Stevens Rearrangement of Ammonium Salts Containing 3-Methyl-3-ethoxycarbonylbutanon-2-yl Group

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Abstract—Ammonium salts containing alongside 3-methyl-3-ethoxycarbonylbutanon-2-yl also 2-alkenyl or benzyl groups under the treatment with $Na_2CO_3 \cdot 10H_2O$ afford products resulting from Stevens rearrangement. In the mentioned salts the ketoester group on treatment with sodium ethylate suspension in ether or benzene suffers partial or total acid cleavage, and then the Stevens 3,2-rearrangement takes place.

The study of steric factors effect on competition between Stevens and Sommelet rearrangements and on formation of products either from Stevens 1,2- or 3,2-rearrangement is of interest. It is known that the competition between the above rearrangements is essentially affected both by the character of the migrating moiety and the nature of the groups adding this moiety, and also by the alkyl groups attached to the nitrogen atom [1–4].

In extension of research in this field we report here on Stevens rearrangement in ammonium salts **Ia–e** containing as the group adding the migrating moiety the 3-methyl-3-ethoxycarbonylbutanon-2-yl group. We used as basic reagents a sodium ethylate suspension in ether or benzene and also $Na_2CO_3 \cdot 10H_2O$ or water solution thereof.

The experiments revealed that regardless of temperature and the solvent character at treatment with sodium ethylate suspension in ether (benzene) the salts with allyl (**Ia**) and benzyl (**Ie**) groups underwent complete acid cleavage rearrangement whereas the salts with 2-butenyl, 3-methyl-2-butenyl, 3-phenyl-2-propenyl groups (**Ib–d**) underwent the acid cleavage rearrangement only partially, and the main products there resulted from Stevens 3,2-rearrangement (Table 1).

The experimental data obtained permit rationalization of the salts **Ia–d** rearrangement under treatment with basic reagents by the following general scheme including reaction directions *a–c*.

Along the path *a* first occurs the cleavage of the ketoester group of ammonium salt effected by sodium ethylate and then proceeds Stevens 3,2-rearrangement providing amines **IIIa–d**. Along path *b* these amines arise from the direct Stevens 3,2-rearrangement as a result of the acid cleavage. In going to a
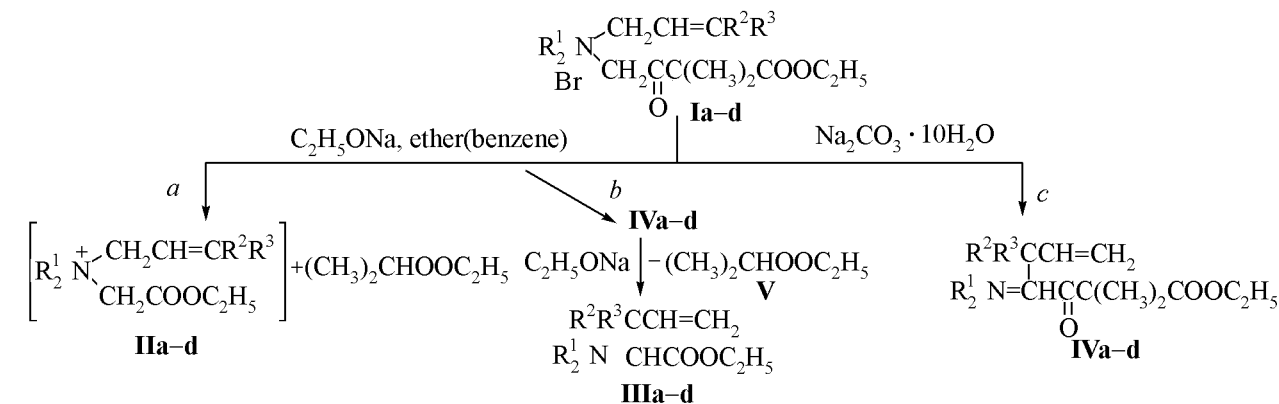
$R^1 = CH_3$, $R^2 = R_3 = H$ (**Ia–IVa**); $R^1 = R^3 = CH_3$, $R^2 = H$ (**Ib–IVb**); $R_2^1 = (CH_2)_5$, $R^2 = R^3 = CH_3$ (**Ic–IVc**); $R^1 = CH_3$, $R^2 = H$, $R^3 = C_6H_5$ (**Id–IVd**).

