

Intramolecular 1,5-Hydride Shift in Products of Stevens 3,2-Rearrangement of Ammonium Salts Containing 3-Phenyl-2-propynyl Group

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Abstract—In products of Stevens 3,2-rearrangement of ammonium salts containing alongside alkoxy carbonylmethyl also 3-phenyl-2-propynyl group an intramolecular 1,5-hydride shift is observed resulting in immonium salts which transform into aminoesters of enamine structure. The hydrolysis of the latter provides the lower aliphatic aldehydes and the corresponding aminoesters. An acid treatment of the reaction mixture affords a mixture of hydrogenated and nonhydrogenated esters of α -ketoacids originating from the mixture of 1,3-diene aminoesters. At treating with concn. HCl of the obtained mixture the nonhydrogenated ketoester undergoes cyclization into 4-methyl-3-phenyl-2-buten-1,4-olide.

We showed formerly that ammonium salts containing both alkoxy carbonylmethyl and 4-penten-2-yl groups treated with sodium alcoholate underwent Stevens 3,2-rearrangement providing products that suffered an intramolecular 1,5-hydride shift [1, 2]. Further treatment of the products with hydrochloric acid resulted in formation of hydrogenated and nonhydrogenated products.

It is known from published sources that tertiary amines containing α -hydrogen atoms are potential donors of hydride ions [3, 4] that are used for intermolecular hydrogenation of multiple bonds, also nitrogen-containing. Among intramolecular hydride

migrations the most interesting are transannular 1,3- and 1,5-hydride shifts [5, 6].

This report concerns the study of hydride shift in the products of Stevens 3,2-rearrangement of ammonium salts containing both alkoxy carbonylmethyl and 4-penten-2-yl. To this end ammonium salts **Ia–f** were synthesized and subjected to treatment with sodium alcoholates in ether (benzene) (Table 1).

The formation of compounds obtained may be rationalized by the following scheme including A and B pathways. According to path A in the products of Stevens 3,2-rearrangement occurs a hydride shift

Table 1. Hydrogenated and nonhydrogenated products of Stevens rearrangement of salts **Ia–f**

