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PHOTOCHEMICAL REACTIONS OF 4-PHENYLQUINAZOLIN-2-ONES[+]

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Abstract ——Irradiation of 4-phenylquinazolin-2-ones (1) in the presence of hydrogen donor such as xanthene (2a), sulfide (2c), and acyclic or cyclic ethers (2b,d-e), gave the C-C bonded 1:1-adducts of (1) and (2) via hydrogen atom abstraction of the excited imino nitrogen of (1), while irradiation of (1) in the presence of triethylamine gave the reduced 3,4-dihydroquinazolin-2-ones.

Although it is generally accepted that the excited states of imines have little tendency to undergo hydrogen abstraction due to the rapid radiationless decay process which results from twisting around the carbon-nitrogen double bond,[1] several reactions analogous to that of carbonyl groups have been observed.[2] In our exploration of the photochemical reactivity of cyclic conjugated nitrogen-carbonyl systems such as pyrimidinones[3] and pyrazinones,[4] we have reported the intramolecular[5] or intermolecular[6] hydrogen abstraction reactions of the pyrimidin-2-ones. As an extension of our interest in the photochemistry of nitrogen-carbonyl systems, we have investigated the photochemical reactions of 4-phenylquinazolin-2-ones (1) and here describe these results.

When a solution of 1-methyl-4-phenylquinazolin-2-one (1a) in benzene or methanol was irradiated in a Pyrex vessel with a high-pressure mercury lamp under argon, no photoproducts could be obtained and the starting material (1a) was quantitatively recovered. Meanwhile, irradiation of (1a) in benzene in the presence of xanthene (2a) as a hydrogen donor under the same conditions for 15 h gave the C-C bonded 1:1-adduct (3) of (1a) and (2a) in 96% yield. The structure of (3) was confirmed on the basis of spectroscopic and elemental analysis. The ir spectrum of (3) showed absorption bands at 3210 and 1665 cm^{-1} assignable to amino and amide

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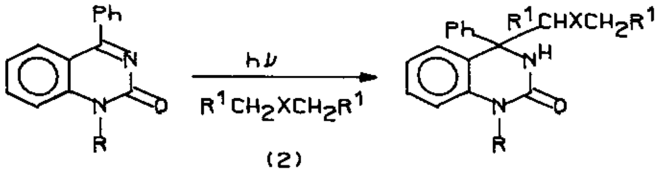
[+] This paper is dedicated to Dr. T. Kametani for his brilliant achievement in the field of heterocyclic chemistry.

carbonyl groups, respectively. The ^1H-nmr spectrum of (3) showed amino and methine protons at δ 4.98 (1H, br s, exchangeable with D_2O) and 5.01 (1H, s), respectively. In the ^{13}C-nmr spectrum, new signals appeared at δ 49.8 (d) and 68.5 (s) due to xanthenyl methine and quaternary carbons at C-4 instead of imino carbon. Accordingly, the addition site of xanthene in the C-C bonded 1:1-adduct (3) was assigned to the C-4 position. Similarly, irradiation of 4-phenylquinazolin-2-ones (1a-b) in hydrogen donating solvent such as tetrahydrofuran and dioxane or in the presence of hydrogen donor such as ether and diethyl sulfide under similar conditions yielded the C-C bonded 1:1-adducts (4-10) in 20-99% yields. In the reaction of (1a-b) with diethyl ether (2b) and diethyl sulfide (2c), two stereoisomeric 1:1-adducts (4-5, 9) and (4'-5', 9') were isolated.[7] The structure of those photoproducts was elucidated on the basis of spectroscopic properties and elemental analyses. Characteristically, the 1:1-adducts (4-10) showed absorptions around 3190-3410 (NH stretching) and 1660-1680 cm^{-1} (CO stretching band) and no C=N absorption was observed in their ir spectra. The ^{13}C-nmr spectra of the 1:1-adducts (3-10) showed a singlet at δ 62.6-68.5 due to C-4 position. When a solution of (1a) and xanthene in benzene was irradiated in the presence of t-stilbene (E_T=50 kcal/mol) as a triplet quencher at the wavelength of 366 nm, the



(1)

(2)

