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Syntheses of 3-(2′,6′ Dimethyl 5′-Heptenyl) Bicyclo (2, 2, 1) 5-heptene 2-Carboxylic Acid and its Ethyl Ester by Diels Alder Reaction and Preparation of 3 Methyl 3-(4-Methyl 3′-Pentenyl) Bicyclo (2, 2, 1) 5 Heptene 2-Carboxylic Acid

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In this work, attempts have been made to prepare bicyclic compounds using citral or citronellal derivatives by Diels Alder reaction.

INTRODUCTION

Sandalwood oil is obtained from the species Santalum album L occurring in Karnataka State, India. It takes a long time to grow the tree to get sandalwood oil economically from the wood. Grass from two cymbopogon species, Cymbopogon flexious (steud) Stapf and Cymbopogon citratus (DC) Stapf[1], yields lemon grass oil containing 70% citral; grass from species Cymbopogon coloratus India and Cymbopogon nardus Jawa[2] yields oil of citronella, percentage of citronellal being 40–50% in the steam distilled oil.

Attempts have been made to prepare bicyclic compounds using citral or citronellal derivatives and cyclopentadiene—a petroleum product by Diels Alder synthesis[3,4], with the intention to see the necessity of the angular methyl group for an olfactory note in sandalwood oil and to prepare compounds which may serve as intermediates in the preparation of santalol type tricyclic compounds and to get a new range of perfume.

Originally the condensation of cyclopentadiene was attempted with geraniol to know whether the adduct reported by Brieger[5] was a single compound or a mixture of two compounds as there are almost two equally feasible sites of attack but a pure compound could not be identified, yields being very low.

EXPERIMENTAL

Citral and citronellal of S. H. Kelkar & Co. were used while all other chemicals such as malonic acid, ethyl cyanoacetate, silver nitrate, pyridine, acetic anhydride are of c.p. quality. Cyclopentadiene was freshly prepared by cracking from bicyclopentadiene J. T. Baker & Co. and was used within ½ hr after cracking.

Preparation of Citronelidene Acetic Acid

The mixture of citronellal (10 g), malonic acid (10.6 g) and pyridine

(18 g) was heated on waterbath for about 8 hrs. The reaction mixture was washed with water (100 ml) twice or thrice to remove all pyridine and unreacted malonic acid and was then steam distilled to remove unreacted citronellal if any. The organic layer was taken in ether and then was extracted with saturated sodium bicarbonate solution. Alkali layer was separated and mixed with fresh ether and acidified with dilute hydrochloric acid, when the separated acid was taken in ether. Ether layer was dried over anhydrous sodium sulphate. Ether evaporated to get crude product which was distilled under vacuum to collect citronelidene acetic acid at 148°C at 2 mm. The yield was 6.55 g. Equivalent wt. found: 172.9, required: 172.0. IR (KBr): 3000 cm^{-1} (OH), 1700 cm^{-1} (unsaturation carbonyl), 1380 cm^{-1} (gem dimethyl), 980 cm^{-1} (trans disubstituted olefin).

PMR ($CDCl_3$): 0.87 to 0.94 (d 3H of C_{12}), 1.22–1.35 (m 3H, 2H, of C_6, 1H of C_5), 1.59 (s 3H of C_{11}), 1.67 (s, 3H of C_{10}), 1.88–3.07 (m 4H, 2H of C_4 and 2H of C_7), 5.07 (t H of C_8), 5.43–5.88 m 1H of C_2), 7.07 (m 1H of C_3), 7.37 (s 1H of COOH).

Preparation of Monoethyl Malonate

To a solution of diethyl malonate (25 g) in ethanol (100 ml) was added dropwise with constant stirring a solution of potassium hydroxide (8.7 g) in ethanol (100 ml) After complete addition the mixture was heated on water bath and then cooled in freezer. The separated potassium ethyl malonate (16 g) was then filtered at pump and dried.