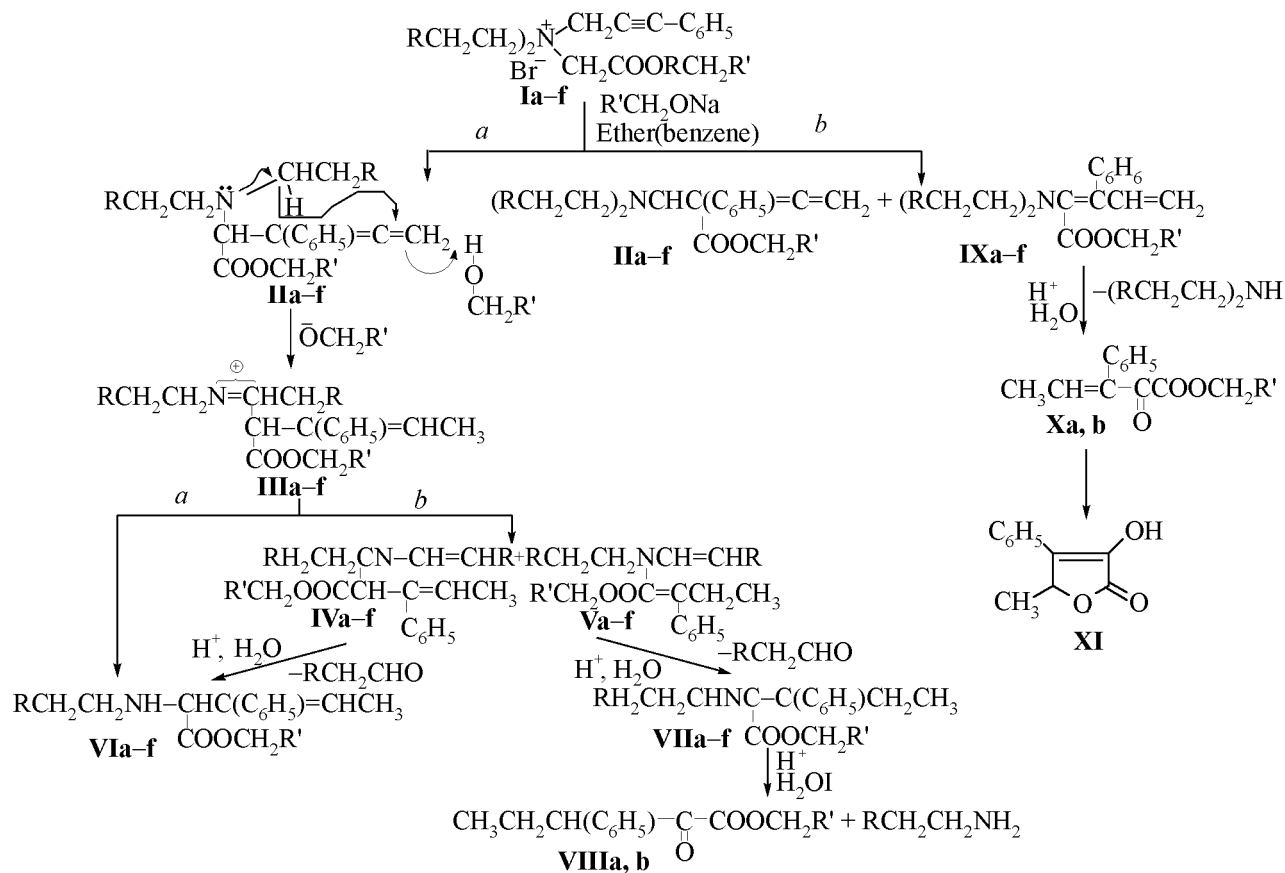
| Initial salt, compd. no. | Amino-ester | Yield, % | bp, °C (mm Hg) | Ratio of hydrogenated and initial amines in the mixture | Found, % | | | Formula | Calculated, % | | |
|--------------------------|-------------|----------|----------------|---|----------|------|------|---|---------------|------|------|
| | | | | | C | H | N | | C | H | N |
| Ia | VIa | 18 | 116–119 (3) | 95:5 | 71.54 | 5.73 | 5.77 | C ₁₄ H ₁₉ NO ₂ + ¹³ H ₁₇ N | 72.56 | 8.20 | 6.07 |
| Ib | VIb | 16 | 161–164 (3) | 94:6 | 73.74 | 8.27 | 5.48 | C ₁₅ H ₂₁ NO ₂ + ¹³ H ₁₇ N | 73.37 | 8.53 | 5.75 |
| Ic | VIc | 14.5 | 148–152 (1) | 96:4 | 72.89 | 8.21 | 5.36 | C ₁₅ H ₂₁ NO ₂ + ¹⁵ H ₂₁ N | 73.25 | 8.55 | 5.70 |
| Id | VIId | 11.3 | 155–160 (1) | 93:7 | 74.48 | 8.37 | 5.85 | C ₁₆ H ₂₃ NO ₂ + ¹⁵ H ₂₁ N | 74.16 | 8.87 | 5.43 |
| Ie | VIe | 13.2 | 173–180 (1) | 94:6 | 73.74 | 8.57 | 5.01 | C ₁₆ H ₂₃ NO ₂ + ¹⁷ H ₂₅ N | 74.15 | 8.90 | 5.39 |
| If | VIIf | 18.7 | 200–206 (3) | 92:8 | 74.39 | 8.88 | 4.78 | C ₁₇ H ₂₅ NO ₂ + ¹⁷ H ₂₅ N | 74.88 | 9.18 | 5.14 |

Table 1. (Contd.)

