

Photochemical Reaction of 2-Acyloxy-1-methoxycarbonylcyclohexenes: an Efficient Aliphatic Photo-Fries Rearrangement and a Novel 1,5-Aroyl Migration

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Upon irradiation 2-acyloxy-1-methoxycarbonylcyclohexenes readily undergo photo-Fries rearrangement to give 2-acyl-2-methoxycarbonylcyclohexanones in good yields and among them 2-aroxyloxy-1-methoxycarbonylcyclohexenes also undergo a novel 1,5-aroxy migration according to irradiation conditions to give 4-aroxy-2-methoxycarbonylcyclohexanones, which result from 1,3-aroxy migration following photo-Fries rearrangement.

From our interest in the photochemical reaction of enol acylates of cyclic ketones and its applicability to construct complex carbon skeletons,¹ we have examined the photochemical reactivity of 2-acyloxy-1-methoxycarbonylcyclohexenes **1**. During this study we have found that irradiation of **1** readily induced 1,3-acyl migration, or photo-Fries rearrangement, to give 2-acyl-2-methoxycarbonylcyclohexanones **2** in good yields and have also discovered an unexpected 1,5-aroxy migration of **1** (R = aryl) to give **3** (R = aryl). The photo-Fries rearrangement² has been extensively studied since the first observation by Anderson and Reese in 1960. Hitherto, however, there has been a limited number of examples of the reaction in aliphatic systems; *i.e.* enol esters,^{2,3} enol lactones² and enamides^{2,4} of carboxylic acids, most of which resulted in low chemical yields. Thus, we report here our results as an example of an efficient aliphatic photo-Fries reaction in the context of the photochemical behaviour of 2-acyloxy-1-methoxycarbonylcyclohexenes.

The results of irradiation[†] of 2-acetyloxy-1-methoxycarbonylcyclohexene **1a** under various conditions are summarized in Table 1. Irradiation of **1a** with a low-pressure mercury lamp (entry 1) led to 1,3-acetyl migration, giving 2-acetyl-2-methoxycarbonylcyclohexanone **2a‡** (62%), which was identified by comparison with authentic material prepared by a conventional method[§] and a trace amount of

[†] In all photoreactions described here, a 2.8×10^{-2} mol dm⁻³ solution of substrate was irradiated at *ca.* 10 °C with bubbling of an argon or nitrogen stream.

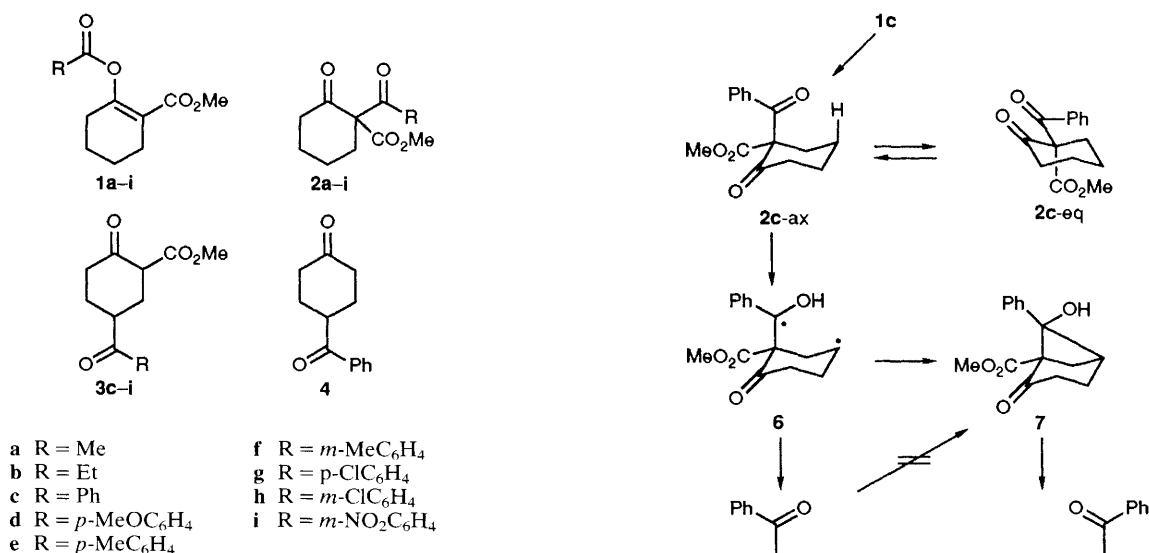
[‡] All new compounds gave satisfactory elementary analyses and spectral data (IR, ¹H and ¹³C NMR, mass).

[§] A 10:3 mixture of **1a** and **2a** was obtained in 95% yield by acetylation of 2-methoxycarbonylcyclohexanone with acetyl chloride and magnesium turnings.⁵

Table 1 Irradiation of compound **1a**

Entry	Light Source ^a	Filter ^b	Solvent ^c	Sensitizer	Time/h	Yield (%) ^d of 2a
1	L	V	A	—	10	62
2	M	P	A	—	10	No reaction
3	M	P	B	Acetone	3.5	64
4	M	P	A	Acetophenone	2	65
5	M	P	A	Benzophenone	2	68

^a L: 60 W low-pressure mercury lamp, M: 300 W medium-pressure mercury lamp. ^b V: Vycor, P: Pyrex. ^c A: acetonitrile, B: acetone. ^d Isolated yields after column chromatography.



