The Preparation of 4-Methoxy-2-butenal, a New Dienophile, and Notes on Related Compounds

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It is thought that the 2-butenals containing a functional substituent in the 4-position may be valuable as new type dienophiles for the practical use of the Diels-Alder reaction. No work on the synthesis of such γ-substituted crotonaldehydes had been found in the literature of the subject, till the formation of 4-dimethylamino-2-butenal was first reported by the authors,[1] who were unable to isolate the free aldehyde, but succeeded in isolating the 2,4-dinitrophenylhydrazone ethylsulfate. In this paper we wish to describe a synthesis of 4-methoxy-2-butenal, which was proved to be a dienophile, and to make several notes on new compounds obtained during the course of investigation on 4-dialkylamino- and 4-hydroxy-2-butenals.

Both attempts to prepare 4-bromo-2-butenal by hydrolysing its diacetate[2] (I) and to prepare 4-diethylamino-2-butenal by hydrolysing the diacetate (II), which had been derived from the bromo-compound through the action of diethylamine, were in vain. The two acetates cited here seemed to be extremely labile in the hydrolysis process.

$$\underset{\text{(I)}}{\mathrm{BrCH_2CH:CHCH(OCOCH_3)_2}} \longrightarrow \underset{\text{(II)}}{\mathrm{(C_2H_5)_2NCH_2CH:CHCH(OCOCH_3)_2}}$$

The second attempt to prepare amino-

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[1] I. Ichikizaki and Yao, the 6th annual meeting of the Chemical Society of Japan at Kyoto University on April 2, 1953.

[2] H. Schmid and E. Crob, *Helv. Chim. Acta*, **32**, 77 (1949).

butenals was carried out by hydrolysing 4-dialkylamino-2-butenal diethyl acetals. 4-Dimethylamino-2-butynal diethyl acetal (III), prepared in a fairly good yield by the interaction of 3-dimethylamino-1-propynylmagnesium bromide and ethyl orthoformate in a benzene-ether solution, was hydrogenated to 4-diethylamino-2-butenal diethyl acetal (IV) in the presence of a catalyst such as palladium-barium sulfate. 4-Dimethylamino-2-butenal diethyl acetal (VI) was obtained from diethylpropargylamine via 4-dimethylamino-2-butynal diethyl acetal (V) through a similar process as above.

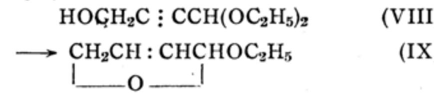
$$R_2NCH_2C \vdots CMgBr \longrightarrow R_2NCH_2C \vdots CCH(OC_2H_5)_2 \quad \begin{array}{ll} (III) & R=C_2H_5 \\ (V) & R=CH_3 \end{array}$$

$$\longrightarrow R_2NCH_2CH:CHCH(OC_2H_5)_2 \quad \begin{array}{ll} (IV) & R=C_2H_5 \\ (VI) & R=CH_3 \end{array}$$

These olefinic acetals were easily hydrolysed with mineral or organic acids, but repeated attempts to isolate the corresponding free aldehydes were all unsuccessful, because they were readily resinified on standing even for short times. Only when 4-dimethylamino-2-butenal diethyl acetal was hydrolysed with an equivalent amount of concentrated hydrochloric acid and immediately treated with Brady's reagent, the formation of 4-dimethylamino-2-butenal was confirmed by charachterizing it as the 2,4-dinitrophenylhydrazone ethylsulfate (VII).

$$(VI) \xrightarrow{\text{HCl, Brady reagent}} \underset{C_2H_5SO_4^-}{(CH_3)_2N^+HCH_2CH:CHCH:NNHC_6H_3(NO_2)_2} \quad (VII)$$

Another investigation was made to prepare 4-hydroxy-2-butenal. By the action of ethyl orthoformate on propargyl alcohol dimagnesiumbromide, 4-hydroxy-2-butynal acetal (VIII) was obtained; however on catalytic reduction it did not yield 4-hydroxy-2-butenal acetal but a low-boiling oil which apparently contained 2-ethoxydihydrofurane (IX).³⁾



$$BrMgOCH_2C \vdots CMgBr \longrightarrow HOCH_2C \vdots CCH(OC_2H_5)_2 \quad (VIII)$$

$$\longrightarrow CH_2CH:CHCHOC_2H_5 \quad (IX)$$

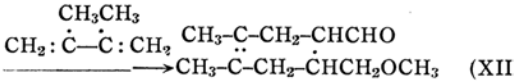
The last attempt to prepare a free aldehyde of the class was made in a way to oxidize 4-methoxy-2-butenol to the corresponding aldehyde and resulted in success.

