Photochemical Reactions of N,N-Disubstituted α-Oxoamides

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Photochemical reactions of α-oxoamides having various substituents have been studied. Irradiation of *N,N*-dialkyl-α-oxoamides (**1b–d,h**) in methanol yielded the corresponding oxazolidin-4-ones (**2b–d,h**), as main products, while that of *N,N*-dibenzyl-α-oxoamides (**1e** and **1i**) in an aprotic solvent gave the corresponding β-lactams (**3e** and **3j**) predominantly. N-Substituted benzoylformanilides (**1k** and **1l**) afforded type II elimination products on irradiation. Mechanisms of these reactions have also been studied.

Photochemical reactions of α-dicarbonyl compounds such as α-diketones and α-oxoesters have been studied extensively.[1,2] However, those of α-oxoamides have received little attention. Akermark and Johanson investigated the photochemical reaction of an α-oxoamide **1a** and some related cyclic α-oxoamides in relation to their studies on penicillin chemistry, and reported that irradiation of **1a** yielded an oxazolidin-4-one **2a** as a major product accompanied by a small amount of a β-lactam **3a** (Scheme I).[3] Their studies were limited to these cyclic amides, and the mechanism for the formation of the unexpected product **2a** has not been clear.

Recently, we reported the photocyclization of α,β-unsaturated amides to β-lactams.[4] These unsaturated amides are isoelectronic with α-oxoamides. This fact and the absence of a systematic investigation on the photochemistry of α-oxoamides prompted us to study the photochemical reactions of these amides. In this paper, we wish to report on the photochemical reactions of α-oxoamides having various substituents, the solvent effects on the reactions, and the mechanism for the formation of the photoproducts.

Pyruvamides. When *N,N*-diethylpyruvamide (**1b**) in methanol was irradiated in a Pyrex vessel under argon with a high-pressure mercury lamp, 2,5-dimethyl-3-ethyloxazolidin-4-one (**2b**) was obtained in a quantitative yield. When an aprotic solvent such as benzene or acetonitrile was used, the yield of **2b** was poorer (56% in benzene and 45% in acetonitrile) and many unidentified by-products were produced. In all cases, analyses of the reaction mixtures by the IR spectra confirmed the absence of β-lactams. Irradiation of *N,N*-di-*n*-propylpyruvamide (**1c**) and *N,N*-diisopropylpyruvamide (**1d**) in methanol also afforded the corresponding oxazolidin-4-ones **2c** and **2d** almost quantitatively.

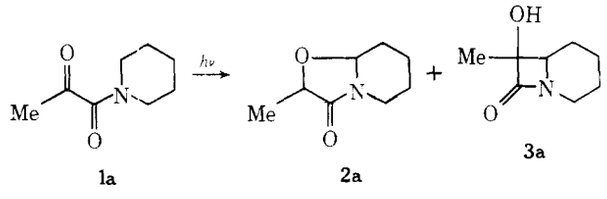
On the other hand, when *N,N*-dibenzylpyruvamide **1e** was irradiated in an aprotic solvent, 1-benzyl-3-hydroxy-3-methyl-4-phenylazetidin-2-one (**3e**) was obtained almost quantitatively. Irradiation of **1e** in methanol gave an oxazolidin-4-one **2e** (78%) as a main product accompanied by small amounts of **3e** (17%). Photochemical reaction of N-substituted pyruvanilides **1f** and **1g** showed similar solvent dependence (see Table I; Scheme II).

Benzoylformamides. Photolysis of *N,N*-diethylbenzoylformamide (**1h**) in methanol gave an oxazolidin-4-one **2h** as a main product, while that in benzene afforded **2h** in a lower yield. *N,N*-Diisopropylbenzoylformamide (**1i**) also gave an oxazolidin-4-one (**2i**) predominantly. However, a small amount of methyl mandelate (in methanol) and mandelanilide (in benzene) was produced in this case.

On the other hand, *N,N*-dibenzylbenzoylformamide (**1j**) yielded a β-lactam **3j** exclusively, both on irradiation in benzene and methanol.

