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The photochemical Wolff rearrangement of 3-diazo-1,1,1-trifluoro-2-oxopropane revisited

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Ethyl 2-diazo-4,4,4-trifluoroacetoacetate (**1a**) and 3-diazo-1,1,1-trifluoro-2-oxopropane (**1b**) exhibit a deviating behavior in solution photolysis (hydrogen abstraction for **1a**; Wolff rearrangement for **1b**) [(*a*) F. Weygand, W. Schwenke and H. J. Bestmann, *Angew. Chem.*, 1958, **70**, 506; (*b*) F. Weygand, H. Dworschak, K. Koch and S. Konstas, *Angew. Chem.*, 1961, **73**, 409]. As shown by ^{13}C-labelling of **1b** this difference is not caused by rearrangement of the primarily formed *α*-oxocarbene to an isomeric *α*-oxocarbene presenting a hydrogen atom as a migrating substituent for the Wolff rearrangement. It is discussed that the singlet *α*-oxocarbene generated from **1a** rapidly undergoes spin equilibration followed by hydrogen abstraction of the triplet *α*-oxocarbene. In contrast, due to a larger singlet–triplet splitting in the singlet *α*-oxocarbene generated from **1b**, the intramolecular Wolff rearrangement on the singlet surface can efficiently compete with the singlet–triplet interconversion.

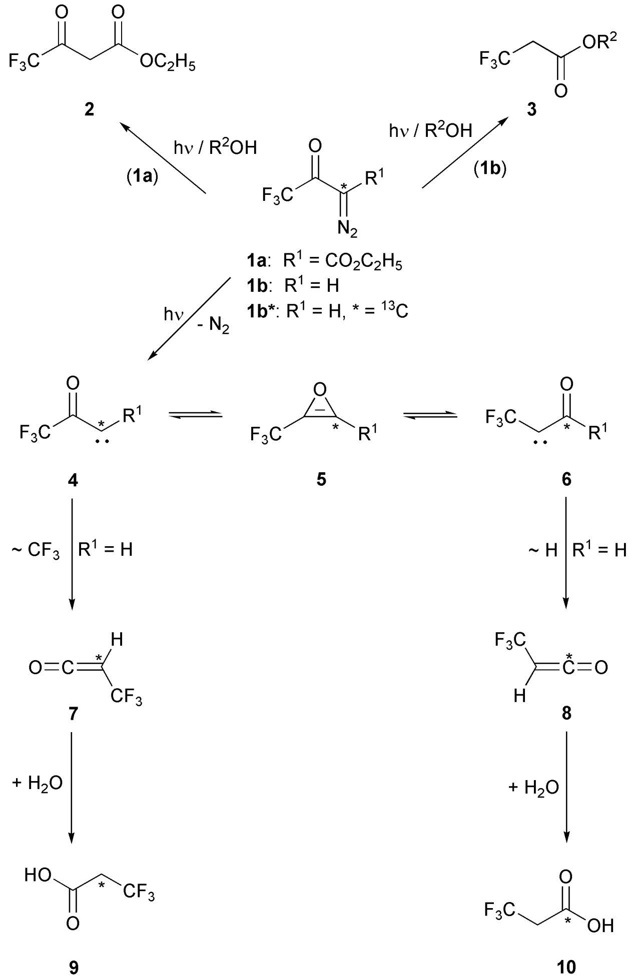
Introduction

More than 100 years after its first report in the literature,[1] the Wolff rearrangement, *i.e.* the photochemical, thermal or catalytic formation of carboxylic acids and acid derivatives from *α*-diazoketones *via* ketenes, has established a firm position in the repertoire of organic synthetic methods.[2] Besides an increasing number of synthetic applications, up to now mechanistic investigations remained the center of interest. Schröter[3] rationalized the rearrangement into ketenes by introducing divalent carbon intermediates (*α*-oxocarbenes). This idea was later incorporated by Eistert[4] into a mechanistic picture based on early electronic theory. Furthermore, in this discussion the hypothetical isomerization of *α*-oxocarbenes into oxirenes was addressed for the first time.

