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Effect of an Extra Chloro Substituent on Photochemistry of *o*-Alkylphenacyl Chloride

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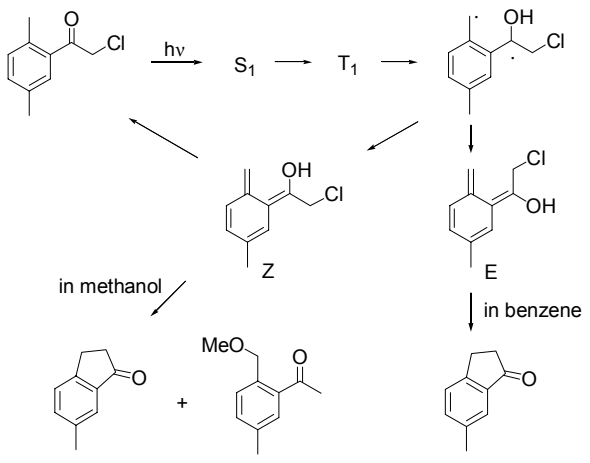
The title compound, α,α-dichloro-*o*-methylacetophenone, was prepared and its photochemical behavior was investigated. Addition of an extra chlorine at alpha position to the carbonyl showed many different features from photochemical reactivities of mono chloro analogue, 2,5-dimethylphenacyl chloride. In benzene, a rearrangement product with a formal 1,5-Cl shift and a reduction product were formed beside indanone. In methanol, solvolysis and cyclization of a common dienol intermediate occurred at comparable reaction rates.

Key Words: Photochemistry, Dichloro ketone, Substituent effect

Introduction

Photochemistry of α-halogenated ketones has received much attention for the last decade not only in their mechanistic interests,[1] but also in their usefulness as synthetic precursors,[2] chain initiators of radical polymerization,[3] and for their atmospheric importance.[4] Reaction routes of the α-halo ketones are known to vary significantly depending upon the halo substituent. Typically, α-bromo ketones give C-Br bond cleavage upon photolysis, while α-chloro ketones often show divergent photobehaviors such as rearrangements or solvolysis beside C-Cl bond cleavage. For example, α-bromovalerophenone gives only the C-Br bond cleavage products, while α-chlorovalerophenone follows the classical Norrish/Yang reaction pathway predominantly.[5]

Bergmark and coworkers have explored photochemistry of 2,5-dimethylphenacyl chloride (DMPC), which gives indanone as only product in benzene, while a mixture of indanone and a solvent incorporated product is obtained in methanol *via* photoenol formation from n, π* triplet excited state.[6] Later, Klan and Wirz reinvesitigated the initial mechanistic work by Netto-Ferreira and Scaiano,[7] and concluded that the reaction in methanol proceeds from *Z*-dienol *via* heterolytic C-Cl cleavage, while in benzene the indanone formation occurs from the *E*-dienol[8] (Scheme 1).



Scheme 1

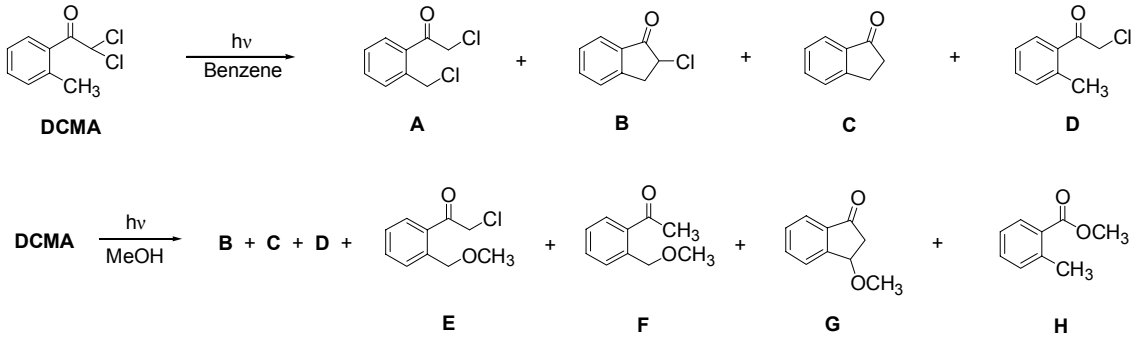
Despite many examples of α-halo ketones in the field of photochemistry, only a few reports on the photochemistry of α,α-dihalo ketones are found in the literature.[9] Addition of an extra halogen at alpha position to the carbonyl often shows quite different photoreactivities from those of the mono halo substituted analogues. Recent study on 1,1-dichloroacetone is of practical interest in atmospheric chemistry, because it explains the role of atmospheric oxidation of volatile organic hydrocarbons by Cl in atmosphere.[4a] In this study, it was revealed that the presence of both chlorines in 1,1-dichloroaetone reduced the compound's reactivity toward chlorine in comparison to monochlorinated analoques. In the course of our studies on substituent effects of ketone photochemistry,[10] we had a chance to investigate photochemical behaviors of α,α-dichloro-*o*-methylacetophenone (DCMA), a dichloro analogue of DMPC, and found an interesting substituent effect on its photoreactivity, which we would like to report here.

