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> SHORT COMMUNICATIONS

Reactions of 2-Diazo-1,3-dicarbonyl Compounds with Aromatic Thioketones (Superdipolarophiles)

V. A. Nikolaev^a, A. V. Ivanov^a, A. A. Shakhmin^a, B. Schulze^b, and L. L. Rodina^a

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

^b Universität Leipzig, Leipzig, Germany

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Cycloaddition reactions of aliphatic diazo compounds are widely used in the synthesis of various nitrogen-containing and other heterocycles [1–3]. In these reactions, the most reactive dipoles are believed to be diazoalkanes and 2-diazo ketones, whereas cycloaddition of 2-diazo-1,3-dicarbonyl compounds to common dipolarophiles is not typical [2, 3].

The goal of the present work was to study cycloaddition of 2-diazo-1,3-dicarbonyl compounds to "superdipolarophiles" [4], i.e., aromatic thioketones which exhibit the highest reactivity in cycloaddition processes, and elucidate the possibility for synthesizing in such a way O- and S-containing heterocycles.

As substrates we used acyclic and carbocyclic 2-diazo-1,3-dicarbonyl compounds, diazoacetylacetone (Ia), ethyl diazoacetoacetate (Ib), and diazodimedone (Ic), and thiobenzophenone (II), thiofluorenone, and other aromatic thioketones were selected as dipolarophiles. We have found that diazodicarbonyl compounds Ia–Ic react with aromatic thioketones even at room temperature to give tetrasubstituted 1,3-oxa-thioles IIIa–IIIc as final products (Scheme 1).

Taking into account that diazodicarbonyl compounds **Ia–Ic** are stable under usual conditions and that they can be stored for a long time without appreciable decomposition, we presumed that the reaction follows a conventional three-step scheme which was proposed for analogous processes with participation of diazo ketones and other diazomonocarbonyl compounds [5, 6]. Initially, [3+2]-cycloaddition of dipolar diazo group at the C=S bond of thioketone gives unstable thiadiazoles IV which lose nitrogen molecule to generate reactive thiocarbonyl ylides V; the latter undergo intramolecular 1,5-electrocyclization leading to 1,3-oxathioles III.

Cyclization of C=S ylide V generated from unsymmetrically substituted diazodicarbonyl compounds could produce two regioisomeric oxathioles. However, in the reaction with diazo ester **Ib**, electrocyclization of the corresponding ylide occurs chemoselectively at the acetyl group, whereas the ester fragment remains intact, and the product is only one regioisomer, 1,3-oxathiole **IIIb**. Cyclic diazodiketone **Ic** reacted with thioketones at a much lower rate, and elevated temperature was necessary to accelerate the process. As a result, the reaction was accompanied by partial decomposition of diazodimedone (**Ic**) with formation of the Wolff rearrangement product, 2-oxoketene. The



I, R = R' = Me (a); R = MeO, R' = Me (b); $RR' = CH_2C(Me)_2CH_2$ (c).



latter reacted with thioketone present in the reaction mixture to give [4+2]-cycloaddition product, oxathiinone VI, the ratio IIIc–VI being ~2.2:1 (Scheme 2).

As in reactions with diazoalkanes and diazoketones [4–6], the most reactive aromatic thioketones toward diazodicarbonyl compounds **Ia–Ic** were thiobenzophenone and thiofluorenone. The structure of oxathioles **IIIa–IIIc** and oxathiinone **VI** was reliably determined by spectral methods.

Thus we have shown that relatively inert (in cycloaddition reactions) 2-diazo-1,3-dicarbonyl compounds react with thioketones to give tetrasubstituted 1,3-oxathioles. Reactions of cyclic diazodiketones with thioketones at elevated temperature are accompanied by Wolff rearrangement of the initial diazodiketone and subsequent [4+2]-cycloaddition of 2-oxoketene at the C=S bond.

