

CHEMISTRY OF FURANIDINE KETONES

III. Some reactions of 4-Diazo-2,2,5,5-Tetramethylfuranid-3-one*

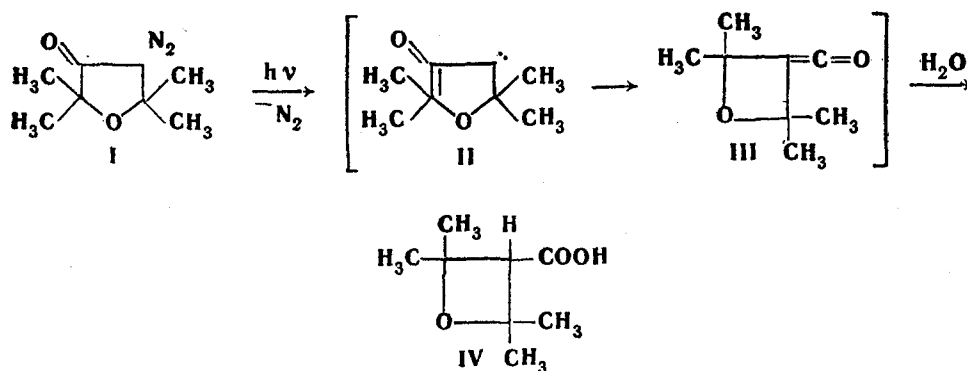
I. K. Korobitsyna, L. L. Rodina, and L. M. Stashkova

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Catalytic cracking of 4-diazo-2,2,5,5-tetramethylfuranid-3-one (I) in inert solvents gives the azine of 2,2,5,5-tetramethylfuranidine-3,4-dione (V), ketene dimer VI, and 2,2,5,5-tetramethylfuranidine-3,4-dione (VII). Treatment of diazoketone I with electrophilic reagents leads to replacement of the diazo group by hydroxyl and chlorine.

Continuing previous research on the reactivities of ketones and α -diketones of the furanidine (tetrahydrofuran) series, under Professor Yu. K. Yur'ev, we have developed a synthesis of a new class of heterocyclic diazoketones, 4-diazo-2,2,5,5-tetraalkylfuranid-3-ones [1, 2], and have investigated some of their chemical reactions. 4-Diazo-2,2,5,5-tetraalkylfuranid-3-ones were rearranged catalytically, thermally, and photolytically, and it was found that the last named method gives the best results. Thus 50 hr irradiation of an aqueous dioxane solution of diazoketone I with a PRK-4 mercury lamp gives a 97% yield of 2,2,4,4-tetramethyloxetane-3-carboxylic acid (IV) [2]. The present paper gives the results of further research on the properties of diazofuranidones.

With a Hanau S81 immersion mercury lamp source of ultraviolet light, the time for rearranging I to IV could be cut fivefold, i.e., to 10 hr, and yields of acid IV were almost quantitative. Apparently the reaction proceeds via a ketocarbene (II):



However, generally, intramolecular rearrangement is not the only possible way in which the ketocarbene formed by splitting of nitrogen from the diazoketone can be stabilized. Thus when diazoketones in inert solvents are cracked with copper catalysts, diacylethylenes formed by dimerization of the intermediate ketocarbenes [3-5] are found among the reaction products. Under such conditions another type of reaction, an intermolecular one, is also possible, i.e., reaction of the intermediate ketocarbene with the starting diazoketone, to give a ketazine [6-8].

We have investigated the pyrolysis of 4-diazo-2,2,5,5-tetramethylfuranid-3-one (I) in inert solvents, with and without added copper catalysts (see Table). 30 hr cracking of diazoketone I over copper bronze catalyst in n-heptane gave the starting diazoketone (23%), and the azine 2,2,5,5-tetramethylfuranidine-3,4-dione (V) (9.8%), identical with the authentic compound as prepared from 2,2,5,5-tetramethylfuranidine-3,4-dione and hydrazine hydrate. Also isolated were inconsiderable amounts of a substance, which from its analysis, molecular weight data, IR and PMR spectra, and analogs described in the literature [9], is probably ketene dimer VI.** Furthermore, thin-layer chromatography showed the products to contain a minute amount of 2,2,5,5-tetramethylfuranidine-3,4-dione (VII).