(3)-(10)

a: R=Me
b: R=Et

	R^1	X
a:	Xanthene	
b:	Me	O
c:	Me	S
d:	$-CH_2CH_2-$	O
e:	$-CH_2OCH_2-$	O

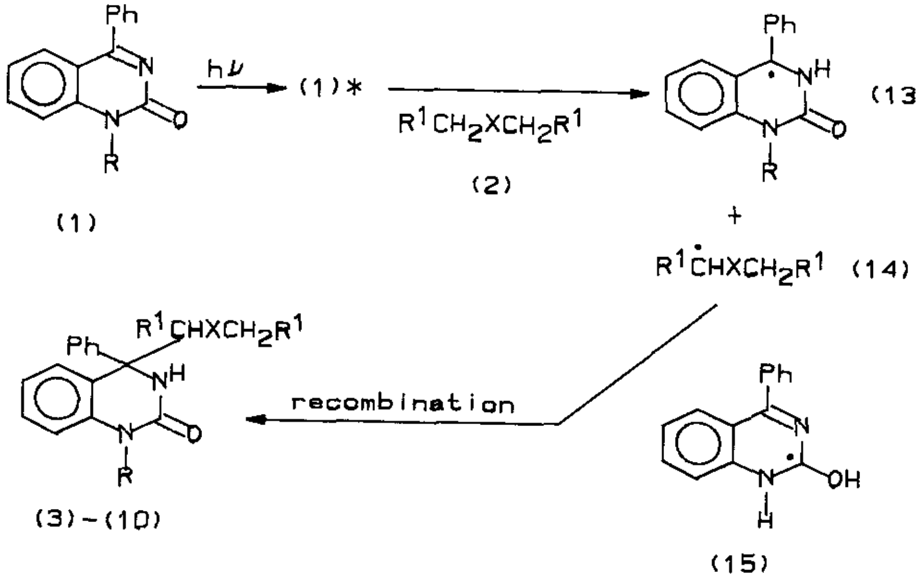
	R	R^1	X
3:	Me	9-Xanthenyl	
4:	Me	Me	O
5:	Me	Me	S
6:	Me	$-CH_2CH_2-$	O
7:	Me	$-CH_2OCH_2-$	O
8:	Et	Xanthenyl	
9:	Et	Me	S
10:	Et	$-CH_2CH_2-$	O

yield of 1:1-adduct (3) decreased drastically to 7% (runs 2,3). These results[8] suggest that the 1:1-adducts might be formed via an excited triplet state of (1a) and a mechanism for the reaction is shown in Scheme. The excited quinazolin-2-one (1) abstracts a hydrogen atom from the hydrogen donor either with the imino

Table 1. Yield of Photoproducts **(3-10)**

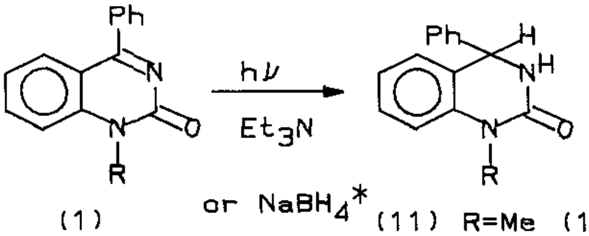
				Yield (%)[a]	
Run	R	R^1	X	Product	Recovered **(1)**
1	Me	Xanthenyl		(3) 96	trace
2[b]	Me	Xanthenyl		(3) 97	trace
3[b,c]	Me	Xanthenyl		(3) 7	93
4	Me	Me	O	(4) 19 (4')[d] 24	38
5	Me	Me	S	(5) 10 (5')[d] 13	75
6	Me	$-CH_2CH_2-$	O	(6) 24	48
7	Me	$-CH_2OCH_2-$	O	(7) 25	35
8	Et	Xanthenyl		(8) 99	trace
9	Et	Me	S	(9) 11 (9')[d] 9	63
10	Et	$-CH_2CH_2-$	O	(10) 58	trace

[a] Isolated yield. [b] Irradiation was carried out at the wavelength of 366 nm for 3 h. [c] Irradiation was carried out in the presence of 2 molar equiv. of t-stilbene as a triplet quencher. [d] Another stereoisomer.



