

Metal-catalysed Organic Photoreactions. Photoreaction of $\alpha\beta$ -Unsaturated Ketones in Alcohols in the Presence of Titanium(IV) Chloride¹

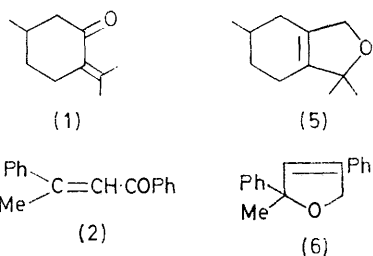
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When $\alpha\beta$ -unsaturated ketones were irradiated in alcohols in the presence of titanium(IV) chloride, a coupling reaction between the carbonyl carbon atom and the α -carbon atom of the alcohol took place, giving dihydrofurans or carbonyl compounds in moderate yields.

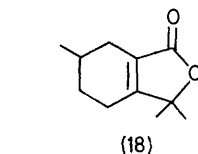
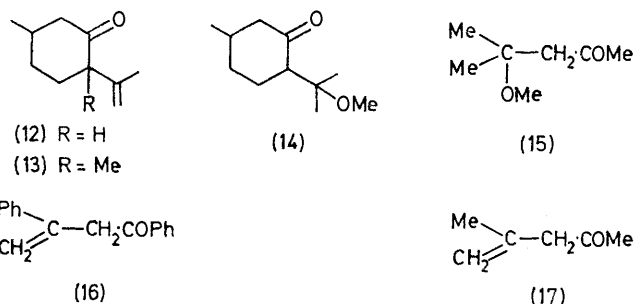
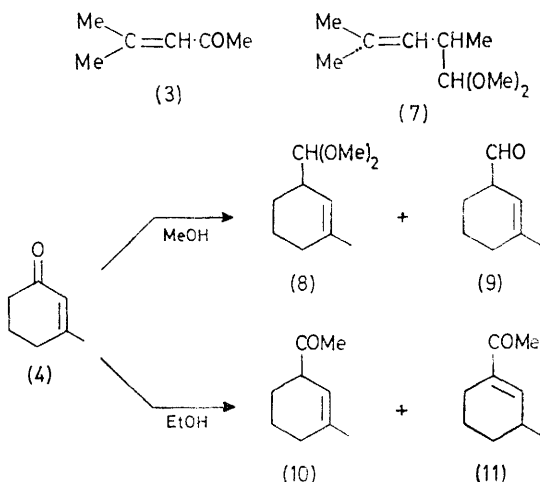
$\alpha\beta$ -UNSATURATED ketones undergo various types of photoreaction in solution, depending on the overall molecular structure, the solvent, the presence or absence of another reactant, and the multiplicity of the excited state. Hart² classified the reactions into six types: (i) β - or γ -hydrogen abstraction, (ii) dimerization to cyclobutane, (iii) inter- or intra-molecular oxetan formation, (iv) isomerization to 'lumi-product', (v) *cis-trans*-isomerization, and (vi) Type I cleavage. Coupling with solvent molecules has received less attention, although a few examples have been described.³ We now report that the coupling reaction proceeds effectively when the irradiation is carried out in the presence of titanium(IV) chloride in alcohols.

titanium(IV) chloride, two types of reaction were observed: (A) cyclization to dihydrofuran, and (B) formation of aldehyde (as acetal) or ketone. The

Type A



Type B



reactions of pulegone (1) and dypnone (2) belong to type A, affording compounds (5) and (6), respectively; those of mesityl oxide (3) and 3-methylcyclohex-2-enone (4) belong to type B, affording compounds (7), and (8) and (9) [or (10) and (11) when ethanol was used as solvent], respectively. These reactions are notable in that a one- (or two-) carbon unit is introduced at the carbonyl carbon atom of the substrate while the carbonyl function is lost. Yields and by-products are summarized in Table 1. Each reaction is fairly clean and the amounts of other products not shown in the Table are negligible, as revealed from the n.m.r. and g.l.c. analyses. The yields of compounds (5), (6), (8), and (9) shown in the Table may be lower than the actual yields because of loss during distillation.

