The Stereochemistry of the Reformatsky Reaction of Methyl 4-Bromo-3-methylbut-2-enoate with *β*-Cyclocitral and Related Compounds

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Received October 11, 1974

R. N. GEDYE, PARKASH ARORA, and A. H. KHALIL. Can. J. Chem. **53**, 1943 (1975).

Both methyl *Z*- and *E*-4-bromo-3-methylbut-2-enoate react with β-cyclocitral in the presence of zinc to give the δ-lactone of 5-hydroxy-3-methyl-5-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2-pentenoic acid as the main product, indicating an *E* to *Z* inversion during the Reformatsky reaction. Similar results were obtained in the Reformatsky reactions of the *Z*- and *E*-bromoesters with benzaldehyde and cyclohexenecarboxaldehyde. Here hydrolysis of the Reformatsky product gave, in each case, the corresponding *Z*-2,*E*-4-acids as the main products, indicating the formation of the δ-lactone as an intermediate. The synthesis of *Z*- and *E*-β-ionylideneacetic acid and the corresponding ring demethyl analogs using a Wittig reaction is also described.

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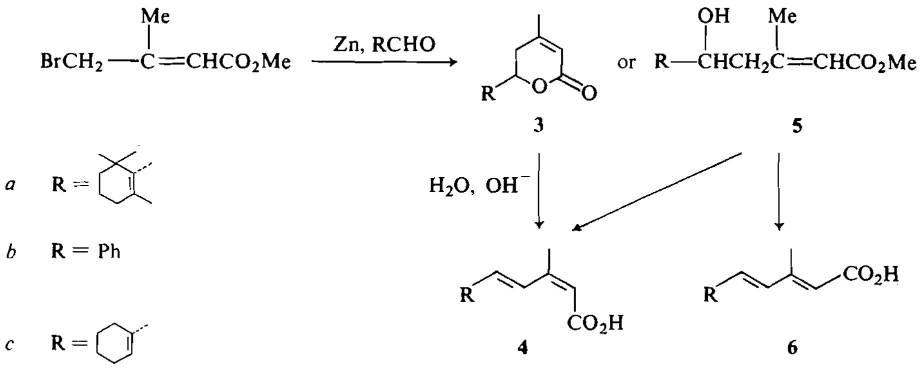
Les bromo-4 méthyl-3 butène-2 oates de méthyle *Z* et *E* réagissent avec le β-cyclocitral en présence de zinc pour conduire à la δ lactone de l'acide hydroxy-5 méthyl-3 (triméthyl-2,6,6 cyclohexène-1 yl-1)-5 pentène-2 oique comme produit principal; ce résultat indique qu'il y a une interconversion de *E* et *Z* au cours de la réaction de Reformatsky. On a obtenu des résultats semblables lors de la réaction de Reformatsky des bromoesters *E* et *Z* avec le benzaldéhyde et le cyclohexènecarboxaldéhyde. Dans chacun de ces cas, l'hydrolyse du produit de Reformatsky conduit aux acides 2-*Z*,4-*E* correspondants comme produits principaux; ces résultats indiquent qu'il y a formation de la δ lactone comme intermédiaire. On décrit aussi la synthèse faisant appel à la réaction de Wittig des acides β-ionylidène acétiques *Z* et *E* ainsi que des analogues desméthyles cycliques correspondants. [Traduit par le journal]

The Reformatsky reactions between benzaldehyde, β-cyclocitral, and β-ionylideneacetaldehyde with esters of 4-bromo-3-methylbut-2-enoic acid have attracted the attention of several laboratories as a possible route to the synthesis of vitamin A and related compounds (1–8). Harper and Oughton (1) and Fuson and Southwick (2) have reported that the Reformatsky reaction between benzaldehyde and methyl 4-bromo-3-methylbut-2-enoate yields a mixture of compounds in which there is a substantial amount of the δ-lactone **3***b*. The bromoester used in these Reformatsky reactions was obtained by the allylic bromination of methyl 3-methylbut-2-enoate with *N*-bromosuccinimide. The formation of the δ-lactone was ascribed either to the presence of the *Z*-bromoester **1** or to the inversion of the *E*-bromoester **2** during the Reformatsky reaction (1).

