Leaf Alcohol

Part XVIII. Condensation of Leaf Aldehyde by Means of Diethylamine

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The diethylamine-catalyzed aldol condensation of *E*-2-hexenal yielded a mixture of 2-*E*,4-*E*,6-*E*- (IV-a) and 2-*E*,4-*Z*,6-*E*-4-ethyldeca-2,4,6-triene-1-al (IV-b). Structural and geometrical elucidation of both alcohols were made by means of spectral evidence as well as by the catalytic hydrogenation leading to the same 4-ethyldecanol (VI). The "b-peak substance" detected in the leaf alcohol reaction products was proved to be identical with 4-ethyldecanol (VI). The treatment of the trienal containing the central *Z*-double bond with sodium under the leaf alcohol reaction condition failed to afford ethyl-propyl-benzyl alcohol, but gave 4-ethyldecanol (VI). This result safely excludes the operation of the previously suspected valence tautomerism (Cope rearrangement) in the leaf alcohol reaction, and accounts for the pathway of the formation of (VI).

In the previous paper,^{1-a)} the mechanism of leaf alcohol reaction has been proposed on the basis of a model reaction with crotonaldehyde (I-a) which on stepwise treatments with diethylamine and metallic sodium gave the leaf alcohol reaction product, *o*-methyl-benzyl alcohol (III-a), via 2-methyl cyclohexadiene aldehyde (II-a).

This was further confirmed by the same reaction sequence with leaf aldehyde as such (I-b) which on treatment with ethanolic sodium hydroxide, instead of diethylamine, yielded a

cyclic intermediate, 2-propyl-5-ethyl-cyclohexadiene-aldehyde (II-b), eventually leading to 2-propyl-5-ethyl-benzyl alcohol (III-b).^{1-b)}

In the case of the previous model reaction with crotonaldehyde, the first Michael-Aldol condensation of crotonaldehyde was easily effected by diethylamine to afford the cyclohexadiene-aldehyde (II-a), whereas the same treatment of leaf aldehyde (*E*-2-hexenal)²⁾ with diethylamine gave acyclic compounds (IV), in contrast to expectation.

In the present paper, the elucidation of structures of the compounds (IV) and the mechanism of formation thereof are described.

E-2-Hexenal when warmed with diethylamine yielded a neutral fraction distilling over

1) a) M. Ohno, Y. Inouye, A. Hatanaka and T. Kajiwaru, *Bull. Inst. Kyoto Univ.*, **43**, 231 (1963).
b) A. Hatanaka, T. Kajiwaru and M. Ohno, *Agr. Biol. Chem.*, **31**, 964 (1967).

2) J. E. Blackwood, *J. Am. Chem. Soc.*, **90**, 509 (1968). For specifying the geometry of polysubstituted ethylenic linkages, the novel *Z*, *E*-system based on the sequence rule and being currently adopted in the Chemical Abstract was preferred here to the conventional *cis*, *trans*-notation.

the range of 72~8°C/3 mm, which consisted of two components as indicated by two peaks on vpc-analysis. A clear-cut separation of the fraction into two components (IV-a and IV-b) was effected by means of preparative vpc and the IR-spectrum of each component suggested the presence of double bonds and aldehyde group. Consistently, both components gave the corresponding 2,4-dinitrophenylhydrazone melting at 132~4°C (IV'-a) and 145°C (IV'-b) respectively and the elemental analyses of both derivatives showed that both parent aldehydes are isomeric to each other and have the same constitution, $C_{12}H_{18}O$, involving one aldehyde group and three double bonds. The UV-spectra of (IV'-a) and (IV'-b) equally showed the absorption maxima at 402 m μ which strongly supported the conjugated triene aldehyde structure of both compounds, in conformity to the IR-analysis. These data when combined with the hydrogenation of (IV-a) and (IV-b) to give the same and identical saturated aliphatic alcohol, 4-ethyldecanol (VI) (*vide infra*) enables one to deduce that both aldehydes are a substituted triene aldehyde of the same carbon skeleton and differ only in the geometry of double bond. In view of the accumulated knowledge of base-catalyzed aldol condensation of aldehyde, in particular of α,β -unsaturated aliphatic aldehydes which have been prosecuted in this series of papers, it is most likely that they are geometrical isomers of 4-ethyl-deca-2,4,6-triene-1-al which resulted from the aldolization and dehydration of two molecules of leaf aldehyde. Accepting this as a reasonable deduction, the geometrical isomerism between (IV-a) and (IV-b) should have originated in the central 4-double bond being newly formed in the C_{12} -system, the other two double bonds at 2- and 6-positions in both condensates inherently possessing the *E*-configuration of the parent leaf aldehyde.

