



Surprising secondary photochemical reactions observed on conventional photolysis of diazotetrahydrofuranones

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ABSTRACT

The formation of C–H insertion products of the terminal N-atom of a diazo group into the α -CH-bond of tetrahydrofuran during direct photolysis of regioisomeric 2,2-dimethyl-5,5-diphenyl and 5,5-dimethyl-2,2-diphenyl-substituted 3-diazotetrahydrofuran-4-ones in THF is dictated by photochemical cycloelimination of the originally formed (1,1-dimethyl-2-oxa-3,3-diphenyl-propano)ketene and oxetanecarboxylic acid derivatives to yield benzophenone. The latter, under subsequent UV irradiation of the reaction mixture, initiates sensitized photolysis of the starting diazoketones resulting in the appearance of the insertion products with the solvent.

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Direct photolysis of cyclic and heterocyclic diazoketones normally proceeds with elimination of nitrogen and subsequent Wolff rearrangement (WR), a process which is widely used in organic synthesis.^{1–3} It was recently demonstrated however that irradiation of 2,2,5,5-tetraphenyl-substituted diazofuranone **A** in tetrahydrofuran (THF), along with the ordinary WR product **B** gave rise to the adduct **C** of the initial diazoketone with THF in yields of up to 50%.⁴ The formation of unexpected α -oxohydrazone **C** can be formally considered as a C–H insertion of the terminal N-atom of the diazo group into the α -CH bond of tetrahydrofuran (Scheme 1).

To the best of our knowledge, the reactions of this type have not been previously described in the chemistry and photochemistry of diazo compounds,^{2,3,5} prompting this study of the origin, along with the scope and limitations of this photochemical process.

As the above-mentioned reaction was observed only with 2,2,5,5-tetraphenyl-substituted diazoketone **A**, and did not occur upon photolysis of the corresponding tetraalkyl-substituted diazo analogues,⁶ it appeared that the α,α -diphenyl substituents adjacent to the diazo group in diazofuranone **A** were pivotal to the outcome of this photochemical process.

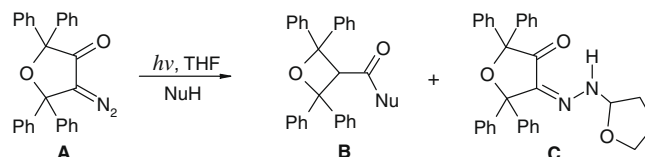
To check this experimentally, regioisomeric 2,2-dimethyl-5,5-diphenyl- and 5,5-dimethyl-2,2-diphenyl-substituted diazoketones **1a** and **1b** were prepared using previously described proce-

dures,⁷ and their photochemical reactions in THF in the presence of different nucleophiles (H₂O, MeOH, Me₂NH) to trap the intermediate ketene were studied.⁸

However, the photochemical reactions of diazoketones **1a,b** showed that both regioisomers exhibited almost identical reactivity and produced, upon photolysis, four basic reaction products **2–5** with similar structures, and essentially in the same ratio (Scheme 2).

Thus, no dependence of the efficiency of the C–H insertion process on the position of the phenyl substituents relative to the diazo group was revealed. At the same time, a well-defined effect of the nature of the nucleophile on the yields of the C–H insertion products **3** was observed (MeOH > H₂O $\gg$ Me₂NH).⁹

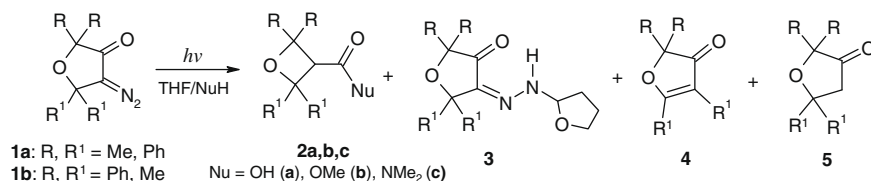
The main objective of the current research was to elucidate the origin of the C–H insertion products **3** in the above-mentioned photochemical reactions as well as the reason behind the unexpected influence of the nucleophile on the yields.



Scheme 1. Ordinary **B** and unusual C–H insertion product **C** formed during photolysis of diazoketone **A**.

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Scheme 2. Major reaction products 2–5 upon photolysis of diazoketones 1a,b.