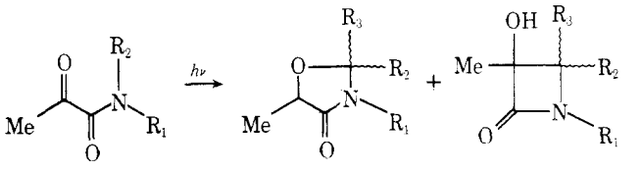
Finally, N-substituted benzoylformanilides **1k** and **1l** showed somewhat different photochemical behavior from other α-oxoamides. Irradiation of these anilides gave methyl

Scheme I



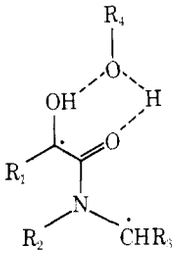
1a **2a** **3a**

Scheme II

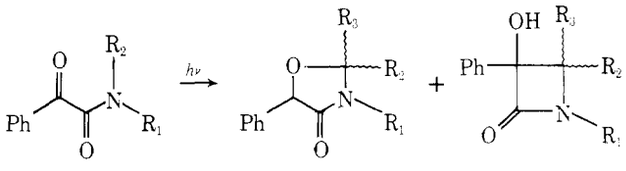


1 **2** **3**

b, $R_1 = R_2$ = Et — b, R_1 = Et; R_2 = Me; R_3 = H
c, $R_1 = R_2$ = *n*-Pr — c, R_1 = *n*-Pr; R_2 = Et; R_3 = H
d, $R_1 = R_2$ = *i*-Pr — d, R_1 = *i*-Pr; $R_2 = R_3$ = Me
e, $R_1 = R_2 = CH_2Ph$ — e, $R_1 = CH_2Ph$; R_2 = Ph; R_3 = H
f, R_1 = Et; R_2 = Ph — f, R_1 = Ph; R_2 = Me; R_3 = H
g, $R_1 = CH_2Ph$; R_2 = Ph — g, $R_1 = R_2$ = Ph; R_3 = H

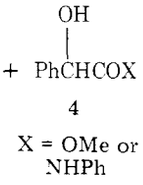


Scheme III



1 **2** **3**

h, $R_1 = R_2$ = Et — h, R_1 = Et; R_2 = Me; R_3 = H
i, $R_1 = R_2$ = *i*-Pr — i, R_1 = *i*-Pr; $R_2 = R_3$ = Me
j, $R_1 = R_2 = CH_2Ph$ — j, $R_1 = CH_2Ph$; R_2 = Ph; R_3 = H
k, R_1 = Et; R_2 = Ph — k, R_1 = Ph; R_2 = Me; R_3 = H
l, $R_1 = CH_2Ph$; R_2 = Ph — l, $R_1 = R_2$ = Ph; R_3 = H



4

X = OMe or NHPh

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Table I. Photochemical Reaction of Pyruvamides

Reactant	Registry no.	Solvent	Yields, % 2	3
1b	22381-21-1	MeOH	100	*a*
1b		C_6H_6	56	*a*
1b		MeCN	45	*a*
1c	38382-90-0	MeOH	~100	*a*
1d	64201-02-1	MeOH	~100	*a*
1d		C_6H_6	86	*a*
1e	64201-00-9	MeOH	78	17
1e		C_6H_6	*a*	94
1f	61110-51-8	MeOH	58	*b*
1f		C_6H_6	*b*	46
1g	64201-20-3	MeOH	13	40
1g		C_6H_6	*a*	~100

[a] Not detected. [b] Trace.

