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CHLORINATION OF ACYCLIC β-DIKETONES. FORMATION OF β-CHLORO-β,γ-UNSATURATED KETONES

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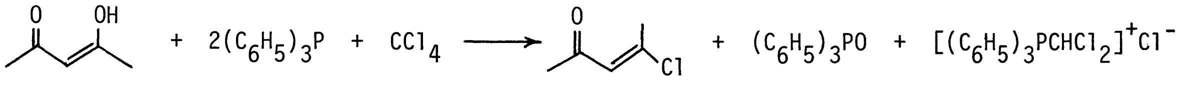
Chlorination of acyclic β-diketones with triphenylphosphine-carbon tetrachloride and the other chlorinating reagents afforded β-chloro-β,γ-unsaturated ketones except when the terminal alkyl group was methyl or *t*-butyl. Unsymmetrical acyclic β-diketones yielded a mixture of the products chlorinated on each carbonyl carbon.

Nucleophilic substitution at a vinyl carbon is generally difficult, but substitution reactions of the halogen on an unsaturated carbon are known to take place easily when an electron-withdrawing group attached to the adjacent carbon. It has been reported that chlorine of β-chloro-α,β-unsaturated ketones can be reduced with zinc-silver couple in methanol,[1)] and substitued with active methylene compounds[2)] and a nitrogen compound.[3)] Although β-chloro-α,β-unsaturated ketone is expected to be an interesting synthone and it has usually been prepared by chlorination of β-diketone, the reactions hitherto reported are limited to those of 2,4-pentanedione and cyclic β-diketones.[1-5)] Thus, we examined the chlorination of some acyclic β-diketones, and we now report the results that acyclic β-diketones gave unexpected β-chloro-β,γ-unsaturated ketones exclusively in some cases.

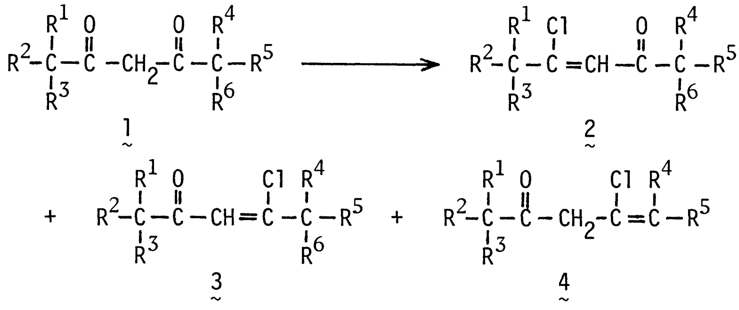
Recently, a useful reagent to substitute an enol-hydroxyl group with a chlorine atom was reported: triphenylphosphine and carbon tetrachloride were used advantageously for the conversion of β-diketones into β-chloro-α,β-unsaturated ketones.[4)] This procedure is regarded to be superior to the various methods



hitherto reported, since the formation of hydrogen halide is not involved and thus the essentially neutral conditions can be maintained throughout the reaction.

We examined the chlorination of several acyclic β-diketones with some modification of this method (method A). To a mixture of diketone (60 mmol) and triphenylphosphine (120 mmol), 47 ml of carbon tetrachloride was slowly added with stirring. After the addition, the mixture was warmed at 40 °C until it became a clear solution. The temperature of the mixture was gradually raised under the separation of the phosphonium salt. The reaction temperature was maintained at about 52 °C until the exothermic reaction ceased. The reaction was complete in 3-4 h. The phosphonium salt was filtered off. To the filtrate was added 20 ml of pentane and a separated white solid, triphenylphosphine oxide, was filtered off.[6] The combined solids were extracted by refluxing with 60 ml of pentane three times. The combined pentane solution was evaporated and the residual product was chromatographed on a silica-gel (Wakogel C-200) column. Unreacted diketone was eluted at first by hexane, then chloroketones were eluted by ethyl acetate-hexane (1:99). The results of chlorination of symmetrical β-diketones are summarized in Table 1 (runs 1-9). The structures of the products were identified mainly by their ^{1}H-NMR spectra (Table 2). The chlorination product of 2,4-pentanedione (1a) was indicated to be a mixture of geometrical isomers (E:Z = 85:15) by vpc analysis (PEG-20M 20% on Chromosorb-W, 2 m). It was confirmed by the comparison of their NMR spectra with the reported data.[7] A long range coupling (J = 1.1 Hz) was observed between vinyl and methyl protons adjacent to the carbon-carbon double bond. In the cases of the chlorination products of 1b and 1c, the signal of vinyl proton of α,β-unsaturated ketone could not be observed around δ = 6.5, but a singlet of methylene protons was observed at δ = 3.5. The other signals were characteristic of the each structure of 4b and 4c. The IR spectra of these com-

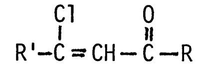
Table 1. Chlorination of β-Diketones



Run	Diketone	R^1	R^2	R^3	R^4	R^5	R^6	Method	Yield (%)[a]	2	3	4
1	1a	H	H	H	H	H	H	A	96	100		0
2[b]	1a							B	50	100		0
3	1a							C	25	100		0
4	1b	Me	H	H	Me	H	H	A	27	0		100
5	1b							B	(15)	0		100
6	1b							C	0[c]			
7	1c	Me	Me	H	Me	Me	H	A	42	0		100
8	1c							B	15	0		100
9	1d	Me	Me	Me	Me	Me	Me	A	8	100		0
10	1e	H	H	H	Me	H	H	A	12	50	0	50
11	1f	H	H	H	Me	Me	H	A	27	50	0	50
12	1g	H	H	H	Me	Me	Me	A	8	100	0	0

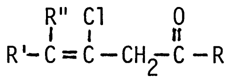
[a] Isolated yield, value given in parentheses was determined by vpc. [b] Lit.[1] [c] Unreacted diketone was recovered.