The reaction medium was acidic owing to the formation of hydrogen chloride from titanium(IV) chloride and the alcohol. Irradiation of these ketones in the presence of hydrogen chloride or boron trifluoride-ether complex, or leaving the solution in the presence of titanium(IV) chloride in the dark, resulted in either addition of the alcohol to the double bond, or isomerization to a $\beta\gamma$ -

RESULTS AND DISCUSSION

When the $\alpha\beta$ -unsaturated ketones (1)–(4) were irradiated in methanol or ethanol in the presence of

¹ Preliminary report, T. Sato, G. Izumi, and T. Imamura, *Tetrahedron Letters*, 1975, 2191.

² H. Hart, D. L. Dean, and D. N. Buchanan, *J. Amer. Chem. Soc.*, 1973, **95**, 6294.

³ (a) Z. Yoshida and M. Kimura, *Tetrahedron*, 1975, **31**, 221; (b) E. F. Ullman and R. Weinkam, *J. Amer. Chem. Soc.*, 1970, **92**, 5256; (c) J. S. Bradshaw, *J.C.S. Chem. Comm.*, 1973, 504; (d) R. C. Cookson, J. Hudec, and N. A. Mirza, *Chem. Comm.*, 1968, 180.

unsaturated ketone, but no trace of the products (5)—(11) was detected (Table 2). Presumably the by-products shown in Table 1 arose from thermal or photochemical reactions induced by the acid. The acidic conditions, however, seem essential for the present reaction: double-bond migration to the $\beta\gamma$ -position was the sole reaction of mesityl oxide on irradiation in

ation observed in the hydrogen chloride-catalysed photoreaction.

The photoreaction of the ketone (4) has been reported to result in dimerization⁷ or isomerization of the double bond to the $\beta\gamma$ -position.⁸ Although a complete product analysis for the photolysis of (4) in the presence of hydrogen chloride has not been achieved, n.m.r. and g.l.c.

TABLE 1
Titanium(IV) chloride-catalysed photolyses of the ketones (1)—(4)

Ketone	Solvent	Irrad. period (h)	Product and % isolated yield		
			Ti-cat. product	By-product	Starting ketone
(1)	MeOH	8	(5) 62	(12) 2, (14) 5	11%
(2)	MeOH	24	(6) 53	Unknowns (12 and 15%) ^a	0
(3) ^a	MeOH	6	(7) 41	(15) 41	18
(4)	MeOH	7	(8) 35, (9) 15		0
	MeOH ^a	7	(8) 61, (9) 30	Unknown (9%)	0
	EtOH ^a	3	(10) 49, (11) 12	Unknown (14%)	1

^a Yields were determined from the peak areas of ¹H n.m.r. spectra and/or g.l.c. of the crude reaction mixture. Yields of unknown substances refer to weight per cent, assuming the molecular weights are the same as those of the starting materials.

TABLE 2
Hydrochloric acid- or boron trifluoride-catalysed photolyses or titanium(IV) chloride-catalysed dark reactions of the ketones (1)—(4)

Ketone	Solvent	Product and % yield ^a		
		Irrad. HCl ^b	Irrad. BF ₃ ^b	Dark TiCl ₄
(1)	MeOH	(1) 41, (12) 33, (14) 21	(1) 60, (12) 20, (14) 15	(1) 60, (12) 7, (14) 29 ^c
(2)	MeOH	(16) 100		<i>cis</i> -(2) 45, <i>trans</i> -(2) 55
(3)	MeOH	(3) 73, (15) 27	(3) 50, (15) 50	(3) 30, (15) 70
(4)	MeOH	(4) 95, unknown (5%)		(4) 100
	EtOH	(4) 80, unknown (9%)		

^a See footnote *a* of Table 1. ^b Irradiations were carried out under the same conditions as those of TiCl₄-catalysed photolyses. Equal volumes of 12N-HCl [3N-HCl in the case of (4)] or BF₃-Et₂O were used in place of TiCl₄. ^c When the solution was refluxed for 3 h, 3-methylcyclohexanone was obtained in 70% yield. Small amounts of compounds (12) and (14) were also detected.

neutralized medium, containing only tetramethoxytitanium as catalyst. The present reaction is characteristic of $\alpha\beta$ -unsaturated ketones; the $\beta\gamma$ -unsaturated ketone (13) was unaffected under these conditions.

