Tetrahedron. Vol. 24, pp. 6557 to 6562. Pergamon Press 1968. Printed in Great Britain

PHOTOCHEMICAL REACTIONS OF BENZOPHENONE WITH ENAMINES

M. KAWANISI, K. KAMOGAWA, T. OKADA and H. NOZAKI
Department of Industrial Chemistry, Kyôto University, Kyôto, Japan

(*Received in Japan* 31 *May* 1968; *Received in the UK for publication* 25 *June* 1968)

Abstract—Work-up of products of the title reaction gives γ-hydroxy ketones produced formally by addition of benzophenone at the β-position of ketones on which the enamines are based. Benzpinacol is the major product isolated in all cases. While morpholine enamines give oxetanes resulting from cycloaddition of benzophenone at the enamine double bond, the reaction of piperidine enamines does not afford similar adducts. Accounts for the reaction mechanism are given by assuming benzophenone triplet as a reactive species.

RECENTLY there has been considerable interest on the photochemical cycloaddition reactions of carbonyl compounds with the unsaturated systems[1] and the photochemical reduction of aromatic ketones has been the subject of many investigations.[2] We wish to record here photochemical reactions of benzophenone with several enamines in which both reactions were observed. In addition, *diphenylhydroxymethylation* was noticed at the β-position of the original ketones from which the enamines were derived.

A solution of an equimolar mixture of 1-N-morpholinocyclohexene (Ia) and benzophenone in benzene was irradiated by means of light of wave length longer than 350 nm under nitrogen atmosphere at room temperature for 50 hr. Under these conditions, the light energy was consumed exclusively for the excitation of benzophenone. Chromatographic separation of the reaction mixture afforded an oxetane V and 3-(diphenylhydroxymethyl)-cyclohexanone (IX) together with benzpinacol (III). 3-N-Morpholino-2-pentene (IIa) under similar conditions gave in addition to III an adduct VI and 6,6-diphenyl-6-hydroxy-3-hexanone (X).

The keto-alcohol IX, III and benzhydrol (IV) were obtained from the piperidine enamine of cyclohexanone (Ib) and the N-methylaniline enamine of cyclohexanone (Ic), whereas the piperidine enamine of diethyl ketone (IIb) afforded the corresponding keto-alcohol X accompanied by III and IV. The reaction sequence is shown below and the product distributions are summarized in Table 1.

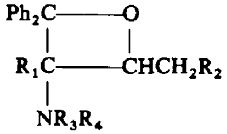
TABLE 1. YIELDS IN MOLE % OF PRODUCTS OF THE REACTION OF BENZOPHENONE WITH ENAMINES

Enamines	III	IV	Oxetane	Keto-alcohol
Ia	56	—	V, 10	IX, 15
Ib	42	12	— —	IX, 23
Ic	57	11	— —	IX, 19
IIa	50	—	VI, 3	X, 21
IIb	60	8	— —	X, 18

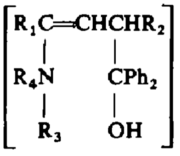
$$R_3R_4N{-}CR_1{=}CHCH_2R_2 + Ph_2C{=}O \xrightarrow{h\nu} Ph_2C(OH)C(OH)Ph_2 + Ph_2CHOH$$

Ia: $R_1, R_2 = (CH_2)_3, R_3, R_4 = (CH_2)_2O(CH_2)_2$
b: $R_1, R_2 = (CH_2)_3, R_3, R_4 = (CH_2)_5$
c: $R_1, R_2 = (CH_2)_3, R_3 = CH_3, R_4 = Ph$
IIa: $R_1 = C_2H_5, R_2 = H, R_3, R_4 = (CH_2)_2O(CH_2)_2$
b: $R_1 = C_2H_5, R_2 = H, R_3, R_4 = (CH_2)_5$