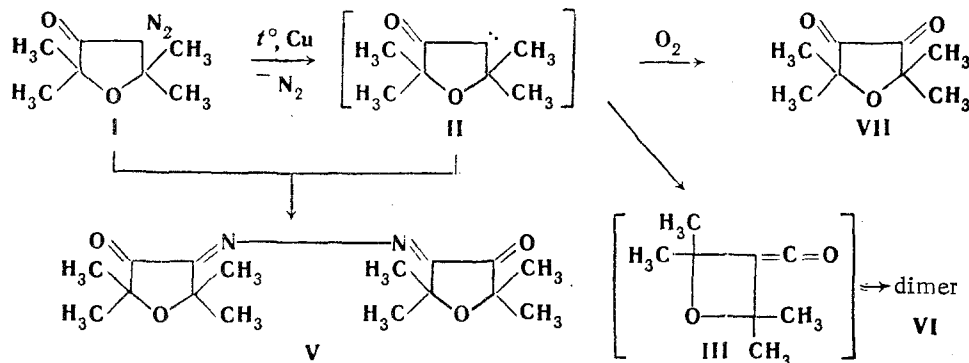
Pyrolysis of diazofuranidone I under more drastic conditions, in n-octane or m-xylene with or without copper bronze, is found to give greater resin formation than when using n-heptane, as described, with lower yields of azine

* For Parts I and II, see [1, 2]

** The results do not preclude the reaction's giving other isomeric compounds, e.g., lactones arising by reaction of ketene III with ketocarbene II [10].

and ketene dimer.

Apparently under the non-catalytic or catalytic conditions used to crack 4-diazo-2,2,5,5-tetramethylfuranid-3-one (I), it splits to ketocarbene II which is stabilized in three different ways: reaction with a molecule of I, to give the azine 2,2,5,5-tetramethylfuranidine-3,4-dione (V); rearrangement to ketene III (which can be isolated only as the dimer VI); and lastly partial oxidation to 2,2,5,5-tetramethylfuranidine-3,4-dione (VII).

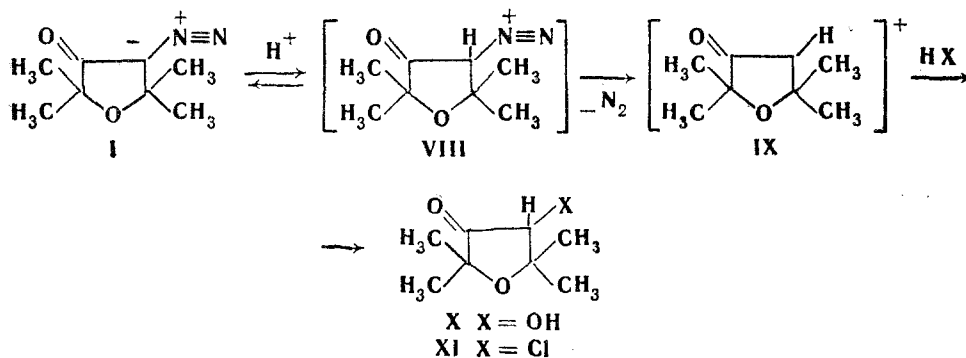


It should be noted that addition of a small amount of water raises the yield of ketone VII to 27%, and that if the reaction is run in ethanol, the yield rises to 42%. Possibly this is connected with both oxygen and the resultant diketone being highly soluble in a polar solvent. Other authors [8,11] have observed oxidation of carbenes too.

So ketocarbene II, formed by decomposition of diazofuranidone I, is stabilized in the way usual for carbenes. The absence of products arising by coupling of two molecules of ketocarbene is a peculiar feature of the reactions under review, and it is evidently due to steric hindrance of that kind of interaction.