Careful study of the conventional photolysis¹⁰ of isomeric diazoketones 1a,b has shown that

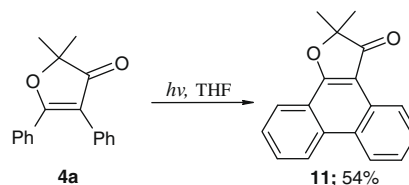
- the primary reaction products were photochemically rather unstable, and during the course of the succeeding UV irradiation, they underwent further transformations. Thus, by the time of complete conversion of diazoketones 1a,b (40–60 min), the reaction mixture usually contained at least 10 reaction products 2–11 (as indicated by ¹H NMR and IR spectroscopy and GC–MS analysis¹¹) (Schemes 2 and 3);
- one of the principal products of these secondary photochemical reactions regardless of the structure of the initial diazoketones 1a,b was benzophenone (7);¹² the content of Ph₂C=O in the reaction mixture usually amounted to 2–5%, and sometimes even more, but then it decreased as irradiation was continued.

We suggest that the appearance of benzophenone (7) during photolysis of diazoketones 1a,b was due to the secondary photochemical processes of the initially formed reaction products.

To check this assumption experimentally, photochemical reactions of a few of the products were studied under the same reaction conditions, namely: photolysis of ketene 6, generated by conventional UV irradiation ($\lambda > 210$ nm) of diazofuranone 1a in neat THF (without addition of NuH); photolysis of the dimethylamide of oxetanecarboxylic acid 2c; irradiation of the product of 1,2-migration of the phenyl group—unsaturated ketone 4a, as well as the sensitized photolysis of diazoketone 1a in the presence of benzophenone.

It was found that ketene 6, initially generated via Wolff rearrangement, on further irradiation of the reaction mixture rapidly disappears,¹³ and according to ¹H NMR data and GC–MS analysis, benzophenone and other reaction products are formed¹⁴ (Scheme 4).

The production of benzophenone (7) was also observed during photolysis of oxetanecarboxylic acid 2a and dimethylamide 2c



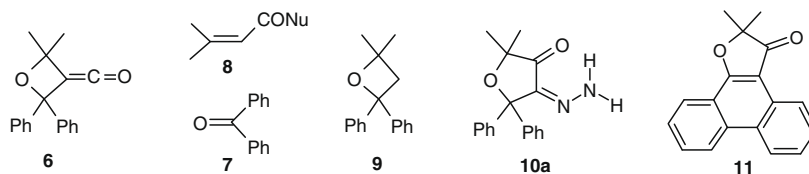
Scheme 5. Intramolecular photochemical cyclization of 4,5-diphenyldihydrofuranone (4a).

(accompanied by the formation of 3,3-dimethylacrylic acid or its dimethylamide 8c) (Scheme 4), while irradiation of unsaturated 4,5-diphenyldihydrofuranone (4a) produced exclusively phenanthrene derivative 11 (Scheme 5).

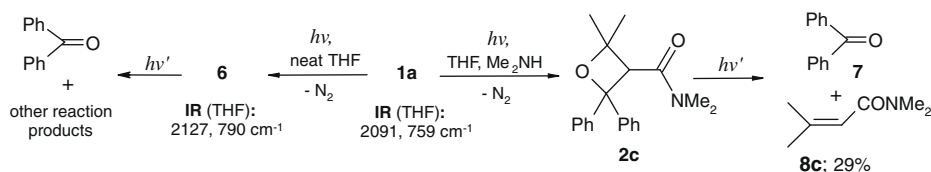
Finally, sensitized photolysis of diazoketone 1a in the presence of 1.5 mol equiv of benzophenone gave rise to the formation of the C–H insertion product 3a (Fig. 1) along with a small amount of monoketone 5a (Scheme 6).

Thus, irradiation with short wavelength UV light ($\lambda > 210$ nm) of ketene 6, acid 2a and amide 2c leads to photochemical cleavage of the oxetane heterocycle, and one of the key products of this process is benzophenone. The observed photochemical transformation can be considered as a reverse Paterno–Büchi reaction.¹⁷ A few examples of similar photochemical cycloelimination processes with aryl-substituted oxetanes have been previously described in the literature.¹⁸

The mechanism of the above-mentioned photochemical reaction in the case of oxetane derivatives 2 and 6 remains unknown. It is conceivable that in the case of ketene 6 the reaction proceeds either by direct photochemical cycloelimination with the formation of benzophenone and isopropylideneketene D (pathway a), or through the initial decarbonylation of ketene 6 followed by cycloelimination of benzophenone from the intermediate oxetanecarbene E with simultaneous generation of isopropylidenecarbene F (Scheme 7, pathways b, c).



Scheme 3. Secondary reaction products 7–11 formed upon photolysis of diazoketones 1a,b.

Scheme 4. Photochemical cycloelimination of oxetane derivatives 6 and 2c to produce Ph₂C=O.