In addition to several other mechanistic problems, *e.g.* the dependency of the reaction path (synchronous *vs.* stepwise ketene formation) from the reaction conditions (*hν*, Δ, cat.), the potential oxirene participation in the photochemical Wolff rearrangement of acyclic *α*-diazoketones has been the subject of numerous experimental and theoretical investigations.[2,5,6] Since all attempts for the direct observation of oxirenes failed,[2,5,7] the prediction of their involvement in the Wolff rearrangement rests on the detection of a partial oxygen migration from the carbonyl carbon to the adjacent, originally diazo substituted carbon by isotopic or substituent labelling (Scheme 1). This oxygen migration should proceed through a species having oxirene geometry. Alternative explanations such as the migration of oxygen in the starting materials (*α*-diazoketones)[8] or products (ketenes) of the Wolff rearrangement[9] and intermolecular oxygen transfer[10] could be excluded experimentally. Thus, the participation of oxirenes in the photochemical Wolff rearrangement can be taken as proven.

Results and discussion

The trifluoromethyl substituent is considered to be a group with a low tendency to migrate in the Wolff rearrangement.[2] In accordance with this, ethyl 2-diazo-4,4,4-trifluoroacetoacetate (**1a**) does not yield the corresponding Wolff rearrangement product when photolyzed in alcoholic solutions. Instead, ethyl 4,4,4-trifluoroacetoacetate (**2**) is obtained as a hydrogen abstraction product. In contrast, solution photolysis of 3-diazo-1,1,1-trifluoro-2-oxopropane (**1b**) proceeds in a smooth reaction to the rearrangement product **3**.[11]



Scheme 1 Photolysis of ethyl 2-diazo-4,4,4-trifluoroacetoacetate (**1a**), 3-diazo-1,1,1-trifluoro-2-oxopropane (**1b**) and [3-^{13}C]3-diazo-1,1,1-trifluoro-2-oxopropane (**1b***).

The different behavior of **1a** and **1b** in solution photolysis could be explained by a carbene–carbene rearrangement *via* the

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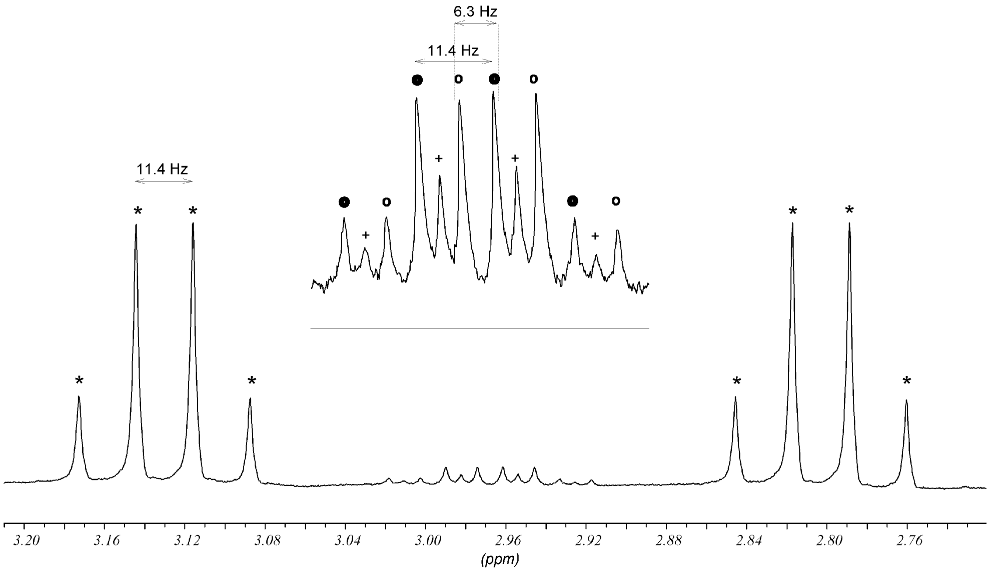


