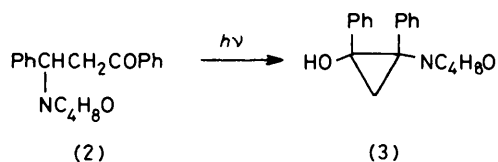# Thermal and Photochemical Behaviour of *N*-(α-Morpholinobenzyl)-benzamide and *N*-(α-Methoxybenzyl)benzamide

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The thermal fragmentation of the title compounds produces benzamide (6), benzaldehyde (7), and *N,N'*-benzylidenebisbenzamide (8) ; in contrast the photochemical reaction gives benzylbenzamide (9) and *meso*- and (±)-1-modifications of *N,N'*-dibenzoyl-1,2-diphenyl-1,2-diaminoethane (10). Evidence is presented which shows that the formation of the various reaction products starts from the *N*-benzyl-idenebenzamide (5).

Although the thermal and photochemical reactions of β-amino-ketones have been investigated,[1,2] there have been no reports on the behaviour of the corresponding α-aza-analogues. In our recent report on the thermal reaction of chalcone, PhCH=CHCOPh (1), with morpholine and piperidine,[1] evidence was presented which showed that the formation of various reaction products involved the intermediate β-amino-ketone (2) initially formed from the addition of amine to chalcone. Previously Roth *et al.*[2] reported that compound (2) upon direct irradiation undergoes photocyclization to give 2-morpholino-1,2-diphenylcyclopropanol (3).

(2)   (3)

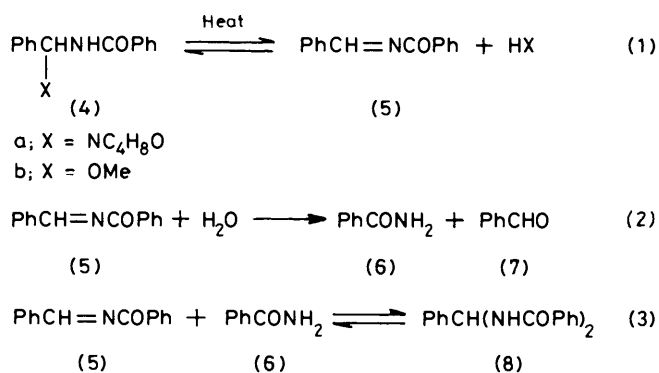We now report the thermal and the photochemical behaviour of *N*-(α-morpholinobenzyl)benzamide (4a), which can be considered the α-aza-analogue of structure (2) and, for a useful comparison, that of *N*-(α-methoxybenzyl)benzamide (4b).
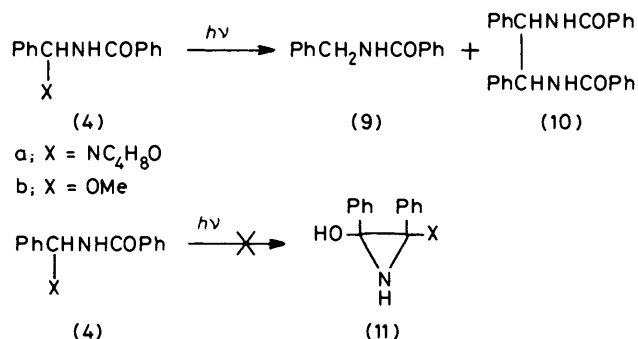
Results and Discussion

When *N*-(α-morpholinobenzyl)benzamide (4a) was heated above its melting point (166—167 °C) decomposition occurred to produce benzamide (6), benzaldehyde (7), and benzylidene-bisbenzamide (8). Similarly *N*-(α-methoxybenzyl)benzamide (4b) also produced compounds (6)—(8). The formation of the latter can be rationalized in terms of the intermediacy of *N*-benzylidenebenzamide (5) derived from the corresponding compound (4) by a thermal elimination. Ben-Ishai *et al.* isolated compound (5) by thermal decomposition from the two benzamides (4b) and (8) in a sublimation apparatus at 200—210 °C and 25—30 mmHg, and described some of their chemical and spectroscopic properties [Scheme 1, equation (1), X = OMe, NHCOPh].[3]

Under our experimental conditions the intermediate (5) both undergoes ready hydrolysis, because of its high hydrophilicity, to give (6) and (7), and the reported addition reaction[3] to give (6) which leads to (8) (Scheme 1).