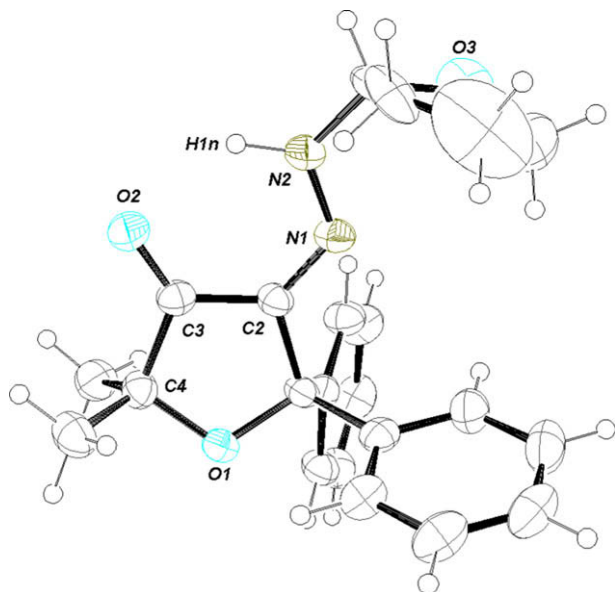
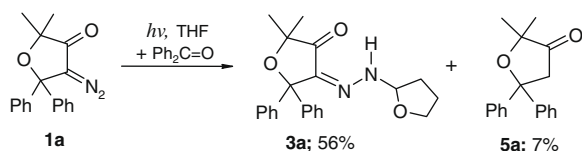


Figure 1. ORTEP plot¹⁵ of the crystal structure of the C–H insertion product **3a**.¹⁶



Scheme 6. Benzophenone-sensitized photolysis of diazoketone **1a**.

The direct cycloelimination (path *a*) is supported by the formation of dimethyl acrylamide (**8c**) during photolysis of oxetane

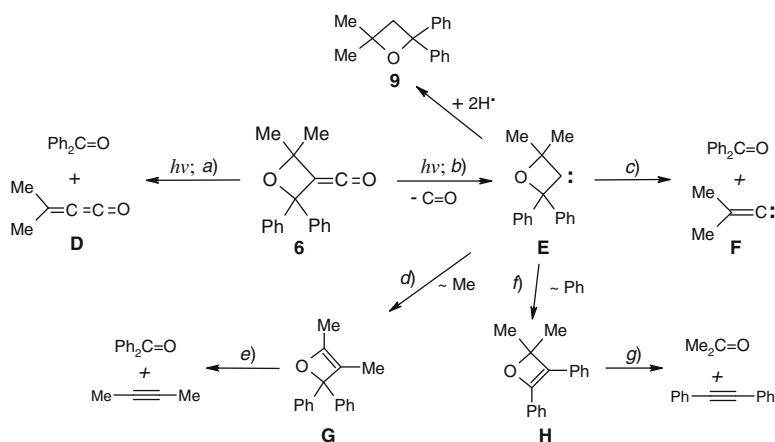
derivative **2c** (Scheme 4), whereas the tandem decarbonylation–cycloelimination process (paths *b*, *c*) is corroborated by the identification of 2,2-dimethyl-4,4-diphenyloxetane (**9**) in the reaction mixture (evidently formed via carbene **E**; Scheme 7) and by analogy to the similar well-known decarbonylation reactions in the chemistry and photochemistry of ketenes.¹⁹ One cannot rule out the formation of benzophenone or the occurrence of the alternative reactions involving 1,2-alkyl(aryl) shifts²⁰ in the assumed oxetanecarbene **E** and subsequent cycloelimination of the relevant oxetenes **G** and **H** (pathways *b*, *d*, *e* or *b*, *f*, *g*) (Scheme 7).

But, independent of the pathways of benzophenone formation, the foregoing experimental data provides evidence in favour of secondary benzophenone-sensitized photolysis of diazofuranones **1a,b** which gives rise to the formation of the C–H insertion products **3** and, at least in part, monoketones **5**.

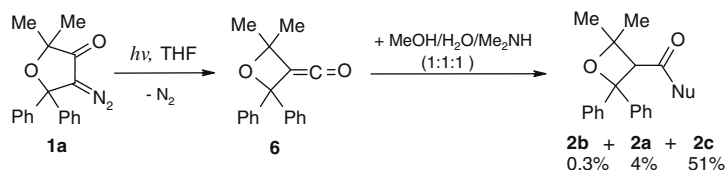
The unexpected effect of the nucleophile on the yield of insertion products **3a,b** may be associated with the rate of nucleophilic interaction with ketene **6**, which is one of the principal sources of benzophenone in the reaction mixture. Photolysis of diazoketone **1a** with an equimolar amount of the nucleophilic reagents (MeOH, H₂O, Me₂NH = 1:1:1) demonstrated that the concurrent reaction of three nucleophiles with ketene **6** furnished predominantly the dimethylamide of oxetanecarboxylic acid **2c** (the ratio of the Wolff rearrangement products **2b/2a/2c** under these reaction conditions was ~1:13:170) (Scheme 8).