Fig. 1 ^{1}H NMR spectrum of ^{13}C labelled sodium 3,3,3-trifluoropropanoate obtained from photolysis of **1b***; *: signals from $CF_3{}^{13}CH_2CO_2{}^-$ (93%), $^{3}J(^{19}F, ^{1}H) = 11.4$ Hz, $^{1}J(^{13}C, ^{1}H) = 130.9$ Hz; ●,**o**: signals from $CF_3CH_2{}^{13}CO_2{}^-$ (6%): $^{3}J(^{19}F,^{1}H) = 11.4$ Hz, $^{2}J(^{19}F,^{1}H) = 6.3$ Hz; +: signals from $CF_3CH_2CO_2{}^-$ (1%), $^{3}J(^{19}F,^{1}H) = 11.4$ Hz. Insert shows the central part expanded and amplified.

oxirene **5**. In the case of **1b** this interconversion would create an isomeric *α*-oxocarbene **6b** with a hydrogen atom in the position capable of migration (R^1 = H), whereas starting from **1a** this site is occupied by an ethoxycarbonyl group of poor migratory aptitude (Scheme 1).

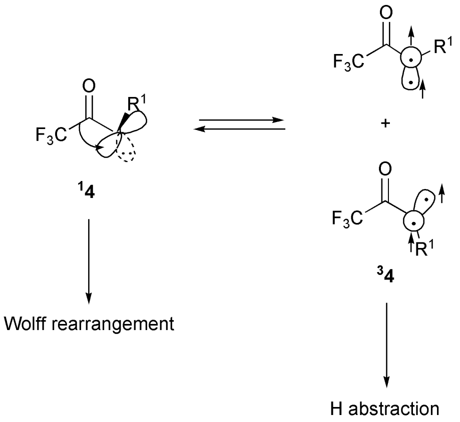
It is generally agreed that hydrogen surpasses all other substituents in its capacity to migrate in the Wolff rearrangement.[2] Thus, the detour *via* **6b** should present a plausible explanation for the contrasting behavior of **1a** and **1b** in the solution photolysis.

To test this interpretation [3-^{13}C]3-diazo-1,1,1-trifluoro-2-oxopropane (**1b***, 99% ^{13}C) has been synthesized and subjected to photolysis in water-saturated ether. The 3,3,3-trifluoropropanoic acid formed has been isolated as the sodium salt and analyzed by ^{1}H, ^{13}C and ^{19}F NMR spectroscopy.

In the $\{^{1}H\}^{13}C$ NMR spectrum an intense signal at $\delta = 42.0$ ppm (q, $^{2}J(^{13}C,^{19}F) = 27.8$ Hz) for the [2-^{13}C]isotopomer **9b*** and a very weak quartet ($^{3}J(^{13}C,^{19}F) = 3.7$ Hz) at 172.6 ppm for the [1-^{13}C]isotopomer **10b*** are detected. The intensity ratio of the two signals indicates that **10b*** contributes very little. Precise values for the contribution of **9b*** and **10b*** can be extracted from the ^{1}H NMR spectrum (Fig. 1). The ^{1}H atoms of the isotopomer **9b*** give rise to a widely split doublet ($^{1}J(^{13}C,^{1}H) = 130.9$ Hz) of a quartet ($^{3}J(^{19}F,^{1}H) = 11.4$ Hz) of high intensity. In the center of this multiplet a weaker group of signals consisting of a doublet ($^{2}J(^{13}C,^{1}H) = 6.3$ Hz) of a quartet ($^{3}J(^{19}F,^{1}H) = 11.4$ Hz) for the isotopomer **10b*** and a quartet ($^{3}J(^{19}F,^{1}H) = 11.4$ Hz) for the unlabelled species present due to incomplete labelling (1%) are seen. From integration it follows that the mixture is composed of 93% **9b***, 6% **10b*** and 1% unlabelled 3,3,3-trifluoropropanoic acid. The ^{19}F NMR spectrum exhibits the expected doublet ($^{2}J(^{13}C,^{19}F) = 27.6$ Hz) of a triplet ($^{3}J(^{19}F,^{1}H) = 11.5$ Hz) for the CF_3 group in **9b***. The corresponding multiplet for **10b*** is too weak to be clearly resolved.