In contrast to the thermolysis, photolysis of compounds (4) in anhydrous benzene with a 450-W medium-pressure lamp equipped with a Pyrex filter under a nitrogen atmosphere gave benzylbenzamide (9) and the *meso* and (±)-modifications of *N,N'*-dibenzoyl-1,2-diphenyl-1,2-diaminoethane (10). It is noteworthy that contrary to our expectations the photocyclization described by Roth *et al.*[2] for the corresponding β-

$$PhCHNHCOPh \overset{Heat}{\underset{}{\rightleftharpoons}} PhCH=NCOPh + HX \quad (1)$$

$$\underset{(4)}{X} \qquad\qquad (5)$$

a; X = NC$_4$H$_8$O

b; X = OMe

$$PhCH=NCOPh + H_2O \longrightarrow PhCONH_2 + PhCHO \quad (2)$$

$$\quad(5)\qquad\qquad\qquad (6)\qquad\quad (7)$$

$$PhCH=NCOPh + PhCONH_2 \rightleftharpoons PhCH(NHCOPh)_2 \quad (3)$$

$$\quad(5)\qquad\qquad (6)\qquad\qquad\qquad (8)$$

Scheme 1

a; X = NC$_4$H$_8$O

b; X = OMe

(4)   (11)

amino-ketone was not observed, no azirinols (11) or their degradation products being detected in the reaction mixtures. The photoreaction also proceeded in a hydrogen-donating solvent such as a cyclohexane–tetrahydrofuran (Cy-THF) with increased yields of compounds (9) and (10); this clearly suggests that the photoreaction of (4) involves a hydrogen abstraction reaction (Table).

The lack of compounds containing the morpholino-residue among the reaction products suggested that the process leading to (9) and (10) starts from *N*-benzylidenebenzamide (5), rather than from the benzamides (4a, b). *N*-Acyl- and *N*-benzoyl-imines are known to undergo reduction and/or reductive dimerization processes upon irradiation according to the imine carbon substituent structure.[4-7] We assume that structures (4a, b) and (8) exist in thermal equilibrium under conditions milder than those of the pyrolysis [Scheme 1, equation (1)]. Our assumption is based on literature reports[3,7,8] and on the results of the experiments reported below. Ben-Ishai,[3] in particular, reported that (4b) undergoes replacement of the methoxy-group upon treatment with piperidine or

Direct irradiation of PhCHXNHCOPh:

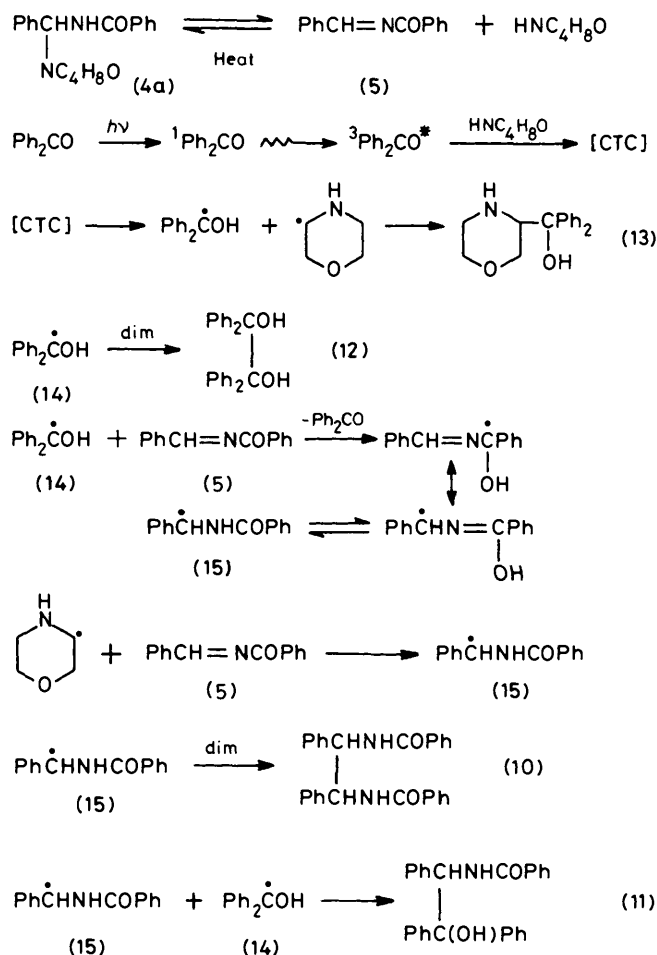| X | Solv. | Time/h | Products (% yield) [a] | | |
			(4) [b]	(9) [b]	(10) [c]
NC4H8O	PhH	44	—	16.2	50
OMe	PhH	44	90	1.2	5
NC4H8O	THF–Cy [d]	30	—	25.0	70
OMe	THF–Cy [d]	30	80	3.3	10

