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Photochemical Dealkylation of 2-Acyl-3-alkylamino-5,5-dimethyl-2-cyclohexen-1-ones

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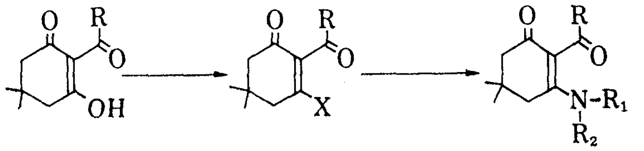
The photochemical behavior of a number of 2-acyl-3-alkylamino-5,5-dimethyl-2-cyclohexen-1-ones has been investigated. Irradiation of these systems resulted in δ-hydrogen abstraction by the excited carbonyl oxygen to form a biradical intermediate, which produces the dealkylation product.

Keywords——synthesis of 2-acyl-3-alkylamino-5,5-dimethyl-2-cyclohexen-1-ones; β-amino-α-acylvinyl ketones; intramolecular photodealkylation; photoelimination; 1,6-hydrogen atom transfers by excited carbonyl oxygen

The intramolecular photoelimination or photocyclization involving 1,6-hydrogen atom transfer by an excited carbonyl oxygen has been the subject of intensive investigation. The reported examples have been limited mainly to 2-benzoyl aromatic ethers,[2)] 2-benzoyl aromatic amines,[3)] acetamides,[4)] and imides,[5)] and little is known about such photochemical behavior of α,β-unsaturated ketone systems. Jorgenson and Yound reported[6)] that some α,β-unsaturated ketones undergo a photo-induced ring closure by intramolecular hydrogen abstraction *via* a seven-membered ring transition state. Sugiyama *et al.* reported[3)] a similar photocyclization of acyclic β-dialkylaminovinyl ketones. In an early paper[7)] in our series of studies on the photochemistry of α,β-unsaturated carbonyl compounds,[7-9)] we reported an example of photochemical demethylation of 2-acetyl-5,5-dimethyl-3-methylamino-2-cyclohexen-1-one (Ia) bearing δ-hydrogen and we now report the generality, limitations, and reaction mechanism of the photodealkylation.

The starting materials, 2-acyl-3-(alkyl and aryl)amino-5,5-dimethyl-2-cyclohexen-1-ones (Ia—i) were prepared by the method of Akhrem;[10)] 3-methoxy and 3-chloro substituted 2-acyl-5,5-dimethyl-2-cyclohexen-1-ones (IIIa, b), readily obtained from 2-acyl-5,5-dimethylcyclohexane-1,3-diones (IIa, b), were treated with amines to give the corresponding 3-(alkyl and aryl)amino compounds (Ia—i). The yields, melting points, and spectral data are listed in Table I.



IIa: $R=CH_3$
IIb: $R=C_6H_5$

IIIa: $R=CH_3$, $X=OCH_3$
IIIb: $R=C_6H_5$, $X=Cl$

Ia: $R=CH_3$, $R_1=H$, $R_2=CH_3$
Ib: $R=CH_3$, $R_1=H$, $R_2=C_2H_5$
Ic: $R=CH_3$, $R_1=H$, $R_2=$iso-C_3H_7
Id: $R=CH_3$, $R_1=H$, $R_2=CH_2C_6H_5$
Ie: $R=R_1=R_2=CH_3$
If: $R=CH_3$, R_1, $R_2=-(CH_2)_4-$
Ig: $R=CH_3$, $R_1=H$, $R_2=$*tert*-C_4H_9
Ih: $R=C_6H_5$, $R_1=H$, $R_2=CH_2C_6H_5$
Ii: $R=CH_3$, $R_1=H$, $R_2=C_6H_5$

Chart 1

Table I. Preparation of 2-Acyl-3-alkylamino-5,5-dimethyl-2-cyclohexen-1-ones (Ia—h)