Potassium ethyl malonate (16 g) was dissolved in minimum amount of water (10 ml). Ether was added to it and the mixture was cooled to 0°C by keeping it in the ice bath. The aqueous layer was then acidified with concentrated hydrochloric acid (4 ml). Ether layer was separated. The solid potassium chloride was again washed with fresh quantity of ether. The ether layer was separated and dried over anhydrous sodium sulphate. Ether was evaporated to get monoethyl malonate. The product was distilled at 147°C at 21 mm. The yield was 11.3 g.

Preparation of Ethyl Citronelidene Acetate

Citronellal (15.4 g) monoethyl malonate (13.2 g) and pyridine (7.9 g) were mixed together and were heated to about 100°C for 8 hrs. The reaction mixture was then taken in ether and the ethereal layer was first washed with very dilute hydrochloric acid to remove pyridine, then with sodium-bisulphite solution to remove unreacted citronellal if any, and then twice or thrice with water. The ether layer was dried over anhydrous sodium sulphate. Ether was evaporated and the residue was fractionally distilled. The fraction boiling at 147°C at 12 mm was collected (7.2 g).

Preparation of Geranic Acid

Citral (3.226 g) was disolved in ethanol (100 ml). A solution of silver nitrate (3.72 g) in water (39 ml) was added to it. To this mixture a solution of sodium hydroxide (3.72 g) in water (150 ml) was added dropwise with constant stirring on a magnetic stirrer. The black precipitate of silver oxide got separated immediately. The whole mixture was stirred continuously for about 3 hrs and then kept overnight.

The supernatant yellow solution was then decanted in a shallow pan and the precipitate was then filtered. The alcohol was allowed to evaporate at room temperature. The neutral fraction was taken up in ether. The aqueous alkaline layer was cooled in ice bath and acidified with dilute hydrochloric acid. The acid was then extracted with ether. To ensure complete removal of citral the ether layer was extracted with alkali. The alkaline layer was taken in fresh lot of ether and again acidified with dilute hydrochloric acid. Ether layer was washed with water to remove mineral acid. Ether layer was then dried over anhydrous sodium sulphate, ether was evaporated to get crude geranic acid (2.25 g). It was distilled at 133°C at 8 mm. Equivalent weight was found to be 167.1. Expected equivalent weight 168.

3-(2′, 6′) Dimethyl 5′-Heptenyl Bicyclo (2, 2, 1) 5-Heptene 2-Carboxylic Acid

Citronelidene acetic acid (3.924 g) freshly cracked cyclopentadiene (1.4 g) were mixed together and heated at 170°C in a sealed pressure tube for 6 hrs.

The whole mass was taken in ether. The ethereal layer was washed with dilute sodium hydroxide (2 N). The alkali layer was washed with ether and then was taken in fresh stock of ether and acidified with dilute hydrochloric acid (2 N). The organic acid was taken in ether, washed with water to make it free from mineral acid and then dried over anhydrous sodium sulphate. Ether was evaporated to get the crude product which was fractionated and the fraction was collected at 179–181°C at 8 mm. The equivalent weight obtained 261.52. Expected equivalent weight 262.

