

SHORT
COMMUNICATIONSThermolysis and Acid-Catalyzed Decomposition
of 4-Diazotetrahydrofuran-3-ones. A New Efficient Synthesis
of Tetrasubstituted Dihydrofuran-3-ones

L. L. Rodina, Yu. Yu. Medvedev, P. N. Moroz, and V. A. Nikolaev

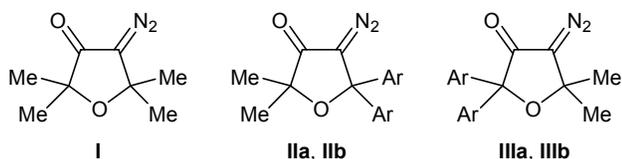
St. Petersburg State University, Universitetskii pr. 26, St. Petersburg, 198504 Russia
e-mail: LRodina@VN6646.spb.edu

Received November 18, 2011

DOI: 10.1134/S1070428012040252

The Wolff rearrangement is one of the most characteristic transformations of diazo ketones [1]. Diazo ketones of the tetrahydrofuran series are thus converted into oxetane derivatives. Using tetramethyl-substituted diazotetrahydrofuranone as an example, we previously showed [2] that its photolytic Wolff rearrangement was the most efficient [2]. Photoinduced reactions of aryl-substituted diazotetrahydrofuranones are characterized by lower selectivity, and they give rise to a number of products [3, 4].

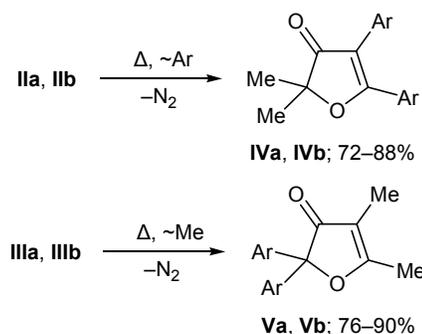
The goal of the present work was to study thermal and acid-catalyzed decomposition of 2,2,5,5-tetrasubstituted 4-diazotetrahydrofuran-3-ones, compare the results with those obtained by photolysis, and estimate synthetic potential of these processes. As substrates we selected 4-diazo-2,2,5,5-tetramethyltetrahydrofuran-3-one (**I**), 4-diazo-2,2-dimethyl-5,5-diphenyltetrahydrofuran-3-one (**IIa**), 4-diazo-5,5-bis(4-fluorophenyl)-2,2-dimethyltetrahydrofuran-3-one (**IIb**), 4-diazo-5,5-dimethyl-2,2-diphenyltetrahydrofuran-3-one (**IIIa**), and 4-diazo-2,2-bis(4-fluorophenyl)-5,5-dimethyltetrahydrofuran-3-one (**IIIb**).

Ar = Ph (a), 4-FC₆H₄ (b).

Preliminary experiments showed that diazo ketones **I–III** are very resistant to heat. Taking into account unexpected thermal stability [5, 6], thermolysis of diazo ketones **II** and **III** was performed at 150–160°C

in the absence of solvent (in melt), and the progress of reactions was monitored by TLC and ¹H NMR.

Diazofuranone **IIa** completely decomposed in 7 h, whereas thermolysis of its di-*para*-fluoro-substituted analog **IIb** required more than 48 h, other conditions being equal. According to the ¹H NMR data, dihydrofuranones **IVa** and **IVb** were formed as almost the only products. Thermal decomposition of regioisomeric diazo ketones **IIIa** and **IIIb** occurred at a much higher rate (in 3 h); like thermolysis of **IIa** and **IIb**, the only observed path of decomposition of **IIIa** and **IIIb** was elimination of nitrogen molecule and 1,2-migration of one methyl group with formation of dihydrofuranones **Va** and **Vb**.



Acid-catalyzed decomposition of diazofuranones **I–III** in trifluoroacetic acid was complete in 5–6 min. The reaction was exothermic, and diazo ketone **I** was converted almost quantitatively into 2,2,4,5-tetramethyl-2,3-dihydrofuran-3-one (**VI**), whereas diazo ketones **I** and **III** gave rise to the same 1,2-alkyl or 1,2-aryl migration products (**IV**, **V**) as in the thermolysis. The structure of newly synthesized compounds **IVb** and

Vb was determined on the basis of their ^1H and ^{13}C NMR spectra and elemental analyses.