Compd.[a]	Yield[b] (%)	mp[c] (°C)	Lit. mp	IR $\nu_{max}^{CHCl_3}$ (cm^{-1})	UV λ_{max}^{EtOH} (nm)
Ia	95	130—131	126—127[10]	1590, 1640	263, 292
Id	79	92—93	—	1570, 1630	261, 291
Ic	85	72—73	—	1570, 1630	261, 291
Id	82	70	92—93[10]	1580, 1590, 1640	258, 293
Ie	79	85	80—81[10]	1530, 1600	263, 295
If	90	34—35	33—34[10]	1530, 1595, 1635	261, 293
Ig	98	75—76	—	1570, 1630	292, 293
Ih	40	206—207	—	1570, 1590, 1635	235, 278, 304
Ii	66	136—137	135—135.5[10]	1560, 1580, 1640	259, 303

a) The results of microanalyses of new compounds were in satisfactory agreement with the calculated values.
b) Yields of isolated products were based on the 3-substituted enone (III).
c) Uncorrected melting points are given.

Irradiation of 2-acetyl-5,5-dimethyl-3-methylamino-2-cyclohexen-1-one (Ia) in methylene chloride for 40 h in a quartz vessel has been shown to give the demethylation product, 2-acetyl-3-amino-5,5-dimethyl-2-cyclohexen-1-one (IV) in 11% yield. We now examined the photo-behavior of Ia under various conditions. When oxygen was continuously bubbled through the methylene chloride solution in the quartz vessel during the irradiation, a 20% yield of IV was obtained. The use of acetophenone as a photosensitizer in methylene chloride solution did not have any effect. Photolysis in other solvents such as benzene, methanol, and ether did not give IV at all, although irradiation of a benzene solution in the presence of acetophenone gave a small amount of IV.

Photodealkylation of other 2-acetyl-3-*N*-monoalkylamino-5,5-dimethyl-2-cyclohexen-1-ones (Ib—d) was performed under similar conditions[11] to give 2-acetyl-3-amino-5,5-dimethyl-2-cyclohexen-1-one (IV) in moderate yields. In the case of 2-acetyl-3-*N*,*N*-dialkylamino compounds (Ie and If), dealkylation of both alkyl substituents on nitrogen was observed. Irradiation of 2-benzoyl-3-benzylamino-5,5-dimethyl-2-cyclohexen-1-one (Ih) gave the dealkylation product (V) selectively, although 2-benzoyl-3-alkyl-5,5-dimethyl-2-cyclohexen-1-ones, which can be regarded as carbon analogs of C-3 amino-substituted Ih, undergo γ-hydrogen

