral data were obtained for liquid film or KBr discs, with a Perkin-Elmer 281 spectrophotometer. NMR spectra were recorded for $CDCl_3$ solutions, with a Bruker AC-200 spectrometer (200 MHz). Elemental analyses were determined by "Servicio de Semimicroanálisis del Centro de Investigación y Desarrollo (CSIC) de Barcelona". MS spectra were done by "Servicios Técnicos de la Universidad de Alicante" with a Hewlett-Packard 5988A Mass Spectrometer. Silica gel Merck 60 (0.06-0.20 mm) was used for column chromatography, and Silica gel Merck 60 (230-400 mesh) for flash column chromatography, with hexane/ether mixtures for elution. Tetrahydrofuran (THF) was distilled from blue sodium diphenylketyl immediately before use. Diethylamine was dried over CaH_2 and distilled before use. All reactions were carried out under an argon atmosphere, using standard conditions for exclusion of moisture. The reaction temperature (-70°C) was achieved by cooling with a CO_2/acetone bath. Evaporation of solvents was carried out with a vacuum rotatory evaporator and a bath at 40°C. Esterifications were performed by treatment of acids with diazomethane in ethyl ether or ethyl acetate.

Cyclohexylidene and cyclopentylidene acetic acids **10** and **11** have been prepared by addition of the lithium enediolate of acetic acid to cyclohexanone or cyclopentanone, and dehydration of the resulting hydroxy acids with cold conc sulfuric acid or acetic anhydride. Cyclohexene and cyclopentene carboxylic acids **8a**, **8b**, and **9** have been prepared through the cyanohydrins of the corresponding ketones, and dehydration with phosphorus oxychloride and hydrolysis with phosphoric acid. 2-Methyl-1-cyclopentene carboxylic acid **12** has been prepared by the method described by Harding and Clement [20]. Melting point values and spectroscopic data for all these starting acids are in agreement with those already described. Other starting compounds were purchased and used without purification.

Most monocyclic ketones **4** to **7** now prepared are well known compounds, and have been identified spectroscopically through their ^1H NMR spectra, and occasionally through their mp. Only recent references or recent references for less common compounds are given. Combustion analysis is given for new compounds, except for ketones which were obtained chromatographically (TLC) and spectroscopically pure (^1H and ^{13}C RMN spectra), but proved unstable.

General method.- Lithium diethylamide in THF was prepared as previously described [11] from lithium metal, naphthalene, and diethylamine in an ultrasonic bath, or from n-butyllithium and diethylamine.

The donor acid (9 mmol) in THF (12ml) was added dropwise to stirred lithium diethylamide (30 mmol) in THF (15 ml) at -70°C. The mixture was stirred at 0°C for 20 min cooled again at -70°C, and the acceptor acid (9 mmol) in THF (12 ml) added dropwise. The mixture was stirred at room temperature for the time stated in each case, and then poured into water (50 ml). The solvent was partly evaporated, and the residue

extracted with ether. The aqueous layer was acidified with conc hydrochloric acid at room temperature or under slight heating, and extracted with ethyl acetate. The combined organic layers were washed with aqueous sodium bicarbonate and then with brine to neutral pH, and dried. Evaporation of the solvent gave the crude ketone, which was purified by column chromatography, bulb to bulb distillation, and/or crystallization.

Isophorone, 4a.- Dimethylacrylic acid (1.8 g, 18 mmol) and lithium diethylamide (33 mmol) for 18 h at rt led to isophorone **4a** (0.40 g, 32 %) as a yellow oil; ν_{max} 1655 (C=O) and 1630 (C=C) cm^{-1}; δ_H 5.83 (1 H, s, C=CH), 2.15 (2 H, s, CH_2), 2.12 (2 H, s, CH_2), 1.89 (3 H, s, $C=CCH_3$) and 0.98 (6 H, s, 2 × CH_3).