Table II. Photochemical Reaction of Benzoylformamides

Reactant	Registry no.	Solvent	Yields, % 2	3	4
1h	34906-86-0	MeOH	73[b]	*a*	*a*
1h		C_6H_6	24[b]	7[b]	*a*
1i	51804-83-2	MeOH	58	22	16[c]
1i		C_6H_6	62	*e*	29[d]
1j	40991-79-5	MeOH	*a*	86	*a*
1j		C_6H_6	*a*	~100	*a*
1k	64201-19-0	MeOH	11	5	36[c]
1k		C_6H_6	14	12	34[d]
1l	64201-18-9	MeOH	*a*	27	35[c]
1l		C_6H_6	*a*	40	24[d]

[a] Not detected. [b] Not completely purified. [c] Methyl mandelate. [d] Mandelanilide. [e] Trace.

mandelate and mandelanilide as major products (see Scheme III).

Mechanism. The formation of the β-lactam, methyl mandelate, and mandelanilide can be explained in terms of a type II photoprocess. A biradical **5** is formed initially by γ-hydrogen abstraction by the ketone carbonyl oxygen. Cyclization of the biradical yields the lactam **3**, while C–N bond cleavage of it affords a hydroxy ketene **6** and an imine **7**. Addition of methanol to **6** gives methyl mandelate, and that of aniline which is formed by hydrolysis of **7** yields mandelanilide.[5] A similar reaction of ethyl benzoylformate to methyl mandelate has been reported by Huyser and Neckers.[2c] Intermediacy of the hydroxyketene **6** in the formation of mandelanilide was confirmed as follows. When **1k** in benzene was irradiated in the presence of an excess of *p*-toluidine, mandel-*p*-toluidide was produced instead of mandelanilide.

The formation of the oxazolidin-4-one (**2**) can be explained as shown in Scheme V. The biradical **5** undergoes 1,4-hydrogen migration to yield another biradical **8**. The biradical cyclizes to an enol **9** which ketonizes to give **2**. Analogous 1,4-hydrogen migration in photocyclization of α-diketones has been reported.[6] Some evidence in support of the intermediacy of the enol **9** was obtained from experiments using methanol-d_1. When a solution of **1b** in methanol-d_1 was irradiated, a deuterated product (**2b**-d_1) was obtained in a quantitative yield. On the other hand, the formation of **2b**-d_1 was not observed when a solution of **2b** in methanol-d_1 was irradiated or heated to 150 °C. An alternative path b, which involves hydrogen abstraction by the amide carbonyl oxygen through a five-membered transition state followed by rotation of the C–N bond, seems to be improbable because (a) reports on intramolecular hydrogen abstraction by an amide carbonyl group are few[7] and (b) intramolecular hydrogen abstraction through a five-membered transition state is the rarely observed process (Schemes IV and V).[8]

Solvent Effects. The formation of the oxazolidin-4-one **2** is apparently enhanced by alcoholic solvents. The photocyclization of **1b** to **2b** proceeded quantitatively in isopropyl or *tert*-butyl alcohol as in the case of methanol. Irradiation of **1b** in benzene containing 5% of methanol or in acetonitrile containing 5% of water gave the same result. It is well known that alcohols, water, and pyridine enhance a type II reaction of ketones by suppressing reverse hydrogen transfer in the biradical intermediate.[9] However, addition of pyridine to a benzene solution of **1b** showed no influence upon the photoreaction, and the yield of **2b** was still poor as in the case of a benzene solution. These results suggest that the alcohols or water play some roles in the 1,4-hydrogen migration step. The migration might proceed intermolecularly in hydroxylic solvents as shown below.

Substituents Effects. Substituents which stabilize the 1,4-biradical **5** seem to enhance the formation of the β-lactam **3**. Thus, *N,N*-Dibenzyl-α-oxoamides **1e** and **1j** gave the lactams **3e** and **3j** almost quantitatively on irradiation in an aprotic solvent. Furthermore, irradiation of *N,N*-dialkylbenzoylformamide **1h** and **1i** gave some amounts of the lactam **3h** and **3i**, while *N,N*-dialkylpyruvamide **1b** and **1d** did not give the corresponding β-lactams. Stabilization of the biradical **5** is presumed to make the 1,4-hydrogen migration inefficient.

