Hydrogen-Bonding Effects in Photo-Fries and Photoanilide Rearrangements

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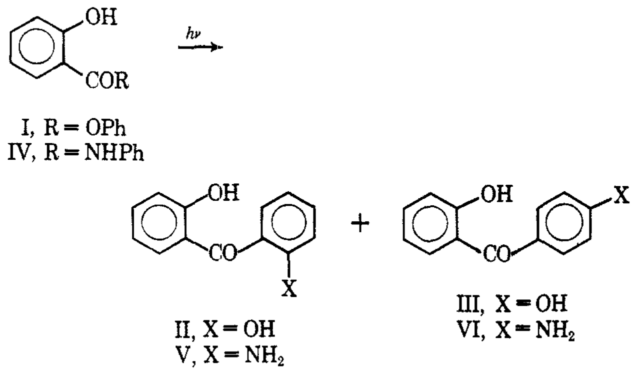
Aryl esters and anilides are known to undergo photochemical rearrangements to give the corresponding *ortho-* and *para*-rearranged hydroxy and amino ketones, respectively. These rearrangements are referred to as the photo-Fries[1] and the photoanilide[2] rearrangements. A typical example is the formation of 2- and 4-hydroxybenzophenone from phenyl benzoate and 2- and 4-aminobenzophenone from benzanilide. We wish to report our findings with phenyl salicylate and salicyanilide and the effect of hydrogen bonding on these rearrangements.

When phenyl salicylate (I) in anhydrous methanol was irradiated for 20 hr, in accordance with earlier findings,[3,4] the expected 2,2′-dihydroxybenzophenone (II) and 2,4′-dihydroxybenzophenone (III) were formed in 28 and 32% yields, respectively. The percentage conversion was 68% based on the recovered starting material. Neither phenol nor salicylic acid was found in the reaction mixture. When the irradiation was carried out in *n*-hexane, the yields of II and III fell to 4 and 1%, respectively, and the percentage conversion went down to 9%.



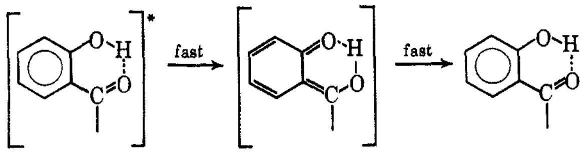
I, R = OPh
IV, R = NHPh

II, X = OH
V, X = NH_2

III, X = OH
VI, X = NH_2

When salicylanilide (IV) was irradiated in methanol, the rearrangement occurred to a very small extent, as indicated by the low percentage conversion (4%). Two products, in extremely small yields, were isolated and they were found to be 2-amino-2′-hydroxybenzophenone (V) and 4-amino-2′-hydroxybenzophenone (VI) from infrared spectral data. Earlier studies in the photo-Fries rearrangement have indicated that solvent polarity has no effect on the extent of reaction.[1c] In the present work, the effect of solvents on the rearrangement of phenyl salicylate and the very low reactivity of salicylanilide compared with that of benzanilide to undergo photoanilide rearrangement are due to the presence of intramolecular hydrogen bonding in these substances.

A good example of the effect of intramolecular hydrogen bonding on photochemical behavior is the case of the photoreduction of benzophenone and the corresponding 2-hydroxy compound. While benzophenone undergoes photoreduction, the corresponding 2-hydroxy compound does not.[5] This inactivity of 2-hydroxybenzophenone was suggested as being due to a fast decay of the excited state in the form of a tautomeric shift *via* hydrogen bonding involving a six-membered ring (eq 1). Recently, Lamola and Sharp have reported[6] that 2-hydroxy-4-methoxybenzophenone at 77°K exhibits phosphorescence in polar solvents but not in nonpolar solvents. They suggested that in nonpolar solvents the molecules exist intramolecularly hydrogen bonded and tautomerization is favored and hence no emission is observed. On the other hand, in polar solvents which are capable of hydrogen bonding, this intramolecular hydrogen bond is broken to a great extent, thereby preventing the tautomerization and favoring emission. The photochromism exhibited by anils of salicylaldehydes was also suggested[7] to be due to a similar proton shift in the excited state.