Table 1. Yields, constants and elemental analysis data of products of rearrangement of salts **Ia–e**

Compd. no.	Base	Solvent	Reaction temperature, °C	Reaction time, h	Reaction product	Yield,[a] %	bp, °C (mm Hg)	n_D^{20}	Found, % C	Found, % H	Found, % N	Formula	Calculated, % C	Calculated, % H	Calculated, % N
Ia	C₂H₅ONa	Ether	30–32	1	**IIIa**	43	71–73 (11)	1.4370	63.45	10.17	8.02	$C_9H_{17}NO_2$	63.16	9.94	8.19
		Benzene	30–32	1	**IIIa**	45	72–73 (11)	1.4367	63.39	10.08	8.05	$C_9H_{17}NO_2$	–	–	–
		Benzene	55–60	1	**IIIa**	46	70–71 (10)	1.4369	63.61	9.67	8.35	$C_9H_{17}NO_2$	–	–	–
	Na₂CO₃·10H₂O	Water	55–60	6	**IVa**	42	95–96 (2)	1.4520	64.45	9.17	6.02	$C_{13}H_{23}NO_3$	64.73	9.54	5.80
			55–60	6	**IVa**	72	104–105 (6)	1.4517	64.31	9.09	6.12	$C_{13}H_{23}NO_3$	–	–	–
Ib	C₂H₅ONa	Ether	30–32	1	**IIIb**	13	73–74 (10)	1.4403	64.72	9.27	6.89	$C_{10}H_{19}NO_2$	64.86	10.27	7.56
					IVb	47	101–103 (2)	1.4572	65.27	9.65	5.71	$C_{14}H_{25}NO_3$	65.88	9.80	5.49
	Na₂CO₃·10H₂O	Water	55–60	6	**IVb**	40	103–105 (3)	1.4575	65.31	9.48	5.88	$C_{14}H_{25}NO_3$	–	–	–
			55–60	6	**IVb**	72	110–112 (6)	1.4570	65.25	9.53	5.77	$C_{14}H_{25}NO_3$	–	–	–
Ic	C₂H₅ONa	Ether	30–32	1	**IIIc**	8.5	115–117 (7)	1.4685	70.55	10.27	5.63	$C_{14}H_{25}NO_2$	70.29	10.46	5.85
					IVc	64	123–125 (2)	1.4735	70.15	10.32	4.28	$C_{18}H_{31}NO_3$	69.90	10.03	4.53
	Na₂CO₃·10H₂O	Ether	50–55	6	**IVc**	60	128–130 (5)	1.4730	70.35	10.38	4.75	$C_{18}H_{31}NO_3$	–	–	–
Id	C₂H₅ONa	Benzene	50–55	1	**IIId**	7	115–118 (1.5)	1.5069	72.51	8.25	5.83	$C_{15}H_{21}NO_2$	72.87	8.50	5.67
					IVd+IVd	58	136–141 (2)	1.5069	71.31	9.05	4.32	$C_{19}H_{27}NO_3$	71.92	8.52	4.44
	Na₂CO₃·10H₂O	Benzene	50–55	6	**IVd**	41	[b]	–	75.26	9.12	4.17	$C_{19}H_{27}NO_3$	–	–	–
Iд	C₂H₅ONa	Ether	30–32	1	**IIIe + VIe**	54	105–108 (1.5)	1.5170	70.34	8.65	6.09	$C_{13}H_{19}NO_2$	70.59	8.59	6.33
		Benzene	50–55	1	**IIIe + VIe**[c]	52	106–109 (2)	1.5170	70.99	8.74	6.57	$C_{13}H_{19}NO_2$	–	–	–
	Na₂CO₃·10H₂O	Benzene	50–55	6	**IVe**	34	135–137 (2)	1.4972	70.00	8.41	4.65	$C_{17}H_{25}NO_3$	70.10	8.59	4.81

[a] Yields of rearrangement products (**IIIa–d**) obtained from salts (**IIa–d**) amount to 68, 77, 74 and 82% respectively.
[b] Identification of compounds performed without distillation for at distillation occurred thermal isomerization.
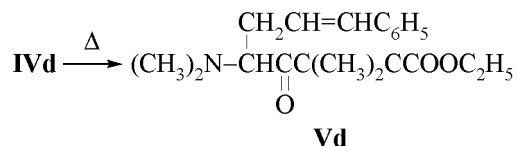[c] Ratio of compounds **IIIe** and **VIe** equals to 87:13.

weaker base, $Na_2CO_3 \cdot 10H_2O$ (path *c*) the acid cleavage is completely suppressed, and the products of Stevens rearrangement are obtained in 60–72% yield.

We showed by an example of salts **Ia, b** that the rearrangement occurred also at the use of 40% water solution of Na_2CO_3; however, the yields of the products were relatively low (Table 1).