| Keto-esters, compd. no. | Ratio VIII:X, % | Overall yield, | bp, °C (mmHg) | Found, % | | Formula | Calculated, % | | Aldehyde, % | mp, °C DNPH | Amines | |
|-------------------------------|-----------------------|-------------------|------------------|----------|------|---|---------------|------|---|----------------|--|---|
| | | | | C | H | | C | H | | | RNH ₂ , % R | R ₂ NH, % R ² |
| VIIIa+Xa | 52:48 | 40.3 | 110-115 (2) | 58.43 | 7.45 | C ₇ H ₁₀ O ₃ + C ₇ H ₁₂ O ₃ | 58.76 | 7.66 | CH ₃ CHO 41.6 | 163-164 | CH ₃ CH ₂ 32 | (CH ₃ CH ₂) ₂ 18 |
| VIIIb+Xb | 40:60 | 46.3 | 118-124 (2) | 60.74 | 8.18 | C ₈ H ₁₂ O ₃ + C ₈ H ₁₄ O ₃ | 61.07 | 8.40 | CH ₃ CHO 45.0 | 164 | CH ₃ CH ₂ 3.0 | (CH ₃ CH ₂) ₂ 19.5 |
| VIIIa+Xa | 17:83 | 54.4 | 105-110 (1) | 58.08 | 7.97 | C ₇ H ₁₀ O ₃ + C ₇ H ₁₂ O ₃ | 58.47 | 8.11 | C ₂ H ₅ CHO 15.3 | 154 | C ₃ H ₇ 14.5 | (C ₃ H ₇) ₂ 37 |
| VIIIb+Xb | 10:90 | 45.7 | 109-115 (1) | 80.61 | 8.47 | C ₈ H ₁₂ O ₃ + C ₈ H ₁₄ O ₃ | 60.84 | 8.74 | C ₂ H ₅ CHO 8.9 | 154-155 | C ₃ H ₇ 9.6 | (C ₃ H ₇) ₂ 41 |
| VIIIa+Xa | 32:68 | 50.2 | 109-115 (2) | 58.11 | 7.62 | C ₇ H ₁₀ O ₃ + C ₇ H ₁₂ O ₃ | 58.60 | 7.92 | C ₃ H ₇ CHO 28.5 | 121-122 | C ₄ H ₉ 31.5 | (C ₄ H ₉) ₂ 36.4 |
| VIIIb+Xb | 47.5:52.5 | 70.3 | 108-114 (1) | 61.49 | 7.96 | C ₈ H ₁₂ O ₃ + C ₈ H ₁₄ O ₃ | 61.13 | 8.31 | C ₃ H ₇ CHO 42.2 | 120-121 | C ₄ H ₉ 28.5 | (C ₄ H ₉) ₂ 33.7 |

followed by prototropic isomerization leading to hydrogenated aminoesters **VIa-f**, **VIIa-f** and ketoesters **VIIIa, b**, and along path B only prototropic isomerization takes place affording aminoesters **IIa-f**, **IXa-f** and ketoesters **Xa, b** (Table 1).

In both cases arise the corresponding aminoesters of enamine structure **IVa-f**, **Va-f**, **VIIa-f**, **IXa-f** which on hydrolysis with diluted hydrochloric acid furnish esters of hydrogenated and nonhydrogenated ketoacids **VIIIa, b**, **Xa, b** (Table 1).



I, II, VI, VII, IX, R = R = H (a), R = H, R = Me (b), R = Me, R = H (c), R = R = Me (d), R = Et, R = H (e), Me (f), (**VIII, X**, R = H (a), Me (b)).

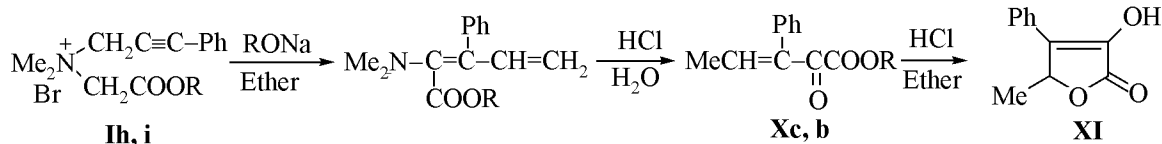
In the ^1H NMR spectrum of the primary product of Stevens 3,2-rearrangement obtained from salt **Ia** before the acid treatment the integral intensity of protons attached to multiple bonds is significantly higher than expected. Besides in case of formation of immonium salt **IIIa** as a single intermediate product the amount of amine compounds in the ether solution should be a lot smaller than that actually observed. This data show that immonium salt **IIIa** if not completely, at least mainly transforms into compounds **IVa**, **Va** under the action of methylate anion [2].