Results and Discussion

The title compound was prepared by dichlorination of *o*-methylacetophenone using either sulfuryl chloride[11] or copper(II) chloride.[12] The purified ketone was irradiated in benzene or methanol using the Pyrex filtered UV light until all the starting material had disappeared. The resulting photoproducts were isolated by routine purification methods using silica gel column chromatography. Each of the isolated products was identified either by analyzing its spectroscopic data or by comparing with authentic samples. The photolysis was also done in an NMR sample scale by attaching the degassed sample solution in an NMR tube by an immersion well equipped with the Hanovia medium pressure mercury arc lamp in order to monitor the reaction more closely. The results from photolysis of DCMA are shown in Scheme 2 and the product distribution at various times is summarized in Table 1 and 2.

The relative amount of each product was dependent upon the irradiation time (Figure 1), which implied that some of them were secondary photoproducts. The product distribution was more complex in methanol than in benzene. Products A, B, D, E and H are primary photoproducts, while the rest of them are secondary photoproducts, *vide infra*.

First of all, it is notable that two other products, A and D,



Scheme 2

beside indanones are formed in photolysis of DCMA in benzene, whereas the indanone is the only product observed for DMPC under the same reaction condition. The photoreduction product, D, has not been observed in the photolysis of DMPC, even though such a reaction is well known for phenacyl chlorides with no ortho alkyls.[13] Apparently, the presence of the ortho methyl diverges the reaction routes and the indanone forming process becomes much faster than the photoreduction path. Adding an extra chloro substituent, however, seems to revive the reduction pathway according to the above results of DCMA.

The photoreduction can be initiated by photochemical β C-Cl bond cleavage reaction of carbonyl compounds, which has been extensively studied before.[14] The driving force for the β C-Cl cleavage can be attributed in part to an overlap of C=O π* orbital and C-Cl σ* orbital. Both homolytic and heterolytic cleavages have been known, which is dependent on substrates and reaction conditions. The homolytic cleavage results in formation of radical pairs, which can be trapped by any hydrogen atom sources in the reaction medium to give a reduction product. On the other hand, electron transfer from the radical pair would form ionic species, which then opens up ionic processes such as rearrangement and solvolysis. Carbocationic intermediates, formed by either direct heterolysis or by homolysis followed by electron transfer, have been proposed to explain some of solvolysis products in photolysis of other dichloro ketones in methanol.[9a] In benzene, however, the radical intermediate is most likely to be the precursor of the photoreduction product. Wagner has shown that addition of 0.05 M benzenethiol can trap efficiently radical intermediates resulting from the β-cleavage.[15] When the photolysis of DCMA was repeated in the presence of 0.05 M benzenethiol, the amount of the photoreduction product D increased about twice as much as that observed without the benzenethiol.

There have been a few reports comparing photoreactivities of mono- and di-halo substituted ketones.[16] In the case of chloro ketones, introduction of the second chlorine atom into alpha position to the carbonyl facilitates the C-Cl bond cleavage and increases the radical character in the cleavage. The result can be explained by relief of steric hindrance upon expulsion of a chlorine atom and the stabilization of the resulting radical by

Table 1. Product Distribution in Photolysis of DCMA in Benzene (Relative Amounts in Percentage)

Irrad. Time (min.)	DCMA	A	B	C	D
0	100				
10	38.1	2.4	20.1	35.8	3.6
20	25.6	3.8	17.1	49.9	3.6
30	18.7	3.4	13.4	61.2	3.3

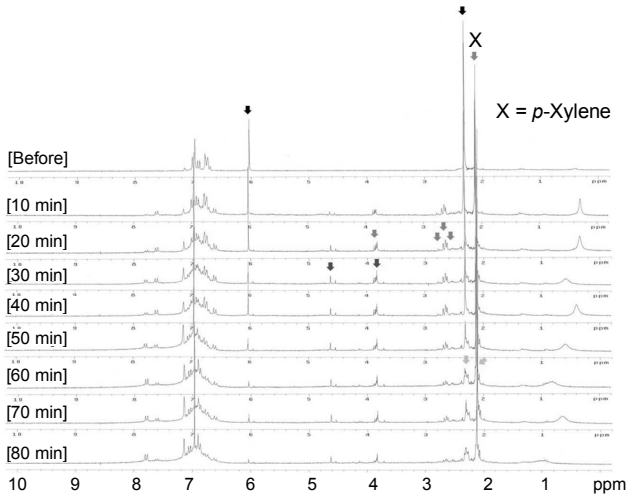
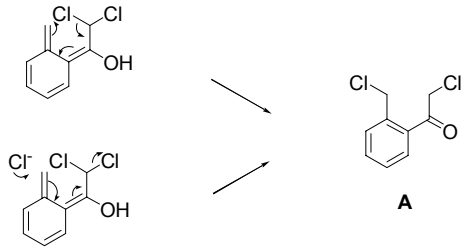