The change in geometrical configuration in polyene systems is sensitively reflected in intensity of UV-absorption and the difference

in intensity was actually observed with the isomeric dinitrophenylhydrazones (IV'-a; ϵ 2.82×10^4) and (IV'-b; ϵ 2.68×10^4). Based on this finding, it may be safely concluded that (IV-a) with the greater intensity is the all-*E* isomer and the other (IV-b) with the smaller intensity is of the remaining possibility *E-Z-E* configuration. In accordance, the IR-spectra of these derivatives showed the presence of *E*-trisubstituted ethylene group (ν_{CH} 834 cm^{-1}) in (IV'-a) and *Z*-trisubstituted ethylene band (ν_{CH} 832, 850 cm^{-1}) in (IV'-b). The scale model inspection revealed that the steric hindrance is comparable in both geometrical isomers, which was actually reflected in the rather anomalously small difference in intensity ($\Delta\epsilon$, 1500) as well as in the isomer ratio of the products (55:45) found by vpc-analysis. Both aldehydes (IV-a, IV-b), when reduced with lithium aluminum hydride followed by catalytic hydrogenation, yielded the same and identical aliphatic alcohol, 4-ethyldecanol (VI), thereby establishing the above-mentioned carbon skeleton.

Since 4-ethyldecanol (VI) was unknown in literature, this compound was synthesized in the present work by the following scheme starting from diethyl malonate: the structure is evidenced by unequivocal sequences of chemical transformation.

Of the two geometrical isomers separated, the aldehyde (IV-b) with *Z*-central double bond may, in principle, be capable of cyclization. In connection with the earlier assumption that the aromatization in the leaf alcohol reaction may proceed through aldol condensation and subsequent Cope rearrangement of the first formed triene aldehyde intermediate, it seems of particular interest to submit this compound to the leaf alcohol reaction conditions. Attempted cyclization

and/or aromatization of (IV-b) by treatment with metallic sodium under the leaf alcohol reaction conditions was doomed to failure since the reaction product isolated here was 4-ethyldecanol (VI) and neither cyclohexadiene intermediate nor substituted benzyl alcohol was formed at all. Consequently, the possibility of operation of aldol condensation followed by Cope rearrangement can be safely excluded, which renewedly furnishes convincing evidence for the proposed mechanism of leaf alcohol reaction.³⁾

Fortuitously enough, 4-ethyldecanol obtained by the metallic sodium treatment of (V) or by the exhaustive hydrogenation of both (IV-a)

leaf aldehyde to give firstly isomeric 4-ethyl-deca-2,4,6-trienealdehyde, (IV-a) and/or (IV-b), followed by the exhaustive reduction of the intermediate with metallic sodium.

The structural elucidation of the diethylamine-catalyzed condensation products of leaf alcohol and their reduction to 4-ethyldecanol as well as the identification of the b-peak substance as 4-ethyldecanol constitute the resolution of the sole pending problem in leaf alcohol reaction *i.e.* it implies that the leaf alcohol reaction has now been completely understood in structure and mechanism of formation of all the reaction products hitherto isolated.

and (IV-b), was found to be identical with one of the by-products in leaf alcohol reaction which was provisionally designated as "b-peak substance" of unknown structure in the earlier work.⁴⁾ It then follows that the formation of 4-ethyldecanol as a by-product in leaf alcohol reaction may be interpreted as the consequence of base-catalyzed aldolization of

EXPERIMENTAL

Condensation of 2-E-hexen-1-al (I-b) using diethylamine. Diethylamine (1.3 g, 0.018 mole) was added to E-hexenal (I-b) (17.60 g, 0.180 mole) during 1 hr with stirring under nitrogen atmosphere and the temperature was kept at 65°C. After addition was completed, the reaction mixture was warmed at 75°C for 1 hr and distilled *in vacuo* to yield the following

3) M. Ohno, Y. Inouye, A. Hatanaka, and T. Kajiwaru, *Bull. Inst. Kyoto Univ.*, **43**, 236 (1965).

