ISSN 1070-4280, Russian Journal of Organic Chemistry, 2017, Vol. 53, No. 2, pp. 178–183. © Pleiades Publishing, Ltd., 2017. Original Russian Text © E.O. Chukhajian, K.G. Shahkhatuni, El.O. Chukhajian, L.V. Ayrapetyan, G.A. Panosyan, 2017, published in Zhurnal Organicheskoi Khimii, 2017, Vol. 53, No. 2, pp. 191–195.

Deamination of 3-(Dialkylamino)-1,4-diarylhex-5-en-1-ynes During Vacuum Distillation

E. O. Chukhajian, K. G. Shahkhatuni, El. O. Chukhajian, L. V. Ayrapetyan, and G. A. Panosyan*

Scientific and Technological Center of Organic and Pharmaceutical Chemistry, National Academy of Sciences of the Republic of Armenia, Institute of Organic Chemistry, pr. Azatutyana 26, Yerevan, 0014 Armenia *e-mail: qnarsh@yandex.ru

Received April 6, 2016

Abstract—During vacuum distillation of 3-(dialkylamino) derivatives of 1,4-diphenyl- and 4-phenyl-1-(p-chlorophenyl)hex-5-en-1-ynes deamination occurs resulting in a high yield of p-diarylbenzenes. The amines transformation into terbenzenes is a domino-reaction: first step consists in the β -elimination of secondary amines with the generation of conjugated dienyne which via an electrocyclic reaction transforms into cyclic allene intermediate. The latter after 1,3- or 1,5-hydride shift quickly converts into the final reaction products.

DOI: 10.1134/S1070428017020063

Many molecular rearrangements of organic compounds are known, in particular, those of unsaturated ammonium salts, among them the rearrangement-cleavage [1], intramolecular cyclization [2]. Basic results of these studies are generalized in reviews [3–5]. Special place among them belongs to Stevens rearrangement [6] proceeding through intermediate formation of ammonium ylides. This is due to the ammonium ylides capability to undergo transformations with the formation of functionally substituted tertiary amines. Stevens rearrangement, along with its fundamental value, provides wide opportunities for the synthesis of amines of various

structures of practical value. For instance, unsaturated amines and quaternary ammonium salts of various structures are present in the molecules of drugs, fungicides, pesticides, metal corrosion inhibitors, surfactants, washing and desinfecting agents etc.

Considering the above information, bringing new unsaturated ammonium salts into Stevens rearrangement providing wide opportunities for the synthesis of new potentially bioactive tertiary amines, is a topical issue.

It is known that Stevens rearrangement of dialkyl(but-2-en-1-yl)(3-phenylprop-2-yn-1-yl)ammonium bromi-





des is followed by the conversion of the migrating group [7]. Recently it was established that similar derivatives in aqueous alkaline surroundings prevailingly underwent Stevens rearrangement, including the conversion of the migrating group and the transfer of the reaction center in the accepting group with the formation of intermediate allenic aminoalcohols **A** (Scheme 1). The intramolecular cyclization of the latter through *O*-alkylation results in amino derivatives of dihydrofuran. The observed reaction is the only known case for Stevens rearrangements [8, 9].

In continuation of the investigations of this rearrangement we explored the behavior of dialkyl(3-phenylprop-2-en-1-yl)(3-phenylprop-2-yn-1-yl)ammonium bromides **1a–1f** [10] and (3-phenylprop-2-en-1-yl)[3-(4-chlorophenyl)prop-2-yn-1-yl]piperidinium and morpholinium bromides **1g** and **1h** [11]. Salts **1a–1h** under the action of two equiv of KOH in the presence of few drops of methanol rearranged with selfheating into 3-(dialkylamino)-1,4-diarylhex-5-en-1ynes **2a–2h**, yellowish viscous fluids, in 60–65% yield (Scheme 2).

Ph



Scheme 3.

R = Me(a), Et(b), Pr(c).

RUSSIAN JOURNAL OF ORGANIC CHEMISTRY Vol. 53 No. 2 2017

Scheme 4.



In case of salts **1a–1c** along with Stevens rearrangement, which is the main direction of interaction, reactions of cyclization-cleavage also occur leading to the formation of a mixture of 3-[(dialkylamino)methyl]-2methyl-1-phenylnaphtalenes **3a**, **3c**, and **5b** and 3methyl-2-[(dialkylamino)methyl]-1-phenylnaphtalenes **4a**, **4c**, and **6b** (Scheme 3) in overall yields 13–15%. Physicochemical characteristics and ¹H and ¹³C NMR spectra of amines mentioned above are identical to the data for compounds that are generated during aqueousalkaline cleavage of cyclization products of salts **1a–1c** in conditions of basic catalysis [10].