4-Methoxy-2-butynol (X) was prepared through a partial methylation of butynediol with dimethyl sulfate in an aqueous alkali, followed by a partial reduction to 4-methoxy-2-butenol (XI) in the presence of palladium-calcium carbonate in ethyl acetate. This was oxidized successfully according to either the method of Oppenauer[4] or that of Attenburrow et al.,[5] into 4-methoxy-2-butenal (XII) which was heated at 140°C with an equivalent amount of 2,3-dimethylbutadiene in a sealed tube to yield an adduct, 4,5-dimethyl-2-methoxymethyl-4-cyclohexene-1-carboxaldehyde (XIII).

$$(\vdots CCH_2OH)_2 \longrightarrow CH_3OCH_2C \vdots CCH_2OH \quad (X)$$

$$\longrightarrow CH_3OCH_2CH:CHCH_2OH \quad (XI)$$

$$\longrightarrow CH_3OCH_2CH:CHCHO \quad (XII)$$



$$\xrightarrow{\overset{CH_3CH_3}{CH_2:\dot{C}-\dot{C}:CH_2}} \begin{array}{l} CH_3-C-CH_2-CHCHO \\ CH_3-C-CH_2-\dot{C}HCH_2OCH_3 \end{array} \quad (XIII)$$

Experimental

4-Diethylamino-2-butenal Diacetate.—Diethylamine (3.2 g.) was dissolved in dry ether (25 cc.), and 4-bromo-2-butenal diacetate (5 g.) was added slowly with stirring and cooling. The mixture was allowed to stand over-night, then filtered. The filtrate was evaporated and the residue distilled to give 4-diethylamino-2-butenal diacetate (1.9 g.), a colorless oil, b.p. 108-109°/3 mm. On standing in air this became dark red. The iodomethylate, m.p. 125° (Found: N, 3.3%. $C_{13}H_{24}O_4NI$ requires 3.6%).

4-Diethylamino-2-butynal Diethyl Acetal and 4-Dimethylamino-2-butynal Diethyl Acetal.—After the most part of ether had been distilled off from an ethereal solution of ethylmagnesium bromide (from 2.5 g. of magnesium, 10.9 g. of ethyl bromide and 80 cc. of ether), dry benzene (100 cc.) was added. Then a solution of diethylpropargylamine[6] (11.1 g.) in benzene (10 cc.) was added dropwise with stirring. After the addition had been completed the solution was stirred for 30 minutes, and ethyl orthoformate (14.8 g.) was added. The reaction mixture thus obtained was heated to 65° and stirred vigorously for 3 hours, cooled and decomposed with a saturated solution of ammonium chloride. The organic layer was separated and the aqueous layer extracted with benzene. The combined extracts were washed, dried and distilled, giving 4-diethylamino-2-butynal diethyl acetal (10.5 g.), b.p. 90°/3.5 mm., $n_D^{16.5}$ 1.4492 (Found: N, 6.7%. $C_{12}H_{25}O_2N$ requires 6.5%).

Following a quite similar procedure, 4-dimethylamino-2-butynal diethyl acetal (10.5 g.) was pre-

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3) I.M. Heilbron, E.R.H. Jones and H.P. Koch, *J. Chem. Soc.*, (1942) 735.
Fernand Quennehen and Henn Normant, *Compt. rend.*, 228, 1301 (1949).

4) A. Lauchenauer and H. Schins, *Helv. Chim. Acta*, 32, 1265 (1949).