In order to isolate individual products **VIIIa, b** the mixture of ketoesters **VIIIa, b**, **Xa, b** was treated with concn. HCl. We presumed that the un-

saturated ketoesters would be converted into lactone **XI**, and the hydrogenated ketoesters **VIIIa, b** would remain intact. We really obtained by this procedure ketoesters **VIIIa, b** and lactone **XI** in pure state. The lactone was also prepared by an independent synthesis through hydrolysis of Stevens rearrangement product obtained from dimethylmethoxy(ethoxy)carbonylmethyl(3-phenyl-2-propynyl)ammonium bromides.

Ketoester **Xa** we synthesized earlier [7].

Thus the spectral and experimental data permit a statement that at 1,5-hydride shift in the products of 3,2-rearrangement of the salts under study the intermediately forming immonium salts **IIIa-f** under the reaction conditions mainly transform into amino-



esters **IVa-f**, **Va-f** which in their turn are converted into the final products. Formation of reaction products along path *a* is also probable. For instance, the treatment with water of the dry residue of salt **Ia** after reaction revealed the presence of compounds **VIa**, **VIIIa** and of acetaldehyde; the latter was identified as 2,4-dinitrophenylhydrazone (4%).

The structure of compounds obtained was established with the use of IR and ^1H NMR spectroscopy (Table 2), and their purity was checked by GLC.

EXPERIMENTAL

IR spectra were recorded on spectrophotometers UR-20 and Specord 75IR, ^1H NMR spectra were registered on spectrometers Perkin-Elmer R-12B and Varian Mercury-300 at operating frequencies 60 and 300 MHz from solutions in CCl_4 and $\text{DMSO}-d_6$ with TMS as internal reference. GLC analysis was carried out on chromatograph LKhM-8MD equipped with catharometer, a column $2000 \times 3\text{mm}$, stationary phase 5% OV-17 on Chromaton N-Super, oven temperature $175\text{--}200^\circ\text{C}$, gas carrier helium, flow rate 60 ml min^{-1} .

General procedure of rearrangement. (a) To a dispersion of 0.03 mol of salts **Ia-f** in 20 ml of anhydrous ether (benzene) was added sodium alcoholate prepared from 0.06 mol of sodium. The reaction mixture was thoroughly stirred. On completion of heat evolution the mixture was boiled for 20 min more, and then ether and water were added. The organic layer was separated, the water layer was twice extracted with ether. The combined extracts were treated with 1.5 N HCl till acid pH. The products other than amines were extracted into ether (3–10 ml), dried with magnesium sulfate, and evaporated. In the ether extract an aldehyde was determined as 2,4-diphenylhydrazone. Ketoesters **VIIIa, b**; **Xa, b** were isolated by distillation (Tables 1, 2). From the water layer after treating with potassium carbonate ($0\text{--}5^\circ\text{C}$) the amine derivatives were extracted into ether (3–10 ml), dried with magnesium sulfate, and the solvent was removed. Aminoethers **VIa-f** were isolated by distillation. The results are compiled in TABLE 1. In the ether extracts

by means of GLC were identified and quantitatively determined the initial dialkyl(3-phenyl-2-propynyl)-amines (8–14%). When needed after adding NaOH to the reaction residue and extraction with ether of alkyl- and dialkylamines their amounts and nature were determined by GLC (Table 1).

(b) To a dispersion of 0.03 mol of salts **Ia-f** in 20 ml of anhydrous ether (benzene) was added sodium alcoholate prepared from 0.06 mol of sodium. On completion of heat evolution the mixture was kept for 20–30 min at $30\text{--}33^\circ\text{C}$ in ether or for 10–15 min at $75\text{--}78^\circ\text{C}$ in benzene. In the organic layer the content of amine products was determined by titration (81–89%).