5,5-Dimethyl-3-phenyl-2-cyclohexenone, 4b.- Addition of β-methylcinnamic acid (1.46 g, 9 mmol) to lithium diethylamide (33 mmol) and then of dimethylacrylic acid (0.90 g, 9 mmol), and 17 h at rt gave a mixture of the title ketone and isophorone, wich was resolved chromatographically to afford 5,5-dimethyl-3-phenyl-2-cyclohexenone **4b** as an oil (54 %); ν_{max} 1660 (C=O) and 1610 (C=C) cm^{-1}; δ_H 7.54-7.50 and 7.41-7.38 (5 H, 2 m, ArH), 6.40 (1 H, t, J 1.3 Hz, C=CH), 2.64 (2 H, d, J 1.3 Hz, C^4H_2), 2.33 (2 H, s, C^6H_2) and 1.11 (6 H, s, 2 × CH_3).

3,5-Diphenyl-5-methyl-2-cyclohexenone, 4c.- β-Methylcinnamic acid (2.92 g, 18 mmol) and lithium diethylamide (33 mmol) for 18 h and work-up gave the title ketone **4c** as a yellow oil (1.40 g, 59 %); ν_{max} 3040 (ArH), 1655 (C=O),1570, 1490 and 1450 (Ar); δ_H 7.55-7.26 (10 H, m, ArH), 6.38 (1 H, s, C=CH), 3.29 (1 H, d, J 17.6 Hz, CH), 3.03 (1 H, d, J 16.1 Hz, CH), 2.99 (1 H, d, J 17.6 Hz, CH), 2.69 (1 H, d, J 16.1 Hz, CH) and 1.46 (3 H, s, CH_3). Found: C, 86.76; H, 7.10 %. Calcd. for $C_{19}H_{18}O$: C, 86.99; H, 6.91 %.

3,5-Dimethyl-2-cyclohexenone, 5a.- When dimethylacrylic acid (0.90 g, 9 mmol) and crotonic acid (0.77g, 9 mmol) were added to lithium diethylamide (33 mmol) according to the general method, and the mixture allowed to react for 4 h at rt, a (84/16) mixture of the title ketone **5a** and isophorone was obtained. The first of them was isolated chromatographically as a colourless oil (0.16 g, 14 %); ν_{max} 1665 (C=O) and 1630 (C=C) cm^{-1}; δ_H 5.84 (1 H, s, C=CH), 2.45-1.97 (5 H, m, 2 × CH_2, CH), 1.93 (3 H, s, $C=CCH_3$) and 1.04 (3 H, d, J 6.0 Hz, CH_3).

5-Ethyl-3-methyl-2-cyclohexenone, 5b.- Addition in the stated order according to the general method of dimethylacrylic acid (0.90 g, 9 mmol) and 2-pentenoic acid **2b** (0.90 g, 9 mmol) and reaction for 19 h at rt gave a (86/14) mixture of ketone **5b** and isophorone. Chromatography allowed isolation of the former ketone as a colourless oil (0.51 g, 41 %); ν_{max} 3030 (C=CH), 1665 (C=O) and 1630 (C=C) cm^{-1}; δ_H 5.84 (1 H, s, C=CH), 2.46-1.90 (5 H, m, 2 x CH_2, CH), 1.93 (3 H, s, $C=CCH_3$), 1.38 (2 H, m, CH_2) and 0.90 (3 H, t, J 7.4 Hz, CH_3) [21].

3-Methyl-5-propyl-2-cyclohexenone, 5c.- Similarly as above, dimethylacrylic acid and 2-hexenoic acid **2c** on reaction for 2 h at rt and usual work-up gave the title ketone **5c** as a yellow oil (0.58 g, 42 %); ν_{max} 3030 (C=CH), 1665 (C=O) and 1630 (C=C) cm^{-1}; δ_H 5.82 (1 H, s, C=CH), 2.45-2.20 (2 H, m), 2.05-1.90 (3 H, m), 1.91 (3 H, s, $C=CCH_3$), 1.35-1.28 (4 H, m, CH_2CH_2) and 0.90-0.84 (3 H, m, CH_3) [22].