This experiment furnishes a plausible explanation concerning the reasons for the profound effect of the nature of the nucleophile on the yields of the insertion products **3**. Since dimethylamine reacts with ketene **6** many times faster than methanol or water, it rapidly consumes the ketene thus preventing subsequent photochemical transformation of the ketene into benzophenone, and thereby strongly minimizing subsequent formation of the C–H insertion products **3**.

In summary, the formation of C–H insertion products **3** during the direct conventional photolysis of regioisomeric diazofuranones **1a,b** is not caused by the effect of the α,α -diphenyl substituents



Scheme 7. The assumed pathways of Ph₂C=O formation upon photolysis of ketene **6**.



Scheme 8. The concurrent action of different nucleophiles with ketene **6**.

adjacent to the diazo group, but results from secondary photochemical processes which give rise to the appearance in the reaction mixture of the sensitizer, benzophenone. The latter, under continued UV irradiation, initiates sensitized photolysis of the diazoketones **1a,b** (in parallel with the direct photochemical reaction), which ultimately give rise to the formation of the C–H insertion products **3**, and presumably the monoketones **5**.

Further investigation of the primary and secondary photochemical reactions of diazotetrahydro-furanones **1**, as well as their tetraphenyl- and tetraalkyl-substituted analogues is currently in progress in our laboratories.

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- The yields of the C–H insertion products, depending on the added nucleophile comprised: 14% (MeOH), 6% (H₂O), 1% (Me₂NH) for diazoketone **1a**, and 6% (MeOH), 3% (H₂O), 0.5% (Me₂NH) for diazoketone **1b**.⁸
- Diazoketones **1a,b** were irradiated at 18–20 °C with a Hanau S-81 medium-pressure mercury lamp (100–130 W) in a 25 ml quartz reactor ($\lambda > 210$ nm). The reactor was charged with a solution of 0.43 g (1.5 mmol) of diazoketone **1a,b** in 10 ml of freshly distilled THF containing (if necessary) 15 mmol of the nucleophilic reagent (H₂O, MeOH, Me₂NH), and the solution was irradiated for 1.5–2 h. The kinetic experiments were carried out by selection of aliquots from the photochemical reactor at certain time intervals. The solvent and nucleophile were removed at 25–35 °C in vacuo (initially at 10–15 mmHg, then at 1–0.5 mmHg), and the residue was immediately analyzed by ¹H NMR spectroscopy using dichloroethane as the internal standard. The reaction products were isolated by recrystallization (**2a–c**) and/or by column chromatography (**3**, **4**, **5**, **7**, **8**, **10a** and **11**) using as the eluents: light petroleum ether (40–65 °C) and Et₂O (or MTBE) in different ratios, or were identified in the reaction mixture by IR spectroscopy and GC–MS analysis (**6** and **9**).
- GC–MS analyses were performed using a Chromato-massspectrometer GCMS-QP2010 Plus. The authors thank Dr. V. Utsal for this work.
- The formation of benzophenone (**7**) in the reaction mixture was confirmed from the ¹H and ¹³C NMR spectra of the isolated compound, together with identification of the corresponding hydrazone (mp 97–98 °C), which was prepared by refluxing the isolated compound with hydrazine-hydrate in EtOH. The presence of benzophenone (**7**) can be easily determined qualitatively and quantitatively from the low-field doublet due to the *ortho*-protons at 7.79–7.82 ppm in the ¹H NMR spectra, which normally does not interfere with the signals of other reaction products.
- Monitoring of ketene **6** formation and its disappearance from the reaction mixture was achieved using IR spectroscopy which indicated the presence of absorption bands at 2127 and 790 cm^{–1}.
- Following 60 min of irradiation of diazoketone **1a** in THF (without NuH) the reaction mixture contained (according to ¹H NMR with the internal standard): benzophenone (**7**) (5%), C–H insertion product **3a** (13%), Ph-group migration product **4a** (2%), monoketone **5a** (1.6%), phenanthrene derivative **11** (2%), along with oxetanecarboxylic acid **3a** (6%).
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- A single crystal of compound **3a** suitable for X-ray diffraction was selected from the analytical sample. Crystallographic measurements were made using an IPDS1 diffractometer [Fa. STOE, Darmstadt, graphite monochromated Mo K α radiation (λ 0.71073 Å)]. The structures were solved by direct methods using the program SIR 2004²¹ and were refined using anisotropic approximation for the non-hydrogen atoms using SHELXL-97.²² All hydrogen atoms were calculated and refined in riding modus. CCDC 724603 for **3a** contains the supplementary crystallographic data. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif from the Cambridge Crystallographic Data Centre.
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