(1)

We feel that in the cases of salicylanilide and phenyl salicylate similar situations also exist. Thus, for phenyl salicylate in methanol, the intramolecular hydrogen bond is broken to a great extent and hence the photo-Fries rearrangement is favored. In *n*-hexane, on the other hand, the molecules are predominantly intramolecularly hydrogen bonded and the rearrangement occurs to a lesser extent. The fact that the rearrangement occurred to a much smaller extent with salicylanilide in methanol is interpreted to mean that the intramolecular hydrogen-bond strength in salicylanilide is much stronger than that in phenyl salicylate.[8,9]

The O-methyl ether of salicylanilide (VII), wherein the intramolecular hydrogen bond between the carbonyl group and the hydroxy group is eliminated, gave three products upon irradiation in ethanol for 48 hr. They were found to be 2-methoxy-2′-aminobenzophenone (VIII), 2-methoxy-4′-aminobenzophenone (IX), and aniline. The yields of the ketones were

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[1] (a) J. C. Anderson and C. B. Reese, *J. Chem. Soc.*, 1781 (1963); (b) H. Kobsa, *J. Org. Chem.*, **27**, 2293 (1962); (c) R. A. Finnegan and J. J. Mattice, *Tetrahedron*, **21**, 1051 (1965).

[2] D. Elad, D. V. Rao, and V. I. Stenberg, *J. Org. Chem.*, **30**, 3252 (1965).

[3] The yellowing of certain plastic films incorporated with phenyl salicylate upon exposure to ultraviolet light and sunlight was reported[4] to be due to such a rearrangement.

[4] G. C. Newland and J. W. Tamblyn, *J. Appl. Polymer Chem.*, **8**, 1949 (1964).

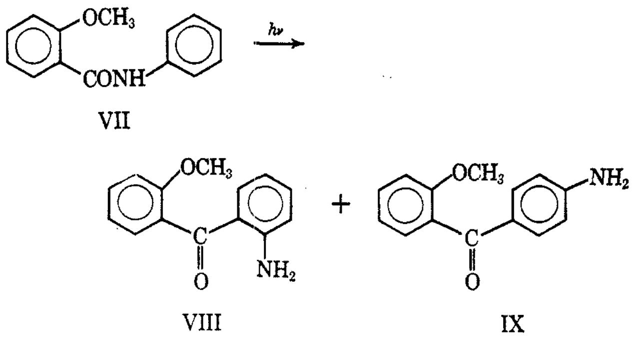
[5] N. J. Turro, "Molecular Photochemistry," 1st ed, W. A. Benjamin, Inc., New York, N. Y., pp 149–154.

[6] A. A. Lamola and L. J. Sharp, *J. Phys. Chem.*, **70**, 2634 (1966).

[7] M. D. Cohen and G. M. J. Schmidt, *ibid.*, **66**, 2442 (1962); M. D. Cohen, Y. Hirshberg, and G. M. J. Schmidt in "Hydrogen Bonding," D. Hadzi, Ed., Pergamon Press Inc., New York, N. Y., 1959, p 293.

[8] From infrared spectral data, the intramolecular hydrogen-bond strengths of salicylanilide and phenyl salicylate were calculated[9] to be 8.5 and 5.8 kcal/mole, respectively. It was suggested[9] that the long wavelength shift of the fluorescence band of salicylanilide in both heptane and acidified ethanol was due to the presence of intramolecular hydrogen bonding.

[9] Y. V. Naboikin, B. A. Zadrozhnyi, and E. N. Pavlova, *Izv. Akad. Nauk. SSSR, Ser. Fiz.*, **23**, 9 (1959).



VII

VIII

IX

very low, although the percentage conversion was 24%. This may be due to some side reaction of the intermediates involved instead of the photoanilide rearrangement. In support of this is the isolation of considerable tarry material during the work-up of the reaction mixture. It is also interesting to note that this reaction differs from benzanilide in that considerable amounts of benzoic acid and no detectable amounts of aniline resulted when benzanilide was irradiated in ethanol.[2]

Experimental Section

Irradiation Procedure.—All irradiations were performed using a 450-w Hanovia mercury lamp (Type 679A 36) and a water-cooled immersion-type quartz probe (Type 19434). A three-neck cylindrical Pyrex flask was used fitted with standard tapered openings for a water-cooled condenser and a nitrogen inlet tube. The reaction mixture was thoroughly flushed with prepurified nitrogen and was kept under a nitrogen atmosphere during the irradiation. The solution was kept stirring with a magnetic stirring apparatus.

Materials.—Spectral grade solvents were used for irradiation and the anilides and phenyl salicylate were purified by recrystallization and thoroughly dried before use. All melting points are uncorrected.