3-Methyl-5-(1-propenyl)-2-cyclohexenone, 5d.- Dimethylacrylic acid (0.60 g, 6 mmol) on reaction with sorbic acid (0.67 g, 6 mmol) for 4 h at rt and after usual work-up and chromatography gave the ketone **5d** (0.34g, 38 %) as a colourless oil; ν_{max} 3025 (C=CH), 1660 (C=O) and 1630 (C=C) cm^{-1}; δ_H 5.84 (1 H, s, C=CH), 5.55-5.31 (2 H, m, CH=CH), 2.78-2.59 (1 H, m, CH), 2.48-2.05 (4 H, m, 2 x CH_2), 1.92 (3 H, s, $C=CCH_3$) and 1.63 (3 H, d, J 5.1 Hz, $CH\underline{CH_3}$); *m/z* (rel intensity, %) 150.2 (M^+, 15), 94.15 (9), 93.15 (19), 82.15 (100), 67.15 (9), 54.0 (15) and 41.05 (11).

3-Methyl-5-phenyl-2-cyclohexenone, 5e.- Dimethylacrylic acid (0.90 g, 9 mmol) and cinnamic acid (1.33 g, 9 mmol) on reaction for 2 h at rt, usual work-up and chromatography gave cyclohexenone **5e** as a yellow oil (1.09 g, 65 %); ν_{max} 3020 (C=CH), 1650 (C=O) and 1630 (C=C); δ_H 7.35-7.21 (5 H, m, ArH), 5.97 (1 H, s, C=CH), 3.40-3.23 (1 H, m, C^5H), 2.70-2.46 (4 H, m, 2 x CH_2) and 1.99 (3 H, s, CH_3).

5-Methyl-3-phenyl-2-cyclohexenone, 5g.- β-Phenylcinnamic (1.46 g, 9 mmol) and crotonic acid (0.77 g, 9 mmol) were allowed to react according to the general method for 17 h at rt. A (70/30) mixture of the title ketone and 3,5-diphenyl-5-methyl-2-cyclohexenone **4c** was obtained, which on chromatography allowed isolation of the former ketone **5g** (0.40 g, 24 %); ν_{max} 3060 (ArH and C=CH) and 1660 (C=O) cm^{-1}; δ_H 7.58-7.48 and 7.42-7.37 (5 H, m, ArH), 6.40 (1 H, s, C=CH), 2.82 (1 H, m), 2.58-2.08 (4 H, m, 2 x CH_2) and 1.16 (3 H, d, J 5.8 Hz, CH_3)[3].

5-Ethyl-3-phenyl-2-cyclohexenone, 5h.- β-Phenylcinnamic acid (1.46 g, 9 mmol) and 2-pentenoic acid (0.90 g, 9 mmol) were allowed to react for 18 h at rt. Usual work-up gave a (90/10) mixture of the title ketone **5h** and 3,5-diphenyl-5-methyl-2-cyclohexenone **4c**, which on chromatography allowed isolation of 5-ethyl-3-phenyl-2-cyclohexenone **5h** as a yellow oil (0.87 g, 48 %); ν_{max} 3060 (ArH and C=CH), 1660 (C=O) and 1610 (C=C) cm^{-1}; δ_H 7.55-7.35 (5 H, m, ArH), 6.40 (1 H, d, J 2.2 Hz, C=CH), 2.85 (1 H, m), 2.64-2.40 (2 H, m), 2.23-2.09 (2 H, m), 1.50 (2 H, m, CH_2) and 0.98 (3 H, t, J 7.4 Hz, CH_3); *m/z* (rel intensity, %) 200.3 (M^+, 39), 171.2 (16), 144.2 (100), 143.2 (25), 116.15 (34), 115.25 (60), 91.15 (9), 77.15 (9) and 51.0 (10).