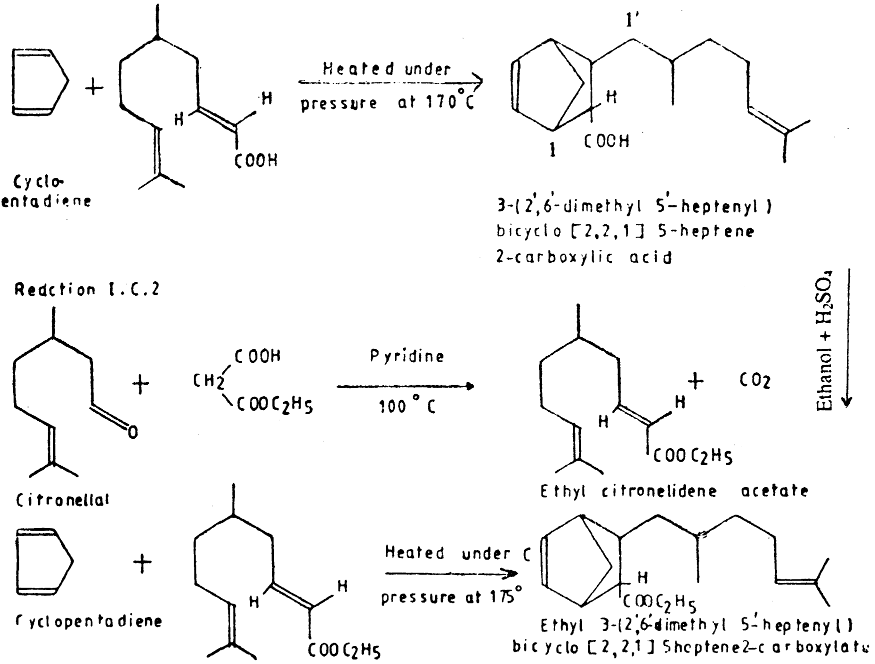
Found % C–76.85, H–10.37% required % C–76.8, H–10.4%.

PMR ($CD\,Cl_3$) : 0.87–0.94 (d 3H of $C_{2'\,\mathrm{methyl}}$), 1.12–1.26 (m 2H of C_7) 1 31–1.47 (m 4H, 2H each of $C_{1'}$ and $C_{3'}$), 1.59–1.67 (s, 6H of 2 CH_3 of $C_{6'}$), 1.95 to 2.2 (m 1H of C_3), 2.34–2.55 (m 1H of $C_{2'}$), 2.99–3.14 (m 2H of $C_{4'}$), 4.72 (s 1H of C_4), 5.07 (t 1H of $C_{5'}$), 5.59 (s 1H of C_1) 5.72 (s 1H of C_2), 6.01–6.3 (m 2H of C_5 and C_6), 8.83 (s 1H of COOH) exchangeable with D_2O.

Above cyclised product (4.5 g) was taken in ethyl alcohol (50 ml). Concentrated sulphuric acid (1.5 ml) was added to it and the mixture was refluxed for about 3 hrs. Excess of alcohol was then partially evaporated. The concentrated residue was taken in ether and washed with water (20 ml) to remove sulphuric acid and alcohol. The ether layer was then washed with saturated bicarbonate solution (20 ml) to remove any unreacted acid. Ether layer was then washed with water and dried over anhydrous sodium sulphate. Ether evaporated and the crude product was distilled under reduced pressure. The fraction (3.7 g) was collected at 172°C at 9 mm. The reduction of ester group is in hand.

Ethyl citronelidene acetate (4.484 g.) and cyclopentadiene (1.41 g.) were heated in a sealed tube at about 175°C. for 10 hrs. The reaction mixture was cooled and distilled under vacuum to collect the fraction at 172°C at 9 mm. (3 g.)

