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PHOTOCYCLOADDITION REACTION OF 3-ARYL-2-ISOXAZOLINES WITH INDENE. GENERATION OF [2+2] CYCLOADDUCT STEREOISOMERS$^{1)}$

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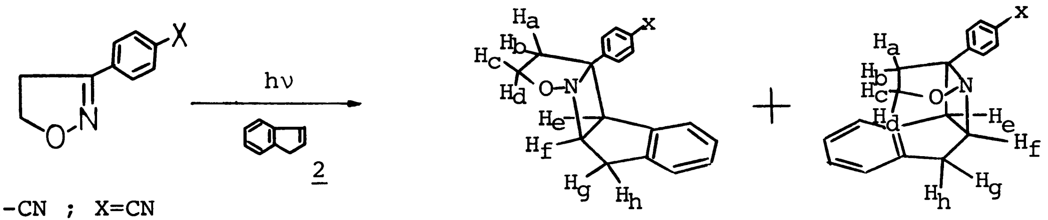
2-Isoxazolines with electron-withdrawing substituents on the 3-aryl moiety (p-cyanophenyl, p-methoxycarbonylphenyl) gave upon irradiation in indene a mixture of syn and anti cycloadducts regiospecifically toward the C=N double bond via their exciplex intermediate.

Recently, we reported that the photocycloaddition reactions of 3-aryl-2-isoxazolines with benzene and five-membered heteroaromatics gave [2+2] cycloadducts across the C=N double bond.$^{2,3)}$ In order to activate the C=N double bond for the photocycloaddition, we consider the necessity of the heteroatom and/or the carbonyl group attached directly to the C=N double bond from the viewpoint of our and several reported examples.$^{3-6)}$ In addition, we suggested that the donor-acceptor (or charge transfer) interaction between 2-isoxazoline and a counterpart was important especially for the success of the photocycloaddition of these systems.$^{3)}$ Therefore, we tried the photoreaction of 3-aryl-2-isoxazolines with indene which has low oxidation potential (1.23 V),$^{7)}$ and founded that hitherto unknown azetidine stereoisomers were formed in good yields.

Upon irradiation of 3-(p-cyanophenyl)-2-isoxazoline 1-CN (1.5×10^{-2} mol dm^{-3}) in indene 2 under N_2 atmosphere through quartz with Rayonet RUL-3000 Å lamps (43 W) for 14 h, two colorless products 5-CN and 6-CN were separated on silica gel by thick layer chromatography. Similar observation was made with 3-(p-methoxycarbonylphenyl)-2-isoxazoline 1-E and 2. These experiments are summarized in Scheme 1. NMR data of 5 and 6 are given in Table 1.$^{8)}$

The compound 5-CN agrees with the formula $C_{19}H_{16}ON_2$ (m/e, M^+=288), which is equivalent to 1 : 1 adduct derived from 1-CN and 2. The NMR spectrum of 5-CN supports that 5-CN is a fused polycyclic compound. In addition, the UV spectrum of 5-CN [λ_{max} (in cyclohexane) 230 nm (ε 14,680), 260 (sh, 2,120), 268 (2,180), 275 (2,060), and 280 (sh, 880)] suggests that the adduct 5-CN is not the adduct between the C=N double bond and the benzene ring of indene, since 5-CN does not show the absorption of 1,3-cyclohexadiene chromophore.$^{9)}$ Based on these facts, we assigned that 5-CN was the adduct between the C=N double bond and the olefinic double bond in 2. The regio- and the stereochemistry were assigned to head-to-head and cis-anti-cis by the following spectroscopic reasons: 1) Methine protons at δ 4.11 (d) and 4.39 (dd) are assigned to the H_e and H_f protons. Since H_f is affected by the neighboring effect of the electronegative N atom, it is shifted to slightly low field in comparison with H_e. 2) Chemical shifts of aromatic protons in indan part



1-CN ; X=CN
1-E ; X=CO_2Me
1-H ; X=H
1-OMe; X=OMe

Yield
5-CN: 64%
5-E : 57%

Yield
6-CN: 11%
6-E : 4%

Scheme 1.