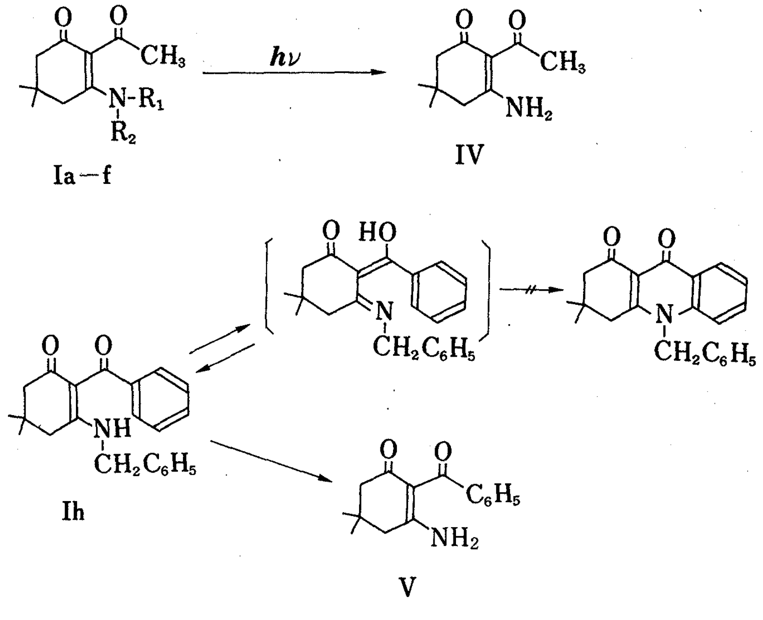


Chart 2

Table II. Reaction Conditions and Yields of Products

	Starting enones (Ia—i and IIIc, d)			Reaction conditions[a]	% yields of product	
	R	R_1	R_2		Dealkylation product (IV or V)	Recovered enone
Ia	CH_3	H	CH_3	Quartz, in CH_2Cl_2, 40 h	11	22
				Quartz, in CH_2Cl_2, O_2, 40 h	20	[b]
				Quartz, in CH_2Cl_2, $CH_3COC_6H_5$, 40 h	11	46
				Quartz, in C_6H_6, 50 h	—	[c]
				Quartz, in CH_3COCH_3, 40 h	18	31
				Quartz, in CH_2Br_2, 40 h	[b]	[b]
				Quartz, in CH_3OH, 50 h	—	[c]
				Quartz, in Et_2O, 50 h	—	[c]
				Pyrex, in CH_2Cl_2, 40 h	31	12
Ib	CH_3	H	C_2H_5	Quartz, in CH_2Cl_2, 40 h	11	27
				Pyrex, in CH_2Cl_2, 40 h	[b]	[b]
Ic	CH_3	H	iso-C_3H_7	Quartz, in CH_2Cl_2, 40 h	20	46
				Pyrex, in CH_2Cl_2, 40 h	[b]	[b]
Id	CH_3	H	$CH_2C_6H_5$	Quartz, in CH_2Cl_2, 40 h	20	56
				Pyrex, in CH_2Cl_2, 50 h	—	[c]
Ie	CH_3	CH_3	CH_3	Quartz, in CH_2Cl_2, 40 h	10	38
If	CH_3	$-(CH_2)_2-$		Quartz, in CH_2Cl_2, 40 h	11	23
Ig	C_6H_5	H	*tert*-C_4H_9	Quartz, in CH_2Cl_2, 50 h	—	[c]
Ih	C_6H_5	H	$CH_2C_6H_5$	Quartz, in CH_2Cl_2, 40 h	24	33
Ii	CH_3	H	C_6H_5	Quartz, in CH_2Cl_2, 50 h	—	[c]

[a] Photolysis was performed with a 350 W high pressure mercury lamp.
[b] The yield was less than 3%.
[c] The starting enone was recovered unchanged.

abstraction to give photo-enols and subsequent oxidative cyclization to give 9-hydroxy-3,4-dihydroanthracenone derivatives.[9] The results are summarized in Table II.

There are three possible routes for the photodealkylation involving the intermediates (A—C) on the basis of published work on aromatic amines and ethers; (i) radical dissociation of the N-C bond into the biradical intermediate (A) (route A),[12] (ii) intermolecular hydrogen abstraction to form the radical cation intermediate (B) by chage transfer interaction with another ketone (route B),[13] and (iii) intramolecular δ-hydrogen abstraction by an excited carbonyl oxygen to give the biradical intermediate (C) (route C).[2–6,14] Although definite evidence could not be obtained, the following results strongly support route C for the dealkylation; (i) photolysis of 2-acetyl-3-*tert*-butylamino- (Ig) and 2-acetyl-3-anilino-5,5-dimethyl-2-cyclohexen-1-ones (Ii) bearing no δ-hydrogens did not cause dealkylation and the