Tanabe (5), Yoshida and Tanabe (6), and Eiter *et al.* (7) have reported that the Reformatsky reaction between β-cyclocitral and the bromoester gave an isolatable δ-lactone **3** which on subsequent hydrolysis yielded *Z*-β-ionylideneacetic acid, **4***a*. Harper and Oughton (1) on the other hand, reported the formation of the hydroxy ester **5***a* but did not mention any investigation of its stereochemistry.

It is almost certain that in all the above reports, a mixture of *Z*- and *E*-bromoesters **1** and **2** has been used (9–11). It has been suggested that the use of the pure *E*-bromoester **2** might be advantageous in the synthesis of all-*trans*-vitamin A(12) but as far as we can ascertain no attempt has been made to examine the stereochemical outcome of the Reformatsky reaction using either pure *Z*-*1* or *E*-*2* to prove or disprove that the presence of the *Z*-bromoester might be responsible for the production of the δ-lactone (1).

Our present investigations have confirmed previous reports (9, 10) that the allylic bromination of methyl 3-methylbut-2-enoate gives a mixture of the two geometrical isomers **1** and **2** in the ratio 2:3. The successful separation of **1** and **2** in stereochemically pure forms enabled us to reexamine the above mentioned Reformatsky reactions using either the pure *Z*-

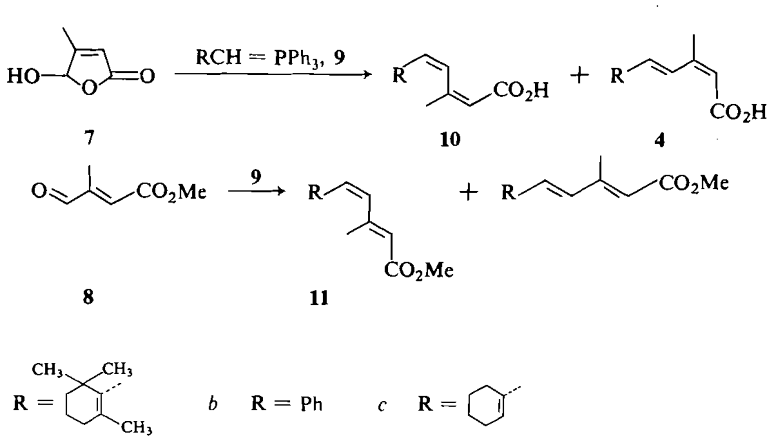


bromoester **1** or *E*-bromoester **2**. Three carbonyl substrates were used in this study: (*a*) benzaldehyde, (*b*) β-cyclocitral, and (*c*) cyclohexenecarboxaldehyde. On the basis of the identification of the products by comparison with reference compounds prepared by unequivocal procedures it was evident that the *Z*-bromoester and the *E*-bromoester afforded the same products under the same conditions. It is therefore not true that the *Z*-bromoester is solely responsible for the formation of the δ-lactone nor is there any real advantage to be gained in the use of the pure *E*-bromoester in the synthesis of vitamin A intermediates using a conventional Reformatsky reaction.

The Reformatsky reaction between benzaldehyde and the *Z*- or the *E*-bromoesters gave similar products. Although we were not successful in isolating the δ-lactone, the product showed an i.r. absorption at 1720 cm^{-1} indicative of the δ-lactone **3*b***. Alkaline hydrolysis followed by isolation of the acidic products and esterification with ethereal diazomethane gave a mixture of the *Z*-2,*E*-4 (70%) and the *E*-2,*E*-4 (30%) isomers of the methyl ester of 3-methyl-5-phenylpenta-2,4-dienoic acid. These results are in agreement with the structural assignments of the Reformatsky products made by Wiley (4), who ascribed the formation of the *Z*-2,*E*-4-isomer **4*b*** to the ring opening of the δ-lactone **3*b*** during the saponification process. The *E*-2,*E*-4-isomer **6*b*** presumably arises, along with **4*b***, from the dehydration of the hydroxy ester **5*b***.

