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Synthesis and unusual photochemistry of a highly reactive pyrimidinedione

Sergey V. Shorunov,*[a] Matthew B. Plutschack,[b] Maxim V. Bermeshev*[a] and Ilia A. Guzei[b]

[a] *A. V. Topchiev Institute of Petrochemical Synthesis, Russian Academy of Sciences, 119991 Moscow, Russian Federation. E-mail: sshorunov@ips.ac.ru, bmv@ips.ac.ru*

[b] *Department of Chemistry, University of Wisconsin-Madison, Madison, 53706 WI, USA*

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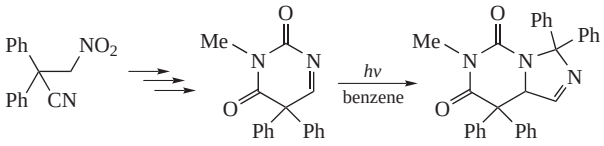
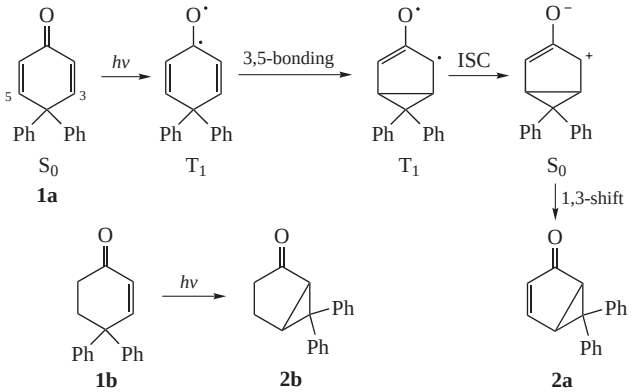
The herein obtained 3-methyl-5,5-diphenylpyrimidine-2,4-(3*H*,5*H*)-dione forms upon photolysis an unusual bicyclic product, namely, 6-methyl-3,3,8,8-tetraphenyl-8,8a-dihydroimidazo[1.5-*c*]pyrimidine-5,7(3*H*,6*H*)-dione in 21% yield. The transformation starts with elimination of carbon monoxide and methyl isocyanate from the molecule of substrate *via* a 'Type A' photochemical process giving 3,3-diphenylazirine. Then 1,3-dipole species generated from the latter is trapped by the starting compound *via* a [3 + 2] cycloaddition.



Disubstituted cyclohexadienones are known to undergo a facile rearrangement from the triplet state.[1] The first described example was the rearrangement of santonin to lumisantonin.[2] In 1961, the mechanism was established by Zimmerman and co-workers using the model compound, 4,4-diphenylcyclohexa-2,5-dienone **1a** which formed bicyclo[3.1.0]hexenone **2a**[3] (Scheme 1). These reactions proceed through an n–π* triplet state which undergoes β,β-bonding. Intersystem crossing produces a zwitterionic singlet which undergoes a 1,3-shift. This type of rearrangement is known as a 'Type A' rearrangement.

To demonstrate that β,β-bonding was occurring between the two double bonds, 4,4-diphenylcyclohexenone **1b** was irradiated resulting in the formation of the rearranged product **2b**. In this case, radical delocalization in a phenyl group results in what is called a 'Type B' rearrangement[4] (see Scheme 1).

Since that time, a systematic study of heterocyclic analogues of the above mentioned carbocyclic photochemical reactants was performed in Zimmerman's group to determine whether there was a parallel reactivity. So far, a number of compounds having nitrogen substituents were synthesized and their photochemistry was explored.[5] They differ from their parent carbon molecules.