[a] The yield of each product was the average of eight runs. Maximum variation in yields was ±6%. [b] Yield determined by g.l.c. [c] Yield determined by weighing the *meso*-form collected by filtration and the (±)-forms separated by column chromatography. [d] Tetrahydrofuran–cyclohexane (1 : 1, v : v).

ethanol at room temperature and proved that the exchange reaction proceeds *via* an elimination-addition mechanism involving the imine (5).

A sample of *N*-(α-methoxybenzyl)benzamide (4b) was subjected to the thermal conditions which gave rise to the isolation of (5) [3] and was then irradiated in a Cy–THF mixture. As expected a 1 : 4 mixture of compounds (9) and (10) together with small amounts of other compounds were formed. The u.v. spectrum of (4a) in cyclohexane at 25 °C showed that the initial maximum absorbance value at 228 nm decreased, while that at 258 nm (shoulder) was enhanced to reach after 3 h a constant value. The addition of an equimolar amount of morpholine resulted in the disappearance of the shoulder at 258 nm and in an increase in the absorbance at 228 nm. The irradiation of (4a) in the presence of morpholine (1 : 2 molar ratio) resulted in complete quenching of the photo-reaction. The results are in agreement with the establishment of the postulated (4) ⇌ (5) equilibrium and its displacement towards the starting material according to the mass effect. The photoreaction of (4a) in the presence of benzophenone in anhydrous benzene (λ > 350 nm) afforded besides the dimers (10) (small amounts) and 1,1,2-triphenyl-1-hydroxy-2-(*N*-benzoylamino)ethane (11), benzpinacol (12) and trace amounts of 3-[diphenyl(hydroxy)methyl]morpholine (13).[9] According to the literature [9,10] the production of the latter compounds, and particularly that of (13), indicates that the process involves benzophenone photoreduction by the free amine, which can derive only by the postulated thermal equilibrium (4) ⇌ (5).

The overall photoreaction of (4a) in the presence of benzophenone can be rationalized by a chemical sensitization sequence similar to that suggested by Padwa for the photoreduction of the *N*-acylimine system [4] (Scheme 2). As was reported for photoreduction of benzophenone in the presence of amine [10,11] one hydrogen is transferred from the amine to the photoexcited ketone through the charge-transfer complex [CTC], to give the ketyl (14) and the amine radicals. The ketyl radical then forms benzpinacol (12) by dimerization, 3-(diphenylhydroxymethyl)morpholine (13) by cross-coupling with amine radical, and the benzyl radical (15) by interaction with the imine structure (5). The benzyl radical (15) in its turn on one hand couples affording (10), on the other cross-couples with ketyl radical (14) affording (11). It cannot be excluded that benzylic radical (15) is also produced by interaction between morpholine radical and (5).

