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THE PHOTOCYCLOADDITION OF CARBOSTYRIL TO OLEFINS

G. R. Evanega and D. L. Fabiny

Union Carbide Research Institute
P.O. Box 278, Tarrytown, New York

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The photochemical dimerization of carbostyril and N-methylcarbostyril has been described by several workers (1,2), and the stereochemistry of the dimers has been elucidated by O. Buchardt (2b). We would like to report another reaction of the excited carbostyril molecule, viz. its addition to olefins to form 1:1 adducts. The adducts of carbostyril with tetramethylethylene, isobutylene, cyclopentene and vinyl methyl ether are presented.

The photochemistry of coumarin, a heteroanalog of carbostyril, is quite unique. Coumarin (E_T = 62 kcal/mole) (3a) is reported to undergo sensitized photocycloaddition to olefins (4) (indene, tetramethylethylene, cyclopentene and ketene diethyl acetal). Benzophenone (E_T = 69 kcal/mole) has been used as a sensitizer (4a,b) although triphenylene (E_T = 67 kcal/mole) should be preferred (4c) for synthetic purposes since oxetane formation (4b,5) and hydrogen abstraction reactions (5) can be avoided. The sensitizer assists in the intersystem crossing of coumarin from the excited singlet to the triplet state (3a). In addition to the cycloaddition reaction with olefins, coumarin forms four different dimers (6) depending upon concentration (7) and energy absorption (sensitized or unsensitized) (3).

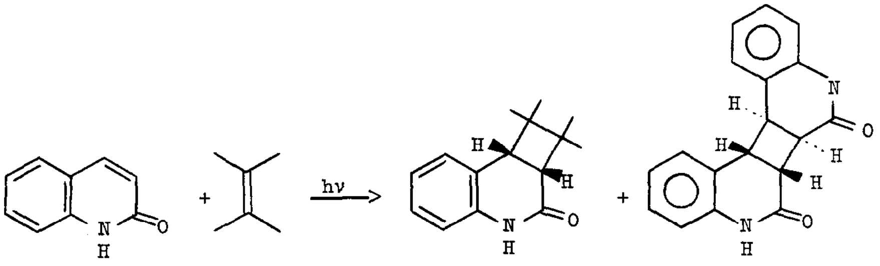
In contrast, carbostyril does not need a triplet energy sensitizer for photocycloaddition to olefins or for dimer formation. The reaction proceeds smoothly to give the adduct and the anti-head-to-head dimer (2b).

A 700 ml ethanol solution containing carbostyril (I, 10.0 g., 0.069 mole) and tetramethylethylene (58 g., 0.69 mole) was purged initially with nitrogen and irradiated for 20 hr. in a quartz vessel in a Rayonet photochemical reactor[†] equipped with 3500 Å Hg vapor black light fluorescent lamps. The dimer (2b) III was obtained in 9.4% yield and the 1:1 adduct II, m.p. 197.5-198.5°, IR (KBr) C=O str 1666 cm^{-1}, in 90% yield. The NMR spectrum,[‡]

[†] Rayonet, Srinivasan-Griffin, Photochemical Reactor, Southern N.E. Ultraviolet Company, Middletown, Conn.

[‡] The NMR spectra were determined in CF_3CO_2D, unless otherwise specified, on a Varian A-60 spectrophotometer.

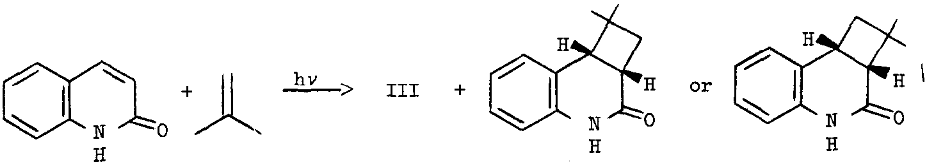
in agreement with structure II, shows four methyl singlets at 0.83 δ, 1.13 δ, 1.32 δ and 1.36 δ, four aromatic hydrogens at 7.13 δ (m) and two cyclobutane hydrogens as an AB pattern at 3.40 δ and 3.57 δ (J_{AB} = 10.5 Hz). Based on the large coupling constant (6,8,9) for the two cyclobutane hydrogens of II and the analogy to olefin adducts of coumarin (4b), the hydrogens are *cis* and the rings are therefore *cis* fused.



I II III

Even though *cis* ring fusion prevails, the photoaddition of carbostyril to less symmetrical olefins such as isobutylene could lead to a mixture of isomers. However, only one adduct was obtained.

