STUDIES ON as-TRIAZINE DERIVATIVES. XV[1].
INTRAMOLECULAR REVERSE-ELECTRON DEMAND DIELS-ALDER REACTION OF 1,2,4-TRIAZINE DERIVATIVES

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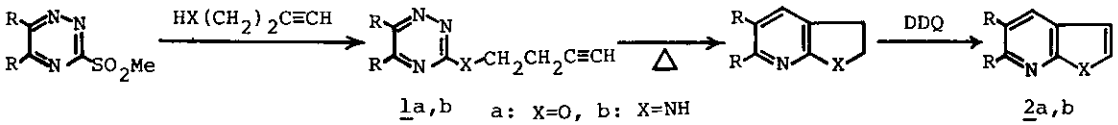
Abstract ——— 5,6-Diphenyl-1,2,4-triazine-3-carboxylic acid esters which have acetylenic function in the alcoholic moiety of the ester group were converted to the pyridine derivatives condensed with lactone ring by means of intramolecular reverse electron-demand Diels-Alder reaction. This type ring-transformation was applicable to the corresponding 3,5-diphenyl-1,2,4-triazine-6-carboxylic acid esters. According to the similar manner, benzofuro[2,3-b]pyridines, benzofuro[2,3-c]pyridines, and benzofuro[2,3-d]pyrimidines were synthesized in satisfactory yields. The intermediates were prepared smoothly by palladium catalyzed cross-coupling reaction of 3-, 6-, and 5-(2-iodophenoxy)-1,2,4-triazines with terminal acetylenes. The Diels-Alder reaction of 3-(2-phenylethynylphenoxy)-1,2,4-benzotriazine afforded 11-phenylbenzofuro[2,3-b]quinoline.

A lot of works have been accumulated[2] on the Diels-Alder reaction of 1,2,4-triazine (as-triazine) derivatives with electron rich dienophiles. The reaction is utilized ingenuously for the synthesis of pyridine and pyrimidine derivatives which are not easily obtained by conventional manners. Furthermore, introduction of intramolecular reactions into this field caused great expansion with the scope of the Diels-Alder reaction. For example, in 1987, Taylor et al.[3] reported a facile synthesis of furo[2,3-b]pyridines (**2a**) by means of thermal transformation of

as-triazine derivatives (**1a**) containing an unsaturated ether chain at the 3-position. The reaction is applicable to the synthesis of pyrrolo[2,3-b]pyridines (**2b**) as shown below (Scheme 1).



Scheme 1

Based on the results described in literatures,[2] the characteristics of the Diels-Alder reaction of as-triazines can be summarized as follows.

(i) The presence of electron-withdrawing groups on as-triazine rings facilitates the reaction.

(ii) In the case of intramolecular reaction, electron-withdrawing groups are unnecessary for the progress of the reaction.

(iii) According to this reaction, various kinds of pyridine condensed rings can be conveniently constructed.

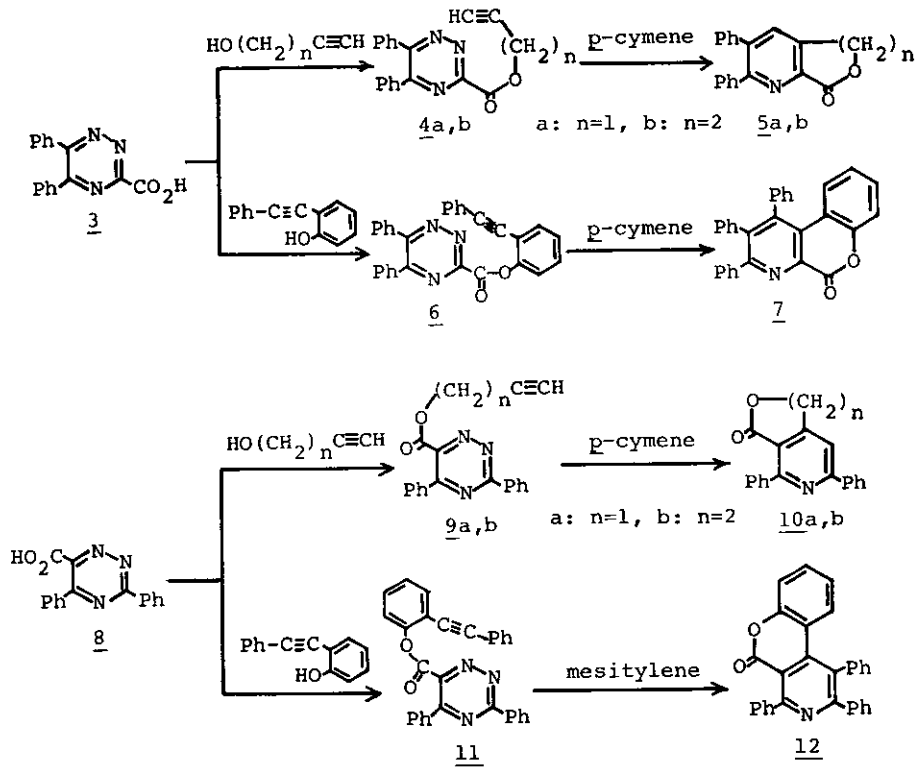
From these points of view, we studied the intramolecular Diels-Alder reation of as-triazine esters containing unsaturated function in the ester group hoping favourable reflection of the electron-withdrawing effect of the ester carbonyl groups.