The solid precipitate was washed with anhydrous ether (3–10 ml). The solvent was removed in a vacuum. The residue was investigated with the use of GLC, ^1H NMR, and IR spectroscopy, then it was acidified with 1.5 N HCl. Further workup was as described under procedure a. To the solid reaction residue was added water, extracted with ether (3–10 ml), the extract was dried with magnesium sulfate, the solvent was distilled off, and in this distillate acetaldehyde was determined as dinitrophenylhydrazone. The composition of the residue was identified by GLC by comparison with the known samples obtained by procedure (a).

Reaction of methyl 3-phenyl-2-oxopenten-3-ate with concn. HCl. To 3.06 g (0.015 mol) of ketoester **VIIIa** at stirring was added dropwise 2 ml of concn. HCl. The mixture was stirred for 2.5 h at $55\text{--}56^\circ\text{C}$. The separated precipitate was filtered off and washed with hexane. We obtained 2.5 g (87%) 3-hydroxy-5-methyl-4-phenyltetrahydrofuran-2-one (**XI**), mp $140\text{--}141^\circ\text{C}$ (from alcohol). Found, %: C 69.02; H 5.53. $\text{C}_{11}\text{H}_{10}\text{O}_3$. Calculated, %: C 69.47; H 5.26.

Similarly from ethyl 3-phenyl-2-oxopenten-3-ate was obtained lactone **XI** in 81% yield.

Reaction of ketoesters VIIIa, Xa mixture with concn. HCl. To 3 g (0.015 mol) of ketoesters **VIIIa, Xa** mixture (52:48) was added at stirring dropwise

Table 2. IR and ¹H NMR spectra of compounds **VIa-f**, **VIIIa-b**, **Xa-b**, **XI**