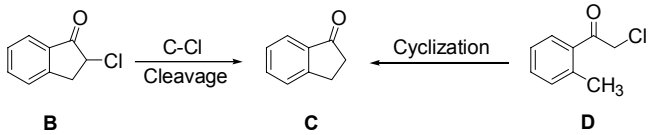
Figure 1. ^{1}H NMR Spectra of Photoproducts of DCMA in Benzene at Various Irradiation Times.

Table 2. Product Distribution in Photolysis of DCMA in Methanol (Relative Amounts in Percentage)

Irrad. Time (min.)	DCMA	B	C	D	E	F	G	H
0	100							
15	39.4	15.2	11.3	3.9	23.0	1.7	3.8	1.7
30	22.4	14.1	18.2	4.8	24.7	4.2	8.5	3.1
45	10.7	10.8	23.0	3.7	23.2	5.6	18.0	5.0
60	4.5	6.9	26.0	2.1	20.7	5.3	29.0	5.5



Scheme 3



Scheme 4

both carbonyl and chlorine. We believe that formation of the product D is the consequence of the similar pathway. Our results imply that the rate enhancement by adding an extra chlorine atom makes the photoreduction pathway competitive with indanone formation.

Formation of product A can be envisaged as either an intramolecular or intermolecular HCl catalyzed rearrangement shown in Scheme 3.

In order to differentiate two possible paths shown in Scheme 3, we repeated the photolysis of DCMA with addition of one equivalent of $NaHCO_3$, and observed that the relative amount of product A decreased significantly. The result implies that the intermolecular path involving HCl is operating for the formation of A. As mentioned above, such a reaction has not been observed in the photolysis of DCMP. It is possible that build-up of HCl from the indanone forming process at the early stage of the photolysis is more significant in the case of DCMA than DCMP.

From mechanistic points of view, the secondary photoproduct C can be formed from both products B and D by β C-Cl cleavage and cyclization of dienol intermediates, respectively (Scheme 4).

In order to evaluate the relative rate of each process, photolysis of 1 to 1 mixture of B and D in benzene was performed. As expected, the only product in this reaction was product C, whose formation was accompanied by decrease of both the starting B and D. Judging from relative amounts of the remaining B and D, the β C-Cl cleavage reaction was about twice as fast as the cyclization of dienol intermediates. The result is in sharp contrast to the similar reactions observed in photolysis of DCMA, where the cyclization of dienol intermediate giving product B is predominant over β C-Cl cleavage to product D as shown in Table 1. The higher reactivity of B than that of DCMA toward the β C-Cl cleavage can be explained by stereoelectronic or conformational effect. The best geometric orientation for the β C-Cl cleavage requires the C-Cl bond to be perpendicular to the carbonyl, such that mixing of the carbonyl π* and C-Cl σ* orbitals are maximized. The rigid structure of B can, therefore, benefit the entropic preference and cleave the C-Cl bond much faster than DCMA does. Similar stereoelectronic effects have been addressed in photolytic cleavage of 4-tert-butyl-2-chlorocyclohexanones.[17]

Photolysis of DCMA in methanol gives a complex mixture of products as shown in Table 2. Major reaction path involves the formation of a solvent incorporated product, E, and the α-chloroindanone, B. The rest of products originate from these primary photoproducts. The fact that product A is not formed in methanol is understandable, considering that its mechanistic origin is common with that of product E, but the methanol outnumbers HCl in attacking the benzylic position of dienol intermediates as shown in Scheme 3. Upon further irradiation, the product E can form F and G *via* photoreduction and photocyclization, respectively. The latter reaction has recently been reported by Klan and coworkers, although only the nonnucleophilic solvents provided the cyclization products in their studies.[18]

A final feature to note in photolysis of DCMA in methanol is the formation of a solvolysis product, H. A control experiment in the dark clearly showed that the reaction was light-driven, which differs from the classical haloform reaction. Our literature searches found that similar observations had been made in photolysis of α,α,α-trichloroacetophenone[19] and α,α-dichloropropiophenone.[9a] The exact mechanism has not been known up until now, but α-cleavage and involvement of oxygen have been suggested. We are currently investigating the mechanism with more similar examples.