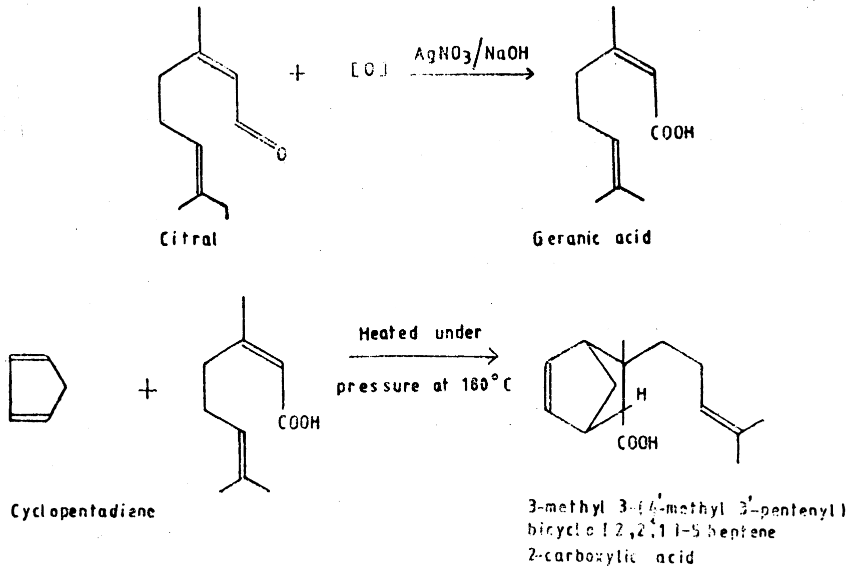
SCHEME I



3-Methyl 3-(4'-Methyl 3'-Pentenyl) bicyclo[2,2,7]-5-Heptene-2-Caboxylic Acid

A mixture of geranic acid and cyclopentadiene in different molar proportions was heated to 180°C. For 12 hrs in a sealed tube. The dark brown reaction mixture was taken in ether. The ethereal layer was washed with 3% sodium hydroxide solution when acidic part was separated from neutral fraction.

SCHEME II



The alkali layer was taken in fresh lot of ether and was acidified with dilute hydrochloric acid. The ether layer was then separated, washed with water and dried over anhydrous sodium sulphate. Ether evaporated to get a mixture of unreacted geranic acid and 3-methyl 3-(4′-methyl 3′-pentenyl) bicyclo (2,2,1) 5-heptene 2-carboxylic acid. This mixture was then fractionated to remove the fraction upto 140°C/8 mm, so that geranic acid was recovered. The undistilled residue was again taken in ether with 3% sodium hydroxide solution. The alkali layer was taken in fresh lot of ether and acidified with dilute hydrochloric acid. The separated organic acid was taken in ether and dried over anhydrous sodium sulphate. Ether was evaporated to get the crude adduct. The quantitative details of these experiments are given in Table 1.

The attempts to distill the adduct failed because the adduct was decomposing. The equivalent weight of the adduct was found to be 233.8 (0.2 g. of the adduct required 31.7 ml of 0.02698 N sodium hydroxide solution). The product gave single spot to T.L.C. on silica gel with a mixture of 50% chloroform and 50% methanol as solvent system with $R_f = 0.91$ whereas geranic acid has shown $R_f = 0.77$. Elemental analysis has shown 77.08% C and 9.37% H; whereas calculated percentages are 76.92% C and 9.402% H.

The structure of the adduct was confirmed by its infrared and nuclear magnetic resonance spectrum.

Table 1

QUANTITATIVE DETAILS OF EXPERIMENTS OF DIEL-ALDER REACTION OF CYCLOPENTADIENE (CPD.) AND GERANIC ACID (G.A.)

Molar proportion G.A. : CPD.	Amount of used substances in grams		Amount of recovered substances in grams		% Yield on the basis of used	
	G.A.	CPD.	G.A.	Adduct	G.A.	CPD.
1 : 3	1.6981	2.00	0.914	0.288	26.37	4.06
1 : 2.32	2.527	2.304	1.517	0.249	17.70	3.049
1 : 1	3.528	1.386	2.356	0.345	21.14	7.94
1 : 0.8155	3.347	1.372	2.013	0.438	23.57	11.53
1 : 0.5064	3.921	0.78	2.115	0.667	26.52	26.43
1 : 0.3	4.368	0.515	3.157	0.438	25.97	93.99

The ethyl ester of the above acid was prepared by the usual method. Its P.M.R. showed the following peaks.

PMR ($CDCl_3$) : 1.07 (s 3A of C_3 Methyl), 1.4 (m 2H of C_7), 1.22 (s, 3H of C_5), 1.27 (s 3H of C_4 Methyl), 1.5 (t 3H of CH_3 of ethyl), 1.88–2.28 (m 4H 2H each of C_1' andC_2'), 4.13 (q 2H of CH_2 of ethyl), 4.68 (m 2H, 1H each of C_1 and C_4), 4.8 (t 1H of C_3'), 5.65 (m 3H, 1H each of C_5, C_6 and C_2).

The reduction of ester is in hand.

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