5) J. Attenburrow, A.F.B. Cameron, I.H. Chapman, R.M. Evans, B.A. Hems, A.B.A. Jansen and T. Walker, *J. Chem. Soc.*, (1952) 1094.

6) John W. Copenhaver and Maurice H. Bigelow, "Acetylene and Carbon Monoxide Chemistry," (1949), p. 110.

pared by the action of ethyl orthoformate (18 g.) on 3-dimethylamino-1-propynylmagnesium bromide (from 2.6 g. of magnesium and 9 g. of dimethylpropargylamine[6]), b.p. 84-86°/6 mm., $n_D^{16.5}$ 1.4419. The iodomethylate, m.p. 139-140° (Found: N, 4.1%. $C_{11}H_{24}O_2NI$ requires 4.2%).

4-Diethylamino-2-butenal Diethyl Acetal and 4-Dimethylamino-2-butenal Diethyl Acetal.—4-Diethylamino-2-butynal diethyl acetal (15.6 g.) was dissolved in ethanol (25 cc.) and hydrogenated in the presence of 3% palladium-barium sulfate (0.5 g.). After 140 minutes one equivalent of hydrogen (1565 cc.) had been absorbed, the catalyst was then separated and the filtrate was distilled, giving 4-diethylamino-2-butenal diethyl acetal, b.p. 80-81°/4 mm., n_D^{15} 1.4402 (Found: N, 58.1%. $C_{12}H_{25}O_4N$ requires 58.2%). The iodomethylate, m.p. 130°.

4-Dimethylamino-2-butynal diethyl acetal was analogously hydrogenated (in 20 cc. of ethanol, 0.2 g. of the catalyst) to 4-dimethylamino-2-butenal diethyl acetal (4.0 g.), b. p. 62-62.5°/3 mm., n_D^{18} 1.4353. The iodomethylate, m.p. 115° (Found: N, 4 0%. $C_{11}H_{24}O_2NI$ requires 4.2%).

2,4-Dinitrophenylhydrazone Ethylsulfate of 4-Dimethylamino-2-butenal.—Concentrated hydrochloric acid (3 drops) was added to 4-dimethylamino-2-butenal diethyl acetal (0.1 g.). With an evolution of heat the mixture became dark red. Brady's reagent (3 cc.) was added to the solution. After 12 hours the reaction mixture was filtered, and the orange reddish needles were recrystallysed from alcohol, m.p. 185-186° (Found: C, 40.3%; H, 4.8%; N, 16.8%. $C_{14}H_{21}O_8N_5S$ requires C, 40.2%; H, 5.0%; N, 17.2%).

4-Hydroxy-2-butynal Diethyl Acetal.—An ethereal solution of ethylmagnesium bromide (from 15 g. of magnesium and 200 cc. of ether) was partly evaporated, 150 cc. of ether being removed. After benzene (200 cc.) had been added, a solution of propargyl alcohol[7] (12.5 g.) in benzene (120 cc.) was added dropwise to the mixture during 1 hour with stirring and heating on a water-bath. After a solution of ethyl orthoformate (49.5 g.) in benzene (50 cc.) had been added in small portions, stirring and heating were continued for 2 hours; then the reaction mixture was cooled and decomposed by adding a saturated aqueous solution of ammonium chloride. The organic layer was dried and fractionated to yield 4-hydroxy-2-butynal diethyl acetal (23.4 g.), b.p. 118-119°/3 mm. (Found: C, 59.8; H, 9.1%. $C_8H_{14}O_3$ requires C, 60.9; H, 8.8%).*

The acetal (18 g.) and a solution of tartaric acid (25 g. in 18 cc. of water) were agitated with a small amount of hydroquinone in an atmosphere of nitrogen, neutralized and then extracted with ether. A part of the extracts was treated with Brady's reagent to yield the 2,4-dinitrophenylhydrazone, orange needles from alcohol, m.p. 119° (Found: N, 27.5%. $C_{10}H_7O_5N_4$ requires 27.5%).