| Compd. | IR spectrum, cm ⁻¹ | ¹ H NMR spectrum, (DMSO- <i>d</i> ₆), δ, ppm (<i>J</i> , Hz) |
|--------------|--|---|
| VIa | 690, 725, 770, 1485, 1530, 1610, 1830, 1890, 3035, 3065, 3085 (C ₆ H ₅), 790, 830, 1640, (CH=C), 1070, 1145, 1240, 1735 (COO), 3375 (NH) | 0.90 t (3H, CH ₂ CH ₃ , <i>J</i> 7), 1.55 br.s (1H, NH), 1.72 d (3H, CH ₃ CH=, <i>J</i> 8), 2.32 q (2H, CH ₂ CH ₃), 3.52 s (3H, OCH ₃), 4.18 s (1H, NCH), 5.69 q (1H, CH ₃ CH=), 7.15 s (5H, C ₆ H ₅) |
| VIb | 700, 730, 775, 1480, 1590, 1610, 1810, 1890, 3030, 3065, 3080 (C ₆ H ₅), 790, 835, 1640 (CH=C), 1065, 1150, 1240, 1735 (COO), 3400 (NH) | 1065, 1150, 1240, 1735 (COO), 3400 (NH) 0.91 t (3H, CH ₂ CH ₃ , <i>J</i> 7.1), 1.23 t (3H, OCH ₂ CH ₃ , <i>J</i> 7), 1.57 br.s (1H, NH), 1.72 d (3H, CH ₃ CH=, <i>J</i> 8), VIc 2.18 q (2H, CH ₂ CH ₃), 3.53 q (2H, OCH ₂), 4.17 s (1H, NCH), 5.68 q (1H, CH=), 7.15 m (5H, C ₆ H ₅) |
| VIb | 710, 725, 770, 1485, 1590, 1610, 1810, 1830, 1890, 3035, 3070, 3085 (C ₆ H ₅), 790, 830, 1640 (CH=C), 1070, 1145, 1235, 1735 (COO), 3380 (NH) | 0.80 t (3H, CH ₃ (CH ₂) ₂ , <i>J</i> 7.1), 1.25 m (2H, CH ₂ CH ₂ CH ₃), 1.49 br.s (1H, NH), 1.73 d (3H, CH ₃ CH=), 2.30 t (2H, CH ₂ CH ₂ CH ₃ , <i>J</i> 7.3), 3.47 s (3H, OCH ₃), 4.17 s (1H, NCH), 5.67 q (1H, CH=, <i>J</i> 8), 7.16 m (5H, C ₆ H ₅) |
| VI d | 700, 725, 765, 1485, 1590, 1610, 1810, 1890, 3035, 3070, 3085 (C ₆ H ₅), 790, 835, 1640 (CH=C), 1070, 1145, 1240, 1740 (COO), 3390 (NH) | 0.81 t [3H, CH ₃ (CH ₂) ₂ , <i>J</i> 7.1], 1.22 t (3H, OCH ₂ CH ₃ , <i>J</i> 7), 1.24 m (2H, CH ₂ CH ₂ CH ₃), 1.51 br.s (1H, NH), 1.73 d (3H, CH ₃ CH=), 2.29 t (2H, CH ₂ CH ₂ CH ₃ , <i>J</i> 7.3), 3.48 q (2H, OCH ₂), 4.16 s (1H, NCH), 5.67 q (1H, CH=, <i>J</i> 8), 7.16 m (5H, C ₆ H ₅) |
| VIe | 700, 730, 770, 1485, 1590, 1605, 1830, 1890, 3035, 3070, 3085 (C ₆ H ₅), 790, 825, 1695 (CH=C), 1065, 1140, 1240, 1735 (COO), 3090 (NH) | 0.70 t [3H, CH ₃ (CH ₂) ₃ , <i>J</i> 7.1], 1.22 m (4H, CH ₂ CH ₂ CH ₂ CH ₃), 1.52 br.s (1H, NH), 1.73 d (3H, CH ₃ CH=), 2.28 t (2H, CH ₂ CH ₂ CH ₂ CH ₃ , <i>J</i> 7.3), 3.47 s (3H, OCH ₃), 4.14 s (1H, NCH), 5.65 q (1H, CH=, <i>J</i> 7.3), 7.15 m (5H, C ₆ H ₅) |
| VI f | 710, 725, 765, 1485, 1590, 1610, 1810, 1830, 1890, 3035, 3070, 3085 (C ₆ H ₅), 790, 825, 1640 (CH=C), 1070, 1145, 1240, 1735 (COO), 3380 (NH) | 0.76 t [3H, CH ₃ (CH ₂) ₃ , <i>J</i> 7.1], 1.21 m (4H, CH ₂ CH ₂ CH ₂ CH ₃), 1.23 t (3H, CH ₃ CH ₂ O), 1.51 m (1H, NH), 1.72 d (3H, CH ₃ CH=), 2.28 t (2H, CH ₂ CH ₂ CH ₂ CH ₃ , <i>J</i> 7.3), 3.51 q (2H, OCH ₂), 4.14 s (1H, NCH), 5.65 q (1H, CH=, <i>J</i> 7.3), 7.13 m (5H, C ₆ H ₅) |
| VIIIa | 700, 725, 770, 1480, 1590, 1610, 1810, 1830, 1890, 3030, 3065, 3080 (C ₆ H ₅), 1675 (C=O), 1070, 1080, 1140, 1240, 1735 (COO) | 0.85 t (3H, CH ₃ CH ₂ , <i>J</i> 7), 1.77 and 2.07 m (2H, CH ₃ CH ₂), 3.75 s (3H, OCH ₃), 4.29 m (1H, CH), 7.10–7.45 m (5H, C ₆ H ₅) |
| Xa | 705, 730, 770, 1485, 1585, 1610, 1830, 1890, 3035, 3065, 3080 (C ₆ H ₅), 790, 835, 1640 (CH=C), 1677 (C=O), 1075, 1145, 1240, 1740 (COO) | 1.94 d (3H, CH ₃ CH=, <i>J</i> 8), 3.87 s (3H, OCH ₃), 7.0 q (1H, CH=), 7.10–7.45 m (5H, C ₆ H ₅) |
| VIIIb | 690, 730, 770, 1485, 1585, 1610, 1810, 1830, 1890, 3030, 3065, 3085 (C ₆ H ₅), 1675 (C=O), 1070, 1140, 1240, 1735 (COO) | 0.90 t (3H, CH ₃ CH ₂ , <i>J</i> 7), 1.23 t (3H, CH ₃ CH ₂ O, <i>J</i> 7), 1.75 and 2.06 m (2H, CH ₃ CH ₂), 4.16 q (2H, CH ₃ CH ₂ O), 4.25 m (1H, CH), 7.09–7.44 m (5H, C ₆ H ₅) |
| Xb | 700, 720, 765, 1485, 1590, 1605, 1830, 1890, 3035, 3070, 3085 (C ₆ H ₅), 790, 835, 1640 (CH=C), 1675 3070, 3085 (C ₆ H ₅), 790, 835, 1640 (CH=C), 1675 (C=O), 1070, 1145, 1240, 1735 (COO) | 1.32 t (3H, CH ₃ CH ₂ O, <i>J</i> 7), 1.92 d (CH ₃ CH=, <i>J</i> 8), 4.32 q (2H, CH ₃ CH ₂ O), 7.04 q (1H, CH ₃ CH=), 7.09–7.44 m (5H, C ₆ H ₅) |
| XI | 710, 775, 1590, 1705, 1960, 3035, 3065, 3085 (C ₆ H ₅), 1125, 1080, 1245, 1745 (COO), 3100–3500 (OH) | 1.44 d (3H, CH ₃ CH, <i>J</i> 6.6), 5.10 q (1H, CH ₃ CH), 7.52 br.s (1H, OH), 7.4 m (5H, C ₆ H ₅) |