Quantum Yields. The quantum yield for the cyclization of **1b** (oxazolidinone formation) was 0.66 in methanol. The reaction was sensitized by 4-methoxyacetophenone ($\Phi = 0.70$, $E_T = 72$ kcal) and less efficiently by 4-aminoacetophenone ($\Phi = 0.23$, $E_T = 65$ kcal), but not by Michler ketone ($E_T = 62$ kcal) or 4-phenylacetophenone ($E_T = 61$ kcal). On the other hand, the quantum yield for the reaction of **1j** (β-lactam formation) was 0.21 in benzene. The photoreaction was also sensitized by 4-methoxyacetophenone ($\Phi = 0.35$) but very inefficiently by 2-acetonaphthone ($\Phi = 0.04$, $E_T = 59$ kcal).

The above results indicate that the triplet states of **1b** and **1j** are reactive. However, both reactions were not quenched by high concentrations (1 M) of 1,3-pentadiene. This fact suggests that the photoreactions of **1b** and **1j** involve either the triplet reaction faster than bimolecular quenching or the singlet reaction faster than intersystem crossing.

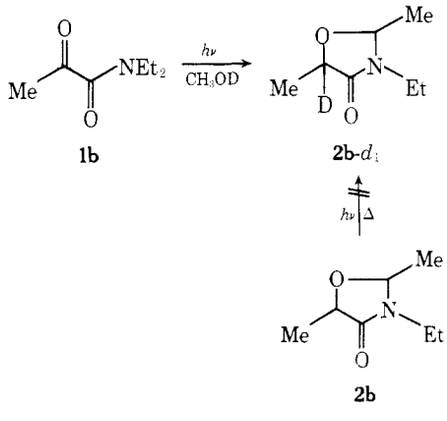
Experimental Section

All melting and boiling points were uncorrected. IR and NMR spectra were obtained on Hitachi EPI and R-20 spectrometers, respectively. A Ushio 450-W high-pressure mercury lamp was used as an irradiation source.

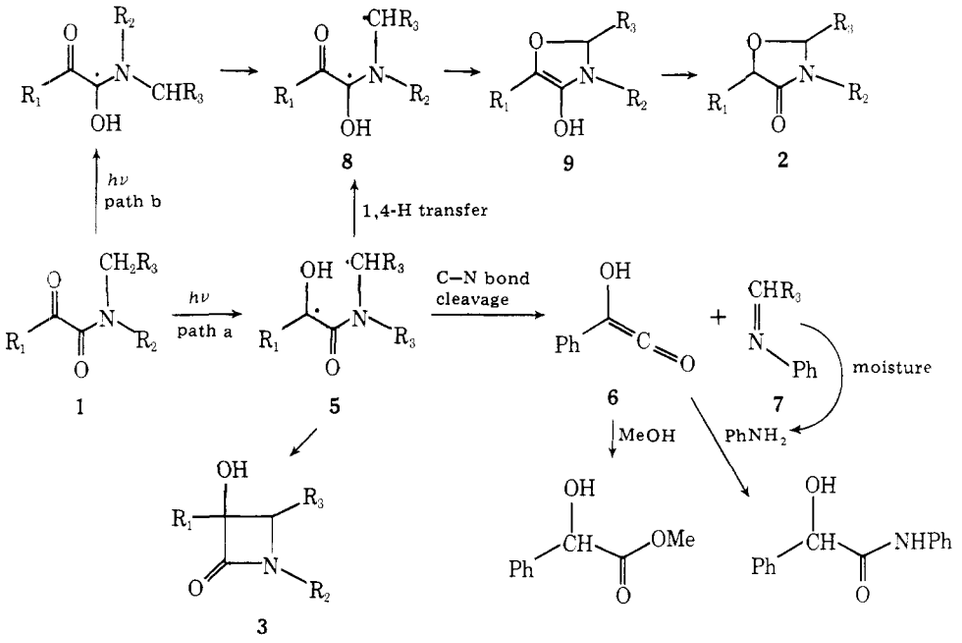
Materials. The oxoamides **1b–1l** were prepared according to the method in the literature.[10]

General Procedure for Photoreactions of α-Oxoamides. A

Scheme IV



Scheme V



solution of the α-oxoamide 1 (1%) was irradiated in a Pyrex vessel under argon with a high-pressure mercury lamp for 10–20 h. After removal of the solvent, the residue was chromatographed on silica gel. Elution with benzene–ethyl acetate afforded the photoproducts.