Scheme

nitrogen or the ureide carbonyl to yield radicals (13) or (15) and (14). The former process might occur preferentially, because it is reported that the hydrogen abstraction reaction in the amide carbonyl is quite inefficient.[5-6,9] Subsequent recombination of the radicals thus formed would give the C-C bonded 1:1-adducts (3-10). On the other hand, irradiation of the quinazolin-2-ones (1a-b) in the presence of triethylamine known as an effective electron and hydrogen donor gave the reduced 3,4-dihydroquinazolin-2-ones (11-12), but in low yields. The structure of (11-12) was confirmed by direct comparison with two authentic samples prepared by the reduction of the quinazolin-2-ones (1a-b) with sodium borohydride.



(1)

(11) R=Me (10%) (84%)*

(12) R=Et (3%) (94%)*

EXPERIMENTAL

Melting points are uncorrected and were measured with Yanaco micro-melting point apparatus. Uv spectra were determined with a JASCO UVIDEC-505 spectrophotometer, ir spectra were recorded on a Hitachi 260-30 spectrophotometer, and nmr spectra were run on a JEOL FX-100 spectrometer (100 MHz) using $CDCl_3$ as solvent and Me_4Si as internal standard. 4-Phenylquinazolin-2-one (1a) was prepared according to literature method[10] and 4-phenylquinazolin-2-one (1b) was prepared by a modification of this method.

1-Ethyl-4-phenylquinazolin-2(1H)-one (1b): mp 183-184 °C(chloroform-hexane); uv(EtOH) 230 (ε 33600), 270 (10200), 356 nm (5600); ir(KBr) 1650 cm^{-1}; ^{1}H-nmr δ 1.45 (3H, t, J=6.8 Hz), 4.38 (2H, q, J=6.8 Hz), 7.13-7.91 (9H, m); ^{13}C-nmr δ 12.3 (q), 38.9 (t), 113.8 (d), 115.9 (s), 121.8 (d), 128.2 (d), 129.4 (d), 130.0 (d), 130.3 (d), 135.1 (d), 136.3 (s), 143.0 (s), 174.4 (s). Found: C, 76.60; H, 5.64; N, 11.11. Calcd for $C_{16}H_{14}N_2O$: C, 76.77; H, 5.63; N, 11.19.

General Procedure for the Photochemical Reactions of the Quinazolin-2-ones (1a-b). A solution of the quinazolin-2-one (1) (200 mg) in a hydrogen donating solvent [THF (2d) or dioxane (2e)] (70 ml) or in ether-benzene (20/50 ml) or in benzene (70 ml) in the presence of a hydrogen donor [ca. 1 ml for diethyl sulfide

(2c) and 2 molar equiv. for xanthene (2a)] was irradiated in a Pyrex vessel with a high-pressure mercury lamp (300 W) under argon for 15-20 h at room temperature. After removal of the solvent, the residue was chromatographed on a silica gel column with benzene-ethyl acetate (4:1 or 2:1) to yield the C-C bonded 1:1 adducts (3-10). The spectral properties of the photoproducts are given in Table 2.[11]

Photochemical Reactions of the Quinazolin-2-ones (1a-b) in the Presence of Triethylamine. A solution of (1) (200 mg) in benzene (70 ml)in the presence of triethylamine (ca. 1 ml) was irradiated under the same conditions as described above. Usual work-up gave the reduced products (11-12).

1-Methyl-4-phenyl-3,4-dihydroquinazolin-2(1H)-one (11): mp 182.5-184 °C (chloroform-hexane); ir(KBr) 3210, 1670 cm^{-1}; ^{1}H-nmr δ 3.32 (3H, s), 5.53 (1H, d, J=2.0 Hz), 5.89 (1H, br s), 6.80-7.00 (3H, m), 7.15-7.35 (6H, m); ^{13}C-nmr δ 29.5 (q), 57.5 (d), 113.0 (d), 122.1 (s), 123.8 (s), 126.8 (d), 127.0 (d), 128.1 (d), 128.3 (d), 128.8 (d), 138.4 (s), 142.4 (s), 154.7 (s). Found: C, 75.35; H, 5.87; N, 11.56. Calcd for $C_{15}H_{14}N_2O$: C, 75.60; H, 5.92; N, 11.75.