Furthermore, since the sensitized fluorene reaction of (4a) resulted in the formation of (9) and (10), while the photoreaction of (4a) was completely quenched by piperylene and markedly retarded by diphenyl sulphide, it may be assumed that the photoreduction of *N*-benzylidenebenzamide (5) proceeds by an electronically excited triplet state [5] according to Scheme 3. It seems likely that the benzyl radical (15) is formed

PhCHNHCOPh (NC4H8O) (4a) ⇌ (Heat) PhCH=NCOPh (5) + HNC4H8O

Ph2CO --hν--> ¹Ph2CO ⇝ ³Ph2CO* --HNC4H8O--> [CTC]

[CTC] --> Ph2C•OH (14) + •N(morpholine) --> (13) [morpholine-CPh2(OH)]

Ph2C•OH (14) --dim--> Ph2COH–Ph2COH (12)

Ph2C•OH (14) + PhCH=NCOPh (5) --(-Ph2CO)--> PhCH=NC•Ph(OH) ⇌ PhC•HNHCOPh (15) ⇌ PhC•HN=CPh(OH)

•N(morpholine) + PhCH=NCOPh (5) --> PhC•HNHCOPh (15)

PhC•HNHCOPh (15) --dim--> PhCHNHCOPh–PhCHNHCOPh (10)

PhC•HNHCOPh (15) + Ph2C•OH (14) --> PhCHNHCOPh–PhC(OH)Ph (11)
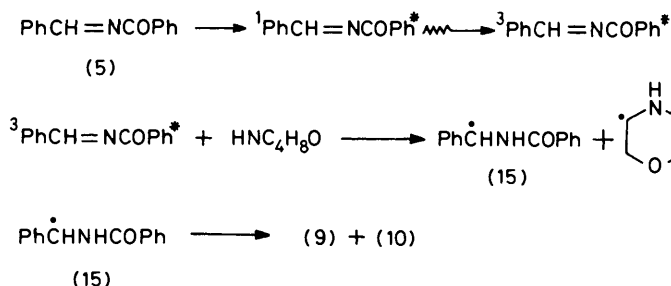
Scheme 2

by a photochemical sequence analogous to that leading to ketyl and amine radicals from benzophenone. From radical (15) in this case besides dimers of (10), the hydrogenation product (9) is obtained.
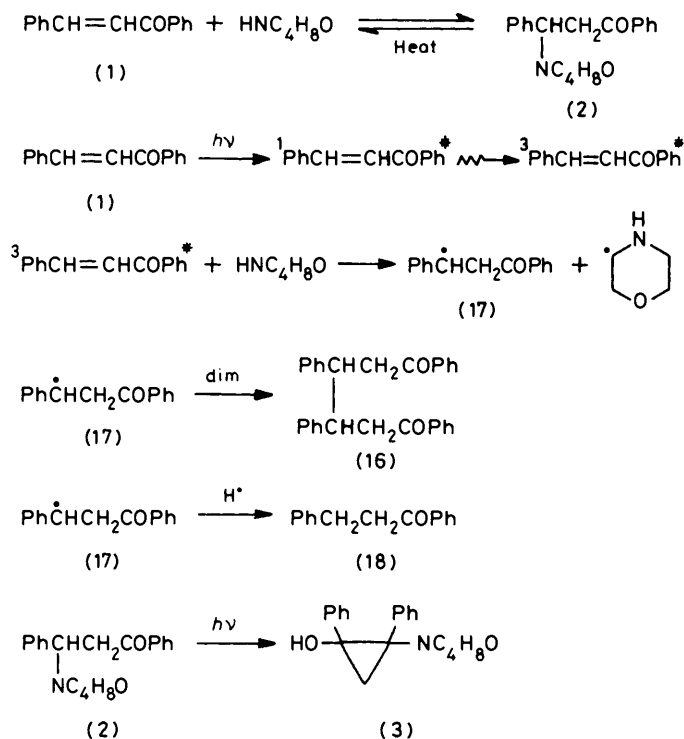
The behaviour of (5) contrasts with the other types of imines investigated [12,13] which give rise to the single dimeric adduct. The formation of a hydrogenation product may be related to the decreased activation energy for disproportionation owing to the presence of carbonyl group bonded to a nitrogen atom and to the presence of amine radicals which are a good hydrogen source.