Before vacuum distillation of the obtained mixtures their IR spectra were recorded. In IR spectra typical absorption bands are present at 1580, 3030 (aromatic ring), 730, 690 (mono-substituted benzene ring) (2a– 2h, 3a, 3c, 4a, 4c, 5b, and 6b) and at 810, 840 cm⁻¹ (*para*-substituted benzene ring) (2g and 2h), and also absorption bands of the terminal vinyl group at 1630, 960, 920 (2a–2h) and 870, 770, 730 cm⁻¹ (penta- and 1,2-substituted benzene ring) (3a, 3c, 4a, 4c, 5b, and 6b).

Analysis of the ¹H NMR spectrum of compounds 2a-2h demonstrates that the structure with the terminal vinyl group prevails in the mixture.

Basing on IR and ¹H NMR spectra we concluded that the Stevens rearrangement of salts **1a–1h** was usually accompanied with the conversion of migrating group.

Unlike the 1-allyl-1-dialkyl(3-phenylprop-2-yn-1yl)-, (but-1-en-2-yl)-1-dimethyl(3-phenylprop-2-yn-1yl)amines [7] and their methallyl analogs [12] amines **2a–2h** during vacuum distillation undergo deamination, and as final products we obtained *p*-diphenylbenzene 7 [13, 14] and *p*-phenyl-*p*-chlorophenylbenzene **8** in 65 and 61% yields correspondingly (Scheme 4).

Deamination of amines **2a–2h** occurred within 20– 25 min. Compounds with simple alkyl groups at the nitrogen atom suffer deamination at higher temperatures: **2a**, at 142°C (1.5–2 mmHg); **2b**, 142°C (1– 1.5 mmHg); **2c**, 75°C (1 mmHg); **2d**, 45–50°C (2 mmHg); **2e** and **2f**, 50–55°C (2–3 mmHg); **2g**, 110°C (1–2 mmHg); **2h**, 70–75°C (3–4 mmHg).

During vacuum distillation of mixture of amines 2a, 2c, 3a, 3c, 4a, 4c, and 2b, 5b, 6b crystals of *p*diphenylbenzene 7 deposited in the side arm of Claisen flask and impeded the distillation of mixture of amines 3a, 3c, 4a, 4c, and 5b, 6b. To avoid this difficulty the distillation of the mixture of amines 2a, 2c, 3a, 3c, 4a,



RUSSIAN JOURNAL OF ORGANIC CHEMISTRY Vol. 53 No. 2 2017



4c, and 2b, 5b, 6b was carried out in a flask with a central tube and a collar. During the vacuum distillation in the central tube of the flask crystals of compound 7 were collected, and in the collar, the mixture of amines 3a, 3c, 4a, 4c, or 5b, 6b that were products of cyclization-cleavage [10]. Physicochemical characteristics and ¹H, ¹³C NMR spectra of amines 3a, 3c, 4a, 4c, and 5b, 6b are identical to the data for amines that form at cleavage of cyclization products of salts 1a–1c in conditions of basic catalysis [10]. The occurrence of cyclization-cleavage in conditions of Stevens rearrangement is a unique case [15, 16].

The vacuum distillation of amines **2d–2h** was performed in a standard Claisen flask. Crystals **7** and **8** deposited in the side arm were collected mechanically.

We suggest a scheme of formation of compounds 7 and 8 (Scheme 5), according to which amines 2a-2hduring vacuum distillation undergo β -elimination first with elimination of secondary amines and simultaneous generation of 1,4-diarylhexa-3,5-dien-1-ynes B, in molecules of which diene and dienophile groups are present that quickly undergo thermal intramolecular cyclization, resulting in compounds whose molecules contain a middle ring with an allene group. Cyclic compounds with an allene group are very unstable, so they quickly isomerize transforming into terphenyls 7 and 8.

The discovered deamination of amines 2a-2hduring vacuum distillation is a unique case in organic chemistry and has a general character. Along with a fundamental it also has a practical value: thus a new accessible method of obtaining the terphenyls 7 and 8 in high yields was developed. The formation of these two compounds is a good chemical proof that Stevens rearrangement of salts **1a–1h** is mainly realized by conversion of migrating group. It is known that compound 7 is a high-temperature carrier and initial compound for preparation of polyphenyls [13]. The structure of compounds 7 and 8 was confirmed by ¹H and ¹³C NMR spectra.

As it is known, 3-(dimethylamino)-1,4-diphenylhex-5-en-1-yne 2a, obtained as a result of Stevens rearrangement of dimethyl(3-phenylprop-2-en-1-yl)(3-phenylprop-2-yn-1-yl)ammonium bromide 1a, at heating in xylene during 1 h affords terphenyl 7 in 70% yield [14]. It was established in the same study that at heating the other similar products of Stevens rearrangement [for example, 3-(dimethylamino)-4-(or -5-)methylhex-5-en-1-yne at 200°C during 3 days or 12 h respectively and -5-phenyl-hex-5-en-1-yne at 140°C during 3 days in an evacuated sealed tube] biphenyles were obtained as final products. In experimental conditions of [14] it is hard to prove in which step the elimination of secondary amine occurs and therefore it is hard to determine the sequence of stages of biphenyls generation. Nevertheless Laird et al. [14] offered two schemes of biphenyls formation, and one of them coincides with Scheme 5 above. However they consider as impossible the generation of cyclic allene intermediate.

