vibrational states to be thermally populated. The unusual feature of formamide is that the frequency of the wagging (pyramidalization) mode of the $NH_2$ is only 289 $cm^{-1}$,[44] which decreases to 222 $cm^{-1}$ in $HCOND_2$.[23] In the pyramidalized transition state this mode becomes an ordinary high-frequency bending vibration. This is not the reaction coordinate, but its excited states are more heavily populated for $HCOND_2$ or HCONHD. The free energy of these reactants is lowered by this degeneracy, thereby raising the free energy of activation so that they rotate more slowly than $HCONH_2$.

From the above frequencies the wagging mode can be calculated to contribute a factor of 1.07 to $k_H/k_D$ at 48 °C. This value is small, but it must contribute to the isotope effect, and it is consistent with the experimental value of 1.16 ± 0.10. To the best of our knowledge this is the first example of a contribution of the excitation term to a KIE. Unfortunately it is not possible to test the temperature dependence of eq 8, since the line-shape method is accurate only over an exceedingly narrow range of rate constants.

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## Conclusions

There is no substantial secondary kinetic isotope effect for C–N rotation in amides, for substitution of deuterium at either carbon or nitrogen. The small effects seen can be attributed to slight changes in zero-point energies of out-of-plane bending modes, rather than conversion of C–H or N–H bends into the reaction coordinate. The large KIE in ethylenes may be a special case. Formamide may also be a special case for which the thermal population of excited vibrational states of HCONHD (or $HCOND_2$) renders the deuterium-substituted amide less reactive toward rotation.

**Acknowledgment.** This research was supported by National Science Foundation Grant CHE90-25113 (to C.L.P.). Purchase of the 500-MHz NMR spectrometer at UCSD was made possible by NIH Grant RR04733 and NSF Grant CHE88-14866.

**Registry No. 1**, 75-12-7; **2**, 123-39-7; **3**, 16135-31-2; **4**, 68-12-2; $D_2$, 7782-39-0.

# Evidence for a 1,4-Dioxy Diradical as an Intermediate in the Thermal Decomposition of 3,3-Dibenzyl-1,2-dioxetane

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**Abstract:** The thermal decomposition of 3,3-dibenzyl-1,2-dioxetane (**1**) in $CDCl_3$ and $CH_2Cl_2$ solutions afforded the expected decomposition product 1,3-diphenyl-2-propanone (**2**) and the novel rearrangement ketone 1-(benzyloxy)-3-phenyl-2-propanone (**3**) in ratios of (73 ± 10):(27 ± 10). A plausible mechanism for the formation of ketone **3** involves homolytic cleavage of the dioxetane peroxide bond with subsequent β cleavage of the benzyl group in the 1,4-dioxy diradical and in-cage combination of the resulting radicals. Moreover, several control experiments render a benzyl radical-induced decomposition of dioxetane **1** unlikely. Thus, the ratio of **2** and **3** was found to be essentially independent of the initial dioxetane concentration, and the presence of radical scavengers did not affect the product ratio and reaction rate. With the electron-rich 1,4-dioxene, the dioxetane **1** afforded the cycloadduct *cis*-3,3-dibenzyl-2,5,7,10-tetraoxabicyclo[4.4.0]decane (**4**) as major product.

The most characteristic reaction of 1,2-dioxetanes[1] is their thermal cleavage to afford efficiently electronically excited carbonyl fragments. While a concerted[2] and a two-step biradical[3] mechanism have been suggested, the "merged mechanism"[4] unifies these two contrary decomposition modes. In a recent theoretical study[5] a decomposition mechanism was proposed in which the formation of the singlet dioxy diradical occurs essentially without activation energy; in fact, the thermal activation is supposedly derived from the production of the triplet diradical. Although the present-day experimental data seem to speak in favor of the biradical mechanism,[3] the only direct evidence constitutes the trapping of the intermediary 1,4-dioxy diradical by 1,4-cyclo-