We have also examined the photochemical behaviour of chalcone, (1), in the presence of an equimolar amount of morpholine in anhydrous benzene. On the basis of the equilibrium (1) ⇌ (2) and the above described results it was expected that the photoreaction would lead to the stereoisomeric dimers of 1,4-dibenzoyl-2,3-diphenylbutane (16) and of cyclopropane derivative (3) [2] *via* two distinct photochemical routes. The one would involve the benzyl radical (17) initially formed in the same way as benzyl radical (15), the other one the cyclization of (2) described by Roth *et al.*[2] according to Scheme 4. We have, in fact, isolated from the photolysed mixture compounds (3) and (16) in 60 and 20% yields respectively together with small amounts of 1,3-diphenylpropan-1-one (18). The unexpected formation of (18) can be rationalized by the presence of amine radicals.

In conclusion, the photoreaction of chalcone, (1), and its α-aza-analogue (5) in the presence of an equimolar amount of

$PhCH=NCOPh \longrightarrow {}^{1}PhCH=NCOPh^{*} \rightsquigarrow \longrightarrow {}^{3}PhCH=NCOPh^{*}$

(5)

${}^{3}PhCH=NCOPh^{*} + HNC_4H_8O \longrightarrow Ph\overset{\bullet}{C}HNHCOPh + $ [morpholinyl radical]

(15)

$Ph\overset{\bullet}{C}HNHCOPh \longrightarrow$ (9) + (10)

(15)

Scheme 3

$PhCH=CHCOPh + HNC_4H_8O \overset{Heat}{\rightleftharpoons} PhCHCH_2COPh$; NC_4H_8O

(1)   (2)

$PhCH=CHCOPh \overset{h\nu}{\longrightarrow} {}^{1}PhCH=CHCOPh^{*} \rightsquigarrow \longrightarrow {}^{3}PhCH=CHCOPh^{*}$

(1)

${}^{3}PhCH=CHCOPh^{*} + HNC_4H_8O \longrightarrow Ph\overset{\bullet}{C}HCH_2COPh +$ [morpholinyl radical]

(17)

$Ph\overset{\bullet}{C}HCH_2COPh \overset{dim}{\longrightarrow} PhCHCH_2COPh$; $PhCHCH_2COPh$

(17)   (16)

$Ph\overset{\bullet}{C}HCH_2COPh \overset{H^{\bullet}}{\longrightarrow} PhCH_2CH_2COPh$

(17)   (18)

$PhCHCH_2COPh$; $NC_4H_8O \overset{h\nu}{\longrightarrow} HO$ [Ph Ph cyclopropane] NC_4H_8O

(2)   (3)

Scheme 4

morpholine can be considered an example of intramolecular chemical sensitization.[5,6,14]

We are continuing to investigate the thermal and photochemical behaviour of an assortment of Mannich adducts and their α-aza-analogues in order to elucidate the role of aza-substitution on the different reactivity of the former with respect to the latter.

Experimental

M.p.s were performed on a Reichert apparatus and are uncorrected. N.m.r. spectra were taken on a Bruker 80 MHz using SiMe₄ as internal standard and deuteriochloroform as the solvent, unless otherwise stated. Mass spectra were obtained with an AIE MS-9 instrument. I.r. spectra were obtained on a Perkin Elmer 237 spectrophotometer. U.v. spectra were recorded with a Beckman DB-GT spectrophotometer using 95% aqueous ethanol as solvent. T.l.c. were carried out on silica gel F 254 plates; Merck silica gel (0.05—0.2) was used for the chromatographic separations. G.l.c. analyses were performed on a Hewlett Packard 5758B instrument equipped with a hydrogen flame ionization detector. The conditions

were: 4% silicone gum rubber UCC-982-methylvinyl on Chromosorb W(60-80 mesh) (5 ft × 1/8 in); nitrogen flow rate 42 ml min⁻¹; column temp. 120 °C for 4 min then 120 → 280 °C at 15 °C min⁻¹; injector temp. 270 °C; detector temp. 330 °C. Michler's ketone was used as internal standard. N-(α-Morpholinobenzyl)benzamide (4a) [λmax.(cyclohexane) 228 (14 215) and 254sh (4 348)] and N-(α-methoxybenzyl)-benzamide (4b) [λmax.(cyclohexane) 226 (12 380) and 252sh (1 700)] were prepared according to the literature.[3,15]

Irradiation.—In a typical irradiation experiment starting materials were dissolved in the appropriate solvent and the solution introduced in a water-jacketted immersion reactor equipped with a Hanovia 450-W medium-pressure lamp and a Pyrex filter, unless otherwise stated. Nitrogen was bubbled through for 20 min before and during irradiation. The irradiation temperature was 30 °C.

