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PHOTOCYCLOADDITION OF 3-ARYL-2-ISOXAZOLINES WITH FIVE-MEMBERED HETEROCYCLES[1)]

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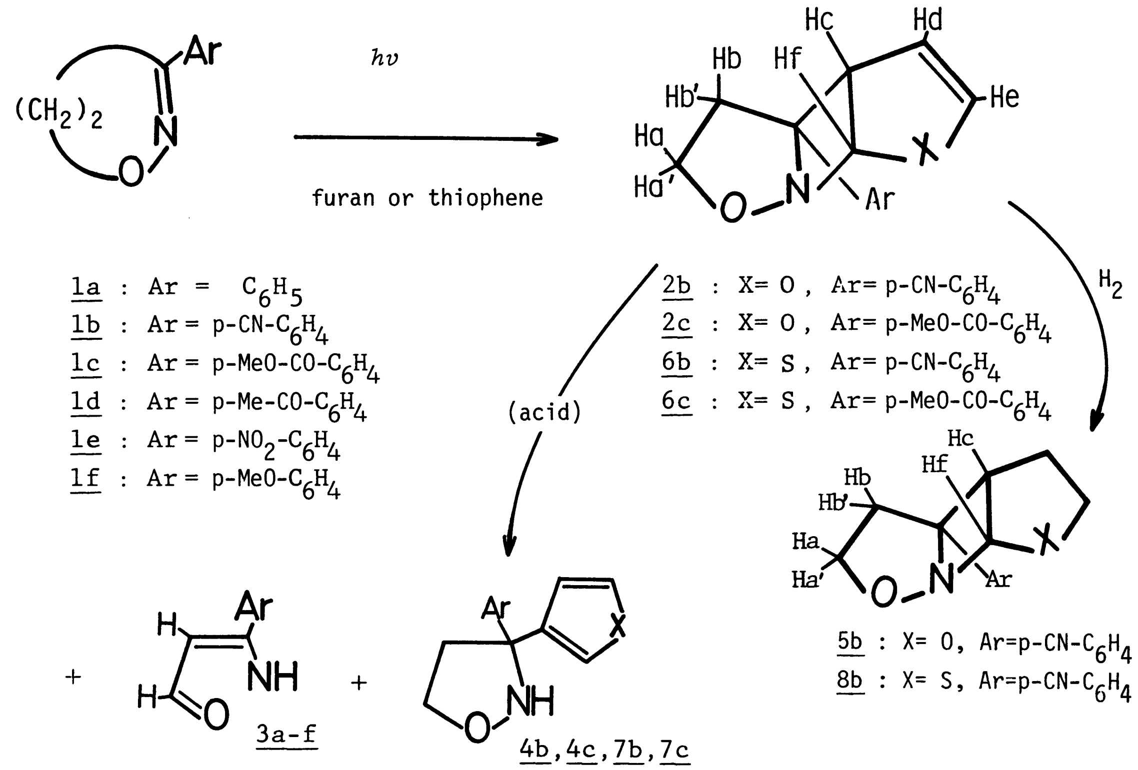
The irradiation of 3-aryl-2-isoxazolines gives novel [2+2] adducts with furan (or thiophene) by addition across the carbon-nitrogen double bond.

As an extention of our interest in the photochemistry of the carbon-nitrogen double bond, we have investigated the excited state behavior of 2-isoxazoline and several related derivatives.[2)] Although photocycloaddition of carbon-nitrogen double bonds is known to occur with oxazolinone, isoindolenone, and oxadiazole, it is not as familiar as that of carbon-carbon double bonds.[3)] Recently, several additional cases have been reported by Ohta, Mariano, Neckers and our own group,[4)] but the generality is not clear in this stage. There is a great deal of interest in the investigation of what factors the photocycloaddition of carbon-nitrogen double bond will occur with. In connection with a photocycloaddition of 3-(p-cyanophenyl)-2-isoxazoline (1b) with benzene,[2)] we wish to describe the second example of the novel photocycloaddition, i.e., the formation of [2+2] adduct with furan and thiophene, in this paper.