A similar Reformatsky reaction between cyclohexene carboxaldehyde and either the *Z*- or the *E*-bromoester showed the formation of an unsaturated δ-lactone (i.r. 1719 cm^{-1}) in all the isolated fractions. Alkaline hydrolysis of the Reformatsky product followed by isolation of the acidic product gave an acid shown to be 5-(cyclohexen-1-yl)-3-methyl-*Z*-2,*E*-4-pentadienoic acid (**4*c***). Again the acid **4*c*** would be expected to arise from the ring opening of the δ-lactone **3*c*** during the saponification process.

The Reformatsky reaction of β-cyclocitral and



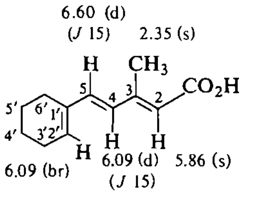
the *Z*- and *E*-bromoesters gave a product from which δ-lactone **3***a* was isolated by column chromatography on alumina. Alkaline hydrolysis of the lactone followed by acidification gave *Z*-β-ionylideneacetic acid (**4***a*).

The products in this study were determined by g.l.c. using reference compounds prepared by standard procedures, notably those of Pattenden and Weedon (13) who showed that the Wittig reaction of 4-hydroxy-3-methylbut-2-enolide (**7**) and of methyl *E*-3-formylcrotonate (**8**) with the Wittig reagent **9***b* gave a convenient method for the synthesis of the four geometrical isomers of 3-methyl-5-phenylpenta-2,4-dienoic acid (**10***b*, **4***b*, **11***b*, and **6***b*).

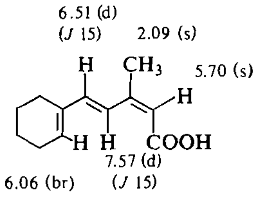
We have applied this method to the synthesis of *Z*- and *E*-β-ionylideneacetic acid. Only one isomer was formed in each reaction, probably due to steric factors, providing a convenient method for the preparation of these important vitamin A intermediates in stereochemically pure forms and in high yield.

Condensation of the Wittig reagent **9***a* (14) with the lactol **7** followed by isolation of the acidic product gave only *Z*-β-ionylideneacetic acid (**4***a*) in 87% yield. The Wittig reaction of **9***a* with methyl *E*-3-formylcrotonate (**8**) gave only the *E*-methyl ester **6***a* in 80% yield.

The *Z*-2,*E*-4 and *E*-2,*E*-4-isomers of 3-methyl-5-(cyclohexen-1-yl)penta-2,4-dienoic acid (**4***c* and **6***c*) were prepared in high yield by similar reactions using the Wittig reagent **9***c* with the lactol **7** and with methyl *E*-3-formylcrotonate, respectively. The n.m.r. properties of these previously unreported isomers **4***c* and **6***c* are shown in the accompanying formulae.



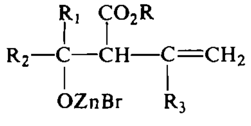
6*c*



4*c*

The relative δ values for the C_3 methyl protons provides a convenient means for determining the stereochemical configuration of compounds of the β-ionylideneacetic acid series, where the absorption in the all-*trans* isomer always occurs at a lower field (11, 15).

On the basis of these experimental results the following points deserve mention. Firstly, under similar conditions in the various Reformatsky reactions the *Z*- and *E*-bromoesters afford the same products, which include the δ-lactone, and it is clear that the δ-lactone does not arise only from the *Z*-bromoester as has been suggested (1). Secondly the formation of the *Z*-2,*E*-4-isomers **4***a*, *b*, and *c*, is only explainable by the formation of δ-lactones as intermediates in the Reformatsky reactions concerned. Unsaturated lactones have been shown to open with conservation of the stereochemistry of the α,β position (16). Finally, in order to account for the formation of the δ-lactones from the *E*-bromoester the following explanations may be considered. (*i*) Excess zinc, usually used in the Reformatsky reaction, might catalyze the stereomutation of the double bond in the *E*-bromoester and result in lactonization. A similar stereomutation has been reported in the presence of iron (17). On refluxing either the pure *E*- (or pure *Z*-) bromoester in benzene with zinc for several hours, however, no stereomutation was observed using g.l.c. or n.m.r. (*ii*) Recently Coffignal and Gaudemar (18) have found that an allylic rearrangement occurs in the condensation of γ-bromocrotonates with aldehydes and ketones and suggested the reaction involved the formation of the rearranged ester **12** (R_3 = H) as the first intermediate. This undergoes equilibration with the "linear" ester **13** (R_3 = H) resulting in a mixture of the rearranged and "linear" β-hydroxy esters after hydrolysis.