4) A. Hatanaka and M. Ohno, *Agr. Biol. Chem.*, **28**, 910 (1964).

fractions; (1) 4 g, bp 73~6°C/3 mm, crude aldehyde (IV); (2) 1.3 g, bp 78~104°C/3 mm; (3) residue.

Isolation of aldehydes (IV-a) and (IV-b) by preparative vpc. The compounds (IV-a) and (IV-b) were isolated by preparative vpc (Barber Colman).

Retention time: (IV-a), 12.5 min; (IV-b), 13.5 min
 Aerograph: A-700, Detector; TCD
 Column: 5% Carbowax 20 M, 150°C
 Detector; 250°C
 Injector: 250°C, Collector 270°C
 Gas flows: 200 ml/min
 Sample size: 2.5 μ l

2.4.-Dinitrophenyl hydrazone of (IV'-a), mp 132~4°C: *Anal.* Found: C, 60.43; H, 6.19; N, 15.22. *Calcd.* for $C_{18}H_{22}N_4O_4$ C, 60.32; H, 6.19; N, 15.63%. (IV'-b) mp 145°C: *Anal.* Found: C, 59.96; H, 6.11; N, 15.68. *Calcd.* for $C_{18}H_{22}N_4O_4$ C, 60.32; H, 6.19; N, 15.63%.

Treatment of (IV) with metallic sodium:—A mixture of (IV) (8 g) and sodium (4.6 g, 0.1 atom) in *p*-xylene was refluxed for 3 hr. The reaction mixture was poured into water and extracted with ether. The extract, after drying and removal of the solvent, gave (VI), bp 130~7°C/12 mm, yield, 0.7 g.

4-Ethyldecatriene alcohol (V). A solution of IV (1.7 g) in ether (10 ml) was treated with lithium aluminum hydride (0.37 g) to give a colorless alcohol (V), bp 80~5°C/3 mm, n_D^{10} 1.4978.

4-Ethyldecanol (VI). A sample of the above alcohol (V) (0.8 g), dissolved in 50 ml of ethyl acetate was hydrogenated in the presence of PtO_2 (0.005 g) until the theoretical amount of hydrogen was absorbed. After filtering the catalyst, ethyl acetate was evaporated *in vacuo*, leaving a mass of brown oil. Distillation of the residue gave 0.5 g of 4-ethyldecanol (VI), bp 130~5°C/12 mm. The alcohol (VI) was identical with the fraction "b-peak substance" in vpc.

Flow rate: 175 ml/min, Temp: 165°C
 Column: P. E. G. 6000 (0.6 $\times$ 60 cm)
 Retention time: Fraction b, (VI); 5 min

Isolation of b-peak substance by preparative vpc. The compound was isolated by preparative vpc (Barber Colman).

Column: 5% Carbowax 20 M, Temp 170°C
 Flow rate: 200 ml/min

3,5-Dinitrobenzoate from b-peak substance; mp 22~

5°C (from ethanol). *Anal.* Found: C, 60.07; H, 7.63; N, 7.15; *Calcd.* for $C_{19}H_{28}O_6N_2$: C, 59.98; H, 7.42; N, 7.36%.

Ethyl ethylmalonate. To a solution of sodium (4.6 g, 0.20 atom) in 75 ml of absolute alcohol was added ethyl malonate (33 g, 0.206 mole) while the liquid was mechanically stirred. The mixture was heated on a steam-bath and stirred while ethyl bromide (25 g, 0.253 mole) was added slowly. The heating was continued for one and a half hrs during which time a copious separation of sodium occurred, and the mixture became neutral to litmus. The greater part of the alcohol was distilled during continued stirring and the residue dissolved in water. The oily layer was separated and treated in the usual way. Fractionation at atmospheric pressure gave a colorless oil boiling at 105~2°C/15~6 mm, 30 g (56.3%), n_D^{25} 1.4130.

Diethyl ethyl, n-hexylmalonate. The ethyl group was introduced first for the reason that a greater difference in boiling point occurs between the mono-alkylated ester and the dialkylated product, thus facilitating purification of the product. To a solution of sodium (7.54 g, 0.328 atom) in 100 ml absolute alcohol were added ethyl ethylmalonate (61.6 g, 0.375 mole) and hexyl bromide (67.1 g, 0.375 mole). Fractionation at 7~8 mm gave 59 g (46.1%) of a colorless oil boiling at 135~8°C, n_D^{25} 1.4284, yield after the procedure described for ethyl ethylmalonate.