When 3-(p-cyanophenyl)-2-isoxazoline (1b) was irradiated in furan with RUL-3000 Å lamps (43 W) using a quartz vessel at room temperature for 9.5 h, a [2+2] photocycloadduct (2b)[5)] was isolated in 42% yield by means of silica gel chromatography. This material was also accompanied by 3-amino-3-(p-cyanophenyl)-2-propenal (3b, 6%), 3-(3-isoxazolidinyl)furan (4b,[7)]1-4%) as well as recovered starting material (9%).[8)] Treatment of the major photoproduct 2b with 0.1 moldm^{-1} HCl gave rise to the furan derivative 4b thereby indicating that the [2+2] adduct 2b possesses a head-to-head orientation. The regiochemistry of 2b was established from the NMR spectrum. The low field doublet (Hf) at 5.66 ppm is adjacent to both the oxygen and the



1a : Ar = C_6H_5
1b : Ar = p-CN-C_6H_4
1c : Ar = p-MeO-CO-C_6H_4
1d : Ar = p-Me-CO-C_6H_4
1e : Ar = p-NO_2-C_6H_4
1f : Ar = p-MeO-C_6H_4

2b : X= O , Ar= p-CN-C_6H_4
2c : X= O , Ar= p-MeO-CO-C_6H_4
6b : X= S , Ar= p-CN-C_6H_4
6c : X= S , Ar= p-MeO-CO-C_6H_4

5b : X= O, Ar=p-CN-C_6H_4
8b : X= S, Ar=p-CN-C_6H_4

nitrogen atom in the head-to-head structure. Heating the [2+2] adduct 2b at 190°C for 12 h produced the starting isoxazoline in 56% yield. On hydrogenation over palladium on charcoal, the cycloadduct 2b afforded 5b[9] in quantitative yield. The chemical shift of the isoxazolidine ring (i.e. protons Ha and Hb) in the NMR spectrum of 5b showed very similar value to those encountered with 2b. This observation strongly suggests that the [2+2] adduct do not have the syn but rather have the anti configuration. The photocycloaddition reaction of 1b with furan is especially noteworthy in view of the high regio- and stereospecificity as well as its high chemical and quantum efficiency.

The formation of an analogous [2+2] cycloadduct (2c,[10] 31%) was also observed in the photolysis of the p-methoxycarbonylphenyl derivative (1c)[11] with furan. Interestingly, 3-phenyl-2-isoxazoline (1a)[2] or the p-methoxy derivative (1f)[2] gave no photoadduct with furan. In addition, no cycloadduct could be detected in the irradiation of 3-arylisoxazoline (1d or 1e)[11] which contains an electron withdrawing substituent (p-acetyl or p-nitro group).

The irradiation of 1b-c was carried out in the presence of other heteroaromatic compounds and olefins in order to establish the scope and generality of the photocycloaddition. With thiophene, 2-isoxazolines 1b and 1c gave rise to analogous [2+2] adducts (6b-c)[12] in 54% and 53% yield, respectively. These isoxazolines, however, did not undergo the photocycloaddition reaction with cyclopentadiene, pyrrole or N-methylpyrrole.[13)] No photoadduct was obtained when all of isoxazolines 1a-f were irradiated with several olefins such as 2,3-dihydrofuran, ethylvinylether, 1,1-dimethoxyethene, enamines or cycloalkenes under similar condition.[14)]

The photolysis of isoxazoline 1b in cyclohexane mainly gives rise to propenal 3b in high quantum efficiency (Φ= 0.15). The reaction efficiency of this process decreased in the presence of furan which exhibited a $k_q\tau$ value of 3.6 $mol^{-1}dm^3$. The quantum yield for the formation of adduct 2b was determined as 0.037 when the irradiation was carried out in furan.[15)] The fluorescence of 1b was also quenched by furan with a $k_q\tau$ value of 3.6 $mol^{-1}dm^3$. This result is only consistent with the cycloaddition proceeding via the singlet excited state of Ar-C=N-O chromophore. The fact that the p-acetylphenyl and p-nitrophenyl derivatives (1d and 1e) do not give photoadducts with furan (or thiophene) can be rationalized by a facile intersystem crossing to the triplet excited state which is unreactive toward cycloaddition. The novel substituent effect observed here suggests that a donor-acceptor interaction between the singlet excited states of 2-isoxazolines (1b-c) and furan (or thiophene) plays an important role in the photocycloaddition reaction of the carbon-nitrogen double bond. The intermediacy of an exciplex in the photocycloaddition of the carbon-nitrogen double bond seems reasonable as a consequence of the electronic requirements of the substituents as well as the regiospecificity of the reaction.[16)] Further studies with these and related systems are in progress.