$$R_2\!-\!\underset{\displaystyle OZnBr}{\overset{\displaystyle R_1}{C}}\!-\!\overset{\displaystyle CO_2R}{CH}\!-\!\underset{\displaystyle R_3}{C}\!=\!CH_2$$

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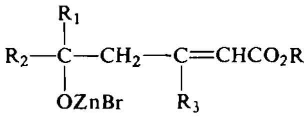

$$R_2\!-\!\underset{\displaystyle OZnBr}{\overset{\displaystyle R_1}{C}}\!-\!CH_2\!-\!\underset{\displaystyle R_3}{C}\!=\!CHCO_2R$$

13

Although no lactone was isolated by these workers, the formation of the δ-lactone in the present study is not inconsistent with this mechanism. The same equilibrium mixture of *Z*-

and *E*-esters **13** (R_3 = Me) would be expected to result from both the *Z*- and *E*-bromoesters **1** and **2**, and the *Z* form may have lactonized during the course of the reaction.

Experimental

All boiling and melting points are uncorrected. Infrared spectra were recorded with a Beckman IR-10 double beam spectrophotometer. The n.m.r. spectra were obtained with a Varian A-60 deuteriochloroform solution unless otherwise stated, with tetramethyl silane as an internal reference. Ultraviolet spectra were recorded with a Hitachi Perkin-Elmer Model 124 double beam spectrophotometer. Gas chromatography was carried out on a Varian Aerograph Model 90-P gas chromatograph using a 160 cm × 6 mm column of 3% SE-30 silicone gum rubber on Chromosorb W with the helium as a carrier gas. Fractional distillations were carried out using a Nester-Faust annular spinning band column with 100 theoretical plates.

Methyl Z- and E-4-Bromo-3-methylbut-2-enoate (1 and 2)

A mixture of *Z*- and *E*-bromoesters was obtained from the reaction of methyl 3-methylbut-2-enoate with *N*-bromosuccinimide according to the literature procedure (9). The product, b.p. 80–88°/12 mm, n_D^{20} 1.5022, was shown by g.l.c. and n.m.r. to consist mainly of two components in the approximate ratio 2:3; the n.m.r. data for the mixture was in agreement with the literature values (9).

Fractional distillation of the isomeric mixture (40.0 g) gave (*i*) methyl *Z*-4-bromo-3-methylbut-2-enoate (**1**) (11.8 g), b.p. 63–65°/7 mm, n_D^{24} 1.4871; λ_{max} (EtOH) 215 nm (ε 11.8 × 10^3); ν_{max} (CCl_4) 1730vs, 1650s, 1440s, 1360s, 1250vs, 1160vs, 1045s, 860s, and 635 cm^{-1}; n.m.r. δ 5.80br (=CH), 4.60s (CH_2Br), 3.70s (OMe).

Anal. Calcd. for $C_6H_9BrO_2$: C, 37.3; H, 4.7; Br 41.5. Found: C, 37.1; H, 4.6; Br, 41.4.

(*ii*) Intermediate fraction (4.3 g), b.p. 65–67°/7 mm; n.m.r. and g.l.c. showed the *Z*:*E* ratio to be about 1:3. (*iii*) Methyl *E*-4-bromo-3-methylbut-2-enoate (**2**) (20.6 g), b.p. 67–8°/7 mm, n_D^{24} 1.4994; λ_{max} (EtOH) 218 nm (13.7 × 10^3); ν_{max} (CCl_4) 1730vs, 1645s, 1435s, 1355s, 1250m, 1230vs, 1210s, 1155vs, 1037s, 925w, 860w, and 620 cm^{-1}; n.m.r. 5.93br (=CH), 393s (CH_2Br), 3.70s (OMe), and 2.26d (J = 2 Hz, MeC=C).

