ISSN 1070-4280, Russian Journal of Organic Chemistry, 2008, Vol. 44, No. 12, pp. 1849–1851. © Pleiades Publishing, Ltd., 2008.
Original Russian Text © D.S. Ryabukhin, A.V. Vasil'ev, 2008, published in Zhurnal Organicheskoi Khimii, 2008, Vol. 44, No. 12, pp. 1875–1877.

SHORT COMMUNICATIONS

Intramolecular Cyclization of *N*-Aryl-3-phenylprop-2-ynamides

D. S. Ryabukhin and A. V. Vasil'ev

St. Petersburg State Academy of Forestry Engineering, Institutskii per. 5, St. Petersburg, 194021 Russia
e-mail: aleksvasil@mail.ru

Received July 2, 2008

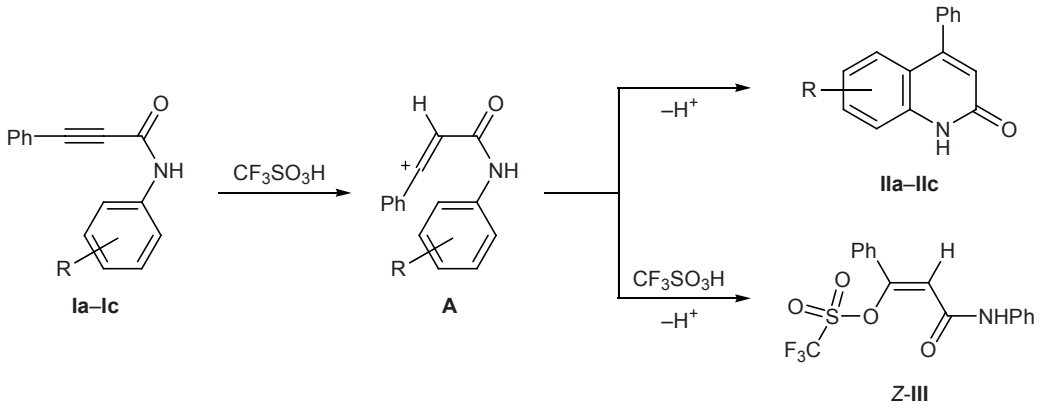
DOI: 10.1134/S1070428008120257

Heterocyclic quinoline system constitutes the basic structural fragment of many natural and synthetic biologically active substances [1–3]. Therefore, development of new methods for the preparation of quinoline derivatives is an important problem of organic chemistry. A promising procedure for the synthesis of 4-arylquinolin-2(1*H*)-ones is based on intramolecular cyclization of *N*,3-diarylprop-2-ynamides by the action of acid reagents. Iwai and Hiraoka [4] were the first to obtain in such a way 4-phenylquinolin-2(1*H*)-one (**IIa**) in 81% yield; it was synthesized by heating *N*,3-diphenylprop-2-ynamide (**Ia**) in polyphosphoric acid at 120°C (reaction time 0.5 h) [4]. The transformation of amide **Ia** into quinolinone **IIa** was also promoted by other reagents, such as solid superacids H-USY and Nafion SAC-13 [5], Lewis acid $AlCl_3$ [6], and superacid CF_3SO_3H [5, 6].

In continuation of our preceding studies on intramolecular reactions of vinyl type cations in various superacidic systems [7], we specially examined the transformation of *N*-aryl-3-phenylprop-2-ynamides **Ia**–**Ic** into 4-phenylquinolin-2(1*H*)-ones **IIa**–**IIc** [8]. Protonation of the triple C≡C bond in **Ia**–**Ic** with trifluoromethanesulfonic acid yields vinyl cations **A** which undergo cyclization to final products **IIa**–**IIc**.

According to the data of [5, 6], *N*-phenyl amide **Ia** in CF_3SO_3H at 25°C in 100 h is converted into quinolinone **IIa** as the only product (yield 97%). We found that the transformation of **Ia** in CF_3SO_3H at a higher temperature (50°C, reaction time 2 h) leads to a mixture of two products, quinolinone **IIa** and vinyl trifluoromethanesulfonate *Z*-**III** (yield 52 and 30%, respectively). Compound **III** was assigned *Z* configuration of the double C=C bond, taking into account that analogous vinyl trifluoromethanesulfonates derived from 3-arylprop-2-ynoates in CF_3SO_3H at elevated temperature also have the structure of *Z* isomers [9, 10]. Presumably, the formation of *Z*-**III** via reaction of intermediate cation **A** with trifluoromethanesulfonic acid molecule is characterized by a higher activation barrier than alternative intramolecular cyclization of **A** to quinolinone **IIa**.