In addtion to the above, the intramolecular reaction of o-ethynylphenoxy-as-triazines which have no electron-withdrawing group in the as-triazine rings was examined. The present paper deals with these two kinds of ring transformation described above, together with some other findings obtained during the investigation.

(I) Ring Transformation of as-Triazinecarboxylic Acid Esters

When the mixed anhydride generated from **3**[4] and ethyl chloroformate was treated with ethynyl alcohols such as 2-propyn-1-ol or 3-butyn-1-ol, **4a,b** were obtained in good yields. Upon heating in p-cymene under reflux, **4a,b** were transformed into **5a,b** with the loss of nitrogen. The phenyl ester (**6**) also derived from **3** was changed to the tricyclic lactone (**7**) under similar conditions.

Similarly, the unsaturated esters (**9a,b**) of as-triazine-6-carboxylic acid (**8**) and the phenyl ester (**11**) underwent the intramolecular ring conversion to give **10a,b** and **12** respectively (Scheme 2).

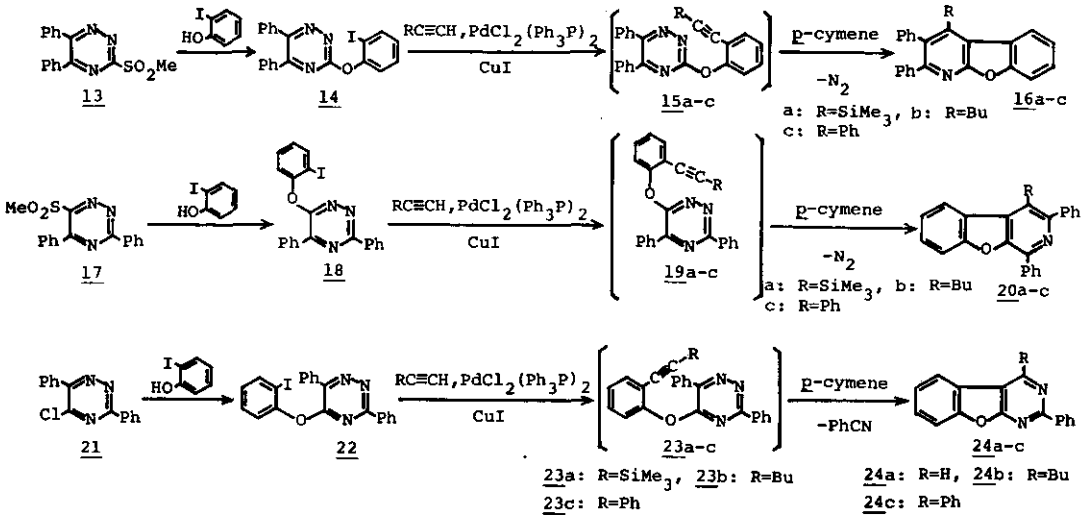


Scheme 2

Based on the results described above, intramolecular Diels-Alder reaction of unsaturated esters of as-triazine-carboxylic acids at positions 3 and 6 seems to have some utility for the synthesis of pyridines fused with lactone rings.

(II) Ring Transformation of o-Ethynylphenoxy-as-triazines

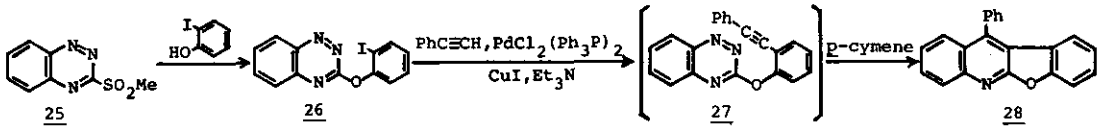
Pd-catalyzed cross-coupling reaction of aryl iodides (or related compounds) with terminal acetylenes such as phenylacetylene, 1-hexyne, and trimethylsilylacetylene is one of the most convenient method for the introduction of ethynyl group into aromatic rings.[5] In order to extend the Diels-Alder reaction of as-triazine derivatives shown in Scheme 1, o-ethynylphenoxy-as-triazines which are analogues of -alkynyloxy-as-triazines (**1a,b**) were synthesized by means of palladium-catalyzed reaction. For example, the o-iodophenyl ether (**14**) preared by the condensation of **13** with o-iodophenol under basic conditions was treated with terminal acetylenes over $PdCl_2(PPh_3)_2$ to give the cross-coupling products (**15a-c**). At the 6-position and 5-position, similar reactions were proceeded, and the corresponding o-ethynyl-phenoxy-as-triazines (**19a-c**, **23a-c**) were obtained in satisfactory yields. The phenyl ethers thus synthesized underwent intramolecular Diels-Alder reaction to give benzofuropyridines (**16a-c**, **20a-c**) and benzofuropyrimidines (**24a-c**)(Scheme 3).