From the ratio of the two isotopomeric acids **9b*** and **10b*** it follows that 93.5% of the 3,3,3-trifluoropropanoic acid is formed from the carbene **4a** by trifluoromethyl migration. Thus, although very attractive at first glance, the rationalization for the deviating results obtained for the photolysis of **1a** and **1b** by a carbene–carbene isomerization, preceding the formation of products, cannot be maintained.

The assertion that the trifluoromethyl substituent in **1a** resists the rearrangement is only valid for the photolysis in solution. The homologous methyl ester of **1a** embedded in an argon matrix at 10 K reacts completely to the corresponding ketene on UV irradiation.[12] The striking difference between photolysis of **1a** in solution and in a cryogenic matrix may be due to competing reactions on the triplet and singlet surface, respectively (Scheme 2).



Scheme 2 Singlet–triplet interconversion of the α-oxocarbenes **4** obtained from **1a** and **1b**.

The hydrogen abstraction is considered as a typical triplet reaction, whereas the Wolff rearrangement must proceed through the singlet state. This would require, that in the solution photolysis the triplet state of carbene **4a** accounts for the only isolated product **2**, however, under matrix conditions the Wolff rearrangement product is obtained through singlet **4a**. On the other hand, the experimental observation that **1b** behaves as an ordinary precursor for the Wolff rearrangement product in solution photolysis, indicates that the primarily formed singlet **4b** is less efficiently converted to the triplet state and can enter the intramolecular reaction path leading to ketene **7**.

How can this deviating reactive behavior of the two *α*-oxocarbenes be correlated with their structural differences? High level theory predicts that carbonyl carbenes such as formylcarbene and alkoxycarbonylcarbenes have triplet ground states of planar geometry, whereas the lowest singlet state is nonplanar.[13,14] The singlet carbene is stabilized by donation from the in-plane lone pair at the carbonyl oxygen to the vacant p-orbital centered at the carbene-carbon and interaction between the sp^2-like lone pair at the carbene with the C=O π*-orbital.[14] This results in a decrease of the singlet–triplet splitting relative to methylene[14] (CH_2: 40 kJ mol^{-1}, HCCHO: 10 kJ mol^{-1}, $HCCO_2CH_3$: 15 kJ mol^{-1}).

In **4a** the divalent carbon is flanked by two carbonyl groups which suggests enhanced stabilization of the lowest singlet state.[15] The combined effect of two carbonyl groups could bring the singlet and triplet state even closer in energy and thus increase the efficiency of the singlet–triplet interconversion.

On the basis of these considerations the different behavior of **4a** and **4b** could be explained by a more rapid singlet–triplet equilibration in **4a** compared to **4b** and a scavenging of triplet **4a** by hydrogen abstraction in solution photolysis. In the photolysis in a cryogenic matrix, where no hydrogen donor is present, the only reaction path accessible after spin equilibration is the intramolecular migration of the trifluoromethyl group in singlet **4a**. Due to the larger S–T splitting expected for the α-oxocarbene **4b**, the singlet–triplet interconversion is less efficient in comparison to **4a** and the rearrangement into **7** and to a smaller extent the ring closure to the oxirene **5** can compete as singlet reactions under the conditions of the photolysis in solution.

Experimental

^{1}H NMR, ^{13}C NMR and ^{19}F NMR-spectra were recorded on Bruker Avance 400 and. Bruker AMX 400 instruments. Infrared spectra were recorded on a JASCO FT-IR-430 spectrometer.

1,1,1-Trifluoro-3-diazo-2-oxopropane 1b

A solution of trifluoroacetic anhydride (1.5 ml, 10.7 mmol) in a dry diethyl ether (35 ml) and a 0.3 molar solution of diazomethane in diethyl ether (110 ml) were reacted together according to ref. 16. Distillation afforded 0.733 g (52%) of **1b**; bp: 70–75 °C, 200 mbar (lit.[16] : 70 °C, 200 mbar). Use of 1 equivalent of triethylamine to save diazomethane resulted in work-up problems and a substantial drop in yield.[16] IR (neat) ν_{max}/cm^{-1} = 2137 (C=N$_2$), 1661 (C=O); ^{1}H NMR (400.16 MHz, CDCl$_3$) δ = 5.78 (s); ^{13}C NMR (100.63 MHz, CDCl$_3$) δ = 55.8 (CHN$_2$), 116.0 (q, $^1J(^{13}C,^{19}F)$ = 288.4 Hz, CF$_3$), (q, $^2J(^{13}C,^{19}F)$ = 37.3 Hz, C=O); ^{19}F NMR (235.36 MHz, CDCl$_3$) δ = −77.5.