Anal. Found: C, 37.1; H, 4.8; Br, 41.3.

Reformatsky Reaction of Benzaldehyde with Methyl Z-4-Bromo-3-methylbut-2-enoate (1)

A portion (5 ml) of a solution of the *Z*-bromoester **1** (15.0 g, 0.078 mol) and benzaldehyde (8.16 g, 0.077 mol) in dry benzene (25 ml) and dry ether (5 ml) was added dropwise to activated zinc (19) (5.23 g, 0.08 g-at.). The mixture was warmed until the reaction started. The mixture was then stirred with gentle warming and the rest of the solution added at such a rate as to maintain a slow reflux. The reaction mixture was refluxed for 30 min, cooled to 0°, and hydrolyzed with ice-cold 10% sulfuric acid (25 ml). The organic layer was separated and successively washed with water, sodium bicarbonate solution, and water and dried over anhydrous sodium sulfate. The solvent was evaporated and the residue distilled giving a pale yellow oil (8.5 g), b.p. 150–175°/3 mm. The i.r. spectrum for the fraction b.p. 169–175°/3 mm (5.9 g) showed a pronounced band at 1725 cm^{-1} indicative of the δ-lactone. Attempts to crystallize the lactone were unsuccessful. The δ-lactone band was less pronounced in the other fractions.

The fraction b.p. 169–175°/3 mm was treated with ethanolic potassium hydroxide for 12 h at 50°, diluted with water, extracted with ether, and acidified with cold 10% sulfuric acid. The white precipitate was taken up in ether, washed with water, and then dried. The ether was evaporated and the resulting crystalline material had m.p. 128–134°. A sample of this product was treated with excess ethereal diazomethane and the resulting oil was shown by g.l.c. to be a mixture of approximately 70% of the *Z*-2,*E*-4 and 30% *E*-2,*Z*-4 isomers of methyl 3-methyl-5-phenylpenta-2,4-dienoate.

Iodine-catalyzed isomerization of the isomeric mixture m.p. 128–134°, according to the directions of Pattenden and Weedon (13) gave the *E*-2,*E*-4-acid **6*b***, m.p. 156–158° (petroleum ether). The acid exhibited the spectral properties as reported (13).

Reformatsky Reaction of Benzaldehyde with Methyl E-4-Bromo-3-methylbut-2-enoate-(2)

Repetition of the preceding experiment with the *E*-bromoester **2**, gave a similar product ratio. The products from both the above reactions were identified by g.l.c. using reference compounds prepared by procedures given below (10, 13).

Reformatsky reaction of Methyl E-4-Bromo-3-methylbut-2-enoate with β-Cyclocitral

The *E*-bromoester (19.3 g, 0.1 mol) was reacted with β-cyclocitral (15.2 g, 0.1 mol) in dry benzene (85 ml) and ether (15 ml) and activated zinc (7.0 g, 0.107 g-at.) using the procedure described above for the benzaldehyde reaction. The product was distilled to give unreacted β-cyclocitral (2.5 g), b.p. 42–44°/1 mm, and a thick syrup (10.4 g), b.p. 130–153°/1 mm, which partly solidified on standing. A portion of the solid was recrystallized from 50% ethanol giving the δ-lactone **3*a***, m.p. 60–63°. Column chromatography of the syrup (2.0 g) on neutral alumina (80–200 mesh) using benzene–hexane as eluent gave the δ-lactone **3*a*** (1.3 g), m.p. 60–63°. A sample obtained by recrystallization from 50% ethanol had m.p. 64–65° (lit. (5) m.p. 65–66°); λ_{max} (EtOH) 209 nm; ν_{max} ($CHCl_3$) 1716 cm^{-1} (δ-lactone). The δ-lactone (2.0 g) was hydrolyzed with ethanolic potassium hydroxide (10%, 10 ml) at room temperature, diluted with water (100 ml), extracted several times with ether, and acidified with cold 10% sulfuric acid. The precipitate was taken up in ether, washed with water, and dried over magnesium sulfate. Evaporation of the ether and recrystallization from petroleum ether (b.p. 30–60°) at 0° gave *Z*-β-ionylideneacetic acid **4*a*** (0.74 g), m.p. 98–99° not depressed on admixture with an authentic sample prepared as described below. The spectral properties were also identical with those of the authentic sample.