Ethyl, hexylmalonic acid. Saponification of the ester was effected by refluxing for 5 hr a homogeneous mixture of 13 g of ester, 25 ml of water and 50 ml of ethyl alcohol with 10 g potassium hydroxide. The solvent was then evaporated and the residue was cooled and acidified with 20 ml of conc. HCl. The free acid separated as an oil. This was extracted with ether and the ether evaporated. The crystals were then dried on a porous plate and washed with a little, petroleum ether. The product consisted of very small, colorless needles melting at 75°C and decomposing at about 140°C with evolution of carbon dioxide. *Anal.* Found: C, 61.01; H, 9.70. *Calcd.* for $C_{11}H_{20}O_4$: C, 61.11; H, 9.26%.

2-Ethyl-octanoic acid. The distillation in Claisen flask of dicarboxylic acid under reduced pressure gave the crude 2-ethyl-octanoic acid. Redistillation of the material gave colorless oil boiling at 145~50°C/12

mm, n_D^{32} 1.4290.

2-Ethyl-octanoic acid ethyl ester. The yield of ester from 2-ethyloctanoic acid (43 g, 0.249 mole), absolute alcohol (115 g), and conc. H_2SO_4 after refluxing for 22 hr, was 41 g (83.9%) of bp 105~115°C/12~3 mm, n_D^{32} 1.4202.

2-Ethyl-octyl alcohol. The lithium aluminum hydride reduction of 2-ethyloctanoic acid ethyl ester (20 g, 0.1 mole) gave the corresponding alcohol, 2-ethyl octyl alcohol, bp 111~5°C/12 mm, n_D^{32} 1.4341, yield 13.5 g (85.5%). 3,5-Dinitrobenzoate: mp 41~2°C (from ethanol). *Anal.* Found: C, 57.98; H, 6.88; N, 7.98. Calcd. for $C_{17}H_{24}N_2O_6$: C, 57.94; H, 6.87; N, 7.95%.

2-Ethyl-octyl bromide. In a flask were placed 48 per cent hydrobromic acid (11 g, 0.065 mole), conc. H_2SO_4 (3 g), and 2-ethyl-octyl alcohol (5 g, 0.025 mole). The mixture was boiled under reflux for 6 hr. The solution was diluted with water and the bromide layer was separated, washed once with a little cold conc. sulfuric acid, then with water and finally with dil. sodium carbonate solution, after usual procedure. The product was collected at 105~9°C/12 mm, n_D^{32} 1.4538 and amounted to 4.6 g (82.4%).

Ethyl 2-ethyl-octylmalonate. To a solution of sodium (0.92 g, 0.04 atom) in 20 ml of absolute alcohol was added ethyl malonate (6.6 g, 0.04 mole) and 2-ethyl octyl bromide (8.8 g, 0.04 mole): this was prepared in the same manner as just described. The yield was 6.2 g (51.5%) boiling at 158~62°C/7~8 mm, n_D^{32} 1.4350.

2-Ethyl-octylmalonic acid. This was prepared in the same manner as the compound just described, using 5.4 g (0.097 mole) of alcoholic potassium hydroxide (water 13.5 ml, alcohol 27 ml).

4-Ethyldecanoic acid. This was prepared in the same manner as the compound just described, using 2-ethyl, octylmalonic acid. The corresponding acid was 3.5 g, bp 173~5°C/14~5 mm, n_D^{32} 1.4384.

4-Ethyldecanol (VI). The lithium aluminum hydride reduction of 2-ethyldecanoic acid (3.5 g, 0.0175 mole) gave the corresponding alcohol, 2-ethyldecanol, bp 134~7°C/10~11 mm, n_D^{32} 1.4402, yield 1.3 g (40%). 3,5-Dinitrobenzoate: mp 23~5°C (from ethanol). *Anal.* Found: C, 59.91; H, 7.76; N, 7.08; Calcd. for $C_{19}H_{28}O_6N_2$: C, 59.98; H, 7.42; N, 7.36%. The melting point was not depressed on admixture with a specimen of the benzoate obtained from "b-peak substance."