Experiments demonstrated that during distillation a part of rearrangement product of salt **Id**, amine **IVd**, underwent thermal isomerizatio yielding a product of Stevens 1,2-rearragement **Vd**.

According to ^{1}H NMR data the content of the latter in the mixture with the product of 3,2-rearrangement amounts to 47%.

Reaction of salt **Ie** with sodium ethylate in ether or benzene afforded a mixture of products originating from Stevens (**IIIe**) and Sommelet (**VId**) rearrangements in the 55:45 ratio whereas under the action of $Na_2CO_3 \cdot 10H_2O$ formed the product of 1,2-rearrangement **IVe**.

$$\textbf{IVd} \xrightarrow{\Delta} \underset{\underset{\displaystyle \textbf{Vd}}{}}{(CH_3)_2N-\overset{\displaystyle \overset{CH_2CH=CHC_6H_5}{|}}{\underset{\underset{O}{\|}}{CH}CC(CH_3)_2CCOOC_2H_5}}$$

Salt **Ie** similar to salts **Ia–d** containing an allyl-type group at treatment with $Na_2CO_3 \cdot 10H_2O$ furnished a Stevens rearrangement product **IVe**. The fact of formation from the salt **Ie** treated with sodium ethylate of products from Stevens and Sommelet rearrangements indicates that for salts **Ia–e** under these conditions first occurs the acid cleavage of the group adding the migrating moiety, and then happens the rearrangement. Otherwise only the product of Stevens rearrangement should have formed as is observed with salts containing both a ketocarbonyl and benzyl groups [6, 7]. It should be noted that the results obtained at carrying out the rearrangement of salt **Ie** in ether (30–32°C) and benzene (50–55°C) (Table 1) are consistent with published data [1, 2]. The different behavior of salts under study is likely to originate from the fact that salts with the 3-substituted allyl group **Ib–d** are more prone to Stevens rearrangement than salts **Ia** and **Ie**. Apparently the substituents create also additional sterical hindrances to the ethylate-ion attack on the 3-methyl-3-ethoxycarbonylbutanon-2-yl group, and therefore it is cleaved only partially. Consequently salts **Ib–d** undergo mainly the ordinary Stevens rearrangement.

The structure of compounds obtained was confirmed by IR and ^{1}H NMR spectra (Table 2), and their purity was checked by GLC. The structure of compounds resulted from acid cleavage-rearrangement was also proved by an independent synthesis: We specially synthesized salts **IIa–d** and subjected them to Stevens rearrangement.

By these reactions aminoesters **IIIa–d** were obtained in high yield (Table 1), and their spectral characteristics (IR, ^{1}H NMR), physical constants, and GLC data were identical to those of the products of acid cleavage-rearrangement **IIIa–d**. The second product of the acid cleavage, ethyl isobutyrate, was identified both by IR and ^{1}H NMR spectra and by GLC comparison with an authentic sample.

EXPERIMENTAL

IR spectra were recorded on spectrophotometers UR-20 and Specord 75IR. ^{1}H NMR spectra were registered from solutions of compounds under study in CCl_4 on spectrometer Perkin Elmer R-12B (60 MHz) and Varian Mercury-300 (300 MHz), internal reference TMS. The GLC analyses were performed on chromatograph LKhM-80 equipped with katharometer, oven temperature programming within 100–220°C (16°C/min), stationary phase 10% Apiezon L on Inerton-AW (0.20–0.25 mm), carrier gas helium, flow rate 60 ml/min.

General procedure for rearrangement of salts Ia–e effected by sodium ethylate. To 0.15 mol of salt in 15–20 ml of anhydrous ether (benzene) was added 0.03 mol of sodium ethylate. If necessary to start the reaction were also added several drops of ethanol On completion of the exothermic reaction the mixture was heated for 1 h at the temperature indicated in Table 1. Then to the reaction mixture water and ethyl ether were added, the ether layer was separated, and the water layer was extracted with ether. In the ether extract the content of reaction products was estimated, and the cleavage products were identified. The combined ether extracts were dried by magnesium sulfate and distilled (Tables 1, 2). From the products of reaction of salts **Ia–e** alongside the other compounds by the distillation was isolated the second component of the acid cleavage-rearrangement, ethyl isobutyrate [8], bp 106–108°C at 680 mm Hg, n_D^{20} 1.3867 (Table 2); in the other cases it was identified only by GLC.