Photoreactions of compounds (1),⁴ (12),⁵ and (13)⁶ are known to give cyclobutanol derivatives. However, no traces of these products were identified in the present reaction.

Titanium(IV) chloride accelerates the reaction: irradiation of pulegone (1) in the absence of titanium(IV) chloride under otherwise identical conditions resulted in no change.

The dihydrofuran (5) was identified from spectroscopic data and by converting it into a lactone (18) by heating in air.

Isomerization to the $\beta\gamma$ -unsaturated ketone (16) was the major reaction path in the case of dypnone (2) in the early stages of titanium-catalysed photolysis, but both isomers [(2) and (16)] had disappeared completely after 24 h. The dark reaction of dypnone (2) in the presence of titanium(IV) chloride resulted in exclusive *cis-trans*-isomerization, in contrast with the double bond isomeriz-

analyses definitively showed that no trace of (8) or (9) was present in the crude reaction mixture. When the acetal (8) was treated with dilute hydrochloric acid, hydrolysis accompanied by double bond isomerization occurred and the aldehyde (19) was isolated as the only product. Its structure was deduced from spectroscopic data and the m.p. of its semicarbazone. The same type of reaction was observed when the photolysis was carried out in ethanol, although the products in this case were ketones rather than acetals. Although the ketone (10) was isolable as such by preparative g.l.c., it was isomerized to (11) upon heating in ethanol-hydrogen chloride.

The present reaction can be visualized as a formal hydrogen abstraction by ketone from alcohol, followed by cross-coupling and dehydration (see Scheme). Although this Scheme sounds reasonable, it deserves further consideration in view of the following points. (a) Although hydrogen abstraction by a ketone from an alcohol is well known, cross-coupling to form a mixed pinacol is rare and ketyl radical dimerization is usually preferred even though the ketyl radical and the α -hydroxy-carbon radical from the alcohol are created in close proximity.⁹ (b) Coupling reaction between $\alpha\beta$ -unsaturated ketones

⁷ H. Ziffer and B. W. Matthews, *Chem. Comm.*, 1970, 294.

⁸ W. G. Dauben, G. W. Shaffer, and N. D. Vietmeyer, *J. Org. Chem.*, 1968, **33**, 4060.

⁹ S. A. Weiner, *J. Amer. Chem. Soc.*, 1971, **93**, 425.

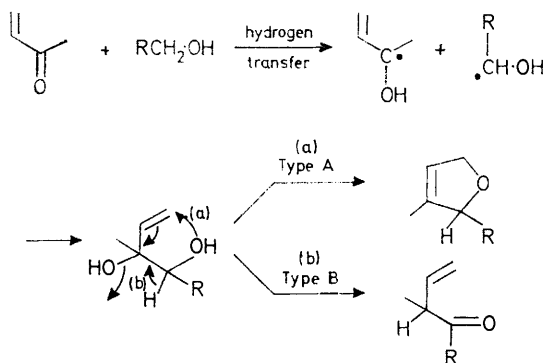
⁴ M. Kawai and K. Naya, *Chem. Letters*, 1972, 389.

⁵ T. Matsui, A. Komatsu, and T. Moroe, *Bull. Chem. Soc. Japan*, 1967, **40**, 2204.

⁶ R. C. Cookson, J. Hudec, A. Szabo, and G. E. Usher, *Tetrahedron*, 1968, **24**, 4353.

and alcohols or ethers are known only in a few cases, and all the known reactions proceed on the β -carbon atom of the ketone.³ The reaction with aliphatic amines is also known to proceed on the β -carbon atom.^{3a}

The abnormality observed in the present reaction may be ascribable to the specific character of titanium. In view of the characteristic role of copper as the mediator for electron transfer from an alcohol to an isoxazole ring,¹⁰ we suggest a similar metal- and photo-assisted electron transfer from alcohol to carbonyl compounds. The electron transfer and the succeeding proton transfer from alcohol to ketone furnish the carbonyl carbon atom and the α -carbon atom of the alcohol with radical character, inducing coupling to form a new C-C bond.