III IV

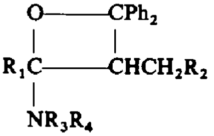


V: $R_1, R_2 = (CH_2)_3$, $R_3, R_4 = (CH_2)_2O(CH_2)_2$
VI: $R_1 = C_2H_5, R_2 = H$, $R_3, R_4 = (CH_2)_2O(CH_2)_2$



→ $R_1COCH_2CHR_2C(OH)Ph_2$
IX: $R_1, R_2 = (CH_2)_3$
X: $R_1 = C_2H_5, R_2 = H$

VII: $R_1, R_2 = (CH_2)_3$
VIII: $R_1 = C_2H_5, R_2 = H$



XVIII

An oxetane structure was assigned to the adduct V on the basis of the following experimental results. The analysis and mass spectroscopy indicated the 1:1-adduct nature. The IR absorption spectrum had an eminent absorption band at 1005 cm^{-1}, which strongly suggested the presence of an oxetane linkage[3] and no absorption due to carbonyl and other unsaturation was found. In the NMR spectrum one proton multiplet signal centered at δ 4·00 ppm was discernible, which may be ascribed to the hydrogen α to the oxygen of an oxetane structure,* although this signal overlapped with the signals due to morpholine protons to form a complex pattern. Conclusive evidence for the adduct nature was deduced from the mass spectrum having eminent peaks at *m/e* 105, 77 and 51, which are possibly due to benzophenone moiety.[4] The rest of the fragmentation pattern is consistent with the oxetane structure mentioned in the literature.[5] The adduct V was actually isolated by chromatographic treatment on Silicagel and recovered unchanged when dissolved in trifluoroacetic acid. Such stability under acidic condition rules out an isomeric O,N-acetal structure (XVIII).[6] Similar oxetane structure was allotted to the adduct VI.

A rationale accounting for the formation of the 1:1-adducts mentioned here can be easily made by assuming the attack of benzophenone in triplet state to the double bone of enamines in ground state. Ample examples of similar reactivity of benzophenone can be found in the literature.[7] An electron-deficient oxygen of the excited benzophenone can attack the more negative center at β-position of the enamine

---

* Ref. 3 states that the oxetanes show the hydrogen α to the oxygen at δ 4·0–5·0 while the hydrogen β to the oxygen on the ring occurs at δ 2·6–3·6 ppm.

followed by the cyclization to form an oxetane. This consideration clearly explains the orientation mode in the formation of the adducts V and VI.*

The structure of the keto-alcohol IX was based on the following data. The IR spectrum consisted of absorptions at 3475 cm^{-1} due to tertiary a OH group and 1700 cm^{-1} due to a 6-membered cyclic ketone. The NMR spectrum of IX showed one proton singlet at δ 2·32 ppm due to an OH group, ten protons multiplet at δ 7·05–7·80 ppm of aromatics and complex nine protons multiplet at δ 1·12–3·10 ppm due to ring methylenes and methine. The final proof for the assigned structure was obtained by the independent synthesis of IX. The keto-alcohol IX was synthesized in a 40% overall yield from methyl 3-oxocyclohexanecarboxylate (XI)[8] by means of ketalization, the conjugative addition of phenyl Grignard reagent followed by deketalization. Dehydration by treatment of IX with dil HCl afforded the hitherto unknown 3-benzhydryl-2-cyclohexenone (XIV) in a 65% yield, possibly due to the isomerization of double bond from *exo*- to *endo*cyclic induced by the acid treatment.[9] Catalytic hydrogenation of XIV gave 3-benzhydrylcyclohexanone† in an almost quantitative yield.

The structure of the keto-alcohol X was also assigned analogously to IX by the spectroscopic data and elemental analysis. Dehydration of X followed by hydrogenation afforded the known ketone, 6,6-diphenyl-3-hexanone (XVII)[12]

The formation of the keto-alcohol IX and X is rationalized by assuming the formation of VII and VIII, which are hydrolyzed to yield the keto-alcohols during the chromatographic treatment. Bradshaw obtained 3-cyclohexenyldiphenylcarbinol by the photochemical reaction of benzophenone with cyclohexene in 27% yield.[13] The formation of seemingly aldol-type addition products, albeit in lower yields, characterized the reaction in the present investigation.