General Procedure for Thermolysis of (4a, b).—The benz-amide (4) in a Pyrex tube was thermolysed at 180 °C under a nitrogen atmosphere for 30 min. Recrystallization from MeOH gave crystalline material, m.p. 230 °C, which was identified as benzylidenebisbenzamide (8) [50% for (4a); 48% for (4b)] as judged by comparison of its n.m.r. and i.r. spectra with those of an authentic sample.[3] After separation of compound (8), the reaction mixture was chromatographed on a silica gel column and compounds (6) [12% for (4a); 9% for (4b)] and (7) [14% for (4a); 8% for (4b)] were obtained. The compounds were identified by g.l.c. and/or t.l.c., u.v. and i.r. spectra comparison with authentic samples.

Irradiation of N-(α-*Morpholinobenzyl*)*benzamide* (4a).—A solution of (4a) (400 mg) in dry benzene or tetrahydrofuran-cyclohexane (300 ml; 1 : 1 v/v) was irradiated for 44 h. The photoreaction led to precipitation of the *meso*-form of the dimers (10). This was filtered off and washed repeatedly with acetone and then chloroform; m.p. 352 °C; νmax. (KBr) 3 360 (NH) and 1 680 cm⁻¹ (NCO); δ(CF₃CO₂D) 5.96br (2H) and 7.28—7.80 (m, 20 H); m/z 210 (m/2 intense peak), 121, 114, 105 (base peak), and 77 (Found: C, 80.2; H, 5.7; N, 6.7. C₂₈H₂₄N₂O₂ requires C, 80.00; H, 5.71; N, 6.68%).

After removal of compound (10) the solvent was distilled off under reduced pressure and the residue was chromatographed on a silica gel column. Elution with benzene–ethyl acetate (4 : 1 v/v) gave successively compound (9) identified by mixed m.p. and i.r. spectra comparison with an authentic sample obtained according to the literature,[16] and a mixture of the (±)-forms of (10); m.p. 297 °C; νmax. (KBr) 3 320 (NH) and 1 680 cm⁻¹ (NCO); δ(CF₃CO₂D) 5.84br (2 H) and 7.25—7.80 (m, 20 H); m/z 210 (m/2 intense peak) 121, 119, 105 (base peak), and 77. The assignment of *meso* and (±)-stereochemistry[17] rests on the assumption that the resonance of the benzyl proton in the *meso*-isomer will appear downfield from

those of the (±)-isomers (10) The table records the yields of compounds (4a), (9), and (10) and the experimental conditions employed.

Irradiation of N-(α-*Methoxybenzyl*)*benzamide* (4b).—A solution containing (4b) (400 mg) in dry benzene or tetrahydrofuran–cyclohexane (300 ml; 1 : 1 v/v) was irradiated for 44 h. The precipitated *meso*-form of (10) was collected by filtration and the solvent was removed under reduced pressure. Inspection of the ^{1}H n.m.r. spectrum showed the presence of (4b), (9) and (±)-dimers of (10) as identifiable products. The Table records the yields of compounds (4b), (9), and (10) and the experimental conditions employed.

Irradiation of N-(α-*Morpholinobenzyl*)*benzamide* (4a) *in the Presence of Morpholine*.—Photolysis of (4a) (1.2 g) and morpholine (0.70 g) in dry benzene (300 ml) for 44 h gave only starting compounds.

