REACTION OF METHYL 4-BROMO-3-BUTYNOATE WITH ALCOHOLS

M.V. Mavrov and V.F. Kucherov

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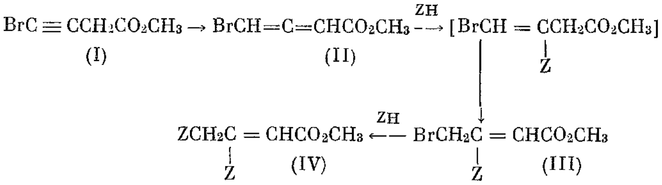
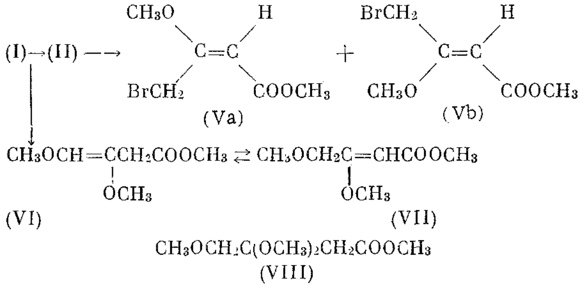
The reaction of methyl 4-bromo-3-butynoate (I) with primary and secondary amines which results in the formation of 3,4-disubstituted derivatives (IV) of methyl crotonate,* proceeds via the scheme



In this communication it is shown that a similar sequence of transformations also occurs during the nucleophilic addition of alcohols to acetylenic ester I. In the presence of alcoholates, the simplest alcohols (CH_3OH and C_2H_5OH) readily react with isomeric esters I and II to form a mixture of V-VIII, the composition of which depends on the amount of alcoholate used and the reaction temperature, which determine the stability and rate of the interconversions of these compounds. The composition of the mixture was determined by gas–liquid chromatography, while the structures of the substances were proved from the UV, IR, and PMR spectra (Table 1). The chief product in the reaction of I with methanol in the presence of 20-50 mole% of sodium methoxide at low temperatures (−5 to −20°C) is methyl 4-bromo-3-methoxycrotonate (V), which is formed as a mixture of isomers (Va and Vb). The PMR spectrum of one of these isomers (the liquid one) contains signals of protons from a $BrCH_2$ group at weaker field, on the basis of which, configuration Va was assigned to it. In contrast to this, the signal of the proton of the vinyl group in the crystalline isomer is shifted to weak field, which confirms configuration Vb for it [1]. Liquid isomer Va, to which the crystalline product is converted on standing and heating, was more stable:



If the reaction of I or Vb with methanol is carried out under more severe conditions (excess sodium methoxide and 20-40°), isomeric compounds V cannot be detected by gas–liquid chromatography in the product formed. Instead, a mixture of three new substances is formed, from which a fraction of the composition $C_7H_{12}O_3$ was isolated by preparative gas–liquid chromatography, and, according to gas–liquid chromatography and the PMR spectra, is an equilibrium mixture (7:3) of the dimethoxyvinylacetic (VI) and dimethoxycrotonic (VII) esters. The third product, being more polar, is converted into a mixture of VI and

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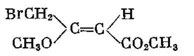
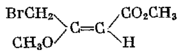
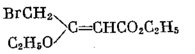
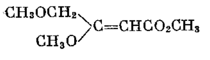
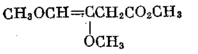
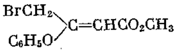
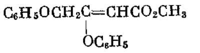
* A special communication will be devoted to this reaction.

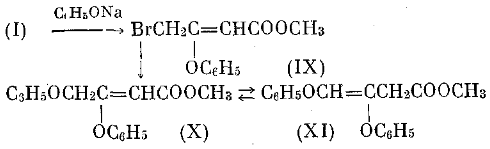
N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No.6, pp.1440-1442, June, 1972. Original article submitted July 29, 1971.

TABLE 1. Spectral Data for the Compounds Obtained

Compound	PMR spectum, ppm			IR spectrum, ν, cm^{-1}	
	δ_α	δ_γ	δ of the other group	C=O	C=C
	5,16	3,82	3,58 (COOCH$_3$) 3,93 (OCH$_3$)	1710	1626
	5,02	4,42	3,60 (COOCH$_3$) 3,65 (OCH$_3$)	1710	1628
	5,06	3,72	3,95 (COOCH$_2$) 4,12 (OCH$_2$)	1710	1626
	4,88	3,54	3,05 (COOCH$_3$) 3,17 (OCH$_3$) 3,33 (OCH$_3$)	1718	1640
 $CH_3OCH{=}\underset{OCH_3}{C}CH_2CO_2CH_3$	2,54	4,29	3,05 (COOCH$_3$) 3,22 (OCH$_3$) 3,50 (OCH$_3$)	1746	1640
	5,48	3,74	3,42 (COOCH$_3$) 6,8—7,0 (OC$_6$H$_5$)	1710	1660
 $C_6H_5OCH_2\underset{OC_6H_5}{C}{=}CHCO_2CH_3$	5,2	4,52	3,48 (COOCH$_3$) 6,6—7,2 (2C$_6$H$_5$O)	1714	1650

VII on attempts to isolate it. This fact provides a basis for assuming for it the methyl 3,4,4-trimethoxybutyrate structure (VIII).