Scheme 3

On the basis of the results illustrated in Schemes 1 and 3, the intramolecular Diels-Alder reaction of unsaturated as-triazinyl ethers which were firstly reported by Taylor et al.[3] became clear to have wide generality and provides a unique method for the synthesis of benzofuran and dibenzofuran aza-analogues.

Finally, the reaction was tested in a 1,2,4-benzotrizine ring system. In reverse electron-demand Diels-Alder reaction of benzene fused diazines and triazines, it is necessary to mobilize aromatic π-electrons in fused benzene rings. Thus, considerable activation energy is supposed to be required for the progress of the reaction. In fact, there are few examples of intermolecular Diels-Alder reaction of benzodiazines[6] and benzotriazines.[1] The o-ethynylphenyl ethers (**27**), however, seems to have favourable structure for the Diels-Alder reaction, because the reaction is intramolecular. As shown in Scheme 4, the ether (**26**) reacted smoothly with phenylacetylene to give **27**. On heating the crude **27** in p-cymene as usual, the tetracyclic compound (**28**) was obtained as expected.



Scheme 4

Generally, as-triazines are synthesized by the condensation of α-dicarbonyl compounds with amidrazones,[7] so as-trizines appear to have good availability as synthetic intermediates, and the Diels-Alder reaction of as-triazine derivatives should be not only theoretically interesting but also practically convenient for

the synthesis of pyridine and pyrimidine derivatives.

EXPERIMENTAL

Melting points were determined in open capillary tubes and were uncorrected. Infrared (ir) spectra were measured with a JASCO IRA-1 spectrophotometer. Proton nuclear magnetic resonance (^{1}H-nmr) spectra were taken at 60 MHz with a JEOL JNM-PMX 60 spectrometer. Tetramethylsilane (TMS) was used as internal standard. Chemical shifts are expressed in δ vaues. The following abbreviations are used : s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, and br=broad.

Ethyl 3,5-Diphenyl-as-triazine-6-carboxylate

To a solution of ethyl 3-phenyl-2,3-dioxopropionate (5.15 g, 25 mmol) in dry EtOH (20ml) a solution of benzamidrazone (30 mmol)[prepared from ethyl benzimidate (4.47 g, 30 mmol) and hydrazine monohydrate (1.5 g, 30 mmol) in EtOH (20 ml)] was added and kept for 48 h at 0°C with continuous agitation. The mixture was refluxed for 2.5 h. After removal of the solvent, the residue was purified by passing it through a silica gel column with hexane-Et_2O (1:1). Recrystallization from pentane gave 5.9 g (77 %) of ethyl 3,5-diphenyl-as-triazine-6-carboxylate, mp 62-64°C, as pale yellow prisms. Ir ($CHCl_3$)cm^{-1}: 1740. ^{1}H-Nmr (CCl_4): 1.36 (3H, t, J=7Hz), 4.36 (2H, q, J=7Hz), 7.2-8.1 (8H, m), 8.4-8.9 (2H, m). Anal. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.80; H, 4.95; N, 13.76. Found: C, 71.07; H, 5.01; N, 13.76.

3,5-Diphenyl-as-triazine-6-carboxylic Acid (8)

To a solution of ethyl 3,5-diphenyl-as-triazine-6-carboxylate (4.58 g, 15 mmol) in EtOH (75 ml) 1N KOH solution (15 ml, 15 mmol) was added and the mixture was stirred for 12 h at room temperature. After removal of the solvent, the residue was diluted with H_2O and acidified with 3N HCl. The resulting precipitate was filtered and dried under reduced pressure to give 4.12 g (99 %) of **8**. Ir (KBr)cm^{-1}: 3600-2400, 1740. ^{1}H-Nmr(pyridine-d_5): 7.1-7.9 (6H, m), 8.1-8.6 (2H, m), 8.6-8.9 (2H, m), 14.5-14.8 (1H, br). Since compound **8** tended to decarboxylate at the stage of recrystallization, **8** was used to the next step without further purification.

2-Phenylethynylphenol

A mixture of methoxymethyl 2-iodophenyl ether (5.28 g, 20 mmol), phenylacetylene (2.24 g, 22 mmol), $PdCl_2(Ph_3P)_2$ (0.63 g, 1.6 mmol), CuI (0.3 g, 1.6 mmol), and Et_3N (50 ml) was refluxed for 1.5 h. After removal of the solvent under reduced pressure, H_2O was added to the residue. The resulting mixture was extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried over Na_2SO_4 and purified by passing it through silica gel column first eluting with hexane, then hexane-Et_2O (10:1). The

hexane-Et_2O (10:1) eluent gave 3.97 g (83 %) of methoxymethyl 2-phenylethynyl ether, bp_6 160°C (bath temp.), as colorless liquid. Ir ($CHCl_3$)cm^{-1}: 2230. ^{1}H-Nmr (CCl_4): 3.50 (3H, s), 5.20 (2H, s), 6.7-7.7 (9H, m). Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92. Found: C, 80.48; H, 5.85.