Presumably, thermolysis of diazo ketones **I–III** with formation of dihydrofuran-3-ones **IV–VI** follows concerted nitrogen elimination–alkyl (aryl) group migration mechanism without intermediate generation of oxocarbenes. The latter are believed to be the most probable intermediate species in the photolysis of such diazo ketones [3, 4], and they tend to undergo Wolff rearrangement and concomitant transformations which were not observed in the thermolysis of diazo ketones **I–III**. Acid-catalyzed decomposition of aliphatic diazo compounds is known to follow two main paths [5, 7]. However, taking into account appreciably higher stability of diazo ketones **I–III** with respect to organic acids, as compared to diazo alkanes, we presume that the initial step is reversible protonation of the carbonyl group in **I–III**, which is followed by elimination of nitrogen to produce finally dihydrofuran-3-ones **IV–VI**.

Thus, unlike photolysis, thermal and acid-catalyzed decomposition of 4-diazotetrahydrofuran-3-ones having alkyl or aryl substituents leads to the formation of unsaturated ketones **IV–VI**, and these reactions may be regarded as an efficient method for the preparation of tetrasubstituted dihydrofuran-3-ones.

Diazo ketone **I** was synthesized from commercial 2,5-dimethylhex-3-yne-2,5-diol according to [8]; diazo ketones **II** and **III** were obtained from 2-methylbut-3-yn-2-ol and benzophenone or 4,4'-difluorobenzophenone according to the procedures described in [9].

Thermolysis of diazo ketones I, IIa, IIb, IIIa, and IIIb (general procedure). The reactions were carried out in a 10–15-ml flask equipped with an air condenser. The progress of the process was monitored by TLC and ^1H NMR. Dihydrofuranones **IV** and **V** were isolated by chromatography on silica gel (gradient elution with petroleum ether–*tert*-butyl methyl ether) or recrystallization from petroleum ether.

2,2-Dimethyl-4,5-diphenyl-2,3-dihydrofuran-3-one (IVa). Yield 44 mg (88%; from 55 mg of **IIa**; 150°C , 7 h), mp $79\text{--}80^\circ\text{C}$ (from petroleum ether), R_f 0.24 (petroleum ether–*t*-BuOMe, 5:1) [4].

4,5-Bis(4-fluorophenyl)-2,2-dimethyl-2,3-dihydrofuran-3-one (IVb). Yield 60 mg (72%; from 88 mg of **IIb**; 160°C , 9.5 h), mp $109\text{--}110^\circ\text{C}$ (from petroleum ether), R_f 0.21 (petroleum ether–*t*-BuOMe, 4:1). ^1H NMR spectrum, δ , ppm: 1.62 s (6H, CH_3), 7.05–7.71 m (8H, H_{arom}). ^{13}C NMR spectrum, δ_{C} , ppm: 23.7 (CH_3), 88.6 (C^2), 113.2 (C^4), 116.4 d (C^m , $^2J_{\text{CF}} = 21.9$ Hz), 116.6 d (C^m , $^2J_{\text{CF}} = 21.9$ Hz), 125.4 d (C^i , $^4J_{\text{CF}} = 4.0$ Hz), 125.9 d (C^i , $^4J_{\text{CF}} = 4.0$ Hz), 131.5 d (C^o ,

$^3J_{\text{CF}} = 9.0$ Hz), 131.9 d (C^o , $^3J_{\text{CF}} = 9.0$ Hz), 161.3 d (C^p , $^1J_{\text{CF}} = 248.3$ Hz), 163.8 d (C^p , $^1J_{\text{CF}} = 248.3$ Hz), 179.5 (C^5), 207.9 ($\text{C}=\text{O}$). Found, %: C 72.06; H 4.68. $\text{C}_{18}\text{H}_{14}\text{F}_2\text{O}_2$. Calculated, %: C 72.03; H 4.66.

4,5-Dimethyl-2,2-diphenyl-2,3-dihydrofuran-3-one (Va). Yield 34 mg (76%; from 50 mg of **IIIa**; 150°C , 4 h), mp $108\text{--}109^\circ\text{C}$ (from petroleum ether), R_f 0.18 (petroleum ether–*t*-BuOMe, 5:1) [4].

2,2-Bis(4-fluorophenyl)-4,5-dimethyl-2,3-dihydrofuran-3-one (Vb). Yield 52 mg (90%; from 65 mg of **IIIb**; 160°C , 8 h), mp $70\text{--}71^\circ\text{C}$ (from petroleum ether), R_f 0.32 (petroleum ether–*t*-BuOMe, 2:1). ^1H NMR spectrum, δ , ppm: 1.75 s (3H, CH_3), 2.35 s (3H, CH_3), 7.01–7.07 m (4H, H_{arom}), 7.42–7.46 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_{C} , ppm: 6.2 (4- CH_3), 15.4 (5- CH_3), 107.8 (C^4), 111.2 (C^2), 115.7 d (C^m , $^2J_{\text{CF}} = 21.9$ Hz), 128.7 d (C^o , $^3J_{\text{CF}} = 8.0$ Hz), 134.6 (C^i), 162.5 d (C^p , $^1J_{\text{CF}} = 247.4$ Hz), 184.3 (C^5), 205.5 ($\text{C}=\text{O}$). Found, %: C 72.16; H 4.71. $\text{C}_{18}\text{H}_{14}\text{F}_2\text{O}_2$. Calculated, %: C 72.03; H 4.66.

