

Solid State Photochemistry of Ternary Cyclodextrin Complexes: Total Selectivity in the Photoreduction of Nitrophenyl Ethers by 1-Phenylethylamine

Miquel Mir, Jorge Marquet,* and Eduard Cayón

Department of Chemistry. Universitat Autònoma de Barcelona.
08193 Bellaterra. Barcelona. Spain

Abstract: The irradiation of the ternary complexes of β -cyclodextrin with several nitrophenyl ethers, and 1-phenylethylamine in the solid state, produces selective photoreduction to the corresponding nitroso derivatives.

Generally, organic chemistry reactions are carried out in isotropic media, therefore, they happen with free tridimensional mobility and random collision orientation of the reagents. Any selectivity is derived from electronic or steric factors. On the other hand, in biological media, the enzyme-substrate complex only allows the movement of the reagents in the direction of the reaction coordinate, achieving that way a high selectivity.

The photoreactions of nitrophenyl ethers in the presence of nucleophiles show an interesting synthetic potential¹, however, their utility is hampered by their complex mechanistic variety², depending on the selectivity of the substrate and the nucleophile in each case. Photosubstitutions at different ring positions³ and photoreductions⁴ are generally observed. Those photoreduction processes give mixtures of nitroso, hydroxylamino and anilino derivatives, and condensation products like azo and azoxy compounds. We wish to report here an example of the limits of the conventional approach to the control of the chemoselectivity of those photoreactions. A novel, and successful, approach to this chemoselectivity control, based on the use of ternary complexes of the reagents with β -cyclodextrin in the solid state, is described.

Cyclodextrins (CDs) are cyclic molecules consisting of either six, seven, or eight glucose units (α -, β - and γ -CD respectively), each having different cavity diameter. They can form inclusion complexes with a variety of guest compounds without any covalent bond being formed. Most reported catalytic reactions of cyclodextrins, either in solution or in the solid state, involve a binary complex of the CD with a single organic substrate⁵. Those binary complexes can associate giving (two guest)-(two host) (2:2) complexes that in some cases show a very interesting photochemistry⁶ (even asymmetric induction has been reported). In a few reports, two dissimilar organic reactants have been contacted within a ternary CD complex in solution⁷. Also

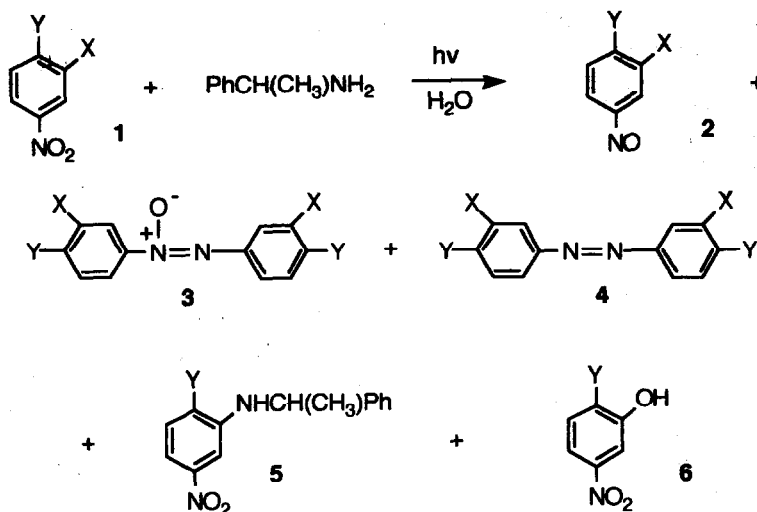
some reports exist about reactions of ternary complexes of CD in the solid state, formed through absorption of one of the guests from the vapour phase⁸.