A mixture of methoxymethyl 2-phenylethynyl ether (3.97 g, 16.7 mmol), conc. HCl (3 ml), and MeOH (60 ml) was stirred for 24 h at room temperature. After removal of the solvent under reduced pressure at room temperature, H_2O was added to the residue. The resulting mixture was extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried over Na_2SO_4, and the CH_2Cl_2 was removed under reduced pressure to give 2.94 g (91 %) of 2-phenylethynylphenol as colorless needles. Ir ($CHCl_3$)cm^{-1}: 3600-3400. ^{1}H-Nmr (CCl_4): 5.3-5.9 (1H, br), 6.6-7.7 (9H, m). 2-Phenylethynylphenol was used to the next step without further purification because of its unstability.

General Procedure for the Preparation of ω-Alkynyl 5,6-Diphenyl-as-triazine-3-carboxylates (4a,b), ω-Alkynyl 3,5-Diphenyl-as-triazine-6-carboxylates (9a,b), 2-(Phenylethynyl)phenyl 5,6-Diphenyl-as-triazine-3-carboxylate (6), and 2-(Phenylethynyl)-phenyl 3,5-Diphenyl-as-triazine-6-carboxylate (11)

To a solution of **3**[4] or **8** (2.6 mmol) in dry THF (20 ml) Et_3N (0.32 g, 3.1 mmol) and ethyl chloroformate (0.31 g, 2.9 mmol) were added at -15°C and the mixture was stirred for 0.5 h at the same temperature. An appropriate acetylenic alcohol or phenol (2.9 mmol) was added to the reaction mixture and the mixture was stirred for 1-3 h at 0°C or room temperature. After removal of the solvent under reduced pressure, H_2O was added to the residue. The resulting mixture was extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried over K_2CO_3, and the resulting solid was purified by recrystallization.

4a: Pale yellow needles (AcOEt-diisopropyl ether), mp 111-113°C, yield (73 %). Anal. Calcd for $C_{19}H_{13}N_3O_2$: C, 72.37; H, 4.16; N, 13.33. Found: C, 72.07; H, 4.34; N, 13.17. Ir ($CHCl_3$)cm^{-1}: 3310, 1760. ^{1}H-Nmr ($CDCl_3$): 2.60 (1H, t, J=2Hz), 5.15 (2H, t, J=2Hz), 7.1-7.9 (10H, m).

4b: Pale yellow needles (AcOEt-hexane), mp 122-124°C, yield (72 %). Anal. Calcd for $C_{20}H_{15}N_3O_2$: C, 72.93; H, 4.59; N, 12.76. Found: C, 72.85; H, 4.51; N, 12.68. Ir ($CHCl_3$)cm^{-1}: 3310, 1745. ^{1}H-Nmr ($CDCl_3$): 2.33 (1H, t, J=2Hz), 2.86 (2H, dt, J=7Hz, J=2Hz), 4.73 (2H, t, J=7Hz), 7.1-7.9 (10H, m).

9a: Pale yellow needles (AcOEt-hexane), mp 147-149°C, yield (87 %). Anal. Calcd for $C_{19}H_{13}N_3O_2$: C, 72.37; H,4.16; N, 13.33. Found: C, 72,10; H, 4.37; N, 13.17. Ir ($CHCl_3$)cm^{-1}: 3310, 1750. ^{1}H-Nmr ($CDCl_3$): 2.60 (1H, t, J=2Hz), 5.00 (2H, d, J=2Hz), 7.3-8.1 (8H, m), 8.4-8.9 (2H, m).

9b: Pale yellow needles (diisopropyl ether), mp 98-100°C, yield (61 %). Anal. Calcd for $C_{20}H_{15}N_3O_2$: C, 72.93; H, 4.59; N, 12.76. Found: C, 72.77; H, 4.88; N, 12.64. Ir ($CHCl_3$)cm^{-1}: 3310, 1740. ^{1}H-Nmr ($CDCl_3$): 2.00 (1H, d, J=2Hz), 2.57 (2H, dt, J=2Hz, J=7Hz), 4.50 (2H, t, J=7Hz), 7.4-7.7 (6H, m), 7.7-8.3 (2H, m), 8.4-8.9 (2H, m).

6: Pale yellow needles (AcOEt-hexane), mp 159-161°C, yield (69 %). Anal. Calcd for $C_{30}H_{19}N_3O_2$: C, 79.45; H, 4.22; N, 9.27. Found: C, 79.20; H, 5.99; N, 9.27. Ir ($CHCl_3$)cm^{-1}: 1765. ^{1}H-Nmr ($CDCl_3$): 6.7-7.9 (m).