1-Ethyl-4-phenyl-3,4-dihydroquinazolin-2(1H)-one (12): mp 150.5-151.5 °C (chloroform-hexane); ir(KBr) 3220, 1675 cm^{-1}; ^{1}H-nmr δ 1.27 (3H, t, J=6.8 Hz), 3.97 (2H, q, J=6.8 Hz), 5.52 (1H, d, J=2.0 Hz), 5.72 (1H, br s), 6.85-7.0 (3H, m), 7.15-7.30 (6H, m); ^{13}C-nmr δ 12.7 (q), 37.0 (t), 57.7 (d), 113.1 (d), 121.8 (d), 123.9 (s), 127.0 (d), 127.2 (d), 128.0 (d), 128.2 (d), 128.8 (d), 137.1 (s), 142.7 (s), 154.2 (s). Found: C, 75.98; H, 6.31; N, 10.97. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10.

Reduction of the Quinazolin-2-ones (1a-b) with Sodium Borohydride. To a stirred solution of (1) (1 mmol) in MeOH (30 ml) was added sodium borohydride (2 mmol) and then the reaction mixture was stirred for 0.5 h at room temperature. Usual work-up gave the dihydroquinazolin-2-ones (11-12).

Table 2. Spectral Properties of Photoproducts (3-10)

	mp (°C)	ir (KBr) cm^{-1}	^{1}H-nmr ($CDCl_3$) δ	^{13}C-nmr ($CDCl_3$) δ
3	166-168	3210, 1665	2.81 (3H, s), 4.98 (1H, s, exchangeable with D_2O), 5.01 (1H, s), 6.36-7.51 (15H, m), 7.69-7.79 (2H, m)	29.1(q), 49.8(d), 68.5(s), 113.1(d), 115.8(d), 117.0(d), 119.5(s), 120.5(d), 121.2(d), 121.8(d), 122.7(d), 123.6(s), 127.5(d), 127.6(d), 127.9(d), 128.3(d), 128.5(d), 130.0(d), 130.2(d), 138.7(d), 142.0(s), 153.0(s), 154.1(s)

Table 2. (continued)

4	158-159	3410, 1670	0.92 (3H, t, J=6.8z), 1.23 (d, J=6.3 Hz), 2.86-3.62 (2H, m), 3.27 (3H, s), 4.26 (1H, q, J=6.3 Hz), 5.82(1H, br s), 6.78-7.50 (9H, m)	14.9(q), 15.1(q), 29.5(q), 65.1(s), 65.2(t), 79.3(d), 113.4(d), 121.5(d), 124.9(s), 125.9(d), 126.2(d), 126.8(d), 128.0(d), 128.1(d), 138.4(s), 144.8(s), 154.4(s)
4'	153-155	3190, 1670	0.96 (3H, t, J=6.8 Hz), 1.19 (3H, d, J=6.4 Hz), 2.90-3.58 (2H, m), 3.26 (3H, s), 4.04 (1H, q, J=6.4 Hz), 5.87 (1H, br s), 6.81-7.03 (3H, m), 7.15-7.55 (6H, m)	14.6(q), 15.3(q), 29.5 (q), 65.2(s), 65.6(t), 80.5(d), 112.9(d), 121.3(d), 125.4(s), 126.9(d), 127.2(d), 128.0(d), 128.8(d), 139.2(s), 143.4(s), 154.3(s)
5	159-160	3410, 1665	0.99 (3H, t, J=6.8 Hz), 1.34 (3H, d, J=6.8 Hz), 1.58-2.02 (2H, m), 3.25 (3H, s), 3.92 (1H, q, J=6.8 Hz), 6.00 (1H, br s), 6.80 (1H, dd, J=1.6, 7.8 Hz), 6.96-7.52 (8H, m)	14.5(q), 18.1(q), 26.0(t), 29.5(q), 48.3(d), 64.5(s), 113.5(d), 121.8(d), 125.1(d), 125.7(s), 125.9(d), 127.1(d), 128.2(d), 138.3(s), 144.1(s), 154.8(s)
5'	141-143	3230, 1665	1.15 (3H, t, J=7.3 Hz), 1.28 (3H, d, J=6.8 Hz), 2.24-2.48 (2H, m), 3.30 (3H, s), 3.71 (1H, q, J=6.8 Hz), 5.79 (1H, br s), 6.80-7.52 (9H, m)	14.7(q), 17.3(q), 26.3(t), 29.6(q), 49.1(d), 65.9(s), 113.3(d), 121.5(d), 125.9(s) 126.2(d), 126.6(d), 127.2(d), 128.2(d), 128.4(d), 138.4(s), 143.8(s), 154.3(s)
6	177-178	3220, 1675	1.78-1.95 (4H, m), 3.31 (3H, s), 3.75-4.02 (2H, m), 4.75-4.90 (1H, m), 5.71 (1H, br s), 6.81-7.55 (9H, m)	25.9(t), 27.5(t), 29.5(t), 63.5(s), 69.7(t), 83.9(d), 113.3(d), 121.8(d), 125.1(s), 126.0(d), 126.4(d), 127.2(d), 128.3(d), 138.0(s), 145.0(s), 154.1(s)
7	215-217	3250, 1675	3.30 (3H, s), 3.53-3.80 (6H, m), 4.48 (1H, dd, J=4.4, 8.3 Hz), 5.84	29.5(q), 62.6(s), 66.2(t), 67.1(t), 67.2(t), 78.6(d), 113.5(d), 122.0(d), 122.6(s),

