

Remarkable Differences in Photo and Thermal (Acid-catalyzed) Reactivities between *ortho*- and *para*-Acylcyclohexadienones as Essential Factors Determining the Overall Efficiency of the Photo-Fries Rearrangement

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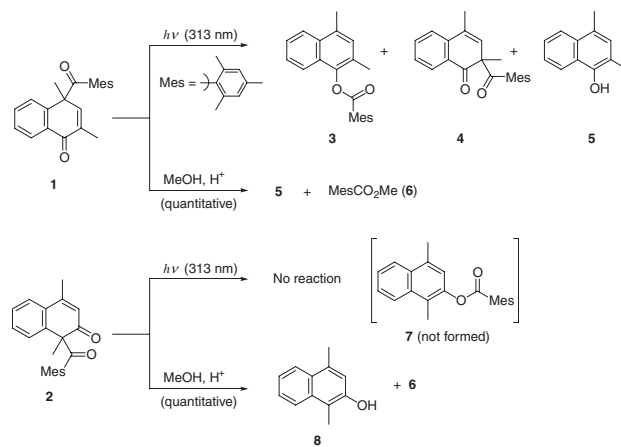
Successful isolation of “*ortho*” and “*para*”-acylcyclohexadienones allowed us to comparatively study their ground- and excited-state behavior under a variety of conditions. In neutral solutions, the two isomeric cyclohexadienones showed completely different reactivities for photochemical and thermal reactions, while in acidic methanol both quantitatively afforded the corresponding transesterification product and naphthol. These studies help us understand the detailed photo-Fries rearrangement mechanism, which involves several crucial photochemical and thermal steps.

The photo-Fries rearrangement has frequently been employed as a bench-mark reaction for assessing the confinement effects of zeolites,^{1,2} cyclodextrins,³ micelles,⁴ and polyethylene films^{2,5} on the fate of geminate organic radical pairs. Nevertheless, the complete photorearrangement mechanism has not yet been fully established. Furthermore, precise reaction control is often difficult to achieve and the reproducibility of product yield and distribution is not good in general, probably owing to the intervention of several consecutive processes, i.e. the initial photocleavage to a geminate radical pair and the subsequent migration of the resulting acyl fragment to the *o*- and *p*-positions to form cyclohexadienone intermediates, which eventually undergo thermal (acid- or base-catalyzed) rearrangements to give the corresponding acylphenols.⁶ For instance, recent studies^{7,8} revealed puzzling solvent effects that by the use of different batch or purification procedures lead to significantly different product distributions. These are rationalized mostly by the side reactions possibly arising from long-lived radical species, but secondary photochemical, as well as thermal, reactions of the intermediate(s) may also be responsible at least in part. Thus, for a comprehensive understanding and precise control of the photo-Fries rearrangement process, it is indispensable to elucidate the photochemical and thermal reactivities of acylcyclohexadienone intermediates. In the preceding paper,⁹ we showed that acylcyclohexadienones **1** and **2**, produced as photo-Fries rearrangement products, are reasonably stable and isolable under ambient conditions. This enabled us to closely examine the photochemical and acid-catalyzed reactions of **1** and **2**.

4-Benzoyl-4-methyl-2,5-cyclohexadienone has been synthesized,¹⁰ and photolyzed to give benzoic acid and *p*-cresol as major products, although no further details have been reported.¹¹ The photobehavior of transient 2,4-cyclohexadienone species obtained upon flash photolysis of phenyl acetate has been investigated.¹² In this two-laser, two-color excitation experiment, the first pulse at 266 nm produces a transient species, which is further photolyzed by the second pulse at 308 nm to give a transient

absorption at 330 nm; these spectral changes are assignable to the initial formation of 6-acetylcyclohexa-2,4-dienone and the subsequent ring-opening to the corresponding dienic ketene. Interestingly, the formation of isomeric 4-acylcyclohexadienone was not detected.

In this study, we comparatively investigated the photoreactivities of “*para*” and “*ortho*”-acylcyclohexadienones **1** and **2** for a more comprehensive understanding of the process. An acetonitrile solution of **1** (0.5 mM) was irradiated under argon at 25 °C in a Pyrex tube at 313 nm with a high-pressure mercury lamp fitted with an aqueous K₂CrO₄ filter, with the photolyzate analyzed by HPLC. Upon short irradiation (5 min), ester **3**, *ortho*-cyclohexadienone **4** and phenol **5** were obtained in 7, 24, and 9% yields, respectively. Although the photolysis of aryl esters is thought to occur in the singlet state, **1** does not fluoresce, suggesting fast intersystem crossing to the triplet. The low material balance may also be explained by a greater contribution of the cage-escape process of a triplet radical pair. These results evoke possible involvement of the secondary photoreaction of acylcyclohexadienones during the photo-Fries reaction of the aryl esters, especially when the conversion is high for synthetic purposes.