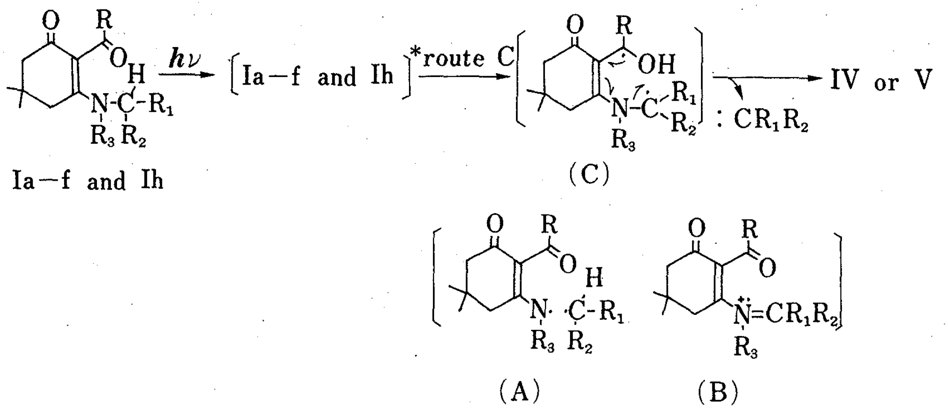


Chart 3

starting enones were recovered unchanged, and (ii) irradiation of the 2-methyl analog instead of the 2-acetyl compound (Ia) gave no dealkylated compound. Route A is eliminated by the first result since the *tert*-butyl radical is the most stable, and route B is ruled out by the result of irradiation of Ia in acetone or in the presence of a carbonyl compound. From a consideration of the above results, the reaction is assumed to begin with intramolecular δ-hydrogen abstraction by the excited carbonyl oxygen to give the biradical intermediate (C), which produces the dealkylation compound (IV or V) with direct elimination of the carbene intermediate or the formation of a radical cation intermediate (B) followed by hydrolysis with a small amount of water contained in the solvent used. In fact, benzaldehyde was isolated by careful examination of the photolysis products of 2-acetyl-3-benzylamino-5,5-dimethyl-2-cyclohexen-1-one (Id). That the photocyclization product could not be obtained at all in our work can be attributed to the instability of the biradical intermediate (C) under the reaction conditions used. More detailed studies are required to account for the above phenomena, including the observed solvent effects.

Experimental

All melting points are uncorrected. Infrared (IR) absorption spectra were recorded on a Shimadzu IR-27 G spectrometer, and nuclear magnetic resonance (NMR) spectra on a Hitachi R-20A or a Hitachi R-22 (90 MHz) spectrometer (with tetramethylsilane as an internal standard). Low- and high-resolution mass spectra (MS) were obtained with a JEOL JMS D-300 instrument, with a direct inlet system. Column chromatography was carried out on Merck Silica-gel 60.

General Procedure for 2-Acyl-3-(alkyl and aryl)amino-5,5-dimethyl-2-cyclohexen-1-ones (Ia—i)——To a stirred solution of 3-methoxy- or 3-chloro-2-acyl-5,5-dimethyl-2-cyclohexen-1-one (IIIa or IIIb, 1 mmol) in methanol (10 ml) was added the corresponding alkylamine (1.2 mmol). The mixture was stirred at room temperature for 2 h and concentrated *in vacuo* to give the crystalline 2-acyl-3-(alkyl or aryl)amino-5,5-dimethyl-2-cyclohexen-1-one (I).

2-Acetyl-3-ethylamino-5,5-dimethyl-2-cyclohexen-1-one (Ib)——This was prepared from IIIa and ethylamine. Recrystallization from petroleum ether gave pure Ib as colorless crystals. *Anal.* Calcd for $C_{12}H_{19}NO_2$: C, 68.86; H, 9.15; N, 6.69. Found: C, 68.59; H, 9.00; N, 6.92. ^{1}H-NMR (10% solution in $CDCl_3$) δ: 1.22 (6H, s, $2\times CH_3$), 1.28 (3H, t, CH_3CH_2), 2.20 (2H, s, CH_2), 2.38 (2H, s, CH_2), 2.45 (3H, s, CH_3CO), 3.35 (2H, m, NCH_2), and 12.55 (1H, br, s NH, disappeared on addition of D_2O).