3-Phenyl-5-propyl-2-cyclohexenone, 5i.- β-Phenylcinnamic acid (1.46 g, 9 mmol) and 2-hexenoic acid (1.03 g, 9 mmol) on reaction for 19 h at rt, usual work-up, chromatography, and bulb to bulb distillation led to cyclohexenone **5i** as a yellow oil (1.10 g, 57 %); ν_{max} 3040 (ArH and C=CH), 1650 (C=O) and 1620 (C=C) cm^{-1};δ_H 7.55-7.00 (5 H, m, ArH), 6.40 (1 H, d, J 1.9 Hz, C=CH), 2.85 (1 H, m), 2.62-2.39 (2 H, m), 2.21-2.12 (2 H, m), 1.50-1.35 (4 H, m, CH_2CH_2) and 0.93 (3 H, t, J 6.9 Hz, CH_3). Found: C, 83.59; H, 8.53 %. Calcd. for $C_{15}H_{18}O$: C, 84.07; H, 8.47 %.

3,5-Diphenyl-2-cyclohexenone, 5j.- β-Phenylcinnamic acid (1.46 g, 9 mmol) and cinnamic acid (1.33 g, 9 mmol) were allowed to react for 2 h at rt. Work-up led to crude ketone (1.43 g, 64 %), which afforded 3,5-diphenyl-2-cyclohexenone **5j** as white prisms (*hexane-ether*) (1.03 g, 46 %), m.p. 83-84.5 °C [lit.[2] m.p. 85°C]; ν_{max} 3060 (ArH, C=CH), 1660 (C=O) and 1640 (C=C) cm^{-1}; δ_H 7.57-7.27 (10 H, m, 2 x C_6H_5), 6.51 (1 H, d, J 2.0 Hz, C=CH), 3.54-3.38 (1 H, m, C^5H), 3.10-2.80 (2 H, m, C^4H_2) and 2.80-2.65 (2 H, m, C^6H_2).

5-Phenyl-2-cyclohexenone, 6a.- Crotonic acid (0.77 g, 9 mmol) and cinnamic acid (1.33 g, 9 mmol)

when allowed to react for 21 h at rt gave a crude oil (0.5 g), which was purified chromatographically to a yellow oil (0.214 g, 14 %) of 5-phenyl-2-cyclohexenone **6a**; ν_{max} 1675 (C=O) and 1630 (C=C) cm^{-1}; δ_H 7.38-7.32 and 7.28-7.24 (5 H, m, ArH), 7.06 (1 H, ddd, J 10.2, 5.6 and 2.7 Hz, $C=C^3H$), 6.13 (1 H, m, $C=C^2H$), 3.35 (1 H, m, C^5H) and 2.75-2.48 (4 H, m, 2 x CH_2) [23].

5-Phenyl-4-methyl-2-cyclohexenone, 6b.- 2-Pentenoic acid (0.90 g, 9 mmol) and cinnamic acid (1.33 g, 9 mmol) for 15 h at rt under the usual reaction conditions led to an oil (0.19 g, 11 %) of crude (>85 %) cyclohexenone **6b**; ν_{max} 3020 (ArH and C=CH), 1675 (C=O), 1600, 1490 cm^{-1}; δ_H 7.19-7.02 (6 H, m, ArH and $C=C^3H$), 6.06 (1 H, d, J 10 Hz, $C=C^2H$), 3.57 (1 H, dt, J 14 and 5 Hz, C^5H), 2.98-2.52 (3 H, m) and 0.82 (3 H, d, J 7.2 Hz, CH_3).

5-Phenyl-2-methyl-2-cyclohexenone, 6c.- When tiglic acid **3a** (0.90 g, 9 mmol) and cinnamic acid (1.33 g, 9 mmol) were allowed to react as above for 14 h at rt, a yellow oil (0.89 g) was obtained, which on chromatography gave the title ketone **6c** (0.54 g, 32 %); ν_{max} 1670 (C=O) and 1635 (C=C) cm^{-1}; δ_H 7.37-7.20 (5 H, m, ArH), 6.78 (1 H, m, C=CH), 3.40-3.24 (1 H, m, C^5H), 2.79-2.62 (2 H, m), 2.60-2.48 (2 H, m) and 1.82 (3 H, m, CH_3) [24].