2,5-Dimethyl-3-ethyloxazolidin-4-one (2b): bp 60–65 °C (bath temp)/5 Torr; IR (neat) 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.16 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 1.42 (d, J = 7.5 Hz, 3 H, 5-CH_3), 1.45 (d, J = 5.5 Hz, 3 H, 2-CH_3), 3.75 (q of AB q, J_q = 7.5 Hz, J_{ABq} = 13 Hz, 2 H, CH_2), 4.25 (d of q, J_d = 1.5 Hz[11], J_q = 7.5 Hz, 1 H, 5-H), 5.18 (d of q, J_d = 1.5 Hz,[11] J_q = 5.5 Hz, 1 H, 2-H).

Anal. Calcd for $C_7H_{13}O_2N$: C, 58.71; H, 9.15; N, 9.78. Found:[12] C, 58.27; H, 9.21; N, 9.62.

5-Deuterio-2,5-dimethyl-3-ethyloxazolidin-4-one (2b-d_1): IR (neat) 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.16 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 1.42 (s, 3 H, 5-CH_3), 1.45 (d, J = 5.5 Hz, 3 H, 2-CH_3), 3.37 (q of AB_q, J_q = 7.5 Hz, J_{ABq} = 13 Hz, 2 H, CH_2), 5.18 (q, J = 5.5 Hz, 1 H, 2-H).

2-Ethyl-5-methyl-3-*n*-propyloxazolidin-4-one (2c): bp 90–95 °C (bath temp)/5 Torr; IR (neat) 1710 cm^{-1}; NMR ($CDCl_3$) δ 0.94 (t, J = 7 Hz, 6 H, two CH_2CH_3), 1.43 (d, J = 7 Hz, 3 H, 5-CH_3), 1.5–2.0 (m, 4 H, two CH_2), 3.24 (t of AB q, J_t = 8 Hz, J_{ABq} = 14 Hz, 2 H, N-CH_2), 4.31 (d of q, J_d = 1.8 Hz, J_q = 7 Hz, 1 H, 5-H), 5.09 (m, 1 H, 2-H).

Anal. Calcd for $C_9H_{17}O_2N$: C, 63.13; H, 10.01; N, 8.18. Found: C, 62.86; H, 10.15; N, 8.18.

2,2,5-Trimethyl-3-isopropyloxazolidin-4-one (2d): mp 34–36 °C; IR (neat) 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.27–1.37 (five CH_3), 3.30 (sep, J = 7 Hz, 1 H, N-CH), 4.11 (q, J = 7 Hz, 1 H, 5-H).

Anal. Calcd for $C_9H_{17}O_2N$: C, 63.13; H, 10.01; N, 8.18. Found: C, 62.78; H, 9.84; N, 8.26.

3-Benzyl-5-methyl-2-phenyloxazolidin-4-one (2e): bp 140–150 °C (bath temp)/5 Torr; IR (neat) 1710 cm^{-1}; NMR ($CDCl_3$) δ 1.52 (d, J = 7 Hz, 3 H, CH_3), 3.40 and 4.87 (AB q, J = 15 Hz, 2 H, CH_2), 4.30 (br q, J = 7 Hz, 1 H, 5-H), 5.55 (br s, 1 H, 2-H), 6.87–7.60 (m, 10 H, aromatic protons).

Anal. Calcd for $C_{17}H_{17}O_2N$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.42; H, 6.47; N, 5.26.