In summary, α,α-dichloro-*o*-methylacetophenone was prepared and its photochemical behavior was investigated. Addition of an extra chlorine at alpha position to the carbonyl showed many different features from photochemical reactivities of mono chloro analogue, 2,5-dimethylphenacyl chloride. In benzene, a rearrangement product with a formal 1,5-Cl shift and a reduction product were formed beside indanone. In methanol, solvolysis and cyclization of a common dienol intermediate occurred at comparable reaction rates.

Experimental Section

Synthesis of α,α-dichloro-*o*-methylacetophenone. Sulfuryl chloride (10.06 g, 74.53 mmol) and *p*-toluenesulfonic acid (0.10 g) were added into 100 mL two neck round bottomed flask containing *o*-methylacetophenone (1.00 g, 7.45 mmol) in 30 mL dichloromethane under argon atmosphere and the mixture was refluxed for 24 hours. Distilled water (40 mL) was added and the organic layer was extracted with dichloromethane. The organic layer was washed with sodium bicarbonate, brine and dried using anhydrous sodium sulfate. After concentration under the reduced pressure, the resulting yellow crude product was purified by column chromatography using dichloromethane and *n*-hexane in 1 to 2 ratio to give 0.95 g of α,α-dichloro-*o*-methylacetophenone (75% yield).

Photolysis. The starting ketone in benzene (typically 0.01 - 0.02 M) was irradiated in an immersion well with argon bubbling using Pyrex (or Uranium) filtered light of a 450 W Hanovia medium pressure mercury arc lamp until all the starting material had disappeared. The reaction mixture was concentrated at reduced pressure and the resulting crude product mixture was separated by column chromatography using *n*-hexane

and ethyl acetate in 7 to 1. The structure of each product was identified either by standard spectroscopic identification or by comparing with authentic samples which had been separately prepared if unavailable commercially.

For NMR scale photolysis, an NMR tube containing ketones in benzene-d_6 was degassed and irradiated by attaching it to the side of an immersion well using Pyrex filtered light of a 450 W Hanovia medium pressure mercury arc lamp. To control reaction temperature the sample was immersed in a temperature control bath during the irradiation.

Spectroscopic properties of photoproducts.

α,α-Dichloro-ortho-methylacetophenone: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.71 (d, 1H, J = 7.8 Hz), 7.37 (m, 3H), 6.69 (s, 1H), 2.53 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 188.3, 140.5, 132.8, 132.3, 128.4, 125.7, 68.9, 21.2. FTIR: 1705 (C=O) cm^{-1}.

α-Chloro-ortho-chloromethylacetophenone: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.60 (m, 4H), 4.92 (s, 2H), 4.69 (s, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 194.1, 138.1, 134.2, 132.7, 131.3, 128.9, 128.4, 47.6, 43.9.

α-Chloroindanone:[16a] ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.86 (d, 1H, J = 7.2 Hz), 7.64-7.56 (m, 3H), 4.60 (dd, 1H, J = 7.6, 4.0 Hz), 3.82 (dd, 1H, J = 17.6, 7.6 Hz), 3.33 (dd, 1H, J = 17.6, 4.0 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 199.7, 151.2, 136.5, 134.2, 128.7, 126.8, 125.4, 56.1, 37.9.

α-Chloro-*o*-methoxymethylacetophenone: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.53-7.77 (m, 4H, aromatic), 4.73 (s, 2H), 4.69 (s, 2H), 3.46 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 194.6, 139.7, 134.1, 132.3, 128.3, 128.2, 127.2, 72.5, 58.7, 47.9.

***o*-Methoxymethylacetophenone:** ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.37-7.45 (m, 4H), 4.78 (s, 2H), 3.50 (s, 3H), 2.61 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 199.8, 132.9, 131.0, 130.4, 128.1, 127.6, 125.1, 72.2, 58.7, 28.9.

3-Methoxyindanone: ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.00 (d, 1H, J = 7.6 Hz), 7.70-7.73 (m, 3H), 5.07 (dd, 1H, J = 6.2, 2.6 Hz), 3.53 (s, 3H), 3.04 (dd, 1H, J = 18.6, 6.2 Hz), 2.69 (dd, 1H, J = 18.6, 6.2 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 202.9, 153.1, 136.8, 134.9, 129.5, 126.5, 123.3, 76.7, 57.1, 43.4.

Methyl *o*-methylbenzoate:[20] ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.88 (d, 1H, J = 6 Hz), 7.43-7.64 (m, 3H), 3.93 (s, 3H), 2.57 (s, 3H). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 167.7, 139.9, 131.7, 131.4, 130.3, 129.2, 125.4, 51.5, 21.5.

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