Scheme 1.

In sharp contrast to **1**, **2** was extremely photostable, being recovered totally under the same conditions and in 98% even after 30 min irradiation, where *ortho*-analogue **4** was completely consumed and 62% of ester **7** was converted.¹³ The dienone **2** was also recovered exclusively when the photolysis was performed in methanol.

Nucleophilic reactions of water and alcohol to 4-benzoylcyclohexadienone have been known,¹¹ but no similar reaction is known for *ortho*-acylcyclohexadienone. We therefore compared

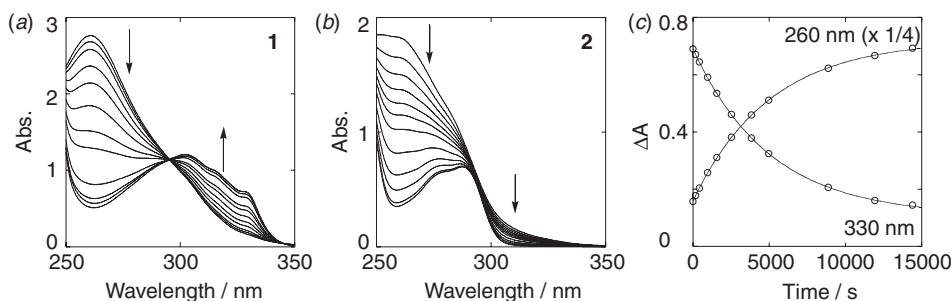


Figure 1. UV spectral changes for the reactions of cyclohexadienones **1** and **2** in methanol in the presence of methansulfonic acid at 25 °C. (a) $[1]_0 = 0.26$ mM, $[\text{MeSO}_3\text{H}] = 0.20$ mM. (b) $[2]_0 = 0.28$ mM, $[\text{MeSO}_3\text{H}] = 0.17$ mM. (c) Typical curve fitting analyses of the absorption changes at 260 and 330 nm for the transesterification of **1** in the presence of acid, with an fitting equation: $\Delta A = c_1 \times \exp(-k_{\text{obs}}t) + c_2 \times [1 - \exp(-k_{\text{obs}}t)]$.

Table 1. Observed rate constants for the acid-catalyzed methanolyses of **1** and **2** in methanol at 25 °C

$[\text{MeSO}_3\text{H}]/\text{mM}$	$k_{\text{obs}}/\text{s}^{-1}$	$[\text{MeSO}_3\text{H}]/\text{mM}$	$k_{\text{obs}}/\text{s}^{-1}$
$[1]_0 = 0.26$ mM		$[2]_0 = 0.28$ mM	
0.097	$<10^{-7}$	0.051	2.2×10^{-6}
0.146	$<10^{-7}$	0.072	2.3×10^{-6}
0.182	1.29×10^{-4}	0.102	4.3×10^{-6}
0.195	1.98×10^{-4}	0.129	7.4×10^{-6}
0.292	9.87×10^{-4}	0.144	8.0×10^{-6}
0.389	1.67×10^{-3}	0.170	1.0×10^{-3}
0.478	2.44×10^{-3}	0.174	3.7×10^{-3}
0.955	5.96×10^{-3}	0.183	8.5×10^{-3}
1.91	1.23×10^{-2}	0.190	1.1×10^{-2}
		0.200	1.9×10^{-2}

the thermal reactivities of **1** and **2**. 4-Benzoyl-4-methyl-2,5-cyclohexadienone was reported to give *p*-cresol and methyl benzoate in methanol at 25 °C in 20% conversion after 17.5 h. In our own case, the both cyclohexadienones were completely stable in methanol at room temperature for more than one week. Such lower reactivities may be attributed to the steric hindrance caused by the two methyls on the mesityl moiety, which protects the carbonyl group from nucleophilic attack by methanol. In the presence of acid (1 mM MeSO_3H added to a 10 mM solution of **1** or **2**), however, the transesterification immediately occurred to give the methyl ester **6** and the corresponding naphthol (**5** or **8**) in quantitative yields (Figure 1). The direct conversion of **1** to **5** was supported by the UV spectral decay of **1** synchronized with the increase of the absorption of **5** (and **6**), with a clear isosbestic point at 290 nm.¹⁴ The decay and formation processes were quantitatively analyzed as functions of $[\text{MeSO}_3\text{H}]$ to give the apparent rate constants (k_{obs}) (Table 1).