References

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5) Product 2b:[6)] colorless needles, mp 136-137.5°C; IR (KBr) 3120, 3070, 2980, 2875, 2230, 1608, 1502 cm^{-1}; NMR($CDCl_3$) δ 2.35(Hb, d d d, J= 12.7, 9.4, 7.8 Hz), 2.79(Hb', d d d, J= 12.7, 6.5, 3.5 Hz), 3.93(Hc, d d d, J= 7.0, 3.0, 1.5

Hz), 4.28(Ha, d d d, J= 8.4, 7.8, 3.5 Hz), 4.45(Ha', d d d, J= 9.4, 8.4, 6.5 Hz), 4.77(Hd, t, J= 3.0 Hz), 5.66(Hf, d, J= 7.0 Hz), 6.34(He, d d, J= 3.0, 1.5 Hz), 7.5(2H, m), 7.7(2H, m); UV(cyclohexane) λmax= 229 (ε 14,640), 261 nm (sh, 1,100).

6) All new compounds gave satisfactory elemental analyses and Mass spectra.

7) Compound 4b:6) colorless oil; IR (oil) 3410, 2970, 2900, 2230, 1609, 1433 cm^{-1}; NMR($CDCl_3$) δ 2.77(2H, t, J= 7.5 Hz), 4.03(2H, t, J= 7.5 Hz), 5.30(NH), 6.23(1H, d d, J= 2.0, 1.0 Hz), 7.31(1H, d d, J= 1.2, 1.0 Hz), 7.34(1H, d d, J= 2.0, 1.2Hz), 7.3-7.7(4H, m).
Compound 7b:6) colorless needles, mp 86.5-88°C.

8) The formations of 3-(p-cyanophenyl)-3-oxazoline and p-dicyanobenzene were observed in 0.2-1% yields.

9) Product 5b:6) colorless needles, mp 136.5-137.5°C; IR (KBr) 2990, 2970, 2940, 2860, 2220, 1603, 1500 cm^{-1}; NMR($CDCl_3$) δ 1.42(Hd, d d d, J= 13.0, 6.5, 1.5 Hz), 1.75(Hd', d d d d, J= 13.0, 9.0, 8.5, 6.5 Hz), 2.30(Hb, d d d, J= 12.5, 9.5, 8.0 Hz), 2.71(Hb', d d d, J= 12.5, 5.8, 3.6 Hz), 3.33(Hc, d d, J= 8.5, 6.1 Hz), 3.62(He, d d d, J= 9.3, 9.0, 6.5 Hz), 3.96(He', d d d, J= 9.3, 6.5, 1.5 Hz), 4.20(Ha, d d d, J= 8.1, 8.0, 3.6 Hz), 4.34(Ha', d d d, J= 9.5, 8.1, 5.8 Hz), 5.28(Hf, d, J= 6.1 Hz), 7.4-7.6(2H, m), 7.6-7.9(2H, m); UV(cyclohexane) λmax 231 (ε 16,600), 268 (sh, 610), 273 nm (sh, 540).
Product 8b:6) colorless needles, mp 157.5-158.5°C.

10) Product 2c:6) colorless needles, mp 152.5-153°C; IR (KBr) 3110, 2990, 2960, 2900, 1714, 1612, 1607 cm^{-1}; The NMR spectrum shows analogous pattern to 2a except for a signal at 3.88 ppm (COOMe).

11) Isoxazoline 1c:6) mp 142.5-143°C; 1d:6) mp 148-148.5°C; 1e: mp 164-165°C.

12) Product 6b:6) colorless needles, mp 145-146°C; IR (KBr) 3050, 2980, 2950, 2870, 2210, 1604, 1499, 1440 cm^{-1}; NMR($CDCl_3$) δ 2.36(Hb, d d d), 2.88(Hb', d d d), 4.25(Ha, d d d), 4.27(Hc, d d d), 4.53(Ha', d d d), 5.06(Hd, d d), 5.48(Hf, d d), 6.10(He, d d d), 7.4-7.6(2H, m), 7.5-7.7(2H, m); UV(cyclohexane) λmax 230 (ε 15,680), 240 (sh, 13,640), 269 nm (sh, 2,840).
Product 6c:6) colorless needles, mp 149.5-150°C.

13) Pyrroles have also quenched both the photoreactions and the fluorescences of 1b and 1c effectively. However, the formation of the analogous photoadduct could not be detected at all indicating the complicating feature of this photoreaction.

14) 2-Isoxazoline 1b gave the [2+2] photoadduct (5b) with 2,3-dihydrofuran in low yield as an unusual exception.

15) The quantum yield was measured using potassium ferrioxalate actinometry when the solution of 1b (5.1 x 10^{-5}moldm^{-3}) was irradiated at 300 nm. The value for 3b was determined to be 0.019 under the same condition.

16) The enhancement of these photocycloadditions was observed when the irradiation were performed at low temperature (5°C). The product yields were improved in 5-15% but the quantitative treatment is so difficult because of the instability of products and the insolubility of isoxazolines. Attempts to detect the exciplex emission were unsuccessful under various conditions.

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