Since enamines are formally analogous to simple olefins, the hydrogen at allylic positions to the double bond can be labile to afford a linearly conjugated allylic radical, which subsequently combines with benzhydrol radical to give VII and VIII. No products arising from the cross-conjugated allylic radical have been obtained.

While IV was isolated in addition to III in some cases, the TLC analysis of the irradiated mixture indicated the absence of IV. The formation of IV is considered to be due to the disproportionation of III during the work-up. Such a disproportionation reaction of III has been observed by Cohen in the photoreduction of benzophenone in the presence of amines.[14] Actually III disproportionated partially into IV and benzophenone when heated under reflux in benzene solution in the presence of Ia.

The hydrogen-source of III must partly exist in the amine part of the enamines, although the products originating from the hydrogen-donor(s) have not been isolated. The following reaction may support this assumption.

When a benzene solution of benzophenone was irradiated (> 350 nm) in the presence of equimolar quantity of morpholine, a 1:1-adduct of benzophenone and mor-

---

* An oxetane with the alternate structure which was not isolated in the present investigation may be unstable to the separation technique, otherwise it may not exist among the reaction products.

† For comparison 2-benzhydrylcyclohexanone was synthesized according to the published method.[10] This compound showed the clear differences in IR, NMR and mp. In addition, the mp of 4-benzhydrylcyclohexanone reported,[11] 170°, was higher than that of XIV. Evidently the diphenylhydroxymethylation took place at 3-position of cyclohexanone.

pholine was isolated, albeit in low yield, in addition to III. The spectroscopic data shows that this adduct is 3-(diphenylhydroxymethyl)-morpholine[15] being produced through the coupling of benzhydrol radical with morpholine radical. The diphenylhydroxymethylation reasonably occurs at the α-position to the nitrogen of morpholine since the N-methylene hydrogen is believed to be more labile than O-methylene.[16]

EXPERIMENTAL

All m.ps and b.ps are uncorrected. The NMR spectra were determined at 60 Mc with a JEOL JMN-C60H spectrometer with $CDCl_3$ as a solvent and TMS as an internal standard. Mass spectra were obtained with a Hitachi RMU-6D mass spectrometer with a direct inlet (200°) and at 80 eV. Plates of Silicagel G were used for TLC and the spots were visualized with I_2 vapour. The UV spectra were taken in EtOH on Hitachi EPS-2 recording spectrophotometer.

General procedure for irradiation. Irradiations were conducted in benzene (200 ml) containing enamines (40 mmoles) and benzophenone (7·3 g, 40 mmoles) by means of 200 W high pressure mercury arc under N_2 atmosphere at room temp through 10% $CuSO_4$ aq as a filter. The progress of the reaction was followed by TLC analysis of aliquots. After all benzophenone had been consumed, the reaction mixture was concentrated *in vacuo* to ca. 20 ml, the crystals of III were collected by filtration and the filtrate was chromatographed on Silicagel.

*2,2-Diphenyl-*3-N-*morpholino-*3,4-*tetramethylenoxetane* (V). This was obtained as colourless crystals, m.p. 112–114° (from benzene–hexane). IR (KBr): 1100 and 1005 cm^{-1} (C—O—C); NMR*: δ 1·20–2·00 (m, 8, CH_2), 2·50–2·90 (t, 4, CH_2—N), 3·30–3·95 (m, 4, CH_2—O), 4·00 (m, 1, CH—O in oxetane), and 7·10–7·60 ppm (m, 10, arom.). The mass spectrum consisted of peaks at *m/e* 349 (P, 22%), 306 (100%), 252 (31%), 206 (10%), 178 (11%), 167 (60%), 152 (13%), 115 (11%), 105 (11%), 77 (16%), 55 (43%), and 41 (27%). (Found: C, 79·3; H, 7·9; N, 3·9. $C_{23}H_{27}NO_2$ requires: C, 79·1; H, 7·8; N, 4·0%). The NMR spectrum of V in trifluoroacetic acid showed the clear differences with the one in $CDCl_3$ indicating the formation of the quartenary salt. Detailed assignments of the signals could not be performed. V was recovered completely unchanged after making the acidic solution alkaline followed by ether extraction.