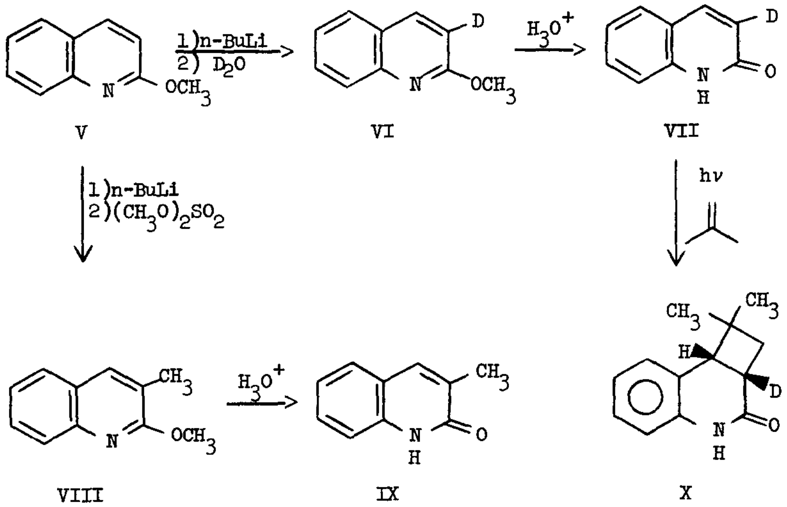
Irradiation of a 700 ml ethanol solution containing carbostyril (10.0 g., 0.069 mole) and isobutylene (17 g., 0.29 mole) as described above gave the dimer III in 40% yield and the adduct IV, m.p. 172.5-173.5°, IR (KBr) C=O str 1667 cm^{-1}, in 57% yield. The NMR of IV is too complex for one to decide between structures IVa or IVb; four aromatic hydrogens at 7.18 δ (m), two methyl singlets at 0.92 δ and 1.38 δ, two cyclobutane hydrogens at 2.49 δ (m) and two more at 3.65 δ (m). The NMR spectrum was simplified by preparing 3-deuteriocarbostyril VII and the corresponding deuterated adduct X.



IVa IVb

By analogy to the work of Gilman (10) on 2-ethoxyquinoline, 2-methoxyquinoline (V) was reacted with n-butyl lithium for 2 1/2 hr. and then quenched with D_2O. Column chromatography gave 3-deuterio-2-methoxyquinoline (VI) in 62% yield, which by acid hydrolysis gave 3-deuteriocarbostyril VII in 95% yield. The NMR spectrum of VII (in DMSO-d6) has a singlet for the olefinic hydrogen at 7.83 δ and an aromatic:olefinic ratio indicating 90% deuterium incorporation. In contrast, the NMR of I has an AB pattern for the olefinic hydrogens at 7.96 δ and 6.62 δ. The 6.62 δ proton signal which corresponds to the 3-position has disappeared in the NMR spectrum of VII.

As further support for the position of deuterium, 2-methoxyquinoline after treatment with n-butyl lithium was reacted with dimethyl sulfate to give after column chromatography 3-methyl-2-methoxyquinoline VIII[†] in 22% yield. The latter was hydrolyzed by acid to give 3-methylcarbostyril (IX), m.p. 238.5-240.0°C (11).



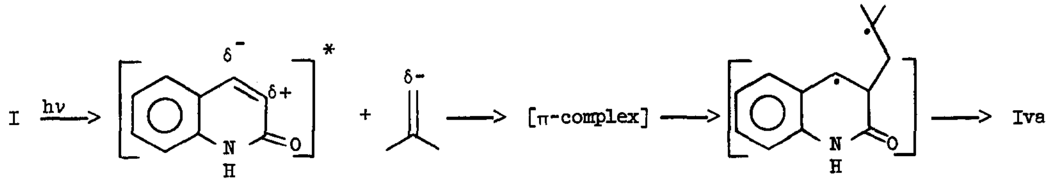
Irradiation of VII with isobutylene afforded an adduct in 90% yield. The NMR of this material was quite simple with an ABM[‡] pattern for the cyclobutane hydrogens: 1 H singlet at 3.68 δ and a 2 H quartet at 2.33 δ and 2.68 δ, J_{AB} = 12 Hz. This is compatible only with X, and therefore, we assign structure IVa to the adduct from I and isobutylene.

The identification of IVa as the only adduct from the photocycloaddition indicates involvement of an excited species with lower electron density at C-3 than at C-4. It is noteworthy that the above correlates with charge distribution calculations (12) of the n,π^* excited state of planar α,β-unsaturated ketones in which C_β is more electronegative than C_α.

[†] According to TLC, six products are found in the reaction mixture. No attempt was made to identify the other products. However, neither V nor 4-methyl-2-methoxyquinoline were present. Gilman (10) reported a 6% yield of the 3-carboxy-2-ethoxyquinoline upon treatment of the lithio compound with CO$_2$.