Reformatsky Reaction of Methyl Z-4-Bromo-3-methylbut-2-enoate with β-Cyclocitral

Repetition of the preceding Reformatsky reaction using the *Z*-bromoester gave similar results. No product other than the δ-lactone was isolated.

Reformatsky Reaction of Methyl E-4-Bromo-3-methylbut-2-enoate with Cyclohexene Carboxaldehyde

The *E*-bromoester (15.0 g, 0.078 mol) was reacted with cyclohexene carboxaldehyde (20) (8.58 g, 0.077 mol) in dry benzene (25 ml) and dry ether (15 ml) and activated zinc (5.23 g, 0.08 g-at.), using the procedure described above for the benzaldehyde reaction. The product was distilled giving a pale yellow oil (7.9 g), b.p. 148–165°/6 mm. The i.r. spectrum for the fraction b.p. 150–165°/6 mm showed a pronounced band at 1719 cm^{-1} indicative of a δ-lactone. This fraction was treated with ethanolic potassium hydroxide at 50° for 12 h, diluted with water, extracted with ether, and acidified with 10% sulfuric acid. The white precipitate was evaporated and the resulting crystalline material had m.p. 158° and showed the same spectral properties as 3-methyl-5-(cyclohexen-1-yl)penta-*Z*-2,*E*-4-dienoic acid (4*c*) prepared as described below.

Reformatsky Reaction of Methyl Z-4-Bromo-3-methylbut-2-enoate with Cyclohexene Carboxaldehyde

Repetition of the preceding Reformatsky reaction with the *Z*-bromoester gave similar results. Alkaline hydrolysis of the product gave the same *Z*-2,*E*-4-acid.

Preparation of the Reference Compounds

The 3-methyl-5-phenylpenta-2,4-dienoic acids and their methyl esters. The four isomeric acids (*Z*-2,*Z*-4, *Z*-2,*E*-4, *Z*-2,*E*-4, and *E*-2,*E*-4 isomers) were prepared using the Wittig reactions between benzyltriphenylphosphonium chloride and 4-hydroxy-3-methylbut-2-enolide and methyl *E*-3-formylcrotonate in the presence of sodium methoxide according to the method of Pattenden and Weedon (13). The methyl esters were obtained by treating the corresponding acids with ethereal diazomethane.

E-β-Ionylideneacetic Acid (6a) and its Methyl Ester

Phenyllithium (0.04 mol) in dry ether (50 ml) was added during 15 min to a well stirred suspension of triphenylcyclogeranyl bromide (14) (12 g, 0.024 mol) in dry ether (300 ml) at 10° under nitrogen. The resulting deep red solution was stirred for 20 min and methyl *E*-3-formylcrotonate (3.07 g, 0.024 mol) in dry ether (40 ml) was added during 15 min. The reaction mixture was stirred for 2 h at 10° and for 1 h at 35° and then diluted with water (300 ml). The mixture was stirred for 30 min at room temperature. The organic layer was separated, washed with water, dried, and then evaporated. The residue was diluted with petroleum ether (b.p. 30–60°), cooled to 0°, and the precipitated triphenylphosphine filtered off. The filtrate was dried over anhydrous sodium sulfate and distilled under reduced pressure giving methyl *E*-β-ionylideneacetate (5.2 g, 87%), b.p. 160–163°/5 mm (lit. (5) b.p. 110–111°/0.5 mm); g.l.c. showed only one peak; λ_{max} (EtOH) 257 and 302 nm; ν_{max} 1720vs (C═O), 1610s (C═C), 970m (CH═CH *trans*).

A sample of this ester (2.0 g) was saponified with ethanolic potassium hydroxide at room temperature and the product acidified giving *E*-β-ionylideneacetic acid (1.2 g) m.p. 125–127° (acetonitrile) (lit. (8) m.p. 126–127°), not depressed on admixture with a sample prepared according to the directions of Ishikawa (21); λ_{max} (EtOH) 258 and 290 nm.