SCHEME

All these processes are considered to be proceeding consecutively within the co-ordination sphere of titanium, thus providing a circumstance favourable for cross-coupling.

When irradiation in the presence of titanium(IV) chloride was carried out while air was bubbled through the mixture, the present reaction did not take place. Under these conditions, formation of dilactone¹¹ and *cis-trans* isomerization, in the case of (2), and addition of methanol to give (15), in the case of (3), were the main reactions. These facts are consistent with the present Scheme which involves reduction and oxidation of the metal.

EXPERIMENTAL

Instrumentation was the same as reported previously.¹¹ ¹³C N.m.r. spectra were obtained with a JEOL PS 100 spectrometer equipped with SD-HC hetero spin-decoupler (CW type) for neat samples. The chemical shifts (δ_0) were determined with reference to external chloroform, and are expressed in p.p.m. from Me₄Si.

All irradiations were carried out on solutions in Pyrex tubes with a high-pressure mercury vapour lamp [Ushio UM 452 (450 W)] and at running-water temperature. After the irradiation or thermal reaction, the solution was poured into water and shaken with carbon tetrachloride. The extract was dried (Na₂SO₄) and the solvent was removed *in vacuo*. The residual oil was treated as indicated.

¹⁰ T. Sato, K. Yamamoto, K. Fukui, K. Saito, K. Hayakawa, and S. Yoshiie, preceding paper.

Photolysis of Pulegone (1) in Methanol-Titanium(IV) Chloride.—Pulegone [(1), containing 7.5% isopulegone (12) and 2.8% of unknown substance] (1.2 ml) was added to a cooled solution of titanium tetrachloride (1.2 ml) in methanol (60 ml), and the solution was irradiated for 8 h. Vacuum distillation afforded two fractions. Fraction (i), b.p. 79–80° at 10 mmHg (0.8 g), was almost pure cyclic ether (5), and fraction (ii), b.p. 80–95° at 10 mmHg (0.6 g), was mainly (5), accompanied by small amounts of compounds (1), (12), and (14). Pure samples were collected by preparative g.l.c. 3,7,7-Trimethyl-8-oxabicyclo[4.3.0]non-1(6)-ene (5) showed *m/e* 151 (*M* – CH₃, base peak), 109, 95, and 81, no i.r. peaks for OH or CO (in CCl₄), δ_H (CCl₄), 1.05 (3 H, d, *J* 8 Hz), 1.20 (6 H, s), 1.5–2.2 (7 H, m), and 4.42br (2 H, s) [signals at δ 1.20 and 4.42 underwent a remarkable downfield shift on adding Eu(dpm)₃], δ_C (neat) 126.6 and 134.5 (C=C), 74.0 and 86.5 (C–O), and 23.3, 23.7, 28.1, 28.5, 30.7, 31.9, and 33.0. 2-Isopropenyl-5-methylcyclohexanone (12) showed ν_{\max} (CCl₄) 2 990, 1 718, and 900 cm⁻¹, δ (CCl₄) 0.99 (3 H, d, *J* 8 Hz), 1.65 (3 H, s), 1.2–1.9 (8 H, m), 4.40br (1 H, s), and 4.57br (1 H, s). 2-(1-Methoxy-1-methylethyl)-5-methylcyclohexanone (14) showed δ (CCl₄) 1.02 (3 H, d, *J* 8 Hz), 1.11 (3 H, s), 1.21 (3 H, s), 1.2–2.5 (8 H, m), and 3.07 (3 H, s).