3,5,6-Trimethyl-2-cyclohexenone, 7a.- Dimethylacrylic acid **1a** (0.90 g, 9 mmol) on reaction with tiglic acid **3a** (0.90 g, 9 mmol) for 15 h at rt gave a (70/30) mixture of the title ketone **7a** and isophorone. Chromatography allowed isolation of a cis/trans mixture (aprox. 1:1) of 3,5,6-trimethyl-2-cyclohexenone **7a** as a yellow oil (0.25 g, 20 %); ν_{max} 3020 (C=CH), 1660 (C=O) and 1630 (C=C) cm^{-1}; δ_H 5.82 (1 H, s, C=CH), 5.79 (1 H, s, C=CH), 2.40-1.72 (8 H, m), 1.90 (6 H, s, 2 x $C=CCH_3$), 1.11 (3 H, d, J 6.4 Hz, CH_3), 1.05 (3 H, d, J 6.2 Hz, CH_3), 1.00 (3 H, d, J 7.2 Hz, CH_3) and 0.92 (3 H, J 6.6 Hz, CH_3) [25].

3-Methyl-4a,5,6,7,8a-hexahydro-1(4H)-naphthalenone, 13.- Dimethylacrylic acid (0.50 g, 5 mmol) **1a**, and 1-cyclohexenecarboxylic acid (0.63 g, 5 mmol) **8a** were allowed to react for 4 h according to the general method, affording a yellow crude oil, which was purified chromatographically, and a diastereoisomeric mixture of the title compound was obtained as a colourless oil (0.37 g, 45%)[8,9]. New chromatography allowed isolation of two diastereoisomers.

Polar isomer: colourless oil; ν_{max} 1660 (C=O) and 1635 (C=C) cm^{-1}; δ_H 5.81 (1 H, s, C=CH), 2.40-2.32 (1 H, m), 2.27 (2 H, s), 1.92 (3 H, s) and 1.89-1.20 (9 H, m).

Less polar isomer: colourless oil; ν_{max} 1660 (C=O) and 1630 (C=C) cm^{-1}; δ_H 5.83 (1 H, s, C=CH), 2.29-2.21 (1 H, m), 2.20 (1 H, dd, J 18.2 and 4.6 Hz, C^4H), 2.09 (1 H, ddq, J 18.2, 10.4 and 1.2 Hz, C^4H), 1.91 (3 H, s, CH_3), 1.87-1.65 (6 H, m, $C^{8a}H$, $C^{4a}H$, and 4 H) and 1.27-1.02 (3 H, m); δ_C(apt) 201.2 (C^1), 160.6 (C^3), 126.2 (C^2H), 49.9 ($C^{8a}H$), 39.8 ($C^{4a}H$), 39.0 (CH_2), 33.5 (CH_2), 25.7 (CH_2), 25.6 (CH_2), 25.5 (CH_2) and 24.2 (C^9H_3).

6-Methyl-1,2,3,3a,7,7a-hexahydro-4H-inden-4-one, 14.- Dimethylacrylic acid **1a** (0.50 g, 5 mmol) and 1-cyclopentenecarboxilic acid **9** (0.56 g, 5 mmol) for 4 h as above gave an orange crude oil (0.26 g). Chromatographic purification allowed isolation of a stereoisomeric mixture of the hexahidroindenone **14** as a pale yellow oil (0.22 g, 29 %) [9]; which was resolved into samples of *cis* and *trans* isomers; ν_{max} 1655 (C=O) and 1630 (C=C) cm^{-1};

Less polar isomer: δ_H 5.82 (1 H, s, C=CH), 2.46 (1 H, dd, J 17.7 and 3.9 Hz), 2.20-2.03 (2 H, m), 1.94 (3 H, s), 1.95-1.57 (6 H, m) and 1.42-1.26 (1 H, m); δ_C(apt) 201.6 (C^4), 161.6 (C^6), 127.0 (C^5H), 53.9 ($C^{3a}H$), 44.3 ($C^{7a}H$), 38.4 (CH_2) 31.4 (CH_2), 24.1 (CH_3), 23.1 (CH_2) and 22.0 (CH_2).