[Methyl-^{13}C]*N*-Methyl-*N*-nitroso-4-toluenesulfonic acid amide (^{13}C-Diazald)

^{13}C-Diazald has was prepared from [^{13}C]methyl iodide (99% ^{13}C) according to a reaction sequence described by Rhee *et al.*[17] ^{1}H NMR (400.16 MHz, CDCl$_3$) δ = 2.43 (s, 3H, CH$_3$), 3.10 (d, 3H, $^1J(^{13}C,^1H)$ = 143.7 Hz, NCH$_3$), 7.35 (m, 2H, 3-H), 7.84 (m, 2H, 2-H); ^{13}C NMR (100.63 MHz, CDCl$_3$) δ = 21.7 (CH$_3$), 28.8 (NCH$_3$), 127.8 (C-2), 130.3 (C-3), 133.9 (C-4), 146.1 (C-1).

[3-^{13}C]3-Diazo-1,1,1-2-oxo-trifluoropropane 1b*

An etheral ^{13}C-diazomethane solution prepared from ^{13}C-Diazald (1.98 g, 9.2 mmol) in the usual way was reacted with trifluoroacetic anhydride (0.275 ml, 2 mmol). When the reaction was over, the methyl trifluoroacetate formed as by-product was removed by concentration with a stream of argon. The remaining concentrated ethereal solution was diluted with diethyl ether (5 ml) and again concentrated with a stream of argon. The residual oil was used for spectral characterization and photolysis without further purification. ^{1}H NMR (400.16 MHz, CDCl$_3$) δ = 5.78 (d, $^1J(^{19}F,^1H)$ = 204.6 Hz, 1H); ^{13}C NMR (100.63 MHz, CDCl$_3$) δ = 55.7 (d, $^3J(^{13}C,^{19}F)$ = 2.0 Hz, CHN$_2$); ^{19}F NMR (235.36 MHz, CDCl$_3$): δ = −77.5 (d, $^3J(^{13}C,^{19}F)$ = 2.3 Hz).

Photolysis of 1b and 1b*

Compound **1b** (113 mg, 0.8 mmol) in water-saturated diethyl ether (110 ml) was exposed to the pyrex-filtered radiation of a Hanovia-450 watt medium pressure lamp for 15 min. The photolysis lamp was placed in a water-cooled immersion well. The reaction vessel was cooled externally with an ice bath and a constant stream of purified nitrogen was bubbled through the etheral solution. After photolysis water was added and the diethyl ether was removed at 40–45 °C, 200 mbar. The remaining solution in water was neutralized with 4.2 ml of 0.1 M NaOH, continuously extracted with diethyl ether and finally brought to dryness yielding 58 mg (48%) of sodium 3,3,3-trifluoropropanoate. ^{1}H NMR (400.16 MHz, D$_2$O): δ = 2.95 (q, $^3J(^{13}C,^{19}F)$ = 11.4 Hz, 2H, CH$_2$); ^{13}C NMR (100.63 MHz, D$_2$O) δ = 42.0 (q, $^2J(^{13}C,^{19}F)$ = 27.8 Hz, CH$_2$), 125.2 (q, $^1J(^{13}C,^{19}F)$ = 275.2 Hz, CF$_3$), 172.6 (t, $^3J(^{13}C,^{19}F)$ = 3.7 Hz, C=O); ^{19}F NMR (235.36 MHz, D$_2$O) δ = −64. The ^{13}C-labelled diazoketone **1b*** was photolyzed analogously and the ^{13}C-distribution in the resulting sodium salt of 3,3,3-trifluoropropanoic acid investigated by ^{13}C, ^{19}F, and ^{1}H NMR spectroscopy. For details see text and Fig. 1.

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