11: Pale yellow needles (AcOEt-diisopropyl ether), mp 154-156°C, yield (66 %). Anal. Calcd for $C_{30}H_{19}N_3O_2$: C, 79.45; H, 4.22; N, 9.27. Found: C, 79.25; H, 4.33; N, 9.20. Ir ($CHCl_3$)cm^{-1}: 1760. ^{1}H-Nmr ($CDCl_3$): 7.1-7.9 (15H, m), 7.9-8.3 (2H, m), 8.6-9.0 (2H, m).

General Procedure for the Intramolecular Diels-Alder Reaction of ω-Alkynyl 5,6-Diphenyl-as-triazine-3-carboxylates (4a,b), ω-Alkynyl 3,5-Diphenyl-as-triazine-6-carboxylates (9a,b), 2-(Phenylethynyl)phenyl 5,6-Diphenyl-as-triazine-3-carboxylate (6), and 2-(Phenylethynyl)phenyl 3,5-Diphenyl-as-triazine-6-carboxylate (11)

The mixture of **4a,b**, **9a,b**, **6**, or **11** (1.6 mmol) and p-cymene (3 ml) was refluxed for 2-48 h. After removal of the solvent under reduced pressure, the residue was purified by passing it through a silica gel column. Recrystallization from appropriate solvents yielded the desired **5a,b**, **10a,b**, **7**, or **12**.

5a: Colorless needles (AcOEt-diisopropyl ether), mp 208-210°C, yield (80 %). Anal. Calcd for $C_{19}H_{13}NO_2$: C, 79.43; H, 4.56; N, 4.88. Found: C, 79.73; H, 4.62; N, 4.90. Ir ($CHCl_3$)cm^{-1}: 1785. ^{1}H-Nmr ($CDCl_3$): 5.46 (2H, s), 7.0-7.6 (10H, m), 7.93 (1H, s).

5b: Pale yellow needles (AcOEt), mp 220-222°C, yield (63 %). Anal. Calcd for $C_{20}H_{15}NO_2$: C, 79.71; H, 5.02; N, 4.65. Found: C, 79.63; H, 5.24; N, 4.60. Ir ($CHCl_3$)cm^{-1}: 1745. ^{1}H-Nmr (DMSO-d_6): 3.23 (2H, t, J=6Hz), 4.63 (2H, t, J=6Hz), 7.0-7.5 (10H, m), 7.96 (1H, s).

10a: Colorless needles (AcOEt), mp 196-198°C, yield (58 %). Anal. Calcd for $C_{19}H_{13}NO_2$: C, 79.43; H, 4.56; N, 4.88. Found: C, 79.54; H, 4.61; N, 4.88. Ir ($CHCl_3$)cm^{-1}: 1770. ^{1}H-Nmr ($CDCl_3$): 5.33 (2H, s), 7.2-7.7 (6H, m), 7.76 (1H, s), 7.9-8.4 (4H, m).

10b: Colorless needles (AcOEt-hexane), mp 205-207°C, yield (25 %). Anal. Calcd for $C_{20}H_{15}NO_2$: C, 79.71; H, 5.02; N, 4.65. Found: C, 79.93; H, 5.09; N, 4.68. Ir ($CHCl_3$)cm^{-1}: 1740, 1720. ^{1}H-Nmr (DMSO-d_6): 3.20 (2H, t, J=6Hz), 4.63 (2H, t, J=6Hz), 7.3-7.8 (8H, m), 8.03 (1H, s), 8.1-8.4 (2H, m).

7: Colorless needles (AcOEt), mp 266-268°C, yield (42 %). Anal. Calcd for $C_{30}H_{19}NO_2$: C, 84.68; H, 4.50; N, 3.29. Found: C, 84.93; H, 4.68; N, 3.25. Ir (KBr)cm^{-1}: 1755. ^{1}H-Nmr (CF_3CO_2H): 6.6-7.8 (m).

12: Colorless needles (AcOEt), mp 280-282°C, yield (49 %). Anal. Calcd for $C_{30}H_{19}NO_2$: C, 84.68; H, 4.50; N, 3.29. Found: C, 84.71; H, 4.25; N, 3.16. Ir (KBr)cm^{-1}: 1740. ^{1}H-Nmr (CF_3CO_2H): 6.9-8.0 (m).

6-Oxo-3,5-diphenyl-1,6-dihydro-as-triazine[8]

To a Grignard solution [prepared from Mg (6.41 g, 260 mg atom) and bromobenzene (40.8 g, 260 mmol) in dry THF (150 ml)] 5,6-dioxo-3-phenyl-1,2,5,6-tetrahydro-as-triazine[9] (15.1 g, 80 mmol) was added and the mixture was refluxed for 20 h under nitrogen. After removal of the solvent under reduced pressure, the Grignard complex was decomposed with 3N HCl and the resulting precipitate was filtered. The precipitate was washed with H_2O and Et_2O. The resulting precipitate was recrystallized from acetone to give 11.8 g (59 %) of 6-oxo-3,5-diphenyl-1,6-dihydro-as-triazine, mp 219-221°C, [lit.[8] mp 218-220°C], as pale yellow needles. ^{1}H-Nmr (DMSO-d_6): 7.2-7.8 (6H, m), 8.0-8.4 (2H, m), 8.5-8.8 (2H, m), 13.4-14.0 (1H, br).