1-Benzyl-3-hydroxy-3-methyl-4-phenylazetidin-2-one (3e): mp 135.5–137 °C; IR (KBr) 3350, 1735 cm^{-1}; NMR ($CDCl_3$) δ 1.51 (s, 3 H, CH_3), 3.43 (s, 1 H, OH), 3.80 and 4.86 (AB q, J = 15 Hz, 2 H, CH_2), 4.28 (s, 1 H, 4-H), 6.91–7.51 (m, 10 H, aromatic protons).

Anal. Calcd for $C_{17}H_{17}O_2N$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.36; H, 6.41; N, 5.17.

2,5-Dimethyl-3-phenyloxazolidin-4-one (2f): mp 106–109 °C; IR (KBr) 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.43 (d, J = 5.5 Hz, 3 H, 2-CH_3), 1.53 (d, J = 6.5 Hz, 3 H, 5-CH_3), 4.42 (d of q, J_d = 1.5 Hz, J_q = 6.5 Hz, 1 H, 5-H), 5.70 (d of q, J_d = 1.5 Hz, J_q = 5.5 Hz, 1 H, 2-H), 7.10–7.50 (m, 5 H, aromatic protons).

Anal. Calcd for $C_{11}H_{13}O_2N$: C, 69.09; H, 6.85; N, 7.33. Found: C, 69.27; H, 6.89; N, 7.47.

3,4-Dimethyl-3-hydroxy-1-phenylazetidin-2-one (3f): mp 141–142 °C; IR (KBr) 3340, 1730 cm^{-1}; NMR ($CDCl_3$) δ 1.40 (d, J = 7 Hz, 3 H, 4-CH_3), 1.47 (s, 3 H, 3-CH_3), 4.12 (q, J = 7 Hz, 1 H, 4-H), 7.20–7.40 (m, 5 H, aromatic protons).

Anal. Calcd for $C_{11}H_{13}O_2N$: C, 69.09, H, 6.85; N, 7.33. Found: C, 68.70; H, 6.78; N, 7.04.

2,3-Diphenyl-5-methyloxazolidin-4-one (2g): mp 97–98 °C; IR (KBr) 1690 cm^{-1}; NMR ($CDCl_3$) δ 1.60 (d, J = 7 Hz, 3 H, CH_3), 4.58 (q, J = 7 Hz, 1 H, 5-H), 6.41 (s, 1 H, 2-H), 7.19 and 7.33 (each s, each 5 H, aromatic protons).

Anal. Calcd for $C_{16}H_{15}O_2N$: C, 75.87; H, 5.97; N, 5.53. Found: C, 76.09; H, 5.95; N, 5.55.

1,4-Diphenyl-3-hydroxy-3-methylazetidin-2-one (3g): mp 153–154 °C; IR (KBr) 3320, 1712 cm^{-1}; NMR ($CDCl_3$) δ 1.67 (s, 3 H, CH_3), 3.04 (s, 1 H, OH), 4.90 (s, 1 H, 4-H), 6.85–7.43 (m, 10 H, aromatic protons).

Anal. Calcd for $C_{16}H_{15}O_2N$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.94; H, 5.84; N, 5.54.

3-Ethyl-2-methyl-5-phenyloxazolidin-4-one (2h) was not completely purified because it decomposed on standing or distillation: IR (neat) 1705 cm^{-1}; NMR ($CDCl_3$) δ 1.17 (t, J = 7 Hz, 3 H, CH_2CH_3), 1.57 (d, J = 6 Hz, 3 H, 2-CH_3), 3.35 (m, 2 H, CH_2), 5.16 (br s, 1 H, 5-H), 5.35 (m, 1 H, 2-H), 7.15–7.45 (m, 5 H, aromatic protons).

1-Ethyl-3-hydroxy-4-methyl-3-phenylazetidin-2-one (3h) did not crystallize and was not completely purified: IR (neat) 3350, 1725 cm^{-1}; NMR ($CDCl_3$) δ 0.78 (d, J = 6 Hz, 3 H, 4-CH_3), 1.13 (t, J = 7 Hz, 3 H, CH_2CH_3), 3.22 (m, 2 H, CH_2), 3.82 (q, J = 6 Hz, 1 H, 4-H), 7.26 (s, 5 H, aromatic protons).