The reaction of 4-diazo-2,2,5,5-tetramethylfuranid-3-one (I) towards electrophilic reagents, dilute sulfuric acid and concentrated hydrochloric acid, was also investigated. When diazofuranidone I is heated with 0.1 N sulfuric acid and copper bronze, it gives a 56% yield of 4-hydroxy-2,2,5,5-tetramethylfuranid-3-one (X), identical with the compound previously prepared [12] by reducing 4-isonitroso-2,2,5,5-tetramethylfuranid-3-one with zinc in acetic acid. When diazoketone I was treated with concentrated hydrochloric acid, a 73% yield of 4-chloro-2,2,5,5-tetramethylfuranid-3-one (XI) was obtained.

From research of recent years on the acid-catalyzed decomposition of diazoketones [13], the mechanism of these reactions is most probably as follows:



The first stage involves addition of a proton to a carbon atom with a negative charge. The resultant diazonium cation VIII then splits off a molecule of nitrogen, to give the carbonium ion IX. The latter gives the hydroxy or chloro ketone by reacting with, respectively, a molecule of water or hydrochloric acid.

Experimental

2,2,4,4-Tetramethyloxetane-3-carboxylic acid (IV). A solution of 2.2 g (0.013 mole) 4-diazo-2,2,5,5-tetramethylfuranid-3-one (I) in 84 ml dioxane, was irradiated in the cylindrical container of the Hanau S81 immersion lamp, for 10 hr. The solvent was then distilled off under a water-pump vacuum. Yield of acid IV 2.02 g (98.2%), mp 114–115° C. The literature [2] gives mp 114–115° C.

Catalytic cracking of 4-diazo-2,2,5,5-tetramethylfuranid-3-one.* A solution of 5 g (0.03 mole) diazoketone I in 50 ml n-heptane and 0.2 g Cu bronze, was stirred and refluxed for 30 hr. On cooling the solution gave 0.25 g colorless crystalline substance VI, mp 212–213° C (ex petrol ether). Found: C 68.79, 69.17; H 8.32, 8.67%; M 278.7; 282.0. Calculated for $C_{16}H_{24}O_4$: C 68.61; H 8.62%; M 280.3. IR spectrum** (cm^{-1}): 1805 weak, 1745 strong, 1681 medium, 1666 weak, 1650 weak, 1469 very strong, 1449 very strong, 1374 very strong, 1319 weak, 1215 medium, 1178 strong, 1134 strong, 1104 medium, 1077 medium, 973 medium, 939 medium, 918 medium, 864 weak, 838 medium, 724 weak. The PMR spectrum*** showed one resonance signal at +3.57 ppm.

Table 2
Catalytic Cracking of Diazoketone I

Run No.	Solvent	Catalyst	Reaction time, hr	Unreacted diazoketone I, %	Yield, %		
					Azine V	Dimer VI	Diketone VII
1	n-Heptane	Cu	10	28	3.3	0.5	Traces
2	n-Heptane	Cu	30	13	9.8	6.0	"
3	n-Heptane	CuSO ₄	30	20	9.0	4.0	"
4	n-Octane	Cu	10	18	1.0	0.5	"
5	n-Heptane + H ₂ O (5:1)	Cu	30	15	1.0	0.5	27

After distilling off the solvent, 0.65 g diazoketone I (13% on the starting quantity) was obtained, bp 64–66° C (6 mm), n_D^{20} 1.4800. A chromatogram**** of the isolated ketone showed an intense spot R_f 0.73 and a weak one R_f 0.042, characteristic respectively of diazofuranidone I and diketone VII [2].

The resinous residue after long standing was diluted with EtOH, to give 0.44 g (9.8% on the initial diazoketone I) azine V, mp 131–132° C (ex EtOH). Undepressed mixed mp with authentic azine V.