When compound (5) was kept at 120 °C for 2 h, or at room temperature for 7 days in air, a viscous oil was obtained. G.l.c. analysis indicated that this was almost pure 4,9,9-trimethyl-8-oxabicyclo[4,3,0]non-1(6)-en-7-one (18). Preparative g.l.c. afforded a pure sample, *m/e* 180 (*M*⁺), 165, 137 (base peak), 123, and 109, ν_{\max} (CCl₄) 1 773, 1 460, and 1 058 cm⁻¹, δ (CCl₄) 1.09 (3 H, d, *J* 8 Hz), 1.40 (6 H, s), and 1.5–2.4 (7 H, m).

Photolysis of Dypnone (2) in Methanol-Titanium(IV) Chloride.—A solution of dypnone (2) (2.7 g) and titanium tetrachloride (2.0 ml) in methanol (40 ml) was irradiated for 24 h. Work-up afforded an oil which was distilled under reduced pressure. A fraction, b.p. 135–139° at 0.05 mmHg (2.2 g), was shown to be a mixture of compound (6) (68%) and two unknowns (14 and 18%) by g.l.c. analysis. A pure sample of 2,5-dihydro-2-methyl-2,4-diphenylfuran (6) was collected by preparative g.l.c.; *m/e* 236 (*M*⁺), 221 (base peak), 115, 105, 91, and 77, no i.r. peaks for OH or CO (in CCl₄), δ (CCl₄) 1.69 (3 H, s), 5.11 (2 H, t, *J* 2 Hz), 6.40 (1 H, t, *J* 2 Hz), and 7.2–7.6 (10 H, m) (Found: C, 86.4; H, 6.7. C₁₇H₁₆O requires C, 86.5; H, 6.8%).

When the irradiation was carried out while air was bubbled through the mixture, a small amount of dilactone¹¹ separated. In the mother liquor, compound (16) and *cis*- and *trans*-isomers of (2) were detected by n.m.r. analysis, but no trace of (6) was observed.

Photolysis of Mesityl Oxide (3) in Methanol-Titanium(IV) Chloride.—A solution of the ketone (3) (1.2 ml) and titanium tetrachloride (1.2 ml) in methanol (60 ml) was irradiated for 6 h. Work-up afforded an oil (1.7 g) which was shown to be a mixture of compounds (3) (13%), (7) (48%), and (15) (39%) from ¹H n.m.r. and g.l.c. analyses. Pure samples of (7) and (15) were collected by preparative g.l.c. 5,5-Dimethoxy-2,4-dimethylpent-2-ene (7) showed *m/e* 127 (*M* – OCH₃), 95, and 75 (base peak), no i.r. peaks for OH or CO (in CCl₄), δ (CCl₄) 0.89 (3 H, d, *J* 8 Hz), 1.62 (3 H, d, *J* 1 Hz), 1.72 (3 H, d, *J* 1 Hz), 2.4–2.8 (1 H, m), 3.24 (3 H, s), 3.32 (3 H, s), 4.0 (1 H, d, *J* 8 Hz), and 5.0br (1 H, d, *J* 10 Hz) (on irradiation at δ 2.4–2.8, signals at δ 0.89, 4.0, and 5.0

¹¹ T. Sato, K. Tamura, K. Maruyama, O. Ogawa, and T. Imamura, *J.C.S. Perkin I*, 1976, 779.

became singlets). 4-Methoxy-4-methylpentan-2-one (15) showed δ (CCl_4) 1.19 (6 H, s), 2.08 (3 H, s), 2.46 (2 H, s), and 3.13 (3 H, s).

Photolysis of Mesityl Oxide (3) in Methanol-Tetramethoxytitanium.—A solution of titanium tetrachloride (1.2 ml) in methanol (60 ml) was neutralized with methanolic sodium methoxide (to pH 7). Sodium chloride was filtered off and mesityl oxide (3) (1.2 ml) was added to the filtrate. The solution was irradiated for 15 h; the work-up afforded an oil, which was shown to be a mixture of compounds (3) (78%) and (17) (22%). 4-Methylpent-4-en-2-one (17) showed δ (CCl_4) 1.73 (3 H, s), 2.18 [s, overlapped with a signal of (3)], 3.02 (2 H, s), 4.79br (1 H, s), and 4.89br (1 H, s).