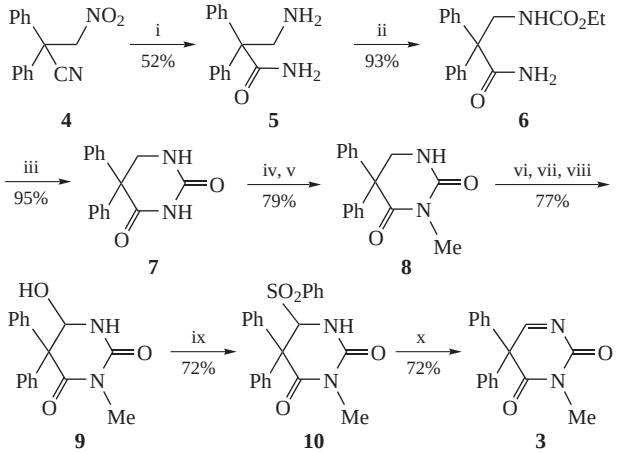


Scheme 1

For example, replacement of the C^2 carbon with a nitrogen, completely alters the course of the reaction giving a regioselective phenyl migration.[6]

We were interested in the photochemistry of 3-methyl-5,5-diphenylpyrimidine-2,4(3*H*,5*H*)-dione **3** (Scheme 2). This particular heterocycle contains two nitrogen atoms (one sp^3 and one sp^2 hybridized) as well as two carbonyl groups (urea and amide ones). We anticipated that each group may alter the usual reaction path of the comparable parent carbocycles. Herein, we describe the synthesis and photochemistry of pyrimidinedione **3** and propose a pathway for formation of the photolysis product.

The synthesis of compound **3** starts from the known 2,2-diphenyl-3-nitropropionitrile **4**[7] (Scheme 2). Reduction with sodium borohydride and palladium on charcoal, followed by an aqueous work up led to amino amide **5**. Carboxylation and base catalyzed ring closure produced compound **7** in excellent yield, and methylation with methyl iodide gave product **8**. The crucial step of this

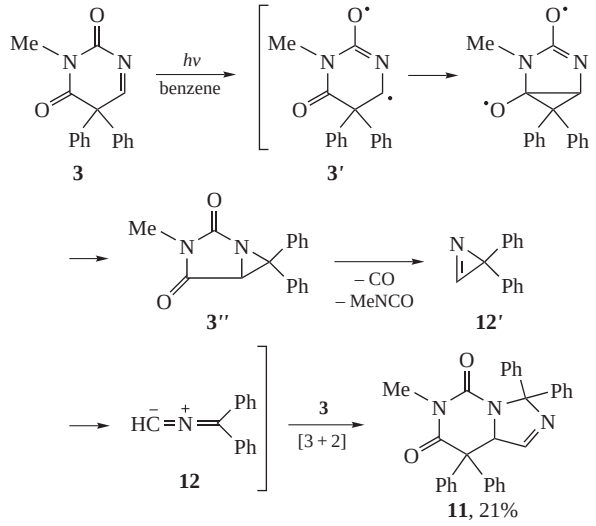


Scheme 2 *Reagents and conditions:* i, $NaBH_4$, Pd/C, EtOH, THF, 20 °C; ii, $ClCO_2Et$, Na_2CO_3, dioxane, EtOH, H_2O, 0 °C; iii, NaOEt, EtOH, dioxane, 20 °C; iv, Bu^tOK, DMF, 20 °C; v, MeI, 20 °C; vi, NaH, THF, 20 °C; vii, $Bu^tN{=}S(Cl)Ph$, –78 °C, viii, H_2O, 20 °C; ix, PhS(O)OH; x, NaH, CH_2Cl_2.

synthesis was the oxidation of CH_2 group of the pyrimidinedione **8** into the hemiaminal **9**, which required the application of the Mukayama's oxidant.[8] ^{1}H and ^{13}C NMR along with HRMS proved the structure of all new compounds (see Online Supplementary Materials for more experimental details including ^{1}H, ^{13}C NMR spectra, and high-resolution mass spectrometry data).

The target compound **3** is a powerful Michael acceptor, reactive towards even weak nucleophiles such as water. Upon short exposure to the atmosphere, it rapidly consumed water vapors forming the hydroxy precursor **9**. Our study of the photochemistry of **3** was carried out with thorough purging the solution of **3** in anhydrous benzene with a stream of deoxygenated nitrogen through syringe needle for 1 h before irradiation in order to remove all traces of oxygen. The irradiation was carried out in a semimicro immersion apparatus with a copper(II) sulfate solution filter. This photolysis led to a single isolated product **11** (Scheme 3) whose structure was established by the NMR spectroscopy and X-ray analyses (Figure 1).[†,9] The rest of the reaction material was a tarry resin with uninterpretable NMR and mass spectra.