3-(*Diphenylhydroxymethyl*) *cyclohexanone* (IX). This was obtained as colourless crystals, m.p. 154° (from benzene–hexane); IR (KBr): 3475 (OH) and 1700 cm^{-1} (C=O); NMR: δ 1·12–3·10 (m, 9, CH_2 and CH), 2·32 (s, 1, OH), and 7·05–7·80 ppm (m, 10, arom.). (Found: C, 81·3; H, 7·2. $C_{19}H_{20}O_2$ requires: C, 81·4; H, 7·2%).

3-*Benzhydrylcyclohexanone* (XV). A mixture of IX (0·1 g, 0·36 mmole), EtOH (30 ml) and 10% HCl (10 ml) was heated under reflux for 5 hr. Evaporation of the solvent, extraction with ether and drying ($MgSO_4$) followed by distillation *in vacuo* afforded an oil (0·06 g), b.p. 170–180° (0·2 mm), which was shown to be 3-*benzhydryl*-2-*cyclohexenone* (XIV); IR (neat): 1675 (C=O) and 1630 cm^{-1} (C=C); UV: 243 nm (log ε 4·21); NMR: δ 1·80–2·50 (m, 6, CH_2), 4·83 (s, 1, CH), 5·55 (s, 1, CH=), and 7·00–7·40 ppm (m, 10, arom.). 2,4-*Dinitrophenylhydrazone* of XIV melted at 205° (from EtOH). (Found: C, 67·7; H, 5·0. $C_{25}H_{22}N_4O_4$ requires: C, 67·9; H, 5·0%).

A soln of XIV (0·05 g, 0·33 mmole) in EtOH (20 ml) containing 10% Pd–C (ca. 0·2 g) was shaken under ordinary pressure of H_2 at room temp. Usual work-up afforded 3-*benzhydrylcyclohexanone* (XV; 0·04 g, 80%), m.p. 98° (from benzene–hexane); IR (Nujol): 1710 cm^{-1} (C=O); NMR: δ 1·30–2·40 (m, 9, CH_2 and CH), 3·57 (d, 1, J = 7 Hz, Ph_2CH), and 7·16 ppm (s, 10, arom). (Found: C, 86·3; H, 7·7. $C_{19}H_{20}O$ requires: C, 86·3; H, 7·6%).

2,2-*Diphenyl*-3-*ethyl*-3-N-*morpholino*-4-*methyloxetane* (VI). This was obtained as colourless crystals, m.p. 83° (from benzene–hexane); IR (Nujol): 1100 and 1010 cm^{-1} (C—O—C); NMR: δ 0·65–1·15 (d and t, 6, CH_3), 1·20–1·55 (q, 2, CH_2), 2·45–2·90 (m, 4, CH_2—N), 3·15–3·90 (m, 4, CH_2—O), 4·00 (m, 1, CH—O in oxetane), and 7·10–7·70 ppm (m, 10, arom). The mass spectrum consisted of peaks at *m/e* 308 (85%), 252 (100%), 167 (96%), 155 (44%), 105 (< 10%), 77 (< 10%), 57 (41%), and 29 (41%). (Found: C, 78·2; H, 8·3. $C_{22}H_{27}NO_2$ requires: C, 78·3; H, 8·1%).

6,6-*Diphenyl*-6-*hydroxy*-3-*hexanone* (X). This was obtained as a colourless oil, which rejected further purification by distillation as well as analyses on account of its property of facile dehydration during the

---

* The NMR data are given in the order of multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = unresolved multiplet), integration, and assignment.

work-up; IR (neat): 3450 (OH) and 1710 cm^{-1} (C═O); NMR: δ 0·95 (t, 3, CH_3), 1·20–3·30 (m, 6, CH_2), 2·80 (s, 1, OH), and 6·90–7·70 ppm (m, 10, arom).