Polar isomer: δ_H 5.83 (1 H, s, C=CH), 2.58-2.37 (2 H, m), 2.17 (1 H, dd, J 18.5 and 3.6 Hz), 2.10-1.52 (9 H, m) and 1.50-1.37 (1 H, m); δ_C(apt) 201.8 (C^4), 160.0 (C^6), 125.3 (C^5H), 48.6 ($C^{3a}H$), 38.6 ($C^{7a}H$), 32.8 (CH_2), 31.0 (CH_2), 27.9 (CH_2), 24.6 (C^8H_3) and 22.8 (CH_2).

4-Phenyl-4,4a,5,6,7,8-hexahydro-2(3H)-naphthalenone, 15.- Cyclohexylideneacetic acid **10** (1.05 g, 7.5 mmol) and cinnamic acid (1,11 g, 7.5 mmol) on reaction for 5 h and work-up according to the general method gave an orange oil (0.68 g), which was purified by column chromatography to obtain a mixture of two diastereoisomers of the title hexahydronaphthalenone as a colourless oil (0.27 g, 16%) which solidified, m.p. 45-70°C (lit [26], m.p. 61-63°C for one of the isomers); ν_{max} 3020 (ArH and C=CH), 1665 (C=O) and 1625 (C=C) cm^{-1}; δ_H 7.36-7.15 (5 H, m, ArH), 5.93 (1 H, s, C=CH), 3.54 (1 H, dt, J 14.7 and 4.7 Hz), 2.95-2.15 (6 H, m) and 1.85-1.10 (5 H, m); δ_C 199.7 ($1C_A$), 199.1 ($1C_B$), 170.0 ($1C_A$), 166.1 ($1C_B$), 142.5 ($1C_B$), 141.2 ($1C_A$), 128.7-122.4 ($6C_A$+$6C_B$), 47.6 ($1C_B$), 45.5 ($1C_A$), 44.8 ($1C_B$), 43.9 ($1C_B$), 42.2 ($1C_A$), 37.6 ($1C_A$), 37.2 ($1C_A$), 35.6 ($1C_B$), 32.3 ($1C_B$), 30.2 ($1C_A$), 28.8 ($1C_A$), 26.5 ($1C_B$), 26.1 ($1C_A$) and 25.4 ($1C_B$).

7-Phenyl-1,2,3,6,7,7a-hexahydro-5H-inden-5-one, 16.- On reaction for 3 h, cyclopentylideneacetic acid **11** (0.35 g, 2.8 mmol) and cinnamic acid (0.42 g, 2.8 mmol) led to apparently a single diastereoisomer of the title hexahydroindenone **16** (0.076 g, 13 %) as a colourless oil; ν_{max} 3025 (Ar-H and C=CH), 1655 (C=O) and 1635 (C=C) cm^{-1}; δ_H 7.36-7.32 and 7.28-7.22 (5 H, m, ArH), 6.00 (1 H, m, C=CH), 2.99-2.92 (1 H, m), 2.83-2.51 (5 H, m) and 1.92-1.19 (4 H, m); δ_C 199.3 (1C), 174.3 (1C), 142.6 (1C), 128.7 (3C), 127.0 (2C), 122.4 (1C), 49.3 (1C), 48.2 (1C), 45.2 (1C), 32.0 (1C), 31.3 (1C) and 23.4 (1C). Found: C, 84.61; H, 7.80 %. Calcd. for $C_{15}H_{16}O$: C, 84.87; H, 7.60 %.