6-Chloro-3,5-diphenyl-as-triazine

A suspension of 6-oxo-3,5-diphenyl-1,6-dihydro-as-triazine (2.5 g, 10 mmol) in $POCl_3$ (20 ml) was refluxed for 3 h with stirring. The reaction mixture was diluted with $CHCl_3$. The $CHCl_3$ layer was washed successively with H_2O, 10 % NH_4OH and sat. aq. NaCl solution, and dried over Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography on active alumina (Sumitomo, KCG-30, 70-230 mesh) using benzene as an eluent. Recrystallization from hexane-Et_2O gave 2.44 g (91 %) of 6-chloro-3,5-diphenyl-as-triazine, mp 101-102°C, as yellow prisms. Anal. Calcd for $C_{15}H_{10}ClN_3$: C, 67.30; H, 3.77; N, 15.70; Cl, 13.24. Found: C, 67.25; H, 3.72; N, 15.80; Cl, 13.00. ^{1}H-Nmr (CCl_4): 7.4-7.7 (3H, m), 8.0-8.3 (1H, m), 8.4-8.8 (1H, m).

6-Methylthio-3,5-diphenyl-as-triazine

a) 15 % aq. MeSNa (8 mmol) was added to the solution of 6-chloro-3,5-diphenyl-as-triazine (1.07 g, 4 mmol) in 1,4-dioxane (20 ml). The mixture was refluxed for 15 h with stirring and concentrated under reduced pressure. H_2O was added to the residue and then the aqueous solution was extracted with $CHCl_3$. The $CHCl_3$ extract was dried over K_2CO_3. After removal of the solvent, the residue was recrystallized from AcOEt-hexane to give 1.02 g (91 %) of 6-methylthio-3,5-diphenyl-as-triazine, mp 114-116°C, as pale yellow needles. Anal. Calcd for

$C_{16}H_{13}N_3S$: C, 68.78; H, 4.69; N, 15.04; S, 11.48. Found: C, 68.90; H, 4.64; N, 14.89; S, 11.58. ^{1}H-Nmr ($CDCl_3$) 2.73 (3H, s), 7.2-7.8 (6H, m), 7.8-8.3 (2H, m), 8.3-8.9 (2H, m).

b) A mixture of 6-oxo-3,5-diphenyl-1,6-dihydro-as-triazine (4.23 g, 17 mmol), P_2S_5 (3.77 g, 17 mmol), and dry pyridine (50 ml) was refluxed for 4.5 h. After removal of the solvent under reduced pressure, H_2O was added to the residue. The resulting precipitate was filtered and dried under reduced pressure at room temperature. This crude precipitate was added to NaOMe solution [prepared from Na (0.42 g, 18 mg atom) and dry MeOH (100 ml)] and MeI (2.73 g, 19 mmol) at room temperature. The reaction mixture was stirred for 3.5 h at room temperature. After removal of the solvent, H_2O was added to the residue, and the resulting mixture was extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried over Na_2SO_4. After removal of the solvent, the resulting residue was recrystallized from diisopropyl ether to give 2.5 g (62%) of 3-methylthio-3,5-diphenyl-as-triazine, mp 114-116°C, as pale yellow needles.

6-Methylsulfonyl-3,5-diphenyl-as-triazine (17)

A solution of $KMnO_4$ (5.18 g, 33 mmol) in H_2O (35 ml) was added to a solution of 6-methylthio-3,5-diphenyl-as-triazine (2.5 g, 9 mmol) and tetra-n-butylammonium bromide (1.0 g) in AcOH (10 ml) and benzene (35 ml). The mixture was stirred at room temperature for 1 h. A sat. $NaHSO_3$ solution was added to the mixture untill the purple color disappeared and the colorless solution was neutrallized with solid K_2CO_3. The benzene layer was separated and dried over Na_2SO_4. After removal of the solvent, the residue was purified by passing it through a silica gel column with benzene. Recrystallization from AcOEt-hexane gave 2.07 g (74 %) of **17**, mp 150-152°C, as pale yellow needles. Anal. Calcd for $C_{16}H_{13}N_3O_2S$: C, 61.72; H, 4.21; N, 13.50; S, 10.30. Found: C, 61.53; H, 4.20; N, 13.31; S, 10.35. ^{1}H-Nmr ($CDCl_3$): 3.53 (3H, s), 7.4-7.9 (6H, m), 7.9-8.4 (2H, m), 8.5-8.9 (2H, m).

General Procedure for the Nucleophilic Substitution Reaction of 5,6-Diphenyl-3-methylsulfonyl-as-triazine (13), 3,5-Diphenyl-6-methylsulfonyl-as-triazine (17), and 5-Chloro-3,6-diphenyl-as-triazine (21) with 2-Iodophenol

60 % NaH in mineral oil (0.31 g, 7.8 mmol) was added to a solution of 2-iodophenol (1.45 g, 6.6 mmol) in dry THF (20 mmol), and the mixture was stirred at room temperature for 5 min. The substrate (**13**,[10] **17**, or **21**[11])(6 mmol) was added thereto, and the mixture was continued with stirring for 4.5-16 h at room temperature. The reaction mixture was concentrated to dryness under reduced pressure and H_2O was added to the residue. The aqueous solution was extracted

with $CHCl_3$, and the $CHCl_3$ extract was dried over Na_2SO_4. After removal of the solvent, the residual precipitate was recrystallized from appropriate solvents to give **14**, **18**, and **22**.