2,2-Dimethyl-3-isopropyl-5-phenyloxazolidin-4-one (2i) was not completely purified because it was readily oxidized on standing to give a peroxide whose structure is not clear at present: IR (neat) 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.39 and 1.49 (each d, each 3 H, J = 4 Hz, isopropylmethyls), 1.52 and 1.55 (each s, each 3 H, 3-Me_2), 3.37 (m, 1 H, N-CH), 5.16 (s, 1 H, 5-H), 7.20–7.63 (m, 5 H, aromatic protons). The peroxide showed a positive KI–starch test: mp 145–146 °C; IR (KBr) 3175, 1695 cm^{-1}. Anal. Calcd for $C_{14}H_{19}O_2N{\cdot}O_2$: C, 63.38; H, 7.21; N, 5.28. Found: C, 63.54; H, 7.16; N, 5.27.

4,4-Dimethyl-3-hydroxy-1-isopropyl-3-phenylazetidin-2-one (3i): mp 140–141 °C; IR (KBr) 3250, 1735 cm^{-1}; NMR ($CDCl_3$) δ 0.82 (s, 3 H, 4-CH_3 cis to Ph), 1.25 (s, 3 H, 4-CH_3 trans to Ph), 1.41 (d, J = 7 Hz, 6 H, isopropylmethyls), 3.58 (sep, J = 7 Hz, 1 H, N-CH), 4.50 (s, 1 H, OH), 7.28 (s, 5 H, aromatic protons).

Anal. Calcd for $C_{14}H_{19}O_2N$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.31; H, 8.28; N, 5.91.

3,4-Diphenyl-1-benzyl-3-hydroxyazetidin-2-one (3j): mp 100–102 °C; IR (KBr) 3325, 1730 cm^{-1}; NMR ($CDCl_3$) δ 3.86 and 4.94 (AB q, J = 15 Hz, 2 H, CH_2), 3.95 (s, 1 H, OH), 4.54 (s, 1 H, 4-H), 6.90–7.50 (m, 10 H, aromatic protons).

Anal. Calcd for $C_{22}H_{19}O_2N$: C, 80.22; H, 5.81; N, 4.25. Found: C, 80.34; H, 5.82; N, 4.19.

3,5-Diphenyl-2-methyloxazolidin-4-one (2k): mp 105.5–107 °C; IR (KBr) 1715 cm^{-1}; NMR ($CDCl_3$) δ 1.57 (d, J = 5 Hz, 3 H, CH_3),

5.35 (br s, 1 H, 5-H), 5.91 (br q, J = 5 Hz, 1 H, 2-H), 7.00–7.70 (m, 10 H, aromatic protons).

Anal. Calcd for $C_{16}H_{15}O_2N$: C, 75.87; H, 5.97; N, 5.53. Found: C, 76.03; H, 6.00; N, 5.55.

1,3-Diphenyl-3-hydroxy-4-methylazetidin-2-one (3k): mp 175–176.5 °C; IR (KBr) 3300, 1725 cm^{-1}; NMR ($CDCl_3$) δ 1.03 (d, J = 6 Hz, 3 H, CH_3), 4.03 (s, 1 H, OH), 4.36 (q, J = 6 Hz, 1 H, 4-H), 6.95–7.55 (m, 10 H, aromatic protons).

Anal. Calcd for $C_{16}H_{15}O_2N$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.98; H, 6.01; N, 5.51.

1,3,4-Triphenyl-3-hydroxyazetidin-2-one (31): mp 172–174 °C; IR (KBr) 3550, 3300, 1735, 1715 cm^{-1}; NMR ($CDCl_3$) δ 5.19 (s, 1 H, 4-H), 6.90–7.72 (m, 15 H, aromatic protons).

Anal. Calcd for $C_{21}H_{17}O_2N$: C, 79.98; H, 5.43; N, 4.44. Found: C, 79.83; H, 5.24; N, 4.42.