1-(5-Methyl-2,2-diphenyl-1,3-oxathiol-4-yl)ethanone (IIIa). A mixture of 785 mg (3.96 mmol) of diphenylmethanethione (II) and 500 mg (3.97 mmol) of ethyl 3-diazopentane-2,4-dione in 5 ml of benzene was left to stand for several days at 18-20°C under nitrogen. According to the ¹H NMR data (using *N*-methylmaleimide as reference), the concentration of oxathiole IIIa in the reaction mixture in 3, 5, and 7 days was 14, 29, and 47%, respectively. After 7 days, the solvent was distilled off under reduced pressure (10–12 mm), and the residue was subjected to chromatography on silica gel (50 g) using petroleum etherdiethyl ether (10:1) as eluent. The major fraction was dried over anhydrous MgSO₄ and evaporated. Yield 425 mg (38%; 54% calculated on the reacted diazoacetylacetone), oily substance which slowly crystallized on cooling to 0°C, mp 54-56°C (from tert-butyl methyl ether), $R_{\rm f}$ 0.45 (petroleum ether-*tert*-butyl methyl ether, 2:1). ¹H NMR spectrum, δ , ppm: 2.26 s (3H, 5-CH₃), 2.38 s (3H, COCH₃), 7.39-7.28 m (6H, H_{arom}), 7.54–7.46 m (4H, H_{arom}). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 15.7 (5-CH₃), 30.5 (COCH₃), 101.1 (C²), 112.6 (C⁴); 126.4, 128.2, 128.5, 142.9 (C_{arom}); 157.1 (C⁵), 191.3 (C=O). Mass spectrum (ESI): m/z 297 $[M + H]^+$.

Methyl 5-methyl-2,2-diphenyl-1,3-oxathiole-4-carboxylate (IIIb). Benzene, 10 ml, was added to 793 mg (4 mmol) of freshly prepared thiobenzophenone, the mixture was heated to 90-95°C, a part of the solvent (~5 ml) was distilled off to remove traces of water, the mixture was cooled to room temperature, a few grains of anhydrous calcium chloride were added, 640 mg (4.5 mmol) of methyl 2-diazo-3-oxobutanoate (Ib) was added, and the flask was flushed with argon, hermetically capped, and kept for 63 days at 18–25°C. After 2 months, the yield of oxathiole IIIb was 61% (74% on the reacted diazo ester Ib) according to the ¹H NMR data. The solvent was distilled off under reduced pressure (15–20 mm), the residue (1.24 g) was applied onto 2.5 g of silica gel and transferred to a column charged with 25 g of silica gel (Woelm Pharma). The column was eluted with petroleum ether-tert-butyl methyl ether (1:0 to 10:1). Yield 442 mg (35%, 43% on the reacted diazo ester **Ib**), $R_{\rm f}$ 0.42 (petroleum ether-*tert*-butyl methyl ether, 3:1), mp 72–73°C (from petroleum ether). ¹H NMR spectrum, δ, ppm: 2.38 s (3H, 5-CH), 3.72 s (3H, OCH₃), 7.38-7.29 m (6H, H_{arom}), 7.52-7.44 m (4H, H_{arom}). ¹³C NMR spectrum, δ_{C} , ppm: 14.9 (5-CH₃), 51.9 (OCH_3) ; 102.0 and 101.3 (C^4, C^2) ; 126.5, 128.3, 128.6, 143.1 (C_{arom}); 158.6 (C⁵), 163.7 (C=O). Found, %: C 69.39, 69.45; H 5.34, 5.44. C₁₈H₁₆O₃S. Calculated, %: C 69.21; H 5.16.

Reaction of 2-diazo-5,5-dimethylcyclohexane-1,3-dione (Ic) with thiobenzophenone (II) at 80°C. A mixture of 1.0 g (6 mmol) of compound **Ic** and 1.19 g (6 mmol) of thioketone **II** in 10 ml of benzene was heated for 4 days under reflux. The solvent was distilled off under reduced pressure (10–12 mm) at 40°C. According to the ¹H NMR data, the crystalline residue (1.9 g) contained 0.256 g (13%) of oxathiinone **VI** and 0.553 g (28%) of oxathiole **IIIc**. The product mixture was separated by column chromatography on silica gel (50 g) using hexane–diethyl ether as eluent (gradient mode); in order of elution, 113 mg of compound **VI** and 502 mg of **IIIc** were isolated.