Similar results were obtained in a study of the reaction of I with sodium ethoxide in phenol. Methyl 4-bromo-3-phenoxycrotonate (IX) and an equilibrium mixture of diphenoxy derivatives (X and XI) were isolated from the reaction mixture; the mixture of X and XI could be partially separated by chromatography on Al_2O_3:



The structures of these products follow quite unambiguously from their IR and PMR spectra and analytical data.

EXPERIMENTAL SECTION

The reaction products were analyzed and identified by gas–liquid chromatography with a chromatograph with a glass vaporizer and a flame-ionization detector on a column containing 10% SE-30 silicone or 10% polyethylene glycol-3000 on silanized Chromosorb-W. The IR spectra were obtained with a UR-10 spectrometer, and the NMR spectra were obtained with an HA-60-1L spectrometer.

Addition of Methanol to Methyl 4-Bromo-3-butynoate (I). A) About 6 ml of 2% sodium methoxide in methanol was added dropwise at −10° to a solution of 1.8 g of ester I in 40 ml of methanol until the starting ester completely disappeared (as monitored by gas–liquid chromatographic analysis). The mixture was decomposed with dry ammonium chloride, the methanol was removed in vacuo, and the residue was extracted thoroughly with ether and dried with $CaCl_2$. The residue (2.1 g) remaining after evaporation of the ether partially crystallized, and 0.9 g of crystalline isomer Vb with mp 59.5-60° [ether–petroleum ether (1:6)] and λ_{max} (heptane) 245 nm (ε 11,000) was isolated. The IR and PMR spectra are given in Table 1. Found%: C 34.53; H 4.40; Br 38.0. $C_6H_9BrO_3$. Calc.%: C 34.47; H 4.34; Br 38.23. The liquid residue (1.2 g) contained no more than 5% Vb according to gas–liquid chromatographic data and, from its PMR spectrum, corresponds to isomeric ester Va with bp 65° (0.4 mm), n_D^{21} 1.5016, and λ_{max} (in heptane) 243 nm (ε 9800).

B) Similarly, 1.8 g of ester I was added at 20° to sodium methoxide (from 0.4 g of Na) in 20 ml of methanol, during which the temperature of the reaction mixture rose to 40°. The mixture was held at this temperature for 2 h, cooled, and worked up as described above. Distillation yielded 1.8 g of a fraction with bp 50-70° (bath temperature) (0.12 mm) and $n_D^{22.5}$ 1.4342. According to gas–liquid chromatography, the mixture contained 60% VI, 15% VII, and 25% VIII. A mixture of 70% of VI and 30% of VII, which did not contain the other substances (according to gas—liquid chromatography and IR and PMR spectroscopy), which was not separable on this column, was obtained by preparative gas—liquid chromatography (silicone elastomer on Chromosorb-W at 150°); n_D^{25} 1.4310. Found%: C 52.28; H 7.68. $C_7H_{12}O_3$. Calc.%: C 52.49; H 7.55.

Addition of Phenol to Methyl 4-Bromo-3-butynoate (I). A total of 2.0 g of ester I was added at 40° to sodium phenoxide in phenol (from 0.1 g of Na and 4 g of phenol); the temperature of the reaction mixture rose to 120° in the process. The reaction product was allowed to stand for 2 h and was then dissolved in ether and washed with 4 N NaOH. Removal of the ether gave 2.4 g of a residue which partially crystallized to give 0.4 g of methyl 4-bromo-3-phenoxycrotonate (IX) with mp 80-80.5° (from hexane) and λ_{max} (in alcohol) 216, 259 nm, (ε 14,200, 7350). The IR and PMR spectra are given in Table 1. Found%: C 48.69; H 4.27; Br 29.40. $C_{11}H_{11}BrO_3$. Calc.%: C 48.72; H 4.08; Br 29.47. The liquid mixture of products obtained after removal of IX was chromatographed on Al_2O_3. Elution with ether—petroleum ether (1:4) yielded 0.3 g of IX and 0.9 g of methyl 3,4-diphenoxycrotonate (X) (see Table 1 for the spectral data) as an oil containing a small amount of a contaminant, apparently the (1,2-diphenoxyvinyl)acetic ester (XI). The IR spectrum contains an absorption band at 1746 cm^{-1} ($COOCH_3$), while the PMR spectrum contains a singlet of low intensity at 6.28 ppm ($=CHOC_6H_5$).

Similarly, 35% of a crystalline isomer of ethyl 3-ethoxy-4-bromocrotonate with mp 45.5° (from petroleum ether) and λ_{max} (in heptane) 247 nm (ε 11,000) could be obtained by the reaction of ethyl 4-bromo-2,3-butadienoate [2] with an equivalent amount of sodium ethoxide in ethanol at −10°. The IR and PMR spectra are given in Table 1. Found%: C 40.3; H 5.32; Br 33.02. $C_8H_{13}BrO_3$. Calc.%: C 40.5; H 5.5; Br 33.75. The substance changed very readily on storage.

CONCLUSIONS

The regularities of the nucleophilic addition of alcohols and phenols to methyl 4-bromo-3-butynoate were studied.

LITERATURE CITED

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2. M. V. Mavrov and V. F. Kucherov, Izv. Akad. Nauk SSSR, Ser. Khim., 1442 (1972).