Spectra.—All ultraviolet spectra were taken on a Beckman DB-G spectrophotometer and infrared spectra on Beckman spectrophotometer, Model IR-4. The nmr spectra were taken on a Varian Associates A-60 spectrometer using tetramethylsilane as internal standard.

Chromatography.—For thin layer chromatography, Eastman chromagram sheets (Type K5301 R) were used. The spots were detected with an ultraviolet lamp (UVSL-13, supplied by Ultra Violet Products, Inc., San Gabriel, Calif.). For column chromatography, silica gel (100–200 mesh, supplied by Bio-Rad Laboratories, Richmond, Calif.) and grade II neutral alumina (made by adding 3 ml of water to 97 g of grade I, supplied by Merck Darmstadt) were used.

Irradiation of Phenyl Salicylate in Methanol.—Phenyl salicylate (5.00 g) in 600 ml of methanol was irradiated for 21 hr. The course of the reaction was followed with tlc. After 1 hr of irradiation, two new products were detected. The yellow alcohol solution was concentrated *in vacuo* on a hot water bath and the residue was dissolved in 25 ml of *n*-hexane. This solution was subjected to column chromatography on silica gel (125 g). Elution of the column with *n*-hexane gave 1.60 g (32%) of a colorless liquid which solidified on standing. It was found to be the unconverted starting material (infrared spectral comparison with phenyl salicylate). Further elution with *n*-hexane gave 1.40 g (28%) of a yellow liquid which solidified on standing. Recrystallization from ligroin gave yellow crystals, mp 61.0–62.0° (lit.[10] mp of 2,2′-dihydroxybenzophenone 59.0–61.0°). This sample was found to be identical with an authentic sample (mixture melting point and infrared). Infrared spectrum ($CHCl_3$) had 3.12, 6.16, 6.30, 6.74, 6.87, 7.47, 7.66, 8.67, 9.66, 10.64, 11.58, 11.90, 12.33, and 15.48 μ. Further elution with *n*-hexane–ether in 4:1 (v/v) gave 1.60 g (32%) of a yellow solid. It was recrystallized from ethanol–water in 1:1 (v/v) to give yellow flakes, mp 146.0–147.0° (for 2,4′-dihydroxybenzophenone, lit.[11] mp 147.0–149.0°). Comparison with an authentic sample (mixture melting point and infrared) showed them to be identical. Infrared spectrum ($CHCl_3$) had 2.78, 3.06, 6.15, 6.24, 6.74, 6.91, 7.50, 7.62, 8.50, 8.60, 9.64, 10.86, and 11.80 μ.

Irradiation of Phenyl Salicylate in *n*-Hexane.—Phenyl salicylate (5.00 g) in 600 ml of *n*-hexane was irradiated for 21 hr. Similar work-up gave 4.55 g (91%) of phenyl salicylate, 0.20 g (4%) of 2,2′-dihydroxybenzophenone, and 0.05 g (1%) of 2,4′-dihydroxybenzophenone.

Irradiation of Salicylanilide.—Salicylanilide (5.0 g) in 600 ml of methanol was irradiated for 3 days. By tlc on silica gel plates using benzene–ether in 4:1 (v/v), two extremely weak brown spots could be detected. Removal of the solvent *in vacuo* left a brown solid residue which was taken up in ether and extracted with 5% $NaHCO_3$ and 10% HCl. Upon evaporation of the ether solution, 4.8 g (96.0% recovery) of the starting material (infrared spectral comparison) was recovered. Work-up of the bicarbonate solution did not give any acidic material. The acid solution was carefully neutralized with 5% $NaHCO_3$ and extracted with ether several times. From the ether solution, an extremely small amount of sticky liquid (*ca.* 15 mg) was obtained. It was chromatographed over 25 g of silica gel using benzene–*n*-hexane in 4:1 (v/v) to give a small amount (*ca.* 5 mg) of a yellow liquid (compound A). Infrared spectrum ($CHCl_3$) had 2.86 and 2.96 (NH_2), 6.2 (C=O), 6.30 (aromatic double bond), and a series of strong bands at 6.76, 6.90, 7.50, 7.66, 8.62, 9.68, 11.70, 11.88, 12.34, and 15.5 μ. Further elution with benzene gave a small amount (*ca.* 5 mg) of a pale yellow solid (compound B), mp 136–138°. Infrared spectrum ($CHCl_3$) had 2.84 and 2.94 (NH_2), 6.16 (C=O), 6.28 (aromatic double bond), and a series of bands at 6.74, 6.93, 7.50, 7.63, 8.84, 8.60, 9.68, 10.70, and 11.90 μ. From the infrared spectral data, the structures of compounds A and B are consistent with those of 2-amino-2′-hydroxybenzophenone and 4-amino-2′-hydroxybenzophenone. No further identification of these ketones was made.