6,6-Diphenyl-5-hexen-3-one (XVI). A soln of crude X (0·1 g) in EtOH (30 ml) containing 10% HCl (10 ml) was refluxed for 5 hr. Evaporation of the solvent, ether extraction and drying ($MgSO_4$) followed by distillation gave XVI, b.p. 160–180° (0·2 mm); IR (Nujol): 1707 (C═O) and 1660 cm^{-1} (C═C). UV: 253 nm (log ε 4·04); NMR: δ 0·98 (t, 3, J = 7 Hz, CH_3), 2·27 (q, 2, J = 7 Hz, CH_2), 3·09 (d, 2, J = 7·5 Hz, CH_2), 6·16 (t, 1, J = 7·5 Hz, CH═), and 6·90–7·30 ppm (m, 10, arom). (Found: C, 86·5; H, 7·3. $C_{18}H_{18}O$ requires: C, 86·4; H, 7·3%).

6,6-Diphenyl-3-hexanone (XVII). A soln of XVI (0·05 g, 0·2 mmole) in EtOH (20 ml) containing 10% Pd–C was treated as mentioned above. Work-up gave XVII (0·05 g, 100%), m.p. 68–69° (lit.[12] m.p. 69–70°); IR (Nujol): 1700 cm^{-1} (C═O). (Found: C, 85·2; H, 8·0. Calc. for $C_{18}H_{20}O$: C, 85·7; H, 8·0%).

Methyl 3-oxocyclohexanecarboxylate ethylene ketal (XII). Treatment of XI[8] (2·3 g, 15 mmoles) with ethylene glycol (0·9 g, 15 mmoles), benzene (150 ml) and *p*-toluenesulphonic acid (0·05 g) for 24 hr at reflux under continuous removing water by Linde Molecular Sieve (4A 1/16) followed by distillation afforded XII (2·0 g, 67%), b.p. 139–140° (23 mm); IR (Nujol): 1740 (ester C═O), 1095 and 1040 cm^{-1} (C—O—C). (Found: C, 60·0; H, 8·2. $C_{10}H_{16}O_4$ requires: C, 60·0; H, 8·1%).

3-(Diphenylhydroxymethyl) cyclohexanone ethylene ketal (XIII). A soln of XII (0·43 g, 2·2 mmoles) in dry ether (10 ml) was added dropwise to the Grignard reagent prepared from bromobenzene (1·2 g, 7·5 mmoles) and Mg (0·18 g, 7·5 mmoles) in dry ether (30 ml) in the course of 2 hr. The reaction mixture was decomposed by excess of NH_4Claq. Ether extraction and drying ($MgSO_4$) followed by concentration afforded XIII (0·66 g, 100%), m.p. 145–146° (from benzene); IR (Nujol): 3500 (OH), 1080 and 1010 cm^{-1} (C—O—C). (Found: C, 77·8; H, 7·4. $C_{21}H_{24}O_3$ requires: C, 77·8; H, 7·5%).

3-(Diphenylhydroxymethyl) cyclohexanone (IX). A soln of XIII (0·35 g, 1·1 mmoles) in EtOH (5 ml) was shaken for several minutes with 5% HCl (50 ml). Ether extraction and drying ($MgSO_4$) followed by concentration afforded IX (0·18 g, 60%), m.p. 154° (from benzene–hexane), whose IR spectrum is completely superimposable with the photoproduct IX. No depression of m.p. when admixed with the photoproduct IX was observed. (Found: C, 81·6; H, 7·1. $C_{19}H_{20}O_2$ requires: C, 81·4; H, 7·2%).

Disproportionation of III *in the presence of* Ia. A 0·1M soln of III in benzene containing equivalent amount of Ia was allowed to stand at room temp for a week. TLC analysis indicated that no reaction occurred. Heating the soln under reflux for 1 hr induced the disproportionation of III into benzophenone and IV as indicated by TLC.