General procedure for rearrangement of salts effected by $Na_2CO_3 \cdot 10H_2O$. A mixture of 0.02 mol of salt and 0.06 mol of $Na_2CO_3 \cdot 10H_2O$ was carefully stirred, heated for 6 h at 50–55°C on a water bath,

Table 2. IR and ^{1}H NMR spectra of compounds **IIIb–e, IVa–e, V, Vd, VIe**

Compd.no.	IR spectrum, δ, cm^{-1}	^{1}H NMR spectrum, δ, ppm (J, Hz)
IIIb	920, 990, 1635, 3030, 3080 (CH=CH$_2$); 1070, 1150, 1240, 1730 (COOR)	0.72 d and 0.84 d (3H, CH3CH, J 7.0); 1.18 t (3H, CH$_3$CH$_2$, J 6.8); 2.52–3.56 m (2H, CHCH); 4.08 q (2H, OCH$_2$), 4.80–5.25 m (2H, CH$_2$=); 5.38–6.15 m (1H, CH=)
IIIc	920, 990, 1640, 3080 (CH=CH$_2$); 1080, 1150, 1240, 1730 (COOR)	1.02 s and 1.07 s (6H, CCH$_3$); 1.22 t (3H, CH$_3$CH$_2$, J 7.0); 1.24–1.60 m (6H, β, γCH2); 2.18–2.38 m and 2.64–2.83 m (4H, CH$_2$); 2.74 s (1H, CH); 4.05 m (2H, OCH$_2$); 4.80–4.96 m (2H, CH$_2$=); 6.03 m (1H, CH=, J110.5; J_2 17.6)
IIId	690, 760, 1600, 3030, 3066 (C$_6$H$_5$), 970, 1605, 3080 (CH=CH$_2$); 1070, 1155, 1240, 1730 (COOR)	1.20 t (3H, CH3CH2, J 6.7); 2.21 s and 2.23 s (6H, NCH$_3$); 3.28–3.98 m (4H, CHCH, OCH$_2$); 4.6–5.25 m (2H, CH$_2$=); 5.65–6.5 m (1H, CH=); 7.18 m (5H, C$_6$H$_5$)
IIIe	690, 750, 1600, 3075 (C$_6$H$_5$), 1075, 1150, 1240, 1730 (COOR)	0.86 t (3H, CH$_3$CH$_2$, J 6.7); 2.08 s (6H, NCH$_3$); 1.40–1.88 t (3H, CH$_2$CH); 3.83 q (2H, OCH2); 6.70–7.20 m (5H, C$_6$H$_5$)
IVa	920, 990, 1640, 3025, 3085 (CH=CH$_2$); 1080, 1130, 1730 (COOR), 1715 (C=O)	1.08 t (3H, CH3CH2); 1.14 s (6H, CCH3); 2.21 s (6H, NCH$_3$); 3.45 d.d (1H, CH, J1 9.3; J2 4.6); 4.05 q (2H, OCH$_2$, J 6.7); 4.75–5.20 m (2H, CH$_2$=), 5.25–6.0 m (1H, CH=)
IVb	920, 990, 1635, 3025, 3080 (CH=CH$_2$); 1070, 1130, 1730 (COOR), 1715 (C=O)	0.72 d and 0.95 d (3H, CH$_3$CH, J 7.0); 1.18 t (3H, CH$_3$CH$_2$, J 6.7); 1.21 s (6H, CCH$_3$); 2.26 s and 2.30 s (6H, NCH$_3$); 2.50–3.55 m (2H, NCHCH); 4.10 q (2H, OCH$_2$, J 6.7); 4.80–5.30 m (2H, CH$_2$=); 5.40–6.20 m (1H, CH=)
IVc	915, 990, 1640, 3025, 3080 (CH=CH$_2$); 1070, 1155, 1180, 1730 (COOR), 1715 (C=O)	1.77 m (19H, CCH$_3$, CH$_3$CH$_2$, αCH$_2$); 2.95 m (6H, β, γCH$_2$); 3.30 c (1H, NCH); 4.04 q (2H, OCH2, J 6.7); 4.60–5.25 m (2H, CH$_2$=); 5.60–6.30 m (1H, CH=)
IVd	690, 750, 1600, 3030, 3070 (C$_6$H$_5$), 910, 990, 1640, 3080 (CH=CH$_2$); 1070, 1150, 1180, 1730 (COOR), 1715 (C=O)	0.86–1.60 m (9H, CCH$_3$, CH3CH2); 2.40 s (6H, NCH$_3$), 3.45–3.90 m (2H, NCHCH); 4.02 q (2H, OCH$_2$, J 6.6); 4.80–5.42 m (2H, CH$_2$=); 5.80–6.65 m (1H, CH=); 7.16–7.50 m (5H, C$_6$H$_5$)
IVe	690, 750, 1600, 3030, 3070 (C$_6$H$_5$), 1070, 1150, 1730 (COOR), 1715 (C=O)	0.72–1.32 m (9H, CCH$_3$, CH$_3$CH$_2$); 2.18 s (6H, NCH$_3$); 1.45–3.40 m (3H, CH$_2$CH); 3.40–4.08 m (2H, OCH2); 6.70–7.20 m (5H, C$_6$H$_5$)
V	1070, 1150, 1240, 1730 (COOR)	1.08 t (3H, CH$_3$CH$_2$, J 7.0); 1.3 d (6H, CCH3, J 7); 2.52 m (1H, CH); 4.03 q (2H, CH$_3$CH$_2$)
Vd	690, 760, 1600, 3030, 3070 (C$_6$H$_5$), 970, 1610, 3080 (CH=CH); 1070, 1160, 1730 (COOR), 1715 (C=O)	0.96–1.44 m (9H, CCH$_3$, CH$_3$CH$_2$); 2.21 s (6H, NCH$_3$), 2.2–2.6 m (2H, CH$_2$); 3.45–4.32 m (3H, NCH, OCH$_2$); 4.70–5.50 m (2H, CH$_2$=); 5.65–6.60 m (1H, CH=); 7.12-7.36 m (5H, C$_6$H$_5$)
VIe	740, 1600, 3075 (C$_6$H$_4$), 1070, 1150, 1240, 1730 (COOR)	0.83 t (3H, CH$_3$CH$_2$, J 7.3); 2.03 s (6H, NCH$_3$); 2.40 s (3H, CH$_3$Ar); 3.20 q (2H, OCH$_2$, J 6.7); 3.32 s (1H, CH); 6.70–7.20 m (4H, C$_6$H$_4$)