Irradiation of O-Methylsalicylanilide.—O-Methylsalicylanilide (5.00 g) in 600 ml of ethanol was irradiated for 48 hr. The resulting red alcoholic solution was concentrated *in vacuo* and the residue taken up in ether. The ether solution was filtered from dark suspended material and extracted with 10% hydrochloric acid and then with 10% sodium bicarbonate. During these extractions a tarry insoluble material precipitated out. The bicarbonate solution gave no product upon acidification followed by extraction with ether. The acid extract was carefully neutralized with sodium hydroxide and extracted several times with ether. After drying over anhydrous magnesium sulfate and evaporation, there was obtained 0.70 g of a dark brown liquid. From the ether solution 3.80 g (76%) of the starting material was obtained.

By glpc the basic material (0.70 g) was found to contain 0.40 g of aniline. Another 0.0275 g was found in the ethanol distillate (ultraviolet estimation), giving a total yield of 8.5%. Aniline was removed from the mixture by steam distillation and the infrared spectrum of the distillate was identical with that of authentic aniline.

The nonsteam volatile residue (0.25 g) was chromatographed over neutral alumina (25.0 g). Elution with *n*-hexane–benzene in 2:3 (v/v) gave 0.035 g (0.7%) of a yellow solid. It was vacuum sublimed, 120° (0.4 mm), and recrystallized from Skellysolve B to give pale yellow needles, mp 111.0–112.0° (for 2-methoxy-2′-aminobenzophenone, lit.[12] mp 110.0–111.0°). It was identical with an authentic sample[13] of 2-methoxy-2′-aminobenzophenone by mixture melting point and infrared spectral comparison.

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.90; H, 5.77; N, 6.16. Found: C, 74.12; H, 5.61; N, 6.32.

Further elution with benzene–ether in 4:1 (v/v) gave 0.142 g (2.8%) of a light brown solid. It was vacuum sublimed, 170° (0.4 mm), followed by recrystallization from ethanol–water in 1:1 (v/v) to give pale cream needles, mp 166.6–167.6°. No direct comparison with an authentic sample of 2-methoxy-4′-aminobenzophenone could be made as this compound has not been reported in the literature. Infrared spectrum ($CHCl_3$) had 2.86 and 2.94 (NH_2), 6.07 and 6.17 (C=O), 8.03 and 9.73 μ (=$COCH_3$); ultraviolet (ethanol), 235 mμ (log ε 3.9901), 330 mμ (log ε 4.3836); nmr ($CDCl_3$), singlet at δ 3.72 (3 H, OCH_3), broad band at 4.18 (2 H, NH_2), set of doublets at 6.56

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[10] C. Graebe and A. Freer, *Chem. Ber.*, **19**, 2609 (1886).

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[12] M. Lamchen and A. J. Wicken, *J. Chem. Soc.*, 2739 (1959).

[13] A sample of this material was kindly furnished by Dr. M. Lamchen, University of Capetown, Rondebosch, Capetown, South Africa.

and 7.65 (4 H, A_2B_2 quartet, $J = 9$ cps, aromatic ring with NH_2), and multiplet between 6.84 and 7.50 (4 H aromatic ring with OCH_3).

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.90; H, 5.77; N, 6.16. Found: C, 74.11; H, 5.76; N, 6.45.

Registry No.—II, 835-11-0; III, 606-12-2; V, 13134-93-5; VI, 13134-94-6; VIII, 1424-76-6; IX, 13134-96-8.

Heterogeneous Photosensitization

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The majority of photosensitized chemical reactions are conducted with the sensitizer and the substrate in the same physical phase and cross-phase sensitization is rarely used. However, use of a sensitizer in a different phase from that of the substrate has the advantage that there are no problems of separation of the sensitizer from the products or reactants. Practically, a suitable solid sensitizer could be placed in a column irradiated by a suitable light source, gaseous or liquid reactant run slowly over the sensitizer, and the reaction products eluted from the bottom of the column.