Provided that the process is controlled thermodynamically (CF_3SO_3H, 20°C, 30 days), amide **Ia** is converted into compound **IIa** as the only product (yield 88%). Under analogous conditions, *N*-(3-meth-



I, R = H (**a**), 3-Me (**b**), 4-Me (**c**); **II**, R = H (**a**), 7-Me (**b**), 6-Me (**c**).

ylphenyl)-3-phenylprop-2-ynamide (**Ib**) gives rise to 94% of quinolinone **IIb**. When the reaction time was shortened to 75 h, the yields of quinolinones **IIb** and **IIc** from amides **Ib** and **Ic** were 40 and 36%, respectively, and the substrate conversion was not complete. In these cases, no vinyl trifluoromethanesulfonates analogous to compound *Z*-**III** were detected in the reaction mixtures.

N-Aryl-3-phenylprop-2-ynamides **Ia**–**Ic** were synthesized by reactions of the corresponding anilines with 3-phenylprop-2-ynoyl chloride at a molar ratio of 2:1 in benzene at 50°C (30 min).

***N*,3-Diphenylprop-2-ynamide (Ia).** Yield 54%, mp 124–126°C; published data [11]: mp 128°C. IR spectrum (KBr), ν, cm^{-1}: 3261 (NH), 2211 (C≡C), 1643 (C=O). ^1H NMR spectrum (400 MHz), δ, ppm: 7.14 t (1H, H_{arom}, J = 7.8 Hz), 7.34 t (2H, H_{arom}, J = 8.0 Hz), 7.35 t (2H, H_{arom}, J = 7.8 Hz), 7.41 t (1H, H_{arom}, J = 8.0 Hz), 7.54 d (2H, H_{arom}, J = 7.8 Hz), 7.59 d (2H, H_{arom}, J = 8.0 Hz), 7.91 s (1H, NH).

***N*-(3-Methylphenyl)-3-phenylprop-2-ynamide (Ib).** Yield 82%, mp 81–83°C. IR spectrum (KBr), ν, cm^{-1}: 3260 (NH), 2211 (C≡C), 1637 (C=O). ^1H NMR spectrum (400 MHz), δ, ppm: 2.34 s (3H, Me), 6.96 d (1H, H_{arom}, J = 7.6 Hz), 7.23 t (1H, H_{arom}, J = 7.6 Hz), 7.34–7.43 m (5H, H_{arom}), 7.55 d (2H, H_{arom}, J = 7.6 Hz), 7.78 s (1H, NH). Found, %: C 81.76; H 5.60; N 6.00. $C_{16}H_{13}NO$. Calculated, %: C 81.68; H 5.57; N 5.95.

***N*-(4-Methylphenyl)-3-phenylprop-2-ynamide (Ic).** Yield 58%, mp 143–145°C. IR spectrum ($CHCl_3$), ν, cm^{-1}: 3400 (NH), 2200 (C≡C), 1650 (C=O). ^1H NMR spectrum (400 MHz), δ, ppm: 2.32 s (3H, Me), 7.13 d (2H, H_{arom}, J = 8.8 Hz), 7.34 t (2H, H_{arom}, J = 7.4 Hz), 7.41 t (1H, H_{arom}, J = 7.4 Hz), 7.47 d (2H, H_{arom}, J = 8.8 Hz), 7.54 t (2H, H_{arom}, J = 7.4 Hz), 7.87 s (1H, NH). Found, %: C 81.63; H 5.59; N 6.02. $C_{16}H_{13}NO$. Calculated, %: C 81.68; H 5.57; N 5.95.

4-Phenylquinolin-2(1*H*)-ones IIa–IIc (*general procedure*). A solution of 0.21–0.84 mmol of amide **Ia**–**Ic** in 2–4 ml of trifluoromethanesulfonic acid was stirred at 20°C for 75 h or 30 days or at 50°C for 2 h. The mixture was poured into ~30 ml of ice water and extracted with chloroform (3×30 ml). The extracts were combined, washed with water, a saturated aqueous solution of $NaHCO_3$, and water again, and dried over Na_2SO_4, the solvent was distilled off under reduced pressure (water-jet pump), and the residue was recrystallized from ethanol or subjected to chromatographic separation on silica gel using hexane–ethyl acetate as eluent.