Table 2. (continued)

			(1H, br s), 6.80-7.51 (9H, m)	126.0(d), 126.2(d), 127.3(d), 128.3(d), 128.8(d), 137.9(s), 144.0(s), 153.5(s)
8	91-93	3225, 1670	0.91 (3H, t, J=6.8 Hz), 3.20-3.56 (2H, m), 4.91 (1H, br s), 5.01 (1H, (1H, s), 6.34-7.50 (15H, m), 7.70-7.84 (2H, m)	12.7(q), 37.0(t), 50.0(d), 68.5(s), 113.0(d), 116.0(d), 117.0(d), 119.5(s), 120.6(d), 120.9(d), 121.9(d), 122.0(d), 123.4(s), 126.7(d), 127.9(d), 128.3(d), 128.5(d), 130.2(d), 130.3(d), 137.6(s), 142.5(s), 152.4(s), 154.2(s)
9	133-134	3270, 1680	1.00 (3H, t, J=7.3 Hz), 1.18 (3H, t, J=6.8 Hz), 1.36 (3H, d, J=6.8 Hz), 1.60-2.06 (2H, m), 3.68-4.10 (3H, m), 5.92 (1H, br s), 6.81-7.51 (9H, m)	12.6(q), 14.6(q), 18.0(q), 26.0(t), 37.1(t), 48.3(d), 64.6(s), 113.6(d), 121.6(d), 125.5(d), 126.0(d), 127.1(d), 128.2(d), 137.2(s), 144.3(s) 154.4(s)
9'	163-165	3210, 1670	1.13 (3H, t, J=7.3 Hz), 1.18 (3H, t), 1.29 (3H, d, J=6.8 Hz), 2.31 (2H, d of q, J=2.4, 7.3 Hz), 3.71 (1H, q, J=7.3 Hz), 3.68-4.07 (2H, m), 5.94 (1H, br s), 6.84-7.53, 6.84-7.53 (9H, m)	12.5(q), 14.7(q), 17.3(q), 26.3(t), 436.9(t), 49.4(d), 65.9(s), 113.3(d), 121.2(d), 126.1(s), 126.7(d), 127.2(d), 128.2(d), 128.3(d), 137.0(s), 144.1(s), 153.9(s)
10	180-181	3230, 1660	1.22 (3H, t, J=7.3 Hz), 1.62-2.02 (4H, m), 3.68-4.14 (4H, m), 4.75-4.90 (1H, m), 5.64 (1H, br s), 6.83-7.55 (9H, m)	12.5(q), 25.8(t), 27.4(t), 36.8(t), 63.5(s), 69.6(t), 83.8(d), 113.3(d), 121.5(d), 125.2(s), 126.5(d), 127.0(d), 128.2(d), 136.6(s), 145.2(s), 153.6(s)

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7. We could not determine the stereochemistry of the 1:1-adducts, because ^{1}H-nmr spectroscopy (using the chiral shift reagent) led no conclusion about it.
8. Sensitization experiments could not be carried out, since no appropriate sensitizer could be found. The extinction coefficient of 4-phenylquinazolin-2-one (1a) at 366 nm (ε 3800) is very high. The uv spectrum of (1a) showed an end absorption until $\lambda \fallingdotseq 390$ nm [λ_{max} (EtOH) 270 (ε 11200) and 358 nm (5900)].
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11. Satisfactory elemental analyses have been obtained for all new compounds.

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