**Table I.** Thermal Decomposition of Dioxetane **1**[a]

| entry | [1] (M) | solvent[b] | additive[c] | product distribution[d] 2 | 3 |
|---|---|---|---|---|---|
| 1 | ca. 4.0 | none | | 44 | 56 |
| 2 | 1.03 | $CH_2Cl_2$ | | 64 | 36 |
| 3 | 0.108 | $CH_2Cl_2$ | | 79 | 21 |
| 4 | 0.010 | $CH_2Cl_2$ | | 80 | 20 |
| 5 | 0.001 | $CH_2Cl_2$ | | 83 | 17 |
| 6 | 0.223 | $CDCl_3$ | | 63 | 37 |
| 7 | 0.245 | $CDCl_3$ | 2,6-di-*tert*-butyl-4-methylphenol (11%) | 65 | 35 |
| 8 | 0.210 | $CDCl_3$ | galvinoxyl (7%) | 78 | 22 |

[a] At room temperature (ca. 25 °C); ca. 48 h were required for complete consumption of the dioxetane **1**, except entry 1 for which only 18 h were necessary. [b] Also in $CCl_4$, $CH_3OH$, $CH_3CN$, and toluene substantial amounts of the rearrangement ketone **3** were observed by $^1H$ NMR. [c] In parentheses, mol % relative to dioxetane **1**. [d] Determined by integration of the appropriate $^1H$ NMR signals (250 MHz), normalized to 100%, error ca. 5% of the stated values, 100% consumption of the dioxetane, the mass balance was >90% in every case.

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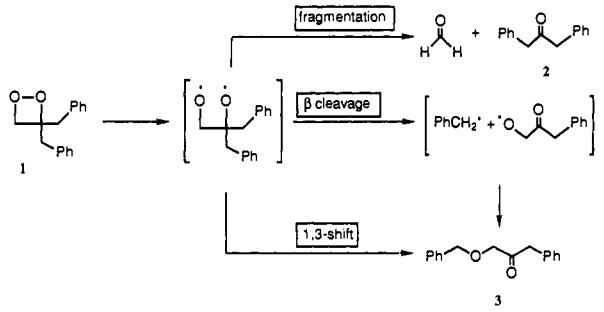
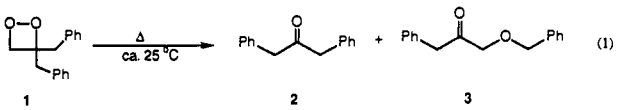
**Scheme I**




hexadiene as a H atom donor.[6]

In recent studies[7a-c] we have employed effectively the readily available 3,3-dibenzyl-1,2-dioxetane[3c] (**1**) for the investigation of the nucleophilic substitution chemistry of 3,3-disubstituted dioxetanes,[7] which constitutes an unfavorable reaction mode for tetrasubstituted derivatives. In this context we observed a novel rearrangement product, namely, 1-(benzyloxy)-3-phenyl-2-propanone (**3**) (eq 1), which was previously not reported[8] in the




(1)

thermal decomposition of dioxetane **1**. Herewith we present a detailed study on the solution thermolysis of this dioxetane and provide evidence for the diradical mechanism.

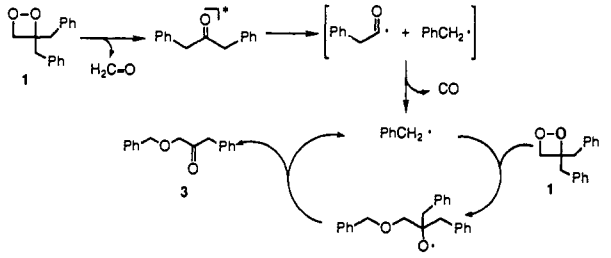
## Results and Discussion

When dioxetane **1** was allowed to decompose without solvent at room temperature, after 18 h the resulting colorless oil contained the expected decomposition product 1,3-diphenyl-2-propanone (**2**) and the novel rearrangement product **3** in a ratio of 44:56 (Table I, entry 1). Decomposition of a ca. 0.2 M solution of dioxetane **1** in $CDCl_3$ afforded the ketones **2** and **3** in a ratio of 63:37 (Table I, entry 6). Alkoxy ketone **3** was isolated by silica gel chromatography, and its structure was unequivocally assigned by means of $^1H$ NMR, $^{13}C$ NMR, and IR spectroscopy and by elemental analysis.