According to Scheme 6 offered in [14] [3,3]signatropic rearrangement of amines may result in allenamine 9, from which by [1,3]-hydrogen shift hexatriene 10 is generated. Electrocyclic reaction of the latter results in compound **11**, from which after elimination of dimethylamine biphenyl **12** is formed.

A good proof that deamination occurs first and then follows the cyclization of intermediate compounds **B** (Scheme 5) was as follows: at heating 3-(dimethylamino)-1,4-diphenylhex-5-en-1-yne **2a** in experimental conditions of [14] we clearly noticed during10–15 min the liberation of dimethylamine that was absorbed with solution of gaseous HCl in anhydrous ether. After finishing the experiment and maintaining the reaction mixture at room temperature terphenyl 7 was filtered from xylene, and decanting of the ether made it possible to separate dimethylamine hydrochloride that was washed with anhydrous ether and dried over P_2O_5 . This salt melted at 171°C and did not provide a depression of the melting point when mixed with an authentic sample.

The phenomenon of deamination of amines **2a–2h** during vacuum distillation has a general character and results in the formation of terphenyls **7** and **8**. This is a good chemical proof that Stevens rearrangement of salts **1a–1h** is mainly realized with the conversion of migrating group.

EXPERIMENTAL

Synthesis and physicochemical characteristics of the initial salts **1a–1h** and amines **3a**, **3c**, **4a**, **4c**, and **5b**, **6b** are described in [10, 11]. IR spectra of amines **2a–2h**, **3a**, **3c**, **4a**, **4c**, **5b**, **6b** were recorded on a spectrometer Specord 75 IR from thin layer, and of compound 8, from solution in CHCl₃. ¹H and ¹³C NMR spectra of compounds 7 and 8 were obtained on an instrument Varian Mercury 300 VX (300 and 75 MHz correspondingly) at 303 K in a mixture of DMSO- d_6 – CCl₄, 1 : 3, internal reference TMS.

Stevens rearrangement of dialkyl(3-arylprop-2en-1-yl)(3-arylprop-2-yn-1-yl)ammonium bromides (1a–1h). General method. To a thoroughly stirred mixture of 8 mmol of powdered salt 1a–1h and 1.46 g (16 mmol) of powdered KOH few drops of methanol was added. Reaction proceeded with self-heating. After 30–40 min the mixture was extracted with diethyl ether (2 × 50 mL). Ether extract was washed with water. An aliquot of ether extract while shaking with water was titrated with 0.1 N H₂SO₄. The titration showed the presence of 5.2–5.4 mmol of amine (yield 65–67%) in the extract. The extract was acidified with 20% HCl. The water layer was separated, neutralized with 10% aqueous KOH, and extracted with ether $(3 \times 40 \text{ mL})$. The extract was washed with water and dried with MgSO₄.

After removing the ether the residual mixture of amines 2a, 2c, 3a, 3c, 4a, 4c, 2b, 5b, 6b, and 2d-2h was subjected to vacuum distillation. General method. Into a flask with a central tube and a collar were placed asbestos fibers operating as capillaries, 6 mmol of the mixture of amines 2a-2c, 3a, 3c, 4a, 4c, and 5b, 6b was charged and subjected to the vacuum distillation. After completing the process of deamination of amines 2a-2c and formation of terphenyl 7 which was collected in the central tube, the distillation started of the mixture of amines 3a, 3c, 4a, 4c or 5b, 6b that were collected in the collar. Crystals of compound 7 were removed mechanically from the central tube, and from the collar with the assistance of a capillary the mixture of 0.78–0.9 mmol of amines 3a. 3c. 4a. 4c. and **5b**, **6b** [10] was isolated in an overall yield of 13– 15%.

Vacuum distillation of amines 2d–2h (6 mmol) was performed in a standard Claisen flask. In the side arm crystals of compounds 7 or 8 were collected that were mechanically removed. After that the crystals and the rest of the Claisen flask were washed with anhydrous ether, the crystals of compounds 7 and 8 were filtered off. After evaporating ether we obtained an insignificant amount of amine products that we failed to identify.

Salts 1a-1h and amines 3a, 3c, 4a, 4c, 5b, and 6b were described in [10, 11].