Considering the electrophilic reactivity of aza enone **3** may suggest that this product arises from the [3 + 2] cycloaddition of the two fragments: reactant **3** and the nitrile ylide **12**. Hence, we suggest that the photolysis of **3** leads to the formation of this



Scheme 3

† A single crystal of **11**·0.45 CH_2Cl_2 for X-ray analysis was obtained after slow evaporation of CH_2Cl_2 from the corresponding solution of **11** in the mixture of CH_2Cl_2 and *n*-heptane (1 : 1 v/v).

Crystal data for **11**: $C_{31}H_{25}N_3O_2 \cdot 0.45\,CH_2Cl_2$ (M = 509.57), monoclinic, space group $P\bar{1}$, at 100 K: a = 8.6152(2), b = 11.1598(3) and c = 13.8826(4) Å, α = 71.752(2)°, β = 89.276(2)°, γ = 80.540(2)°, V = = 1249.29(6) Å^3, Z = 2, d_{calc} = 1.355 g cm^{-3}, μ(CuKα) = 1.530 mm^{-1}, F(000) = 266.9. Intensities of 20009 reflections were measured and 4605 independent reflections (R_{int} = 0.0356) were used in a further refinement. The refinement converged to wR_2 = 0.0916 and GOF = 1.043 for all independent reflections [R_1 = 0.0356 was calculated against F for 3458 observed reflections with $I > 2\sigma(I)$]. The measurements were made on a Bruker Apex Smart CCD diffractometer with graphite-monochromated CuKα radiation (λ = 1.54178 Å). A successful solution by the direct methods provided most non-hydrogen atoms from the E-map. The remaining non-hydrogen atoms were located in an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined with anisotropic displacement coefficients. All hydrogen atoms were included in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients.

CCDC 1813479 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

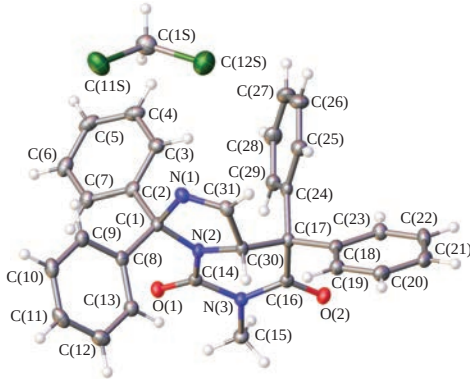


Figure 1 A molecular drawing of solvate **11**·0.45 CH_2Cl_2 shown with 50% displacement probability ellipsoids (the solvent molecule of dichloromethane is 45% occupied).

1,3-dipole **12**. A plausible mechanism for this transformation is shown in Scheme 3. Excitation of **3** could lead to biradical **3′**, which can undergo β,β-bonding similar to the cyclohexadienone structures mentioned above. A Type A-like rearrangement could then result in compound **3″**, which then undergoes decomposition evolving carbon monoxide and methyl isocyanate. Rearrangement of **12′** would provide the 1,3-dipole fragment **12**, which could then react with starting material and form the isolated bicyclic compound **11**.

In summary, the unique photochemical behavior of substituted pyrimidines was demonstrated by example of photochemical rearrangement of 3-methyl-5,5-diphenylpyrimidine-2,4(3*H*,5*H*)-dione **3**. The formed bicyclic structure **11** seems to be hardly accessible by non-photochemical approaches. Probably, pyrimidinedione **3** might be employed as a photochemical precursor of unusual 1,3-dipole, $Ph_2C{=}N^+{=}CH^-$, to be trapped by suitable dipolarophiles.

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Dedicated to the memory of Professor Howard E. Zimmerman.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2018.09.016.

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