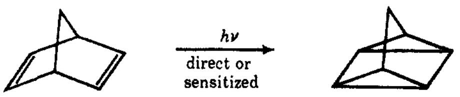
We have used the solid polymer polyvinylphenyl ketone (polyacrylophenone), the photosensitizing properties of which have been briefly investigated previously,[1] as a photosensitizer for the systems piperylene, norbornadiene, and myrcene.

Polyvinylphenyl ketone is closely analogous to acetophenone which is commonly used as a photosensitizer. Acetophenone has a triplet energy of 74 kcal/mole[2] and an intersystem crossover efficiency of 0.99.[3] A polymer with properties similar to these would be an efficient sensitizer of the three systems investigated.

Phenyl vinyl ketone was prepared as a pale yellow oil from β-chloropropionyl chloride.[4,5] Polymerization was effected by azobisisobutyronitrile initiation at 55° in benzene. The polymer was obtained as a plastic mass by precipitation from benzene by petroleum ether (bp 60°) and became quite brittle when vacuum dried. It was cut into small pieces (~2 mm^3) for sensitization experiments. The ultraviolet spectrum shows absorption at 280 mμ associated with the $n-\pi^*$ transition of the carbonyl group and the infrared spectrum shows the absorption at 1675 cm^{-1} characteristic of an aromatic carbonyl. The emission spectrum in an ether-tetrahydrofuran glass at 77°K showed a well-resolved progression of bands with maxima at 395 (0–0 band, triplet energy of 72.4 kcal), 420, 450, and 485 mμ, which compares to acetophenone under the same conditions with peaks at 380 (0–0 band, 74.0 kcal), 412, 440, and 472 mμ. Clearly the triplet state of the polymer is much like that of acetophenone.

Initially the polymer was used to sensitize the *cis-trans* isomerization of a 1.0 *M* solution of *cis*-piperylene in Spectrograde isopentane, a solvent in which the polymer was shown to be totally insoluble (to the limits of ultraviolet detection in the 280–320-mμ region). All energy transfer, then, must be heterogeneous. Typically, a well-stoppered test tube containing 0.3 g of the solid polymer and 2 ml of an isopentane solution of piperylene was attached to and irradiated by a water-cooled Hanovia 450-w medium-pressure reactor fitted with a Pyrex envelope to prevent direct excitation of the diene. A photostationary state *trans/cis* of 1.18 was obtained after 24 hr irradiation. This ratio is in the range expected from a sensitizer with a triplet energy close to that of acetophenone.[6]

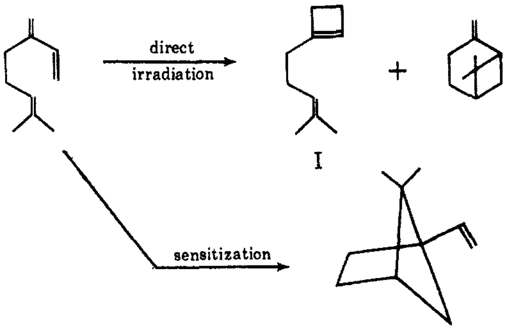
The valence isomerization of norbornadiene to quadricyclene (eq 1) has been found to be a quite clean reaction either by direct irradiation[7] or by sensitization with a variety of sensitizers.[8] A yield of 90% quadricyclene has been obtained with acetophenone as sensitizer in isopentane solution.[8]



(1)

Sensitization of neat norbornadiene by the polymer over a period of 17 hr gave a net yield (by vpc) of approximately 60% quadricyclene and a number of minor products. The conversion was kept to less than 10%. Identification of the quadricyclene was on the basis of comparison of its retention times with an authentic sample on vpc columns of S.E. 30 and S.F. 96 and its nmr spectrum. The nmr shows a broad group with its highest peak at τ 8.58 owing to the protons on the cyclopropane rings and a triplet owing to the methylene protons at τ 8.04.[7] During irradiation the polymer changed its form from solid pieces to a single plastic mass; however, a neat aliquot of supernatent liquid showed negligible absorption in the 300–320-mμ region indicating virtually no dissolution of the polymer.

The direct photolysis of myrcene produces a number of products of which 54% is the cyclobutene I and 9% is β-pinene.[9] In contrast, the sensitized photolysis produces just one product, 5,5-dimethyl-1-vinylbicyclo[2.1.1]hexane, with a quantum yield of 0.05[10] (eq 2).



(2)

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