4-Phenylquinolin-2(1*H*)-one (IIa). *a*. The reaction of 50 mg (0.23 mmol) of amide **Ia** in 2 ml of CF_3SO_3H at 20°C in 30 days gave 44 mg (88%) of **IIa**.

b. Quinolinone **IIa** was obtained together with compound *Z*-**III** from 50 mg (0.23 mmol) of amide **Ia** and 2 ml of CF_3SO_3H at 50°C in 2 h. Yield 26 mg (52%), mp 256–258°C; published data [4]: mp 259–261°C. IR spectrum (KBr), ν, cm^{-1}: 3320 (NH), 1661 (C=O). ^1H NMR spectrum (400 MHz), δ, ppm: 6.68 s (1H, =CH), 7.17 t (1H, H_{arom}, J = 7.6 Hz), 7.43–7.57 m (8H, H_{arom}), 12.07 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 116.73 d.d (J = 161, 7 Hz), 119.59 m (J = 4 Hz), 120.75 d (J = 166 Hz), 122.51 d.d (J = 161, 7 Hz), 126.69 d.d (J = 160, 7 Hz), 128.59 d.d (J = 160, 7 Hz), 128.77 d.m (J = 160, 7 Hz), 128.84 d.m (J = 160, 7 Hz), 130.66 d.d (J = 161, 8 Hz), 137.17 m (J = 5 Hz), 138.98 t (J = 8 Hz), 153.44 s, 164.28 s. Mass spectrum, m/z (I_{rel}, %): 221 (100) $[M]^+$, 193 (26), 165 (35), 139 (7). Calculated: M 221.08.

7-Methyl-4-phenylquinolin-2(1*H*)-one (IIb). *a*. The reaction of 50 mg (0.21 mmol) of amide **Ib** in 2 ml of CF_3SO_3H at 20°C in 30 days gave 47 mg (94%) of **IIb**.

b. Quinolinone **IIb** was obtained from 200 mg (0.84 mmol) of amide **Ib** in 4 ml of CF_3SO_3H at 20°C in 75 h. Yield 80 mg (40%), mp 260–263°C. IR spectrum (KBr), ν, cm^{-1}: 3300 (NH), 1658 (C=O). ^1H NMR spectrum (400 MHz), δ, ppm: 2.46 s (3H, Me), 6.65 s (1H, =CH), 6.98 d (1H, H_{arom}, J = 8.8 Hz), 7.33 s (1H, H_{arom}), 7.43–7.50 m (6H, H_{arom}), 12.69 s (1H, NH). Mass spectrum, m/z (I_{rel}, %): 235 (100) $[M]^+$, 234 (28), 206 (15), 178 (7), 165 (8), 152 (14), 77 (12). Found, %: C 81.72; H 5.62; N 5.97. $C_{16}H_{13}NO$. Calculated, %: C 81.68; H 5.57; N 5.95. M 235.10.

6-Methyl-4-phenylquinolin-2-2(1*H*)-one (IIc) was obtained from 50 mg (0.21 mmol) of amide **Ic** in 2 ml of CF_3SO_3H at 20°C in 75 h. Yield 18 mg (36%), mp 243–245°C. IR spectrum ($CHCl_3$), ν, cm^{-1}: 3400 (NH), 1670 (C=O). ^1H NMR spectrum (500 MHz), δ, ppm: 2.32 s (3H, Me), 6.65 s (1H, =CH), 7.30 s (1H, H_{arom}), 7.33–7.36 m (2H, H_{arom}), 7.45–7.52 m (5H, H_{arom}), 11.88 s (1H, NH). Mass spectrum, m/z (I_{rel}, %): 235 (100) $[M]^+$, 234 (16), 152 (11), 77 (20). Found, %: C 81.59; H 5.53; N 5.88. $C_{16}H_{13}NO$. Calculated, %: C 81.68; H 5.57; N 5.95. M 235.10.