2-Acetyl-3-isopropylamino-5,5-dimethyl-2-cyclohexen-1-one (Ic)——This was prepared from IIIa and isopropylamine. Recrystallization from water gave pure Ic as colorless crystals. *Anal.* Calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 69.79; H, 9.28; N, 6.34. ^{1}H-NMR (10% solution in $CDCl_3$) δ: 1.04 (6H, s, $2\times CH_3$), 1.22 (3H, d, CH_3), 1.32 (3H, d, CH_3), 2.22 (2H, s, CH_2), 2.41 (2H, s, CH_2), 2.47 (3H, s, CH_3CO), 3.85 (1H, dd, CH), and 12.75 (1H, br s, NH, disappeared on addition of D_2O).

2-Acetyl-3-*tert*-butylamino-5,5-dimethyl-2-cyclohexen-1-one (Ig)——This was prepared from IIIa and *tert*-butylamine. Recrystallization from acetone gave pure Ig as colorless crystals. *Anal.* Calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found: C, 70.72; H, 9.69; N, 6.12. ^{1}H-NMR (10% solution in $CDCl_3$) δ: 1.03 (6H, s, $2\times CH_3$), 1.44 (9H, s, $3\times CH_3$), 2.20 (2H, s, CH_2), 2.51 (2H, s, CH_2), 2.45 (3H, s, CH_3CO), and 13.15 (1H, br s, NH, disappeared on addition of D_2O).

2-Benzoyl-3-benzylamino-5,5-dimethyl-2-cyclohexen-1-one (Ih)——This was prepared from IIIb (described below, 303 mg, 1.2 mmol) and benzylamine (300 mg, 2.8 mmol) in benzene (10 ml). Recrystallization from benzene gave pure Ih as colorless crystals, mp 206—207°C. *Anal.* Calcd for $C_{22}H_{23}NO_2$: C, 79.25; H, 6.95; N, 4.20. Found: C, 79.24; H, 6.98; N, 4.38. ^{1}H-NMR (10% solution in $CDCl_3$) δ: 1.11 (6H, s, $2CH_3$), 2.27 (2H, s, CH_2), 2.51 (2H, s, CH_2), 4.58 (2H, br d, $J=7$ Hz, CH_2N), 7.1—7.6 (10H, m, ArH), and 11.69 (1H, br s, NH).

2-Benzoyl-3-chloro-5,5-dimethyl-2-cyclohexen-1-one (IIIb)——Oxalyl chloride (0.7 ml, 7.9 mmol) was added dropwise to IIb[10] (700 mg, 2.9 mmol) at 0°C. After the reaction mixture had been stirred at 0°C for 1 h, excess oxalyl chloride was removed *in vacuo* to give a solid. The solid was recrystallized from petroleum ether to give a 63% yield (480 mg) of IIIb as colorless crystals, mp 95—96°C. *Anal.* Calcd for $C_{15}H_{15}ClO$: C, 68.57; H, 5.79. Found: C, 68.29; H, 5.68. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1580, 1595, 1615, 1660, and 1680. ^{1}H-NMR (10% solution in $CDCl_3$) δ: 1.23 (6H, s, $2\times CH_3$), 2.42 (2H, s, CH_2), 2.74 (2H, s, CH_2), and 7.3—7.9 (5H, m, ArH).

Typical Procedure for the Photodealkylation of 2-Acyl-3-(alkyl and aryl)amino-5,5-dimethyl-2-cyclohexen-1-ones (Ia—i)——A solution of I (300 mg) in methylene chloride (50 ml) was irradiated in a quartz or Pyrex vessel for the period indicated in Table II. Removal of the solvent *in vacuo* followed by preparative TLC on silica gel (chloroform: methanol = 10: 1) gave the dealkylated product (IV or V) and the starting enone

(I). These products were identical with the corresponding authentic specimens.[7,10] The reaction conditions and yields of the products are listed in Table II.

References and Notes

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