For both substrates, the effect of acid was discontinuous, exhibiting a sudden increase in k_{obs} at $[\text{MeSO}_3\text{H}] = 0.15\text{--}0.17$ mM. However, even at low $[\text{MeSO}_3\text{H}]$, **2** suffers transesterification in appreciable rates, giving a good linear correlation with $[\text{MeSO}_3\text{H}]$, whilst **1** does not react in a comparable time scale. At $[\text{MeSO}_3\text{H}] > 0.17$ mM, the rate constants are well described by $k_{\text{obs}} = k_a[\text{MeSO}_3\text{H}] + k_0$, where $k_a = 7.1 \pm 0.1$ and $590 \pm 40 \text{ M}^{-1} \text{ s}^{-1}$ for **1** and **2**, respectively. The much larger k_a for **2** may be attributed to the 1,3-diketonic structure.

We have demonstrated that the *ortho*- and *para*-acylcyclohexadienones, sharing an apparently similar dienone structure, are totally different in stability and reactivity upon photochemi-

cal and thermal (acid-catalysis) activations. More detailed and quantitative studies are currently in progress for revealing the origin of differences in the photochemical and thermal reactivities, with the aim of eventually understanding the overall photo-Fries rearrangement mechanism.

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References and Notes

- K. Pitchumani, M. Warrier, and V. Ramamurthy, *J. Am. Chem. Soc.*, **118**, 9428 (1996); R. Suau, G. Torres, and M. Valpuesta, *Tetrahedron Lett.*, **36**, 1311 (1995).
- W. Gu, M. Warrier, B. Schoon, V. Ramamurthy, and R. G. Weiss, *Langmuir*, **16**, 6977 (2000); W. Gu, M. Warrier, V. Ramamurthy, and R. G. Weiss, *J. Am. Chem. Soc.*, **121**, 9467 (1999).
- S. Koodanjeri, A. R. Pradhan, L. S. Kaanumalle, and V. Ramamurthy, *Tetrahedron Lett.*, **44**, 3207 (2003); A. V. Veglia, R. H. de Rossi, *J. Org. Chem.*, **58**, 4941 (1993); M. S. Syamala, B. N. Rao, and V. Ramamurthy, *Tetrahedron*, **44**, 7234 (1988); A. V. Veglia, A. M. S'anchez, and R. H. Rossi, *J. Org. Chem.*, **55**, 4083 (1990).
- A. K. Singh and S. N. Sonar, *Synth. Commun.*, **15**, 1113 (1985).
- W. Gu and R. G. Weiss, *J. Photochem. Photobiol., C*, **2**, 117 (2001); J. Xu and R. G. Weiss, *Org. Lett.*, **5**, 3077 (2003); C. Cui and R. G. Weiss, *J. Am. Chem. Soc.*, **115**, 9820 (1993).
- For a general review on the mechanism of photo-Fries rearrangement, see: J. A. Pincock, in "CRC Handbook of Organic Photochemistry and Photobiology," 2nd ed., ed. by W. M. Horspool and F. Lenci, CRC Press, Boca Raton, Florida (2004), Chap. 66.
- C. Cui, X. Wang, and R. G. Weiss, *J. Org. Chem.*, **61**, 1962 (1996).
- T. Mori, M. Takamoto, T. Wada, and Y. Inoue, *Photochem. Photobiol. Sci.*, **2**, 1187 (2003).
- T. Mori, M. Takamoto, H. Saito, T. Furo, T. Wada, and Y. Inoue, *Chem. Lett.*, **33**, 254 (2004).
- L. B. Jackson and A. J. Waring, *J. Chem. Soc., Chem. Commun.*, **1985**, 857; *J. Chem. Soc., Perkin Trans. 1*, **1988**, 1791.
- L. B. Jackson and A. J. Waring, *J. Chem. Soc., Perkin Trans. 2*, **1990**, 907; *J. Chem. Soc., Perkin Trans. 2*, **1990**, 1893.
- M. C. Jiménez, M. A. Miranda, J. C. Scaiano, and R. Tormos, *J. Chem. Soc., Chem. Commun.*, **1997**, 1487.
- Note that absorption coefficient of **10** is much higher than that of **9** at 313 nm, being 7900 and $720 \text{ M}^{-1} \text{ cm}^{-1}$, respectively.
- Note that the absorption coefficient of **10** is always larger than that of **12**, thus not showing an isosbestic point. However, the reaction does not involve any side reactions, as judged from the results of curve-fitting analysis.