(*Z*)-*N*,3-Diphenyl-3-(trifluoromethylsulfonyloxy)-prop-2-enamide (III) was obtained (together with compound **IIa**) from 50 mg (0.23 mmol) of amide **Ia** in 2 ml of CF_3SO_3H at 50°C in 2 h. Yield 25 mg

(30%), mp 130–132°C. IR spectrum (KBr), ν, cm^{-1}: 3280 (NH), 1670 (C=O). ^1H NMR spectrum (400 MHz), δ, ppm: 6.33 s (1H, =CH), 7.16 t (1H, H_{arom}, J = 8.0 Hz), 7.34–7.59 m (9H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 114.81, 118.28 q (CF_3, J_{CF} = 319 Hz), 120.24, 125.02, 126.37, 129.02, 129.06, 131.46, 131.94, 137.12, 152.46, 159.89. ^{19}F NMR spectrum: δ_F –70.35 ppm. Mass spectrum, *m*/*z* (I_{rel}, %): 371 (8) $[M]^+$, 279 (14), 238 (10), 221 (12), 149 (22), 129 (100), 105 (42), 93 (71), 77 (29). Found, %: C 51.86; H 3.09; N 3.81. $C_{16}H_{12}F_3NO_4S$. Calculated, %: C 51.75; H 3.26; N 3.77. *M* 371.04.

The ^1H NMR spectra were recorded on Bruker AM-500 and Bruker WM-400 spectrometers (500 and 400 MHz, respectively). The ^{13}C and ^{19}F NMR spectra were measured on a Bruker AM-500 spectrometer at 125 and 470 MHz, respectively, using $CDCl_3$ as solvent. The chemical shifts were determined relative to the residual proton signal of $CHCl_3$ (^1H, δ 7.25 ppm), signal of $CDCl_3$ (^{13}C, δ_C 77.0 ppm), and $CFCl_3$ signal (^{19}F, δ_F 0.0 ppm). The mass spectra were obtained on an MKh-1321 mass spectrometer. The IR spectra were recorded on an FSM-1201 instrument with Fourier transform.

REFERENCES

1. Gilchrist, T.L., *Heterocyclic Chemistry*, Harlow, Essex, England: Longman Scientific & Technical, 1992, 2nd ed.
2. Joule, J.A. and Mills, K., *Heterocyclic Chemistry*, Malden, MA: Blackwell Science, 2000, 4th ed.
3. Soldatenkov, A.T., Kolyadina, N.M., and Shendrik, I.V., *Osnovy organicheskoi khimii lekarstvennykh veshchestv* (Principles of Organic Chemistry of Medicinal Agents), Moscow: Mir, 2007, p. 192.
4. Iwai, I. and Hiraoka, T., *Chem. Pharm. Bull*., 1963, vol. 11, p. 638.
5. Koltunov, K.Yu., Walspurger, S., and Sommer, J., *Chem. Commun*., 2004, p. 1754.
6. Koltunov, K.Yu., Walspurger, S., and Sommer, J., *Eur. J. Org. Chem*., 2004, p. 4039.
7. Vasilyev, A.V., Walspurger, S., Haouas, M., Sommer, J., Pale, P., and Rudenko, A.P., *Org. Biomol. Chem*., 2004, p. 3483; Vasil'ev, A.V., Walspurger, S., Pale, P., Sommer, J., Haouas, M., and Rudenko, A.P., *Russ. J. Org. Chem*., 2004, vol. 40, p. 1769.
8. Ryabukhin, D.S. and Vasil'ev, A.V., *Materialy Vserossiiskoi molodezhnoi nauchnoi konferentsii "Molodezh' i nauka na severe"* (Proc. All-Russian Youth Scientific Conf. "Youth and Science in the North"), Syktyvkar, 2008, p. 110; Ryabukhin, D.S., Vasil'ev, A.V., and Fukin, G.K., *Materialy Mezhdunarodnoi konferentsii po organicheskoi khimii "Khimiya soedinenii s kratnymi uglerod-uglerodnymi svyazyami"* (Proc. Int. Conf. on Organic Chemistry "Chemistry of Compounds with Multiple Carbon–Carbon Bonds), St. Petersburg, 2008, p. 214.
9. Walspurger, S., Vasil'ev, A.V., Sommer, J., Pale, P., Savechenkov, P.Yu., and Rudenko, A.P., *Russ. J. Org. Chem*., 2005, vol. 41, p. 1485.
10. Vasilyev, A.V., Walspurger, S., Chassaing, S., Pale, P., and Sommer, J., *Eur. J. Org. Chem*., 2007, p. 5740.
11. Braun, J. and Ostermayer, H., *Chem. Ber*., 1937, vol. 70, p. 1002.