4-Nitroanisole^{2c,3a,9} (1, X=H, Y=OMe, Scheme), 3-nitroanisole¹⁰ (1, X=OMe, Y=H, Scheme) and 4-nitroveratrole^{2a,3a} (1, X=OMe, Y=OMe, Scheme) photoreact in water solution with primary amines, and even with secondary amines giving rise mainly to photosubstitution products. Competition between photosubstitution and photoreduction, for a particular case, and providing the initial electron transfer step is feasible, will probably depend on the proton transfer ability of the amine cation radical¹¹ (in basic water solution). We considered that the use of a primary amine with a high tendency to proton transfer (following the electron transfer step) would translate into a change with respect to the normal behavior of primary amines, photoreduction as a major process, being expected in this case. The results of the photoreactions between 1-phenylethylamine and 4-nitroanisole, 3-nitroanisole and 4-nitroveratrole in water solution are reported in the Table (entries 1, 3 and 5). The results in the cases of 4- and 3- nitroanisoles (entries 1 and 3) are remarkable since no photosubstitution products are obtained. In the case of 4-nitroveratrole (entry 5), the same tendency is observed (presence of photoreduction products), but the photoreaction is more complicated, the major process being substitution by OH⁻. Those results show clearly the limits of a classical approach to the control of these photoreactions in solution. In addition to photosubstitution products (4-nitroveratrole case), condensation photoreduction products like azoxy, 4, and azo, 5, derivatives are obtained in variable amounts.

In addition to the just demonstrated reductand ability of 1-phenylethylamine in our photoreactions, their structural features (presence of a phenyl ring) made it suitable for complexation with cyclodextrins. Ternary [(nitrophenyl ether)/(1-phenylethylamine)/(β-CD)] complexes were precipitated from water. A mixture of 0.11 mmols of nitrophenyl ether, 0.24 mmols of 1-phenylethylamine and 0.35 mmols of β-CD in 20 ml of water was sonicated for 1.5 h. On cooling, a precipitate identified as a crystalline mixed inclusion complex by FTIR spectroscopy, forms. The guest-host molar ratio was determined by ¹H NMR in DMSO-D₆, being 1:1:2 (nitrophenyl ether / 1-phenylethylamine / β-CD). These complexes were stable to air. Irradiation of the ternary complexes in the solid state afforded in all the cases (Table, entries 2, 4 and 6) the corresponding nitroso compound in practically quantitative amounts as unique photoproduct derived from the nitrophenyl ether. Conversions were limited to less than 20%. Acetophenone (resulting from oxidation and hydrolysis of the 1-phenylethylamine) was also obtained. To our knowledge, those are the first examples of bimolecular photoreactions between dissimilar reagents in a solid CD phase. In blank experiments, mechanical mixtures of the nitrophenyl ethers and the complex of 1-phenylethylamine with β-CD were irradiated. No photoreaction was detected.

The photoreaction of 4-nitroanisole (1, X=H, Y=OMe) and 1-phenylethylamine was also studied in water solution in the presence of β-CD. A small catalytic effect was observed ($\Phi_{\beta\text{-CD}}/\Phi = 1.16$) in the production of 4-nitrosoanisole. This result suggests the presence in solution of associations of binary complexes CD-(4-nitroanisole) and CD-(1-phenylethylamine) in such an arrangement the nitro and amino groups are placed close enough to interact.

Our results in the solid state could be rationalized assuming the ternary complex (in our cases) crystallizes in channel structures¹². Those channels would behave as a pseudofluidal medium only allowing certain reagent movements (enough to produce



Scheme

Table. Comparison between the Photoreactions of Nitrophenyl Ethers with 1-Phenylethylamine in Water Solution, and the Corresponding Photoreactions of the Ternary Complex (Nitrophenyl Ether/ β -CD/1-Phenylethylamine) in the Solid State.

Entry	Substrate	Conditions ^a	Product ^b yields				
			2	3	4	5	6
1	1 (X=H, Y=OMe)	Water solution, 1h	66	4	2	-	-
2	1 (X=H, Y=OMe)	Solid state, 1h β -CD ternary complex	>95	-	-	-	-
3	1 (X=OMe, Y=H)	Water solution 1h	37	21	-	-	-
4	1 (X=OMe, Y=H)	Solid state, 1h β -CD ternary complex	>95	-	-	-	-
5	1 (X=OMe, Y=OMe)	Water solution, 1.5 h	17	c	-	7	41
6	1 (X=OMe, Y=OMe)	Solid state, 30m β -CD ternary complex	>95	-	-	-	-

a) 400W Medium pressure Hg lamp with pyrex filter. Room Temperature. Excess of amine in the photoreactions carried out in water solution. b) The new products gave correct elemental analyses. Their full characterization will be reported elsewhere. Yields based in non recovered starting material. c) Traces.

redox photochemistry, specially if the proper arrangement suggested by the solution experiment is maintained in the solid state), but strongly restricting some others (needed to form covalent bonds). Structural studies are currently in progress and a full account will be published in the near future.