The ratio of the ketone products **2** and **3**, as determined by $^1H$ NMR monitoring (cf. Experimental Section), was essentially independent of the initial concentration of dioxetane **1** during its decomposition in solution. This lack of concentration dependence becomes quite evident for the decompositions of 0.001 M to ca. 1 M solutions of dioxetane **1** in methylene chloride at room temperature (Table I, entries 2–5), i.e., within the error limit of $^1H$ NMR spectroscopy the ratio of ketones **2** and **3** was (73 ± 10):(27 ± 10) at low conversion (first ca. 10%) and complete conversion (ca. 100%), an insignificant change over the $10^3$-fold concentration range. These results speak against induced decomposition of dioxetane **1**, a point that will be reiterated after presentation of a plausible mechanism for the formation of the unusual ketone product **3**.

Significant is the fact that a rearrangement product such as **3** is so far unknown in the thermal decomposition of dioxetanes.[1] Homolysis of the dioxetane peroxide bond with subsequent β cleavage of the benzyl group in the resulting 1,4-dioxy diradical and radical cage recombination (Scheme I) accounts best for the results in Table I. Alternatively, a concerted 1,3-shift of the benzyl group in the primary 1,4-dioxy diradical would also explain the formation of ketone **3**; however, our present results cannot distinguish between these two pathways. Attempts to observe CIDNP effects during the decomposition of **1** in the NMR spectrometer (200 MHz, ca. 0.2 M solution of dioxetane **1** in $CDCl_3$, 60 °C) failed, but it would be presumptuous to argue on the basis of such negative evidence that the mechanism with the concerted 1,3-shift (Scheme I) applies.

**Scheme II**




Irrespective of these mechanistic details, the intervention of the 1,4-dioxy diradical appears to be essential in rationalizing the formation of the ketone **3**. The preservation of the four-membered ring C–C bond during the thermolysis of dioxetanes is indeed unusual for such labile peroxides, for which fragmentation into carbonyl products with light emission is the prominent course of action. Nevertheless, some examples have been reported,[9] but only for dioxetanes which carry amino or thio substituents, in which the cleavage of the heteroatom substituent (C–N or C–S cleavage) is preferred over that of the dioxetane C–C bond to afford 1,2-diketones.[9]

The observed competition between β cleavage of a benzyl radical with the established C–C bond fragmentation into carbonyl products is quite reasonable for the 1,4-dioxy diradical if one recalls the ease with which alkoxy radicals suffer β scission of benzyl substituents.[10,11] For example, the preference of benzyl versus methyl cleavage in alkoxy radicals is more than $10^4$-fold.[10a] In fact, an absolute rate constant of $2.5 \times 10^7$ $s^{-1}$ was determined for the benzyl scission in the denitrogenation of hyponitrites,[11b] which corresponds to an activation energy of only ca. 5 kcal/mol.[11b]

As an alternative mechanism the benzyl radical-induced decomposition[12] of dioxetane **1** needs to be considered, especially since it has been reported[3c] that the thermal cleavage of dioxetane **1** affords benzyl radical by Norrish type I cleavage of triplet-excited dibenzyl ketone (**2**) (Scheme II). Several facts, however, render the benzyl radical-induced decomposition of dioxetane **1** unlikely. On the one hand, typical benzyl radical products like dibenzyl[13] (dimerization) or toluene (hydrogen abstraction) should have been observed, but such products were not detected in our product studies by $^1H$ NMR spectroscopy (detection limit less than 2%). On the other hand, higher yields of ketone **3** would have been expected with increasing initial concentration of dioxetane **1**. As already mentioned, the yield of ketone **3** was essentially independent of the dioxetane concentration (Table I, entries 1–6).

For the rigorous exclusion of the benzyl radical-induced formation of ketone **3** (Scheme II), additional control experiments were performed. For example, when catalytic amounts of 2,6-di-*tert*-butyl-4-methylphenol and galvinoxyl were employed as radical scavengers (Table I, entries 7, 8), in both cases no significant change in the ratio of products **2** and **3** or in the rate of reaction was observed. Thus, *free benzyl radicals are not produced in sufficient amounts* during the decomposition of dioxetane **1**

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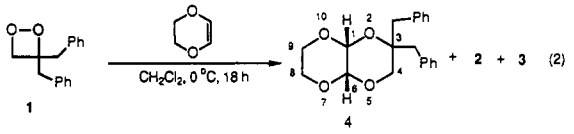
(13) Richardson detected 2.2% of dibenzyl (ref 3c) during the decomposition of a ca. $10^{-3}$ M solution of dioxetane **1** in benzene at 60 °C.

to be responsible for the formation of ketone **3** through radical-induced chain decomposition (Scheme II).