6-Phenyl-1,2,3,5,6,7-hexahydro-4H-inden-4-one, 17a.- 2-Methyl-1-cyclopentenecarboxylic acid **12** (0.70 g, 5.5. mmol) and cinnamic acid (0.81 g, 5.5 mmol) for 4 h, and usual work-up gave a crude orange oil (0.85 g). Column chromatography allowed isolation of the hexahydroindenone **17a** as a yellow oil (0.70 g, 60 %); ν_{max} 3020 (Ar-H), 1660 (C=O) and 1635 (C=C) cm^{-1}; δ_H 7.36-7.32 and 7.27-7.22 (5H, m, Ar-H), 3.43-3.32 (1H, m), 2.69-2.51 (8H, m) and 2.01-1.90 (2H, m); δ_C 196.7 (1C), 164.6 (1C), 143.5 (1C), 137.7 (1C), 128.7 (2C), 126.8 (1C), 126.7 (2C), 44.6 (1C), 41.9 (1C), 37.6 (1C), 34.6 (1C), 28.9 (1C) and 21.7 (1C). *m/z* (rel intensity, %) 212.25 (M^+, 17), 108.15 (100), 79.15 (19) and 77.15 (10).

6-Ethyl-1,2,3,5,6,7-hexahydro-4H-inden-4-one, 17b.- 2-Methyl-1-cyclopentenecarboxylic acid **12** (0.76 g, 6 mmol) and 2-pentenoic acid **2b** (0.60 g, 6 mmol) for 3 h and work-up led to an orange crude oil (0.65 g). Column chromatography allowed isolation of the ethylhexahydroindenone **17b** as a colourless oil (0.42 g, 43 %); ν_{max} 1660 (C=O) and 1630 (C=C) cm^{-1}; δ_H 2.53-2.36 (6 H, m), 2.05-1.80 (5 H, m), 1.44-1.32 (2 H, m) and 0.89 (3 H, t, J 7.4 Hz, CH_3); δ_C 197.9 (1C), 165.1 (1C), 137.5 (1C), 43.9 (1C), 37.9 (1C), 37.6 (1C), 32.8 (1C), 28.9 (1C), 28.6 (1C), 21.7 (1C) and 11.2 (1C). Found: C, 80.23; H, 9.82 %. Calcd. for $C_{11}H_{16}O$: C, 80.44; H 9.82 %.

6-Propyl-1,2,3,5,6,7-hexahydro-4H-inden-4-one, 17c.- Methylcyclopentenecarboxylic acid **12** (0.76 g, 6 mmol) and 2-hexenoic acid **2c** (0.69 g, 6 mmol) for 4 h led to a yellow crude oil (0.69 g), which was purified as usual to obtain a yellow oil (0.46 g, 43%) of the title ketone **17c**; ν_{max} 1665 (C=O) and 1635 (C=C) cm^{-1}; δ_H 2.55-2.34 (6 H, m), 2.12-1.81 (5 H, m), 1.36-1.27 (4 H, m, CH_2CH_2) and 0.92-0.86 (3 H, m, CH_3); δ_C 198.0 (1C), 165.3 (1C), 137.5 (1C), 44.2 (1C), 38.0 (1C), 37.6 (1C), 35.9 (1C), 33.1 (1C), 28.8 (1C), 21.7 (1C), 19.7 (1C) and 14.0 (1C). *m/z* (rel intensity, %) 178.3 (M^+, 13), 135.2 (9), 108.15 (100), 79.15 (19) and 77.15 (9).

Addition of 2-methyl-1-cyclopentenecarboxylic acid 12 to 1-cyclohexenecarboxylic acid 8a.- 2-Methyl-1-cyclopentenecarboxylic acid **12** (0.63 g, 5 mmol) and 1-cyclohexenecarboxylic acid **8a** (0.63 g, 5 mmol) were allowed to react for 4 h at rt, and the mixture was poured into water. The solvent was partly evaporated, the residue was washed with ether, the aqueous layer acidified with conc hydrochloric acid, and then extracted with ethyl acetate. When the solvent was evaporated, a mixture (1,10 g) of an oil and a precipitate was obtained. Addition of hexane and filtration gave white small crystals of the dicarboxylic acid **20a** (0.21 g, 17 %), m.p. 197-198°C; ν_{max} 3500-2500 (CO_2H), 1690 (C=O), 1670 (C=O) and 1625 (C=C) cm^{-1}. Found: C, 66.64; H, 7.99 %. Calcd. for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99 %.