1,1':4',1''-Terphenyl (7). Yield 0.9 g (3.9 mmol, 65%), white crystals, mp 210°C (xylene) [13]. ¹H NMR spectrum, δ , ppm: 7.31 m (2H, H⁴ Ph), 7.42 m (4H, H^{3.5} Ph), 7.61 m (4H, H^{2.6} Ph), 7.66 s (4H, C₆H₄). ¹³C NMR spectrum, δ , ppm: 126.3 (4CH), 126.7 (2CH, C⁴ Ph), 126.8 (4CH), 128.2 (4CH), 139.3 (2C), 139.9 (2C).

4-Chloro-1,1':4',1''-terphenyl (8). Yield 0.96 g (3.66 mmol, 60%), yellow crystals, mp 205°C (xylene) [17]. IR spectrum, v, cm⁻¹: 1580 (aromatic ring), 820 (*p*-substituted benzene ring), 720, 680 (mono-substituted benzene ring). ¹H NMR spectrum, δ , ppm: 7.32 m (1H, H⁴ Ph), 7.39–7.45 m (4H, H^{3,5} Ph and C₆H₄Cl), 7.59–7.63 m (4H, H^{2,6} Ph and C₆H₄Cl), 7.65 s (4H, C₆H₄). ¹³C NMR spectrum, δ , ppm: 126.3 (2CH), 126.7 (2CH), 126.8 (CH), 126.9 (2CH), 127.7 (2CH), 128.2 (2CH), 128.3 (2CH), 132.5, 137.9, 138.4, 139.6, 139.7.

REFERENCES

- Babayan, A.T., Indzhikyan, M.G., and Bagdasaryan, G.B., Dokl. Akad. Nauk Arm. SSR, 1962, vol. 34, p. 75.
- Babayan, A.T., Chukhadzhyan, E.O., Babayan, G.T., and Abramyan, I.A., *Dokl. Akad. Nauk Arm. SSR*, 1969, vol. 48, p. 54.
- Chukhadzhyan, É.O., Chem. Heterocycl. Compd., 1993, vol. 29, p. 363. doi 10.1007/BF00529871
- Chukhajian, E.O., Shahkhatuni, K.G., and Chukhajian, El.O., *Chem. Sustainable Develop.*, 2013, vol. 21, p. 263.
- Chukhajian, E.O., Gevorkyan, H.R., Chukhajian, El.O., Shahkhatuni, K.G., Panosyan, H.A., and Tamazyan, R.A., *J. Heterocycl. Chem.*, 2003, vol. 40, p. 1059. doi 10.1002/jhet.5570400614
- Stevens, T.S., Greighton, B.M., Gordon, Q.B., and MacNikol, M., J. Chem. Soc., 1928, p. 3193. doi 10.1039/JR9280003193
- Babayan, A.T., Anayan, E.S., and Chukhadzhyan, E.O., Arm. Khim. Zh., 1969, vol. 22, 894.
- Chukhajian, E.O., Gabrielyan, A.S., Chukhajian, El.O., Shahkhatuni, K.G., and Panosyan, H.A., *Chem. Heterocycl. Compd.*, 2009, vol. 45, p. 1302. doi 10.1007/s10593-010-0425-1

- Chukhadjian, E.O., Gabrielyan, A.S., Chukhadjian, El.O., Shahkhatuni, K.G., and Panosyan, H.A., *Chem. Heterocycl. Compd.*, 2011, vol. 47, p. 418. doi 10.1007/ s10593-011-0775-3
- Chukhajian, E.O., Ayrapetyan, L.V., Chukhajian, El.O., and Panosyan, H.A., *Chem. Heterocycl. Compd.*, 2012, vol. 48, p. 1314. doi 10.1007/ s10593-012-1138-4
- Chukhajian, E.O., Ayrapetyan, L.V., Chukhajian, El.O., and Panosyan, H.A., *Chem. Heterocycl. Compd.*, 2013, vol. 49, p. 1274. doi 10.1007/s10593-013-1375-1
- 12. Atomyan, A.V., Chukhadzhyan, E.O., and Babayan, A.T., *Arm. Khim. Zh.*, 1983, vol. 36, p. 639.
- Chemistry of Carbon Compounds, Rodd, E.H., Ed., 1956, vol. 3, Amsterdam: Elsevier, Ullmann's Encyclopedia, Weinheim, 1977, 4 ed.
- Laird, T., Ollis, D., and Sutherland, I.O., J. Chem. Soc., Perkin Trans. 1, 1980, p. 1473. doi 10.1039/ P19800001473
- 15. Kocharyan, S.T., *Doctoral (Chem.) Dissertation*, Yerevan, 1986.
- Manukyan, M.O., Candidate Sci. (Chem.) Dissertation, Yerevan, 2008.
- 17. Bahurel, Y., Billion, J., and Descotes, G., *Bull. Soc. Chim.*, 1968, p. 4255.