Irradiation of benzophenone in the presence of morpholine. A soln of morpholine (5·2 g, 60 mmoles) and benzophenone (10·9 g, 60 mmoles) in benzene (300 ml) was irradiated in an analogous manner as the case of enamines. The reaction mixture was concentrated *in vacuo* to ca. 15 ml, the crystals of III were removed by filtration and the filtrate was chromatographed on Silicagel. From benzene eluants an additional III was isolated, which totally weighed 8·8 g (80%). From benzene–ether (8:2) eluants there was obtained 3-(diphenylhydroxymethyl)-morpholine (0·08 g, 0·5%), m.p. 127° (from EtOH) (lit.[15] m.p. 126–128°); IR (KBr): 3450 (OH), 3350 (NH) and 1100 cm^{-1} (C—O—C); NMR: δ 1·55–1·75 (broad s, 1, NH), 2·55–3·25 (m, 2, CH_2—N), 3·35–3·95 (m, 5, CH_2—O and CH—N), 4·10–4·50 (broad s, 1, OH), and 7·00–7·80 ppm (m, 10, arom). (Found: C, 75·6; H, 7·0; N, 5·4. Calc. for $C_{17}H_{19}NO_2$: C, 75·8; H, 7·1; N, 5·2%).

Acknowledgements—The authors wish to thank Prof. K. Sisido for help and encouragement. They are also indebted to the staff of Kao Soap Co. for measurement of mass spectra. This work was supported in part by the Grant-in-Aid administered by the Ministry of Education, Japanese Government, to which the authors express their appreciations.

REFERENCES

[1] O. L. Chapman and G. Lenz, *Advances in Organic Photochemistry* (Edited by O. L. Chapman) Vol. I; p. 286. Marcel Dekker, New York, N.Y. (1967).

[2] For the pertinent Refs, [a] J. G. Calvert and J. N. Pitts, Jr., *Photochemistry* p. 532. Wiley, New York, N.Y. (1966); [b] D. C. Neckers, *Mechanistic Organic Photochemistry* p. 163. Reinhold, New York, N.Y. (1967).

[3] D. R. Arnold, R. L. Hinman and A. H. Glick, *Tetrahedron Letters* 1425 (1964).

[4] F. W. McLafferty, *Interpretation of Mass Spectra* p. 45. Benjamin, New York, N.Y. (1966).

[5] L. A. Singer and G. A. Davis, *J. Am. Chem. Soc.* **89**, 598, 941 (1967).

[6] Houben-Weyl, *Methoden der organischen Chemie* 4 Aufl., Vol. XI/2; p. 90. Georg Thieme Verlag, Stuttgart (1958).

[7] N. C. Yang, *Pure and Appl. Chem.* **9**, 591 (1964); also Ref. 3.

[8] D. K. Banerjee, J. Dutta and G. Bagavant, *Proc. Indian Academy of Science* Bangalore Sec A **46**, 80 (1958).

[9] M. Pfau, R. Dulou and M. Vilkas, *C.R. Acad. Sci., Paris* **254**, 1817 (1962).

[10] S. O. Winthrop and L. G. Humber, *J. Org. Chem.* **26**, 2834 (1961).

[11] M. Fetizon, M. Golfier and A. Rassat, *C. R. Acad. Sci., Paris* **252**, 139 (1961).

[12] A. D. Petrov and V. M. Vdovin, *Zh. Obsch. Khim.* **27**, 45 (1957); *Chem. Abstr.* **51**, 12044 (1957).

[13] J. S. Bradshaw, *J. Org. Chem.* **31**, 237 (1966).

[14] S. G. Cohen and R. J. Baumgarten, *J. Am. Chem. Soc.* **89**, 3471 (1967).

[15] S. O. Winthrop, U.S.Pat. 2,947,749, Aug. 2, 1960; *Chem. Abstr.* **55**, 3624 (1961).

[16] S. G. Cohen and H. M. Chao, *J. Am. Chem. Soc.* **90**, 165 (1968).