An alternative approach to inhibiting triplet-state-mediated induced decomposition of dioxetanes, as displayed in Scheme II, is to employ triplet quenchers such as electron-rich olefins.[14,15] The ratio of ketones **2** and **3** (ca. 80:20) was not significantly influenced in the presence of equimolar amounts of the very efficient triplet quencher 1,3-cyclohexadiene.[15] Moreover, ketone **3** was also observed (ca. 6%) when dioxetane **1** was allowed to react with the electron-rich 1,4-dioxene at 0 °C (eq 2). In the




1 4

latter case, the major product was the cycloadduct **4** (54%) through competitive direct reaction of the dioxetane **1** with 1,4-dioxene, a process which was recently reported[7b] by us for other 3,3-disubstituted dioxetanes. Significant is the fact that at the low temperature (0 °C) at which these reactions were conducted, the formation of triplet-excited dibenzyl ketone (**2**) by thermolysis of dioxetane **1** is negligible. Again, free benzyl radicals are unlikely to be responsible for the rearrangement ketone **3** through induced decomposition (Scheme II).

To summarize, the facts that the formation of rearrangement ketone **3** is independent of dioxetane concentration, that radical scavengers such as 2,6-di-*tert*-butyl-4-methylphenol and galvinoxyl do not affect significantly the product distribution and reaction rate, and that the ketone **3** is formed under conditions at which thermolysis of dioxetane **1** into triplet-excited ketone **2** is negligible (thus, no benzyl radicals are produced through Norrish type I cleavage) speak against the chain mechanism proposed in Scheme II. Instead, a more plausible mechanistic rationalization is to invoke the 1,4-dioxy biradical as bona fide intermediate, produced through O–O bond homolysis of dioxetane **1**, subsequent $\beta$ cleavage of a benzyl radical, and in-cage coupling to afford the rearrangement ketone **3** (Scheme I). Our novel finding that cleavage of a lateral benzyl C–C bond is competitive with that of the central dioxetane C–C bond opens up new perspectives in regard to the thermal behavior of dioxetanes.

## Experimental Section

**General Aspects.** For common analytical instruments and spectral calibrations, cf. ref 7a. Column chromatography: silica gel (63–200-$\mu$m particle size) from Woelm as stationary phase with an adsorbance/substrate ratio of 100:1. Dioxetane **1** was prepared according to the literature procedure[7a] by NaOH-catalyzed cyclization of the corresponding $\beta$-bromo hydroperoxide.

*Caution! 3,3-Disubstituted 1,2-dioxetanes are hazardous compounds, especially when handled in neat form.*

**Decomposition of Dioxetane 1 without Solvent.** A neat sample of dioxetane **1** (250 mg, 1.04 mmol) was kept at room temperature (ca. 25 °C) for 18 h under an argon gas atmosphere. The resulting colorless oil (231 mg, 98%) contained a mixture of **2** and **3** in a ratio of 44:56 (by $^1$H NMR, 250 MHz). $^1$H NMR spectroscopy revealed traces of nonidentified products. Silica chromatography ($CH_2Cl_2$ as eluent) afforded first 79.0 mg (36%) of 1,3-diphenyl-2-propanone (**2**) and then 101 mg (40%) of **3** as colorless oils.

**1-(Benzyloxy)-3-phenyl-2-propanone (3)**: TLC ($CH_2Cl_2$) $R_f$ = 0.55; $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 3.70 (s, 2 H, Ph$CH_2$CO), 4.05 (s, 2 H, CO$CH_2$O), 4.50 (s, 2 H, Ph$CH_2$O), 7.20 (m, 10 H, aromatic H); $^{13}$C NMR ($CDCl_3$, 63 MHz) $\delta$ 46.2 (t, Ph$CH_2$CO), 73.3 (t, Ph$CH_2$O), 74.3 (t, CO$CH_2$O), 127.0 (d), 127.9 (d), 128.0 (d), 128.4 (d), 128.6 (d), 129.4 (d), 133.4 (s), 137.0 (s), 205.9 (s, C=O); IR ($CCl_4$) 3100, 3080, 3050, 2930, 2870, 1730 (C=O), 1600, 1500, 1465, 1440 cm$^{-1}$. Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.90; H, 7.04.