2-methoxycarbonylcyclohexanone (<0.5%, estimated by GLC analysis) along with some unidentified products. An acetonitrile solution of **1a** was stable to Pyrex-filtered irradiation with a medium-pressure mercury lamp (entry 2), which was in accord with the UV spectrum of **1a** [$\lambda_{\text{max}} = 221.5$ nm (ϵ ca. 8200) in acetonitrile] which exhibited no absorption at wavelengths over than ca. 300 nm. However, under the same irradiation conditions, the rearrangement readily proceeded either when the reaction solvent was replaced by acetone (entry 3), or when 2.0 equiv. of acetophenone or benzophenone was added to the reaction system (entries 4 and 5). These findings show that this reaction is efficiently sensitized by these ketones. Likewise, propionoyl derivative **1b** also gave the Fries product **2b** in good yield, whose photoreactivity was nearly parallel to that of **1a**.

In contrast, the photoreactivity of 2-benzoyloxy-1-methoxycarbonylcyclohexene **1c** proved to be far more complicated than that of **1a**. Irradiation of **1c** in acetone with a medium-pressure mercury lamp equipped with a Pyrex filter for 10 h afforded the 1,5-aryl migration product, 4-benzoyl-2-methoxycarbonylcyclohexanone **3c**† (43%), as a major product, along with 1,3-aryl migration product, 2-benzoyl-2-methoxycarbonylcyclohexanone **2c** (6%), and a ring cleavage

product **5**‡ (6%), where **1c** (9%) was also recovered. As well, under the same conditions a range of aryloxy compounds **1d-i** afforded **3d-i** in 25–50% yields which have not been optimized. On the other hand, acetophenone- or benzophenone-sensitized irradiation of **1c-i** in acetonitrile by using the same combination of light source and filter enhanced the yields of photo-Fries rearrangement products **2c-i**. The yields of **2a-i** from **1a-i** under irradiation conditions optimal so far, *i.e.* benzophenone-sensitized irradiation, are shown in Table 2, where 1,5-aryl migration and ring cleavage were completely eliminated.

Since **3c** (54%) and **5** (6%) were also obtained by acetone-sensitized irradiation of the isolated **2c**, the formation of these compounds would be reasonably explained as a result of Norrish type II reactions⁷ of the photoexcited **2c** as illustrated in Scheme 2. Upon irradiation, photo-Fries rearrangement of **1c** takes place to form **2c** which may exist as an equilibrium mixture of two major chair conformers, with the benzoyl group either axial **2c-ax** or equatorial **2c-eq**. The carbonyl group of the benzoyl moiety in **2c** is photoexcited again, then on the basis of stereoelectronic grounds the conformer **2c-ax** undergoes intramolecular γ -hydrogen abstraction to form a 1,4-biradical intermediate **6**. Subsequently, **6** proceeds to two typical competitive reactions of Norrish type II process; *i.e.* β -cleavage to yield **5** and bonding of biradical to form a cyclobutanol **7**, of which the latter is followed by retroaldol reaction to yield **3c**. Another possible route to **3c** via **5**; *i.e.* intramolecular [2 + 2] photocycloaddi-

† The structure of **3c** was confirmed on the basis of the NMR spectra of **3c** and **4** derived from **3c** by decarbomethoxylation (NaCl, H₂O, DMSO, 150 °C; 70%). ⁶ **3c**: ¹H NMR (CDCl₃): δ 1.70–2.70 (6H), 3.24–3.94 (1.3H), 3.73 (3H, s), 7.36–7.76 (3H), 7.76–8.16 (2H), 12.30 (0.7H, s). **4**: ¹H NMR (CDCl₃): δ 1.80–2.34 (4H), 2.34–2.73 (4H), 3.49–3.90 (1H, m), 7.33–7.78 (3H), 7.78–8.16 (2H). ¹³C NMR (CDCl₃): δ 28.8 (t), 39.9 (t), 42.7 (d), 128.2 (d), 128.8 (d), 133.3 (d), 135.7 (s), 201.8 (s), 210.0 (s).

‡ For determination of the structure, **5** was hydrolysed with NH₄Cl and NH₄OH in H₂O,⁸ giving known compounds, methyl benzoyl-acetoacetate and pent-4-enoic acid in 56 and 43% yields, respectively.

Table 2 Yields of photo-Fries rearrangement products **2** from **1** with benzophenone-sensitized irradiation^a

Substrate	Product	M.p./°C	Yield (%) ^b
1a	2a	Oil	68
1b	2b	Oil	70
1c	2c	170–174	76
1d	2d	115.5	72
1e	2e	200–202	65
1f	2f	83.5	88
1g	2g	80.0	84
1h	2h	81.5	79
1i	2i	57.0–58.0	59

^a An acetonitrile solution of a substrate was irradiated with medium-pressure mercury lamp equipped with a Pyrex filter in the presence of 2.0 equiv. of benzophenone, and irradiation time was 1–2 h except for the case of **1i** of 15 h. ^b Isolated yield after column chromatography.

tion of the enol of **5** followed by retroaldolization of the resulting **7**, was completely eliminated by the fact that under the same irradiation conditions the isolated **5** was stable. As it is generally accepted that Norrish type II process proceeds *via* a triplet excited state, the above results show that the triplet energies (E_T)⁹ of **2a–i** and the sensitizers employed lie in the order, **2a,b** > acetone ($E_T = 78\text{--}82 \text{ kcal mol}^{-1}$) > **2c–i** > acetophenone (74.1), benzophenone (69.2) (1 cal = 4.184 J).

From a synthetic point of view, the photo-Fries reaction of **1a–i** to **2a–i** offers an efficient method for the C-acylation of

2-methoxycarbonylcyclohexanone whose acylation by conventional methods preferentially give the *O*-acylation product (**1a–i**). Furthermore, the 1,5-aroyl migration of **1c–i**, or 1,3-aroyl migration of **2c–i** through the Norrish type II process, would suggest a new synthetic methodology for remote functionalization (aroxylation) of inactive carbon atoms. Currently, we are studying these migration reactions in more detail with a view to establishing their mechanisms and scopes.

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