Quantum Yield Determinations. Benzophenone–benzhydrol actinometry was used for quantum yield determination. The 313-nm line was isolated with a filter solution containing 0.002 M potassium chromate in 5% aqueous potassium carbonate. Samples (0.10 M solution) in Pyrex tubes were degassed to ca. 10^{-3} mm in three freeze–thaw cycles and sealed. The samples were irradiated individually in succession. Photolyses were carried out to 30–50% conversion. The degree of reaction was determined by NMR spectroscopy. Concentrations of the sensitizer were adjusted so that 5% or less of the incident light was absorbed by the oxoamides (**1b** and **1j**).

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Registry No.—**2b,** 64201-17-8; **2b-d_1,** 64201-16-7; **2c,** 64201-15-6; **2d,** 64201-14-5; **2e,** 64201-13-4; **2f,** 64201-12-3; **2g,** 64201-11-2; **2h,** 64201-10-1; **2i,** 64201-09-8; **2k,** 64201-08-7; **3e,** 64201-07-6; **3f,** 64201-06-5; **3g,** 64201-05-4; **3h,** 64201-04-3; **3c,** 64201-03-2; **3j,** 64201-01-0; **3k,** 64200-99-3; **3l,** 64201-21-4.

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Regio- and Stereoselectivity of the Formation of Halohydrins from 3-Methyl- and 3-*tert*-Butylcyclohexene and from the Corresponding Epoxides

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In order to explain large variations in product regio- and stereochemistry observed in several types of ionic additions to cycloalkenes involving different reagents, the product compositions obtained in some reactions leading from 3-methyl- and 3-*tert*-butylcyclohexene to chlorohydrins, bromohydrins, and bromoacetoxy derivatives have been investigated in detail. Whereas with *N*-chlorosuccinimide, preformed HOBr, or CH_3COOBr electrophilic attack was nonstereoselective for the methyl and anti stereoselective for the *tert*-butyl derivative, with NBS a high syn stereoselectivity was observed for the attack by electrophilic bromine, which indicated that repulsive steric effects operating during the nucleophilic step should be the main product-determining factor in the latter case, and that this step should be the rate-limiting one. Support of this hypothesis was brought by the reactions of the corresponding epoxides with HBr and HCl, since the observed regioselectivities of these reactions, which can be taken as models for the nucleophilic opening of the halonium intermediates of the electrophilic additions to olefins, are in agreement with those deduced from the product compositions of the latter reactions.

As a part of a research program concerning the influence of steric, polar, and conformational effects on electrophilic additions involving different types of reagents and different mechanisms,[1-4] we undertook a comparative product and kinetic study of additions to 3-alkylcyclohexenes involving epihalonium ion intermediates and of the ring-opening reactions of diastereoisomeric couples of 3-alkyl-1,2-epoxycyclohexanes, which can be taken as models for the nucleophilic steps of the additions. A methyl and a *tert*-butyl group were chosen as alkyl substituents having, respectively, a relatively small and very large size. In this paper, we report the results of the product study.[5]

Results

3-*tert*-Butylcyclohexene Derivatives. As reported by Richer,[6] the epoxidation of 3-*tert*-butylcyclohexene (**1a**) with peroxyacids yielded a 90:10 mixture of the trans and cis epoxides **2a** and **3a.** Opening of this mixture with hydrogen bromide afforded three isomeric bromohydrins, which were separated by column chromatography. The most abundant compound was identified as the diequatorial bromohydrin **5c** on the basis of its NMR spectrum[7] and of its conversion back to **2a** by treatment with base. The other two isomers were trans diaxial bromohydrins, as shown by the narrow signals, due to equatorial protons α to bromine and hydroxyl, appearing in the medium-field part of their NMR spectra; they were identified as **4c** and **6c** by conversion, respectively, into the epoxides **2a** and **3a.**

This method was convenient for the preparation of the pure trans epoxide **2a,** since the separation of bromohydrin **5c** from

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