6,6-Dimethyl-2,2-diphenyl-4,5,6,7-tetrahydrocyclopenta[e][1,3]oxathiin-4-one (VI). Yield 113 mg (6%), mp 112–113°C, R_f 0.57 (diethyl ether–hexane, 1:1). ¹H NMR spectrum, δ , ppm: 0.98 s (6H, CH₃), 2.29 s (2H, 7-H), 2.46 s (2H, 5-H), 7.54–7.33 m (10H, H_{arom}). ¹³C NMR spectrum, δ_C , ppm: 29.4 (C⁶), 34.7 (CH₃), 48.6 and 42.0 (C⁵, C⁷), 98.4 (C²), 114.2 (C^{4a}); 127.2, 128.4, 129.0, 141.4 (C_{arom}); 171.4 (C^{7a}), 181.5 (C⁴).

6,6-Dimethyl-2,2-diphenyl-4,5,6,7-tetrahydro-1,3-benzoxathiol-4-one (IIIc). Yield 237 mg (13%), R_f 0.50 (petroleum ether–*tert*-butyl methyl ether, 2:1), colorless crystals, mp 157–158°C (from *tert*-butyl methyl ether). ¹H NMR spectrum, δ , ppm: 1.12 s (6H, CH₃), 2.30 s (2H, 7-H), 2.50 s (2H, 5-H), 7.38–7.31 m (6H, H_{arom}), 7.50–7.47 m (4H, H_{arom}). ¹³C NMR spectrum, δ_C , ppm: 28.4 (CH₃), 34.2 (C⁶), 38.7 (C⁷), 50.9 (C⁵), 105.2 (C⁶), 111.5 (C^{3a}=C); 126.5, 128.2, 128.6, 142.7 (C_{arom}); 165.5 (C^{7a}), 191.5 (C⁴). Found, %: C 75.22, 75.00; H 5.99, 5.91. C₂₁H₂₀O₂S. Calculated, %: C 74.97; H 5.99.

The ¹H and ¹³C NMR spectra were measured on a Varian Gemini 300 spectrometer at 300 and 75.45 MHz, respectively, using CDCl₃ as solvent and tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV) were obtained on a Quadrupole-MS VG 12-250 instrument. Quantitative analysis of the reaction mixtures was performed using *N*-methylmaleimide or 1,1,2,2-tetrachloroethane as internal reference. The elemental compositions were determined on a Heraeus CHNO rapid analyzer. The progress of reactions was monitored, and $R_{\rm f}$ values were determined, on Silufol UV-254 plates (Kavalier, ČSSR). Diazodicarbonyl compounds Ia-Ic were synthesized from the corresponding commercial 1,3-dicarbonyl compounds by diazo transfer reaction [7]; thiobenzophenone and thiofluorenone were prepared from the corresponding ketones according to known procedures [8, 9].

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REFERENCES

- Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products, Padwa, A. and Pearson, W.H., Eds., Hoboken, NJ: Wiley, 2002, p. 539.
- Regitz, M. and Heydt, H., *1,3-Dipolar Cycloaddition* Chemistry, Padwa, A., Ed., New York: Wiley, 1984, vol. 1, p. 393.
- Korobitsyna, I.K., Bulusheva, V.V., and Rodina, L.L., *Khim. Geterotsikl. Soedin.*, 1978, p. 579.
- 4. Huisgen, R. and Langhals, E., *Tetrahedron Lett.*, 1989, vol. 30, p. 5369.
- Mloston, G. and Heimgartner, H., Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products, Padwa, A. and Pearson, W.H., Eds., Hoboken, NJ: Wiley, 2002, p. 315.
- Mloston, G. and Heimgartner, H., *Polish J. Chem.*, 2000, vol. 74, p. 1503; Kagi, M., Linden, A., Mloston, G., and Heimgartner, H., *Helv. Chim. Acta*, 1998, vol. 81, p. 285; Kagi, M., Linden, A., Mloston, G., and Heimgartner, H., *Helv. Chim. Acta*, 1996, vol. 79, p. 855.
- Regitz, M. and Maas, G., Diazo Compounds. Properties and Synthesis, New York: Academic, 1986, p. 326; Doyle, M.P., McKervey, M.A., and Ye, T., Modern Catalytic Methods for Organic Synthesis with Diazo Compounds, New York: Wiley, 1998.
- 8. Pedersen, B., Scheibye, S., Nilsson, N., and Lawesson, S., *Bull. Soc. Chim. Belg.*, 1978, vol. 87, p. 223.
- Scheibye, S., Shabana, R., and Lawesson, S., *Tetra*hedron, 1982, vol. 38, p. 993.