Methyl ester: δ_H 3.70 (3 H, s, CO_2CH_3), 3.65 (3 H, s, CO_2CH_3), 2.97 (1 H, dd, J 13.0 and 9.7 Hz), 2.65-2.09 (7 H, m), 1.86-1.55 (7 H, m) and 1.44-1.22 (3 H, m); δ_C 175.1, 166.5, 158.3, 128.5, 51.2, 50.9, 45.4, 38.3, 36.1, 33.7, 30.4, 28.5, 25.4, 24.0, 22.5 and 21.6.

The filtered hexane solution was washed with aqueous sodium bicarbonate and then with brine. Evaporation of the solvent gave an oil (0.59 g), which on purification allowed isolation of **1,2,3,4a,5,6,7,8,8a-decahydrobenz[d]inden-4(4H)-one 18a** (0.43 g, 45 %) as a yellow oil. Column chromatography allowed isolation of two diastereoisomers.

Less polar isomer: white solid, m.p. 46-47 °C; ν_{max} 1655 (C=O) and 1635 (C=C) cm^{-1}; δ_H 2.56-2.42 (4 H, m), 2.35-2.23 (2 H, m), 2.13-1.64 (8 H, m) and 1.28-0-98 (4 H, m); δ_C(apt) 199.2 (C^4), 163.4 (C^{9a}), 137.1 (C^{3a}), 50.6 ($C^{4a}H$), 41.2 ($C^{8a}H$), 37.5 (CH_2), 34.4 (CH_2), 33.9 (CH_2), 29.2 (CH_2), 25.8 (CH_2), 25.7 (CH_2), 25.6 (CH_2) and 21.6 (CH_2). *m/z* (rel intensity, %) 190.3 (M^+, 23), 148.2 (10), 147.2 (19), 108.15 (100), 81.15 (14), 79.15 (27), 53.0 (11) and 41.05 (20).

Polar isomer: colourless oil; ν_{max} 1655 (C=O) and 1635 (C=C) cm^{-1}; δ_H 2.64-2.53 (1 H, m), 2.53-2.21 (6 H, m), 2.11-2.01 (2 H, m), 1.92-1.62 (5 H, m) and 1.56-1.10 (4 H, m).

Addition of 2-methyl-1-cyclopentenecarboxylic acid 12 to 6-methyl-1-cyclohexenecarboxylic acid 8b.- 2-Methyl-1-cyclopentenecarboxylic acid **12** (0.76 g, 6 mmol) and 6-methyl-1-cyclohexenecarboxylic acid **8b** (0.84 g, 6 mmol) were allowed to react as usual for 4 h. On work-up as in the preceding reaction, the dicarboxylic acid **20b** was obtained as a precipitate of white small crystals (0.50 g, 31 %), m.p. 224-226 °C, pure on washing with hexane; ν_{max} 3400-2500 (CO_2H), 1685 (C=O) and 1635 (C=C) cm^{-1}; δ_H 3.53 (1 H, t, J 13.5 Hz), 2.83-2.69 (1 H, m), 2.67-2.53 (2 H, m), 2.40-2.28 (2 H, m), 2.06-1.70 (6 H, m), 1.68-1.23 (5 H, m) and 0.94 (3 H, d, J 6.6 Hz, CH_3); δ_C 181.0, 172.7, 159.5, 129.4, 48.3, 38.8, 37.6, 34.6, 34.5, 33.5, 28.7, 27.7, 26.0, 21.4 and 20.0. Found: C, 67.90; H, 8.41 %. Calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33 %.

A negligible amount of ketone **18b** resulted from the hexane solution.

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