14: Pale yellow prisms (AcOEt-hexane), mp 152-154°C, yield (75 %). Anal. Calcd for $C_{21}H_{14}IN_3O$: C, 55.89; H, 3.13; N, 9.31. Found: C, 55.97; H, 3.28; N, 9.42. ^{1}H-Nmr ($CDCl_3$): 6.8-8.0 (m).

18: Pale yellow needles (AcOEt), mp 188-189°C, yield (74 %). Anal. Calcd for $C_{21}H_{14}IN_3O$: C, 55.89; H, 3.13; N, 9.31. Found: C, 55.82; H, 3.19; N, 9.35. ^{1}H-Nmr ($CDCl_3$): 6.9-8.0 (m), 8.5-8.8 (m). The integrated ratio of the former signal and the latter signal is 5:2.

22: Pale yellow needles (AcOEt-hexane), mp 172-174°C, yield (87 %). Anal. Calcd for $C_{21}H_{14}IN_3O$: C, 55.89; H,3.13; N, 9.31. Found: C, 55.79; H. 3.21; N, 9.21. ^{1}H-Nmr ($CDCl_3$): 6.9-8.6 (m).

General Procedure for the Preparation of Benzofuro[2,3-b]pyridines (16a-c), Benzofuro[2,3-c]pyridines (20a-c), and Benzofuro[2,3-d]pyrimidines (24a-c)

A mixture of diphenyl-2-iodophenoxy-as-triazine (**14**, **18**, or **22**)(1.0 mmol), acetylene (1.2 mmol), $PdCl_2(Ph_3P)_2$ (31 mg, 0.08 mmol), CuI (15 mg, 0.08 mmol), and Et_3N (15 ml) was refluxed for 3.5-24.5 h. In the case of trimethylsilylacetylene as acetylene, the same conditions mentioned above were adopted except for Et_3N (1.2 mmol) and DMF (1 ml) in sealed tube at 80°C. After removal of the solvent under reduced pressure, H_2O was added to the residue. The resulting mixture was extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried over Na_2SO_4. After removal of the solvent, the resulting residue was chromatographed on a silica gel column. The eluate with an appropriate solvent gave a crude diphenyl-2-ethynylphenoxy-as-triazine (**15a-c**, **19a-c**, or **23a-c**).

A solution of the crude substrate (**15a-c**, **19a-c**, or **23a-c**) in mesitylene (or p-cymene)(5 ml) was refluxed under nitrogen for 13-25 hr depending on the substrate. The solvent was evaporated under reduced pressure and the residual solid was purified by passing it through a silica gel column eluting with appropriate solvents to yield the desired **16a,b**,[12] **c**, **20a,b**,[12] **c**, or **24a**,[13] **b,c**.

16a: Pale yellow needles (hexane), mp 161-163°C, yield (43 %). Anal. Calcd for $C_{26}H_{23}NOSi$: C, 79.35; H, 5.89; N, 3.56. Found: C, 79.52; H, 6.10; N, 3.39. ^{1}H-Nmr ($CDCl_3$): 0.15 (9H, s), 7.2-7.8 (13H, m), 8.0-8.3 (1H, m).

16b: Pale yellow prisms (pentane), mp 106-107°C, yield (50 %). Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14; N, 3.71. Found: C, 85.87; H, 6.12; N, 3.70. ^{1}H-Nmr ($CDCl_3$): 0.82 (3H, t, J=7Hz), 1.0-1.8 (4H, m), 3.00 (2H, t, J=7Hz),

7.1-8.0 (14H, m).

16c: Colorless needles (AcOEt-hexane), mp 232-234°C, yield (48 %). Anal. Calcd for $C_{29}H_{19}NO$: C, 87.63; H,4.82; N, 3.52. Found: C, 87.47; H, 4.78; N, 3.59. ^{1}H-Nmr ($CDCl_3$): 6.8-7.8 (m).

20a: Pale yellow needles (hexane-Et_2O), mp 195-197°C, yield (36 %). Anal. Calcd for $C_{26}H_{23}NOSi$: C,79.35; H, 5.89; N, 3.56. Found: C, 79.30; H, 6.01; N, 3.44. ^{1}H-Nmr ($CDCl_3$): 0.22 (9H, s), 7.3-7.8 (14H, m), 8.1-8.4 (1H, m), 8.5-8.7 (2H, m).