The azine of 2,2,5,5-tetramethylfuranidine-3,4-dione (V). 0.125 g (0.0025 mole) hydrazine hydrate was poured into a solution of 0.8 g (0.005 mole) 2,2,5,5-tetramethylfuranid-3,4-dione in 5 ml glacial AcOH, when heat was evolved. After cooling the solution was added dropwise to water, the precipitate filtered off, and air-dried. Yield 0.6 g (75%), mp 131–132° C (ex EtOH). Found: N 8.82, 8.91%. Calculated for $C_{16}H_{24}N_2O_4$: N 9.08%.

The table gives the results of catalytic cracking runs with diazoketone I.*****

Decomposition of 4-diazo-2,2,5,5-tetramethylfuranid-3-one (I) in ethanol. A solution of 5 g (0.03 mole) I in 50 ml dry EtOH, plus 0.5 g Cu bronze, was stirred and heated for 30–40 hr in a Wood's metal bath, the bath temperature being held at 90–100°C*****. After cooling the catalyst was filtered off, the EtOH distilled off, and the residue vacuum-distilled to give 4 g bright-crimson compound, bp 54–57° C (3 mm), n_D^{20} 1.4440, and a resinous residue.

The substance isolated was chromatographed on grade 3 activity neutral alumina, when elution with petrol ether gave 1.0 g (20%) of the starting diazoketone I. Elution with ether gave 3.0 g (42% based on the diketone) of the dihydrate of diketone VII, giving an undepressed mixed mp with authentic 2,2,5,5-tetramethylfuranid-3,4-dione dihydrate [14]. The literature gives the mp of 2,2,5,5-tetramethylfuranid-3,4-dione dihydrate as 74–75° C [14].

On prolonged standing the resinous residue deposited yellow crystals of azine V, mp 130.5–131° C (ex EtOH), giving an undepressed mixed mp with authentic compound.

*See table, Run 2.

**The IR spectra were determined with a nujol suspension between glass using an IKS-14 instrument with a NaCl prism.

***The PMR spectrum was determined with a JNM 3 spectrometer, at 40 Mc, field homogeneity 10^{-8} , external standard water.

****Alumina activity grade 2 was used for the thin-layer chromatography, and the eluant was petrol ether + ether (1:1).

*****Diazoketone I was cracked similarly in n-heptane, n-octane, and m-xylene, very small amounts (0.5–1%) dimer VI and azine V being isolated.

*****With 5 g starting compound, and heating for 10 hr in a water-bath at 50–60°C, 4.8 g was recovered unchanged.

4-Hydroxy-2, 2, 5, 5-tetramethylfuranid-3-one (X). 15 ml 0.1 H₂SO₄ and 0.1 g Cu bronze were added to a solution of 1.7 g (0.01 mole) diazoketone I in 5 ml EtOH, and the whole refluxed and stirred mechanically on a water-bath (bath temperature 55–60° C) for 5 hr. The EtOH was then distilled off under a water-pump vacuum, and the residue extracted with ether. The extracts were dried over MgSO₄, and the ether distilled off, when the residue crystallized. Yield of X 0.9 g (56%), mp 97.5–98° C (ex petrol ether), giving an undepressed mixed mp with authentic 4-hydroxy-2, 2, 5, 5, -tetramethylfuranid-3-one [12]. The literature [12] gives mp 98.5–99° C.

4-Chloro-2, 2, 5, 5-tetramethylfuranid-3-one (XI). 1.2 ml (0.014 mole) concentrated HCl was added dropwise to 2.2 g (0.013 mole) diazoketone I, when there was vigorous evolution of N₂, and the mixture heated up. After cooling it was neutralized with NaHCO₃ solution, and carefully extracted with ether, the ether vacuum-distilled off from the extracts after drying with MgSO₄, to give 1.6 g (73%) XI, bp 68–70° C (10 mm); d₄²⁰ 1.0813; n_D²⁰ 1.4500. Found: Cl 19.76, 19.81%; MR_D 43.89. Calculated for C₈H₁₃ClO₂: Cl 20.09%; MR_D 43.77. The literature [15] gives 65–66° C (8 mm); d₄²⁰ 1.0820; n_D²⁰ 1.4470.

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Zhdanov Leningrad State University