Z-β-Ionylideneacetic Acid (4a)

Phenyllithium (0.05 mol) in dry ether (60 ml) was added during 20 min to a cooled (0°) and well stirred suspension of triphenyl-β-cyclogeranylphosphonium bromide (12.2 g, 0.026 mol) in dry ether (300 ml) under nitrogen. The resulting deep red solution was stirred for 20 min and 4-hydroxy-3-methylbut-2-enolide (3.0 g, 0.026 mol) added during 15 min. The reaction mixture was stirred for 2 h at 0° and for an additional 2 h at room temperature. It was then diluted with water (300 ml) and stirred for 30 min. The aqueous layer was separated, extracted with ether, acidified with cold 20% sulfuric acid, and the acidic product extracted several times with ether. The combined ether extracts were washed with water, dried, and evaporated leaving *Z*-β-ionylideneacetic acid (4*a*) (5.2 g, 85%), m.p. 98–99° (petroleum ether) (lit. (8) m.p. 98.5–99.5°); λ_{max} (EtOH) 256 and 305 nm; λ_{max} 1680(s) (C═O), 1620 (C═C), and 850 cm^{-1}. The n.m.r. spectra of the *Z*- and *E*-acids were the same as reported (11). Iodine-catalyzed isomerization of *Z*-β-ionylideneacetic acid according to the procedure of Robeson *et al.* (8) gave the *E* isomer (g.l.c.). A sample of the *Z*-acid was treated with ethereal diazomethane giving the methyl ester, g.l.c. one peak; λ_{max} 257, 310 nm.

3-Methyl-5-(cyclohexen-1-yl)penta-E-2,E-4-dienoic Acid (6c) and its Methyl Ester

The reaction was carried out according to the procedure used for *E*-β-ionylideneacetic acid and its methyl ester. Methyl *E*-3-formylcrotonate (5.9 g, 0.046 mol) in dry ether (50 ml) was allowed to react with a mixture of phenyllithium (0.064 mol) in dry ether (50 ml) and triphenyl(1-cyclohexen-1-yl-methyl)phosphonium bromide (22) (20.0 g, 0.046 mol) in dry ether (300 ml). After a similar work-up procedure the product was distilled giving methyl 3-methyl-5-(cyclohexen-1-yl)-penta-*E*-2,*E*-4-dienoate (8.5 g, 89%) as a pale yellow oil, b.p. 155–158°/7 mm, n_D^{24} 1.5341; g.l.c. one peak; λ_{max} (EtOH) 207 and 318 nm; ν_{max} ($CHCl_3$) 1720vs (C═O), 1615s (C═C), 962s (CH═CH *trans*), and 880w cm^{-1}.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.73; H, 8.74. Found: C, 75.64; H, 8.56.

A sample of the ester (2.0 g) was saponified as described above for the preparation of 6*a* giving the *E*-2,*E*-4 acid (1.1 g), m.p. 172–175° (dec.) (benzene – petroleum ether). The acid is very sensitive to either air or light.

3-Methyl-5-(cyclohexen-1-yl)penta-Z-2,E-4-dienoic Acid (4c)

The reaction was carried out according to the procedure for *Z*-β-ionylideneacetic acid (above): 4-hydroxy-3-methylbut-2-enolide (3.4 g, 0.03 mol) in dry ether (25 ml) was reacted with a mixture of the above phosphonium salt (13.0 g, 0.03 mol) in dry ether (250 ml) and phenyllithium (0.05 mol) in dry ether (40 ml). After a similar work-up procedure the *Z*-2,*E*-4 acid 4*c* (5.2 g, 90%), m.p. 161–162° (benzene – petroleum ether) was obtained.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 75.00; H, 8.33. Found: C, 74.31; H, 7.95.

A sample of the acid was treated with excess ethereal diazomethane giving the methyl ester; g.l.c. one peak; λ_{max} (EtOH) 206 and 316 nm; ν_{max} ($CHCl_3$) 1740vs (C═O), 975s (CH═CH *trans*).

The n.m.r. spectra of these isomers (4*c* and 6*c*) are shown in the formulae above.

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