Photolysis of 3-Methylcyclohex-2-enone (4) in Methanol-Titanium(IV) Chloride.—A solution of the ketone (4) (1.2 g) and titanium tetrachloride (1.2 ml) in methanol (100 ml) was irradiated for 7 h. Work-up afforded an oil (1.7 g), which was shown to be a mixture of compounds (8) (66%) and (9) (24%) by g.l.c. analysis. Vacuum distillation afforded two fractions: (i), b.p. 60–64° at 23 mmHg (0.24 g), a mixture of (8) (37%) and (9) (45%); and (ii), b.p. 64–67° at 23 mmHg (0.64 g), another mixture of (8) (85%) and (9) (12%). Pure samples of (8) and (9) were collected by preparative g.l.c. 3-Dimethoxymethyl-1-methylcyclohexene (8) showed m/e 139 ($M - \text{OCH}_3$), 107, 95, and 75 (base peak), no i.r. peaks for OH or CO (in CCl_4), δ_{H} (CCl_4) 1.61 (3 H, s), 1.1–2.4 (7 H, m), 3.15 (3 H, s), 3.19 (3 H, s), 3.82 (1 H, d, J 9 Hz), and 5.21br (1 H, s), δ_{C} (neat) 124.7 and 137.9 (C=C), 111.5 (O–C–O), 53.8 and 54.0 (C–O), and 24.8, 26.8, 27.3, 32.8, and 40.3. 3-Methylcyclohex-2-enecarbaldehyde (9) showed ν_{max} (CCl_4) 2 950 and 1 730 cm^{-1} , δ (CCl_4) 1.78 (s), 1.7–2.1 (m), 2.93br (1 H, s), 5.57br (1 H, s), and 9.73 (1 H, d, J 2 Hz).

When compound (8) (0.3 g) was refluxed in ethanol (15 ml)

containing 3N-hydrochloric acid (15 ml), 3-methylcyclohex-1-enecarbaldehyde (19) was obtained, which was isolated by preparative g.l.c.; m/e 124 (M^+) and 109, ν_{max} (CCl_4) 1 680, 1 625, and 1 160 cm^{-1} , δ (CCl_4) 1.13 (3 H, d, J 8 Hz), 1.2–2.5 (7 H, m), 6.51br (1 H, s), and 9.45 (1 H, s); semicarbazone, m.p. 196–197° (lit.,¹² 197.5–199°).

Photolysis of 3-Methylcyclohex-2-enone (4) in Ethanol-Titanium(IV) Chloride.—A solution of the ketone (4) (0.15 ml) and titanium tetrachloride (0.15 ml) in ethanol (15 ml) was irradiated for 3 h. Work-up afforded an oil (0.14 g) which was shown to be a mixture of compounds (10) (67%) and (11) (16%), starting material (2%), and two unidentified products (15 and 1%). Chromatography over alumina afforded a fraction (55 mg) as a mixture of (10) (75%) and (11) (16%). Complete separation of the two isomers could not be achieved by column chromatography, but was effected by preparative g.l.c. 3-Acetyl-1-methylcyclohexene (10) showed m/e 138 (M^+) and 95 (base peak), ν_{max} (CCl_4) 2 950, 1 710, 1 440, 1 352, and 1 154 cm^{-1} , δ (CCl_4) 1.71br (3 H, s), 1.5–2.1 (6 H, m), 2.09 (3 H, s), 2.99br (1 H, s), and 5.54br (1 H, s). 1-Acetyl-3-methylcyclohexene (11)¹³ showed ν_{max} (CCl_4) 2 970, 1 663, and 1 234 cm^{-1} , δ (CCl_4) 1.13 (3 H, d, J 8 Hz), 1.1–2.6 (7 H, m), 2.22 (3 H, s), and 6.72br (1 H, s).

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¹² P. Seifert and H. Schinz, *Helv. Chim. Acta*, 1951, **34**, 728.

¹³ Cf. H. Rupe, R. Haecker, E. Kambli, and N. Wasslieff, *Helv. Chim. Acta*, 1933, **16**, 685.