**Concentration Dependence of the Decomposition of Dioxetane 1.** Solutions of dioxetane **1** (30.0 mg, 0.125 mmol) in $CH_2Cl_2$ which were ca. 1.0, 0.1, 0.01, and 0.001 M were kept at room temperature for 48 h. When the dioxetane had completely decomposed (negative KI test), the solvent was evaporated at 20 °C/15 Torr, and the residue (mass balance >90% in every case) was taken up in $CDCl_3$. The product distributions were determined by $^1$H NMR spectroscopy (250 MHz), and the results are given in Table I (entries 2–5).

**Decomposition of Dioxetane 1 in $CDCl_3$.** Aliquots (0.6 mL) of 0.2–0.3 M solutions of dioxetane **1** in $CDCl_3$ which contained the additives given in Table I (entries 7, 8) and hexamethyldisiloxane as internal NMR standard were kept at room temperature until the dioxetane was completely consumed ($^1$H NMR monitoring). The product distributions were determined by $^1$H NMR spectroscopy, and besides ketones **2** and **3** only traces of nonidentified products were detected (mass balances >90% in every case). The results are given in Table I (entries 6–8). Throughout the NMR monitoring the ratio of ketones **2** and **3** stayed constant within experimental error (ca. 5%).

**Reaction of Dioxetane 1 with 1,4-Dioxene.** A solution of dioxetane **1** (202 mg, 0.841 mmol) in 3 mL of methylene chloride was cooled to 0 °C under an argon gas atmosphere, and a solution of 1,4-dioxene (79.0 mg, 0.841 mmol) in 3 mL of methylene chloride was added. After 18 h the dioxetane was completely consumed, and the solvent was evaporated at ca. 20 °C/15 Torr. The crude product mixture contained the dioxetane–dioxene adduct **4** and the ketones **2** and **3** in a ratio of 54:40:6; the mass balance was 92%. Adduct **4** was isolated by silica gel column chromatography [petroleum ether (bp 30–50 °C)/ethyl acetate = 7:1] as a colorless oil (100 mg, 36%), which was crystallized on treatment with petroleum ether to afford colorless plates, mp 82–84 °C.

***cis*-3,3-Dibenzyl-2,5,7,10-tetraoxabicyclo[4.4.0]decane**: $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ AB pattern ($\delta_A$ = 2.73, $\delta_B$ = 2.98, $J$ = 14.1 Hz, 4 H, $CH_2$Ph), 3.42 (m, 2 H, 8-H or 9-H), 3.46 (m, 2 H, 8-H or 9-H), AB pattern ($\delta_A$ = 3.38, $\delta_B$ = 3.88, $J$ = 11.7 Hz, 2 H, 4-H), 4.62 (d, $J$ = 1.8 Hz, 1 H, 1-H or 6-H), 5.07 (d, $J$ = 1.8 Hz, 1-H or 6-H), 7.23 (m, 10 H, aromatic H); $^{13}$C NMR ($CDCl_3$, 63 MHz) $\delta$ 39.6 and 42.4 (t, $CH_2$Ph), 60.2 (t, C-4), 63.4 (t, C-8 or C-9), 63.8 (t, C-8 or C-9), 70.0 (s, C-3), 88.6 (d, C-1 or C-6), 90.6 (d, C-1 or C-6), 126.5 (d), 127.9 (d), 128.3 (d), 128.5 (d), 130.6 (d), 130.9 (d), 136.2 (s), 136.7 (s); IR (KBr) 3100, 3040, 2980, 2920, 1600, 1500, 1460, 1350, 1290, 1250 cm$^{-1}$. Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.92; H, 7.11.

**Acknowledgment.** We thank the Deutsche Forschungsgemeinschaft (SFB 172 "Molekulare Mechanismen kanzerogener Primärveränderungen") and the Fonds der Chemischen Industrie for generous financial support.

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