and then the reaction mixture was thrice extracted with ether (benzene). The combined extracts were dried with magnesium sulfate and distilled. On removed the solvent the distillation of the residue afforded the reaction products (Tables 1, 2). Similarly was carried out the rearrangement of salts **Ia, b** at treatment with triple molar excess of 40% water solution of Na_2CO_3 (Tables 1, 2).

General procedure for rearrangement of salts IIa–d. To 0.015 mol of salt in 15–20 ml of anhydrous ether was added 0.03 mol of sodium ethylate. The reaction mixture was ground, and on completion of the exothermic reaction it was boiled for 20 min, then ethyl ether and water was added. The ether layer was separated, the water layer was extracted with ether, the combined ether extracts were dried with magnesium sulfate, and distilled. We obtained compounds **IIIa–d** (Tables 1, 2). Physical constants of compound **IIIa** (bp 73°C at 11 mm Hg, n_D^{20} 1.4370) coincide with published data [9]. Physical constants of compounds **IIIb–d** prepared also by an independent synthesis are given in Tables 1, 2.

REFERENCES

1. Babayan, A.T., Kocharyan, S.T., and Ogandzhanyan, S.M., *Arm. Khim. Zh.,* 1976, vol. 29, p. 403.
2. Razina, T.L., Ogandzhanyan, S.M., and Kochanyanryan, S.T., and Babayan, A.T., *Arm. Khim. Zh.,* 1982, vol. 35, p. 644.
3. Karapetyan, V.E., Kocharyan, S.T., and Babayan, A.T., *Zh. Org. Khim.,* 1985, vol. 21, p. 56.
4. Kocharyan, S.T., Karapetyan, V.E., and Churkina, N.P., *Zh. Obshch. Khim.,* 2000, vol. 70, p. 1169.
5. Kocharyan, S.T., Voskanyan, V.S., Grigoryan, V.V., Panosyan, G.A., and Babayan A.T., *Arm. Khim. Zh.,* 1985, vol. 38, p. 37.
6. Ollis, W.D., Rey, M., Sutherland, J.O., and Closs, G.L., *J. Chem. Soc., Perkin Trans. I* 1983, p. 1009.
7. Ollis, W.D., Rey, M., and Sutherland, J.O., *Chem. Commun.,* 1974, no. 14, p. 543.
8. *Organikum. Organisch-Chemisches Grundpraktikum,* Berlin: VEB Deutscher Verlag der Wissenschaften, 1976, 15th ed.
9. Kocharyan, S.T., Ogandzhanyan, S.M., and Babayan, A.T., *Arm. Khim. Zh.,* 1976, vol. 29, p. 42.