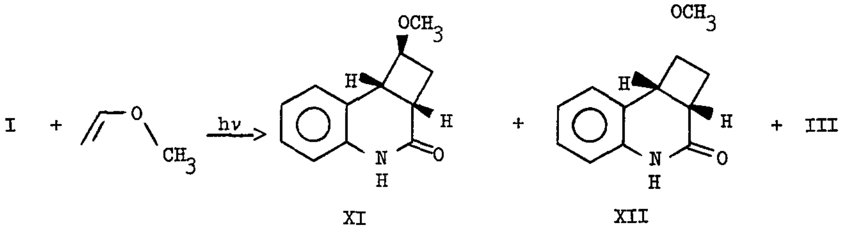
[‡] $J_{AM} = J_{BM} \simeq 0$ Hz.

In addition, Corey et al. (12) have proposed the formation of an oriented π-complex by interaction of the n,π* excited state of the cycloalkenone with the olefin. A similar proposal was used to explain the stereochemistry of products from coumarin (4b). Since both the coumarin and the carbostyril adducts have the same stereochemistry, we favor a similar pathway for carbostyril at this time.

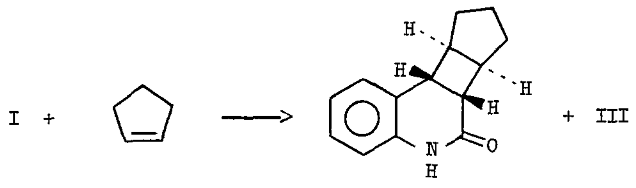


We do not have sufficient data from sensitization experiments to arrive at any conclusions about the nature of the excited species responsible for dimerization or photocycloaddition of carbostyril. However, on dilution, with a constant ratio of the reactants, the ratio of dimer to cycloaddition product decreases and approaches zero. This suggests that dimerization and photocycloaddition are due to two excited species with different lifetimes. For example, dimerization could be due to either a singlet species or an excimer and photocycloaddition due to a triplet species.

The photocycloaddition of carbostyril to vinyl methyl ether and cyclopentene was also investigated. With a 6.4:1 molar ratio of vinyl methyl ether to carbostyril, a 36% yield of the dimer III and a 65% yield of a mixture of two adducts (3:2 ratio as analyzed by g.l.p.c. and NMR) were obtained. By analogy to the discussion above, we have assigned the structures XI and XII to the two adducts.



A 10:1 molar ratio of cyclopentene to carbostyril gave the dimer III in 46% yield and an adduct XIII in 59% yield.



XIII

The NMR spectra of XIII and the deuterated analog were too complex for confirmation of the assigned stereochemistry, but on steric grounds the proposed structure is more reasonable. Further work on carbostyril photocycloaddition, including efforts to define the reactive species, is in progress.

REFERENCES

1. E. C. Taylor and W. W. Pandler, *Tetrahedron Letters*, 1 (1960).
2. (a) O. Buchardt, *Acta. Chem. Scand.* **17**, 1461 (1963); (b) O. Buchardt, *Acta. Chem. Scand.* **18**, 1389 (1964).
3. (a) G. S. Hammond, C. A. Stout and A. A. Lamola, *J. Am. Chem. Soc.* **86**, 3103 (1964); (b) G. O. Schenck, I. V. Wilucki, and C. H. Krauch, *Chem. Ber.* **95**, 1409 (1962).
4. (a) G. O. Schenck, W. Hartmann, S. P. Mannsfeld, W. Metzner and C. H. Krauch, *Chem. Ber.* **95**, 1642 (1962); (b) J. W. Hanifin and E. Cohen, *Tetrahedron Letters*, 1419 (1966); (c) Photocycloaddition of coumarin to tetramethylene in acetonitrile does occur by direct irradiation but is more efficient with triphenylene as sensitizer. Unpublished results of D. L. Fabiny and G. R. Evanega.
5. D. R. Arnold, R. L. Hinman, and A. H. Glick, *Tetrahedron Letters*, 1425 (1964).
6. C. Krauch, S. Farid and G. O. Schenck, *Chem. Ber.* **99**, 625 (1966).
7. H. Morrison, H. Curtis and T. McDowell, *J. Am. Chem. Soc.* **88**, 5415 (1966).
8. R. H. Bible, Jr., "Interpretation of NMR Spectra," Plenum Press, New York, N. Y., 1965, p. 36.
9. I. Fleming and D. H. Williams, *Tetrahedron* **23**, 2747 (1967); H. Weitkamp and F. Korte, *Tetrahedron*, Supplement No. 7, 75 (1966).
10. H. Gilman and J. A. Beel, *J. Am. Chem. Soc.* **73**, 32 (1951).

11. G. Ornstein, *Chem. Ber.* **40**, 1088 (1907) reports a m.p. of 234-235°C for 3-methylcarbostyril. The IR and NMR of this material were distinctively different from a purified commercial sample (Aldrich Chem. Co.) of 4-methylcarbostyril, m.p. 222-223°.

12. E. J. Corey, J. D. Bass, R. LeMahieu and R. B. Mitra, *J. Am. Chem. Soc.* **86**, 5570 (1964).