Table 1. NMR data of 5 and 6[a)]

Compound	H_a	H_b	H_c	H_d	H_e	H_f	H_g	H_h
5-CN[b,c)]	2.56 J_{ab}=12.5 J_{ac}=3.3 J_{ad}=6.8	3.00 J_{bc}=8.1 J_{bd}=9.2	4.23 J_{cd}=8.9	4.52	4.11 J_{ef}=7.3	4.39 J_{fg}=6.3 J_{fh}=2.0	3.17 J_{gh}=16.8	3.39
6-CN[b,c)]	1.87 J_{ab}=13.5 J_{ac}=3.3 J_{ad}=7.2	2.24 J_{bc}=8.3 J_{bd}=9.2	3.57 J_{cd}=12.0	3.71	3.97 J_{ef}=6.9	4.86 J_{fg}=9.0 J_{fh}=2.3	3.10 J_{gh}=17.0	3.70
5-E[b,c)]	2.64 J_{ab}=12.7 J_{ac}=8.1 J_{ad}=9.3	3.02 J_{bc}=3.4 J_{bd}=6.9	4.27 J_{cd}=8.1	4.60	4.14 J_{ef}=7.5	4.42 J_{fg}=7.5 J_{fh}=1.1	3.23 J_{gh}=17.3	3.41
6-E[b,c)]	1.95 J_{ab}=12.6 J_{ac}=8.3 J_{ad}=9.0	2.26 J_{bc}=6.9 J_{bd}=3.7	3.59 J_{cd}=8.3	3.88	4.05 J_{ef}=6.9	4.88 J_{fg}=9.3 J_{fh}=2.0	3.18 J_{gh}=18.3	3.76

a) The spectra of 5-CN and 6-CN were measured at 100 MHz in $CDCl_3$; the spectra of 5-E and 6-E were measured at 200 MHz in $CDCl_3$; resonance positions are given as δ values relative to internal TMS; J values are given in Hz.

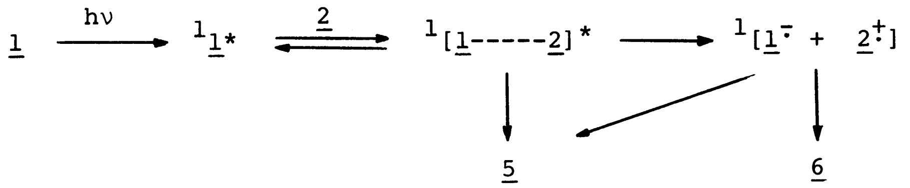
b) Chemical shifts of methoxy protons of 5-E and 6-E are δ 3.88 and 3.66; aromatic protons of 5-CN, 6-CN, 5-E, and 6-E are δ 6.46-7.50, 7.25-7.80, 6.45-7.85, and 7.30-8.19, respectively.

c) All new compounds gave satisfactory elemental analyses and mass spectra.

in 5-CN are shifted to high field, i.e., δ 6.46-7.22. If the regiochemistry of 5-CN is head-to-tail, we are not able to expect this remarkable anisotropic effect due to the p-cyanophenyl group, because the benzene ring and the p-cyanophenyl group are very far apart from each other. 3) Chemical shifts of the p-cyanophenyl group are also shifted to high field from δ 7.74 (4H, m) in 1-CN to 7.25 (2H, d, J=8 Hz) and 7.40 (2H, d, J=8 Hz). Again these suggest the relatively close position between the benzene ring in indan part and the p-cyanophenyl group in 5-CN. Based on the above data, the compound is assigned to 4,5-benzo-7-(p-cyanophenyl)-10-oxa-1-azatricyclo[5.3.0.$0^{2,6}$]deca-4-ene.