20b: Colorless needles (diisopropyl ether), mp 133-135°C, yield (48 %). Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14; N, 3.71. Found; C, 85.86; H, 6.25; N, 3.93. ^{1}H-Nmr ($CDCl_3$): 0.88 (3H, t, J=7Hz), 1.0-2.0 (4H, m), 3.18 (2H, t, J=7Hz), 7.4-7.8 (10H, m), 7.9-8.2 (2H, m), 8.4-8.6 (2H, m).

20c: Colorless needles (benzene-Et_2O), mp 224-226°C, yield (40 %). Anal. Calcd for $C_{29}H_{19}NO$: C, 87.63; H, 4.82; N, 3.52. Found: C, 87.69; H,4.92; N, 3.35. ^{1}H-Nmr ($CDCl_3$): 7.0-7.9 (17H, m), 8.5-8.7 (2H, m).

24a: Colorless needles (benzene-hexane), mp 161-163°C, yield (40 %). Anal. Calcd for $C_{16}H_{10}N_2O$: C, 78.04; H, 4.09; N, 11.38. Found: C, 78.04; H, 4.22; N, 11.18. ^{1}H-Nmr ($CDCl_3$): 7.3-8.1 (7H, m), 8.5-8.8 (2H, m), 9.33 (1H, s).

24b: Colorless needles (hexane), mp 86.5-88.5°C, yield (60 %). Anal. Calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.66; H, 6.08; N, 8.93. ^{1}H-Nmr ($CDCl_3$): 1.03(3H, t, J=7Hz), 0.9-2.4 (4H, m), 3.32 (2H, t, J=7Hz), 7.2-8.1 (7H, m), 8.4-8.8 (2H, m).

24c: Pale yellow needles (AcOEt), mp 194-196°C, yield (37 %). Anal. Calcd for $C_{22}H_{14}N_2O$: C, 81.97; H, 4.38; N, 8.69. Found: C, 81.95; H, 4.42; N, 8.63. ^{1}H-Nmr ($CDCl_3$): 7.3-8.3 (6H, m), 8.6-8.8 (1H, m).

3-Methylsulfonyl-1,2,4-benzotriazine (25)

To a stirred solution of the 3-methylthio-1,2,4-benzotriazine[14] (1.06 g, 6 mmol) in $CHCl_3$ (50 ml) at room temperature, m-chloroperbenzoic acid (2.96 g, 12 mmol) was added in small portions over the course of a few minutes. The resulting mixture was stirred at room temperature for 3.5 h. The mixture was washed with aq. K_2CO_3 solution. The $CHCl_3$ layer was separated and dried over K_2CO_3. After removal of the solvent, the resulting solid was recrystallized from AcOEt gave 0.96 g (77 %) of **25**, mp 140-142°C, as pale yellow needles. Anal. Calcd for $C_8H_7N_3O_2S$: C, 45.92; H, 3.37; N, 20.09; S, 15.33. Found: C, 45.68; H, 3.41; N, 19.97; S, 15.25. ^{1}H-Nmr ($CDCl_3$): 3.66 (3H, s), 7.9-9.0 (4H, m).

3-(2-Iodophenoxy)-1,2,4-benzotriazine (26)

Following the procedure for the preparation of **14**, **18**, or **22**, treatment of **25** (0.83 g, 4 mmol) with 2-iodophenol (1.06 g, 4.8 mmol) and 60 % NaH in mineral oil (0.192 g, 4.8 mmol) in dry THF (20 ml) for 1 h followed by recrystallization from AcOEt-hexane gave 1.21 g (86 %) of **26**, mp 115-117°C, as pale yellow needles. Anal. Calcd for $C_{13}H_8IN_3O$: C, 44.72; H, 2.31; N, 12.04. Found: C, 44.51; H, 2.38; N, 11.92. ^{1}H-Nmr ($CDCl_3$): 6.9-8.2 (7H, m), 8.4-8.8 (1H, m).

11-Phenylbenzofuro[2,3-b]quinoline (28)

Following the procedure for the preparation of **16a-c**, **20a-c**, or **24a-c**, **26** (0.7 g, 2 mmol) was treated with phenylacetylene (0.25 g, 2.4 mmol), $PdCl_2(Ph_3P)_2$ (63 mg, 0.16 mmol), and CuI (30 mg, 0.16 mmol) in Et_3N (20 ml). The reaction time was 3.5 h, and hexane-Et_2O (1:1) was used as eluting solvent on silica gel column chromatography. The Diels-Alder reaction was performed in p-cymene (5 ml) for 2 h. The residual solid was purified by silica gel column chromatography eluting with hexane and then with hexane-Et_2O (1:1). The resulting crystals obtained from the hexane-Et_2O (1:1) eluate were recrystallized from MeOH to yield 0.34 g (58 %) of **28**, mp 204-206°C, as colorless needles. Anal. Calcd for $C_{21}H_{13}NO$: C, 85.40; H, 4.44; N, 4.74. Found: C, 85.20; H, 4.70; N, 4.86. ^{1}H-Nmr (CF_3CO_2H): 7.2-8.5 (m).

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12. In these cases, the Diels-Alder reaction proceeded in Et_3N.

13. In this case, trimethylsilylacetylene was used as a starting material.

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