4-Methoxy-2-butynol.—Butynediol[8] (40 g.) was dissolved in an aqueous solution of sodium hydroxide (24 g. in 100 cc. of water). Dimethyl sulfate (31 g.) was added dropwise with agitating at the temperature not higher than 70°. After stirring had been continued at 80° for a further 2 hours, the reaction mixture was extracted continuously with ether over 12 hours. The extract was washed, dried and evaporated. The residue was fractionated cautiously to give dimethoxybutyne (4.1 g.), b.p. 54-55°/15 mm., and 4-methoxy-2-butynol (18.8 g.),[9] b. p. 96-97°/15 mm., 81-82°/5 mm., n_D^{20} 1.4593, d_4^{20} 1.0462 (Found: C, 58.0%; H, 8.2%. $C_5H_8O_2$ requires C, 59.9%; H, 8.0%).

4-Methoxy-2-butenol. — 4-Methoxy-2-butynol (28.9 g.) was hydrogenated, in ethyl acetate (30 cc.), in the presence of 3% palladium-calcium carbonate (2.5 g). One equivalent of hydrogen (7065 cc.) was absorbed within 5 hours. 4-Methoxy-2-butenol, b.p. 87-88°/20 mm., n_D^{20} 1.4485, d_4^{20} 0.9910 (Found: C, 58.3; H, 9.6%. $C_5H_{10}O_3$ requires C, 58.8; H, 9.9%).

4-Methoxy-2-butenol.—*A. By the Method of Attenburrow et. al.*—4-Methoxy-2-butenol (16.9 g.) was stirred for 30 minutes with a suspension of manganese dioxide (98.9 g.) in carbon tetrachloride (290 cc.). The mixture was filtered and evaporated at room temperature under a reduced pressure. The residue, with a small amount of hydroquinone, was distilled to give 4-methoxy-2-butenal (2.1 g.), a colorless oil with irritating odor, b.p. 72-75/26 mm. (Found: C, 59.5; H, 8.2%. $C_5H_8O_2$ requires C, 59.9; H, 8.0%). The 2,4-dinitrophenylhydrazone, m. p. 139-140° (Found: N, 19.8%. $C_{11}H_{12}N_2O_5$ requires 18.9%). The final residue (7.9 g.), an odorless oil, has not been investigated,

B. By the Method of Oppenauer (Modified).—Aluminium isopropoxide (9.9 g.) and 4-methoxy-2-butenol (15 g.) were heated gradually to 70-100° at 12 mm., the replaced isopropyl alcohol being distilled off through a Vigreux column (1.2×20 cm.). After 50 minutes, cinnamic aldehyde (23.9 g.) was added dropwise and the temperature of the oil-bath was kept at 130-150°. The distillate, b.p. 70-88° at 25-27 mm., amounted to 10.4 g. On rectification 4-methoxy-2-butenal (7.1 g.) was obtained. The analytical data was identical with that of the sample in A.

4,5-Dimethyl-2-methoxymethyl-4-cyclohexene-1-carboxaldehyde.—2,3-Dimethylbutadiene[10] (0.77 g.), 4-methoxy-2-butenal (0.61 g.) and petroleum ether (1 cc.) were heated at 140° in a sealed glass tube for 8 hours. The light yellow reaction mixture was fractionated to yield the adduct, a colorless oil with citral-like odor (0.66 g.), b.p. 82-84°/2.5 mm. (Found: C, 72.5%; H, 9.9. $C_{11}H_{18}O_2$ requires C, 72.1; H, 10.0%). The thiosemicarbazone, m.p. 152° (Found: C, 56.1;

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[7] ibid., p. 105.

* All the acetylenic compounds reported in this paper gave too low analytical values of carbon; these values were reproduced identically on repeated combustions. This analytical problem is serious, but has not been solved by the authors.

[8] ibid., p. 98.

[9] Hans J. Pistor, *Gem. Pantent*, 804, 569 (April 26, 1951).

[10] Louis F. Fieser, "Experiments in Organic Chemistry." D.C. Health and Company, (1941), p. 383.

H, 8.2; N, 16.1%. $C_{12}H_{25}ON_3S$ requires C, 56.5; H, 8.2; N, 16.4%).

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