Irradiation of N-*Benzylidenebenzamide* (5).—N-Benzylidenebenzamide (5) [λ$_{max.}$(cyclohexane) 268 (17 200); δ(CDCl$_3$) 7.2—7.8 (m, 10 H), and 8.75 (s, 1 H, CH=N)] was obtained by pyrolysis of N-(α-methoxybenzyl)benzamide (4b) (600 mg) under the experimental conditions reported by Ben-Ishai.[3] Irradiation in cyclohexane–tetrahydrofuran (300 ml; 1/1 v/v) for 44 h afforded compounds (9) and (10) in 10 and 40% yields respectively (determined as recorded in the Table).

Irradiation of N-(α-*Morpholinobenzyl*)*benzamide* (4a) *in the Presence of Diphenyl Disulphide*.—A solution of (4a)(1.18 g) and diphenyl disulphide (0.436 g) in dry benzene (300 ml) was irradiated for 44 h. Compounds (9) and (10) were obtained in 1 and 5% yields respectively.

Irradiation of N-(α-*Morpholinobenzyl*)*benzamide* (4a) *in the Presence of Fluorene*.—Compound (4a) (300 mg) and fluorene (400 mg) in dry benzene (300 ml) were irradiated for 44 h through a uranium filter. Compound (9), *meso*- and (±)-dimers of (10) were obtained in 10 and 50% yields respectively (determined as recorded in the Table).

Irradiation of N-(α-*Morpholinobenzyl*)*benzamide* (4a) *in the Presence of Piperylene*.—A solution of (4a) (29.5 mg) and piperylene (81.7 mg) in dry benzene (10 ml) in a Pyrex tube (1.5 cm int. diam. and 20 cm length) was degassed at 10^{-4} mmHg in several freeze-pump cycles, sealed, and then irradiated externally with a 450-W Hanovia lamp. After 44 h the solvent was removed under reduced pressure and (4a) recovered (100% yields).

Irradiation of N-(α-*Morpholynobenzyl*)*benzamide* (4a) *in the Presence of Benzophenone*.—A solution containing (4a) (400 mg) and benzophenone (200 mg) in dry benzene (300 ml) was irradiated through a uranium filter. After all the N-(α-morpholinobenzyl)benzamide (4a) was consumed (4 h), the photoreaction was stopped and the white solid, the *meso*-form of the dimers (10) (5%), was collected by filtration. Evaporation of the solvent left an oil which was chromatographed on a

silica gel column. Elution with benzene–ethyl acetate (4 : 1 v/v) gave benzpinacol (12), benzophenone, 3-(diphenylhydroxymethyl)morpholine (13) (trace), all identified by g.l.c. and i.r. comparison with authentic samples, and 1,1,2-triphenyl-1,1-hydroxy-2-benzoylaminoethane (11) (63%); m.p. 269—270 °C; ν$_{max.}$ (KBr) 3 460 (OH), 3 390 (NH), and 1 650 cm^{-1} (NCO); δ(CDCl$_3$) 3.0br (1 H), 6.25 (d, 1 H, J 7.6 Hz), and 7.3—7.1 (m, 21 H); m/z 375 (M − H$_2$O), 270, 256, 211 (base peak), 210, 193, 183, 182, 106, 105, 91, and 77 (Found: C, 82.4; H, 5.85; N, 3.6. C$_{21}$H$_{23}$NO$_2$ requires C, 82.44; H, 5.85; N, 3.56%).

Irradiation of ω-*Benzylidenacetophenone* (1) *in the Presence of Morpholine*.—A solution containing compound (1) (2.91 g) and morpholine (1.21 g) in dry benzene was irradiated until all the ω-benzylideneacetophenone (1) was consumed (24 h). On precipitation, the white solid was collected by filtration and identified as the *meso*-form of 1,4-dibenzoyl-2,3-diphenylbutane (16) (15%) by comparison with an authentic sample. Evaporation of the solvent left an oil which was chromatographed on a silica gel column. Elution with benzene gave 1,3-diphenylpropan-1-one (18) (2%), 2-morpholino-1,2-diphenylcyclopropanol (3) (60%), and (±)-forms of the dimer (16) (5%) identified by t.l.c., i.r., n.m.r. and m/z comparison with authentic samples obtained according to literature reports.[2,18]

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