Table 2. ^{1}H-NMR Spectral Data of Chloroketones[a]



$R'-C(Cl)=CH-C(=O)-R$

Chloroketone			Chemical shifts (δ)		
	R'	R	R'	CH	R
2a	Me	Me	2.56	6.48	2.21[b]
			2.26	6.27	2.33[c]
2d	*t*Bu	*t*Bu	1.26	6.57	1.17
2e	Me	Et	2.57	6.45	1.09, 2.48
2f	Me	*i*Pr	2.57	6.52	1.11, 2.5
2g	Me	*t*Bu	2.55	6.71	1.14



$R'-C(R'')=C(Cl)-CH_2-C(=O)-R$

Chloroketone				Chemical shifts (δ)			
	R'	R"	R	R'	R"	CH_2	R
4b	Me	H	Et	1.82	5.83	3.49	2.59, 1.05
4c	Me	Me	*i*Pr	1.75	1.88	3.51	2.62, 1.11
4e	Me	H	Me	1.80	5.72	3.39	2.21
4f	Me	Me	Me	1.79	1.92	3.47	2.20

[a] Taken in $CDCl_3$ solution. The chemical shifts are expressed in δ downfield from internal TMS. [b] Lit.[7)] 2.52 (R'), 6.47 (-CH=), 2.20 (R) for *E*-isomer. [c] Lit.[7)] 2.26 (R'), 6.27 (-CH=), 2.33 (R) for *Z*-isomer.

pounds were also concordant with their structures.

As shown in Table 1, β-chloro-α,β-unsaturated ketones were obtained from the corresponding β-diketones when the terminal alkyl groups were methyl (**1a**; run 1) or *t*-butyl group (**1d**; run 9), but β-chloro-β,γ-unsaturated ketones were obtained exclusively when the terminal alkyl groups were ethyl (**1b**; run 4) or isopropyl (**1c**; run 7).

The enol form of β-diketones is considered to take certainly an α,β-unsaturated ketone structure. Thus the formation of β-chloro-β,γ-unsaturated ketones should involve the rearrangement of double bond during the reaction process. In order to confirm whether these interesting result is on account of the chlorinating reagent or not, we examined the reactions using other chlorination reagents, oxalyl chloride (method B)[1)] and phosphorus trichloride (method C).[2,5)] These reactions were carried out by the same way as reported. No discrepancy in the regioselectivity was observed between each preparation method (Table 1).

As the regioselective formation of α,β- or β,γ-unsaturated ketones appeared to depend on the substrates and not on the preparation reagents, unsymmetrical β-diketones were treated with triphenylphosphine and carbon tetrachloride as aforementioned (method A). In these reactions, one of the terminal alkyl groups of β-diketones was fixed to methyl and the other was changed as ethyl, isopropyl and *t*-butyl groups (Table 1, runs 10-12). The isomer distributions of the products were determined by vpc. The each isomer was separated by column chromatography and submitted to NMR measurements. In the cases of 2,4-hexanedione (**1e**) and 5-methyl-2,4-hexanedione (**1f**), the chlorination occurred at both C^2 and C^4 in an equal probability, and no selectivity due to the terminal alkyl groups could be observed. The C^2-chlorination products were α,β-unsaturated ketones, but the C^4-chlorination products were exclusively β,γ-unsaturated compounds. In the case of 5,5-dimethyl-2,4-hexanedione (**1g**), the product was a sole kind of α,β-unsaturated ketone. The ^{1}H-NMR chemical shift of *t*-butyl group of the product (δ = 1.14) was almost identical with that of the starting diketone (δ = 1.14) and a long range coupling (J =

1.2 Hz) was observed between methyl and vinyl protons. Thus the chlorination product was identified with 2-chloro-5,5-dimethyl-2-hexen-4-one (**2g**). The result that the chlorination occurred at the carbon adjacent to methyl group may be due to the steric reason of *t*-butyl group. It is also consistent with the fact that the reaction of **1a** gave better yield than that of **1d**.

Although the product (**2a**) derived from **1a** was a mixture of geometrical isomers, the other β-chloro-α,β-unsaturated ketones (**2d**, **2e**, **2f**, and **2g**) were all single isomers. These products showed vinyl proton signals at δ = 6.45-6.71 and signals of methyl protons adjacent to the carbon-carbon double bond at δ = 2.55-2.57 in their NMR spectra. These data indicated that these products were all *E*-isomers.

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