On the other hand, the compound 6-CN also has the formula $C_{19}H_{16}ON_2$ (m/e, M^+= 288), suggesting 1 : 1 adduct of 1-CN and 2. The NMR spectrum of 6-CN shows similar pattern to 5-CN, but the methylene protons of H_a-H_d are equally shifted to high field (ca. 0.7 ppm) in comparison with those of the adduct 5-CN. This high field shift is ascribed to the shielding effect of the benzene ring in the indan system which is covered with the fused isoxazolidine system. So the regio- and the stereochemistry of 6-CN can be assigned to a head-to-head cis-syn-cis cycloadduct as depicted in Scheme 1. In the case of 2-isoxazoline 1-E, similar cycloadducts 5-E and 6-E were isolated in 57 and 4% yield, respectively.

In order to obtain the information about the reaction mechanism for the photocycloaddition of this system, some mechanistic studies were done. The UV spectra did not show any absorption due to the CT (charge transfer) complex between 1-CN and 2. Although the exciplex emission was not observed, the fluorescence of 1-CN was quenched by 2 with quenching constant $k_q\tau=32.8\ M^{-1}$. Irradiation of benzene solution of 1-CN and 2 (40 equivalents) in the presence of a triplet sensitizer such as Michler's ketone preferentially gave the anti head-to-head indene dimer,10) instead of 5-CN and 6-CN. Photocycloaddition of 1-CN and 2 as well as the photolysis of 1-CN itself2) was depressed in the presence of O_2. These results are compatible with the cycloaddition proceeding via the singlet state of Ar-C=N-O chromophore. The proposed reaction pathway is depicted in Scheme 2.



Scheme 2.

Since 3-phenyl-2-isoxazoline 1-H or p-methoxyphenyl derivative 1-OMe gave no photoadduct with indene, the intermediacy of an exciplex seems reasonable as a consequence of the electronic requirement of the substituent as well as the regiospecificity of the reaction. As far as we know on this stage, there are no clear examples for the two discrete exciplexes responsible for the formation of different photoproducts except for the intramolecular case.11) Therefore, the major product 5 was formed via the singlet exciplex. The regio- and the stereochemistry of 5 can be interpreted in terms of the most stabilized sandwich type configuration12) between the 3-aryl group and the benzene ring in indene.

On the other hand, as the oxidation potential of indene is low, indene has a tendency to give one electron to isoxazolines. This minor pathway gives rise to the radical ion pair which gives 6 as well as 5. Since we could not detect the formation of indene dimer formed via the attack of the neutral indene to the indene radical cation, the radical ion pair is presumably in cage. On the reported examples, nucleophiles add the 2-position of the indene radical cation.13) And the electron density of the isoxazoline radical anion is expected to higher in 2-position than in 3-position. So we can exclude the possibility of the formation of the head-to-tail adduct on the stage of the coupling of this radical ion pair, i.e., the electronic character of the radical ions is the chief determining factor for the regiospecificity on this stage.

As of now, it is rare for the radical ion pair to collapse to the 4-membered ring mentioned above and other Diels-Alder type adducts.[14)]

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7) This value was measured with Ag electrode in CH_3CN; H.Lund, Acta Chem. Scand., 11, 1323 (1957).
8) Product 5-CN; colorless needles, mp 149-149.5 °C, IR (KBr) 2970, 2900, 2210, 1604 cm^{-1}. Product 6-CN; colorless needles, mp 100.5-101 °C, IR (KBr) 2910, 2230, 1609 cm^{-1}. Product 5-E; colorless needles, mp 181.5-182 °C, IR (KBr) 3000, 2950, 1714, 1612 cm^{-1}. Product 6-E; colorless needles, mp 103-106 °C, IR (KBr) 2950, 1713, 1610 cm^{-1}.
9) 1,3-cyclohexadiene; λ_{max} (in hexane) 256 nm (ε 8,000) from R. M. Silverstein and G. C. Bassler, "Spectrophotometric Identification of Organic Compounds," 2nd ed , John Wiley and Sons, Inc., New York, NY (1967), p. 157.
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14) The closest example of this process is found in the reaction of the 9,10-dicyanoanthracene radical anion and the methyl diphenylcyclopropene carboxylate radical cation; K. A. Brown-Wensley, S. L. Mattes, and S. Farid, J. Am. Chem. Soc., 100, 4162 (1978).

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