Reaction of diazo ketones I–III with trifluoroacetic acid (general procedure). Trifluoroacetic acid, 0.4–0.8 mmol, was added dropwise to 0.3–0.6 mmol of diazo ketone **I**, **IIa**, **IIb**, **IIIa**, or **IIIb**. When the exothermic reaction ceased and evolution of nitrogen terminated, the mixture was cooled, volatile components were removed under reduced pressure (10–15 mm), and the residue was purified by chromatography on silica gel or by recrystallization from petroleum ether. From 97 mg (0.6 mmol) of **I** and 96 mg (0.8 mmol) of CF_3COOH we obtained 80 mg (95%) of **VI**; from 100 mg (0.34 mmol) of **IIa** and 58 mg (0.42 mmol) of CF_3COOH , 83 mg (92%) of **IVa**; from 100 mg (0.3 mmol) of **IIb** and 60 mg (0.5 mmol) of CF_3COOH , 88 mg (98%) of **IVb**; from 100 mg (0.3 mmol) of **IIIa** and 70 mg (0.61 mmol) of CF_3COOH , 81 mg (90%) of **Va**; from 100 mg (0.3 mmol) of **IIIb** and 60 mg (0.5 mmol) of CF_3COOH , 86 mg (95%) of **Vb**.

The ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 spectrometer at 300 and 75.5 MHz, respectively (CDCl_3 , TMS). Reaction mixtures were separated by chromatography on Silicagel L (40–100 μm , activity grade I). The progress of reactions was monitored, and R_f values were determined, by TLC on Silufol UV-254 plates (Kavalier, ĀSSR).

REFERENCES

1. Krimse, W., *Eur. J. Org. Chem.*, 2002, p. 2193; Meier, H. and Zeller, K.P., *Angew. Chem., Int. Ed. Engl.*, 1975, vol. 14, p. 324; Rodina, L.L. and Korobitsyna, I.K., *Usp. Khim.*, 1967, vol. 36, p. 260.

2. Korobitsyna, I.K. and Rodina, L.L., *Zh. Org. Khim.*, 1965, vol. 1, p. 932; Korobitsyna, I.K., Rodina, L.L., and Shuvalova, V.G., *Zh. Org. Khim.*, 1968, vol. 4, p. 201.
3. Rodina, L.L., Mishchenko, V.L., Malashikhin, S.A., Platts, M.S., and Nikolaev, V.A., *Russ. J. Org. Chem.*, 2003, vol. 39, p. 1530; Rodina, L.L., Galkina, O.S., Supurgibekov, M.B., Grigor'ev, Ya.M., and Utsal', V.A., *Russ. J. Org. Chem.*, 2010, vol. 46, p. 1542; Nikolaev, V.A., Galkina, O.S., Sieler, J., and Rodina, L.L., *Tetrahedron Lett.*, 2010, vol. 51, p. 2713.
4. Rodina, L.L., Malashikhin, S.A., Galkina, O.S., and Nikolaev, V.A., *Helv. Chim. Acta*, 2009, vol. 92, p. 1990.
5. Regitz, M. and Maas, G., *Diazo Compounds. Properties and Synthesis*, Orlando: Academic, 1986, pp. 65, 96; Regitz, M. and Bartz, W., *Chem. Ber.*, 1970, vol. 103, p. 1477.
6. Popik, V.V. and Nikolaev, V.A., *J. Chem. Soc., Perkin Trans. 2*, 1993, p. 1791.
7. Bethell, D., *Adv. Phys. Org. Chem.*, 1969, vol. 7, p. 153; Jugeld, W. and Brseck, L., *Tetrahedron*, 1970, vol. 26, p. 5557.
8. Korobitsyna, I.K. and Rodina, L.L., *Zh. Obshch. Khim.*, 1964, vol. 34, p. 2851; Korobitsyna, I.K., Rodina, L.L., and Stashkova, L.M., *Zh. Obshch. Khim.*, 1963, vol. 33, p. 3109.
9. Rodina, L.L., Malashikhin, S.A., Linden, A., Heimgartner, H., and Nikolaev, V.A., *Helv. Chim. Acta*, 2008, vol. 91, p. 1662.