3 ml of concn. HCl. The stirring at 55–60°C was continued for 10 h, the reaction mixture was then cooled, the separated precipitate was filtered off and washed with hexane. We obtained 1.2 g of lactone **XI** (76% with respect to ketoester **Xa**), mp 140–141°C (from alcohol). No depression of melting point was observed in a sample mixed with compound obtained in the previous experiment. The solvent was removed from the filtrate, and the residue was distilled in a vacuum. We obtained 0.7 g of compound **VIIIa** (44% with respect to ketoester **VIIIa** in the initial mixture), bp 96–98°C (1 mm Hg), n_D^{20} 1.5078.

Similarly from 3.3 g (0.015 mol) of ketoesters **VIIIb**, **Xb** in 40:60 ratio and 3 ml of 36% HCl we obtained 1.2 g (73%) of lactone **XI** (with respect to ketoester **Xb**), mp 140–141°C (from alcohol), and 0.53 g (41%) of compound **VIIIb** (with respect to ketoester **VIIIb** in the initial mixture), bp 96–98°C (2 mm Hg), n_D^{20} 1.5107.

REFERENCES

1. Kocharyan, S.T., Ogandzhanyan, S.M., Churkina, N.P., Voskanyan, V.S., Razina, T.L., and Babayan, A.T., *Arm. Khim. Zh.*, 1990, vol. 43, p. 136.
2. Kocharyan, S.T., Razina, T.L., Gyul'nazaryan, A.Kh., and Babayan, A.T., *Zh. Obshch. Khim.*, 2001, vol. 71, p. 294.
3. Kaitmazov, G.S., Gambaryan, N.P., and Rokhlin, E.E., *Usp. Khim.*, 1989, vol. 58, p. 2011.
4. Parnes, Z.N. and Kursanov, D.N., *Reaktsii gidridnogo peremeshcheniya v organicheskoi khimii* (Reaction of Hydride Shift in Organic Chemistry), Moscow: Nauka, 1969, 161.
5. Cope, A.C., Berchald, G., Peterson, P., and Sherman, S., *J. Am. Chem. Soc.*, 1960, vol. 82, p. 6364.
6. Prelog, V., Kiing, N., and Toljenovic, T., *Helv. Chim. Acta*, 1962, vol. 45, p. 1352.
7. Kocharyan, S.T., Ogandzhanyan, S.M., and Babayan, A.T., *Arm. Khim. Zh.*, 1976, vol. 29, p. 409.