Acknowledgements.- We thank the DGICYT (Ministerio de Educación y Ciencia of Spain, Project PB90-0693) for financial support, and Prof. M. Moreno-Mañas for helpful discussions

References

1. Cornelisse, J.; Havinga, E. *Chem. Rev.* 1975, 75, 353.
2. (a) Cantos, A.; Marquet, J.; Moreno-Mañas, M.; Castelló, A. *Tetrahedron* 1988, 44, 2607. (b) Van Eijk, A.M.J.; Huizer, A.H.; Varma, C.A.G.O.; Marquet, J. *J. Am. Chem. Soc.* 1989, 111, 88. (c) Cantos, A.; Marquet, J.; Moreno-Mañas, M.; Gonzalez-Lafont, A.; Lluch, J.M.; Bertrán, J. *J. Org. Chem.* 1990, 55, 3303. (d) Cayón, E.; Marquet, J.; Lluch, J.M.; Martín, X. *J. Am. Chem. Soc.* 1991, 113, 8970. (e) Marquet, J.; Cantos, A.; Moreno-Mañas, M.; Cayón, E.; Gallardo, I.; *Tetrahedron* 1992, 48, 1333.
3. (a) Cervelló, J.; Figueredo, M.; Marquet, J.; Moreno-Mañas, M.; Bertrán, J.; Lluch, J.M. *Tetrahedron Lett.* 1984, 25, 4147. (b) Cantos, A.; Marquet, J.; Moreno-Mañas, M. *Tetrahedron Lett.* 1989, 30, 2423.
4. (a) Dopp, D. *Topics in Current Chem.* 1975, 55, 49. (b) Marquet, J.; Moreno-Mañas, M.; Vallribera, A.; Virgili, A.; Bertrán, J.; Gonzalez-Lafont, A.; Lluch, J.M. *Tetrahedron* 1987, 43, 351. (c) Petersen, W.C.; Letsinger, R.L. *Tetrahedron Lett.* 1970, 3509.
5. (a) Bender, M.L.; Komiyama, M. *Cyclodextrin Chemistry*, Springer-Verlag, Berlin, 1978. (b) Saenger, W. *Angew. Chem. Int. Ed. Engl.* 1980, 19, 344. (c) Ramamurthy, V. *Tetrahedron* 1986, 42, 5753.
6. (a) Tamaki, T.; Kokuba, T.; Ichimura, K. *Tetrahedron* 1987, 43, 1485. (b) Rao, V.P.; Turro, N.J. *Tetrahedron Lett.* 1989, 30, 4641.
7. Schaeffer, H.J.; Beauchamp, L.; Miranda, P. de; Elion G.B.; Bauer, D.J.; Collins, P. *Nature*, 1978, 272, 583.
8. (a) Gountzos, H.; Jackson, W.R.; Harrington, K.J. *Aust. J. Chem.* 1986, 39, 1135. (b) Wernick, D.L.; Yazbek, A.; Levi, J. *J. Chem. Soc. Chem. Commun.* 1990, 956. (c) Tanaka, Y.; Sakuraba, H.; Nakanishi, H. *J. Org. Chem.* 1990, 55, 564. (d) Shimada, M.; Harada, A.; Takahashi, S. *J. Chem. Soc. Chem. Commun.* 1991, 263.
9. Kronenberg, M.E.; Van der Heyden, A.; Havinga, E. *Recl. Trav. Chim. Pays-Bas.* 1966, 85, 56.
10. Havinga, E.; De Jongh, R.O. *Bull. Soc. Chim. Belg.* 1962, 71, 803.
11. (a) Sundararajan, K.; Ramakrishnan, V.; Kuriacose, J.C. *Indian J. Chem., Sect B* 1983, 22B, 257. (b) *Ibid. J. Photochem.* 1984, 27, 61.
12. (a) McMullan, R.K.; Saenger, W.; Fayos, J.; Mootz, D. *Carbohydr. Res.* 1973, 31, 211. (b) Hamilton, J.A.; Chen, L. *J. Am. Chem. Soc.* 1988, 110, 5833.

(Received in UK 10 July 1992)