# Ene Syntheses in the s-Triazine Series.

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β-Oxo-s-triazines undergo an ene synthesis with dienophiles. The ease of the reaction depends
on the substituents of the triazine ring and on the nature of the enophile.

The Diels-Alder reaction has been used extensively in
the synthesis of heterocyclic compounds (1a, 1b). In add-
ition, acetylene dicarboxylic acid and its esters react with
nitrogen heterocycles by a number of pathways (1c). Hav-
ing prepared a series of β-oxo-s-triazines and demonstrated
that they exist as enols (2,3), we examined the possibility
of effecting a diene synthesis with them. The products ob-
tained were, however, those from an ene synthesis.
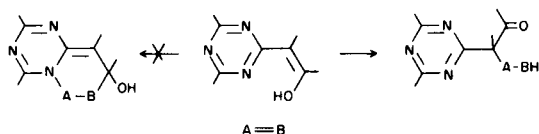
The ease of the reaction depends on the substituents of
the triazine ring and on the nature of the enophile; in our
case this was mainly dimethyl acetylenedicarboxylate I.
With the diamino-β-oxo-s-triazines II and III, the latter gives
practically quantitatively IV and V when the reaction is
carried out in refluxing benzene for 3 to 4 hours. Similarly
VII was obtained from the dimethoxy-s-triazine VI, but
only after 24 hours reflux in toluene. On the other hand,
I reacts neither with the dichloro-s-triazine VIII nor with
the bismethylthio-s-triazine IX, even under forcing condi-
tions (200° in toluene in the autoclave), and IX does not
react in the presence of stannic chloride.

The action of ethyl azodicarboxylate on II results in for-
mation of X after 3 hours refluxing in benzene, ethyl pro-
piolate giving XI in only 30% yield under these conditions.
Stronger conditions are necessary for acrylonitrile to react
with II, XII being formed at 200° in toluene in the auto-
clave.

Although an excess of enophile was always present, we
never observed addition of a second enophile molecule on
the diene systems obtained: IV, VII and XI.

The structure of the products obtained was determined
by elemental analysis, and mass, nmr and ir spectra (the
intense band at 1560 cm⁻¹ arising from the triazine ring
being retained).
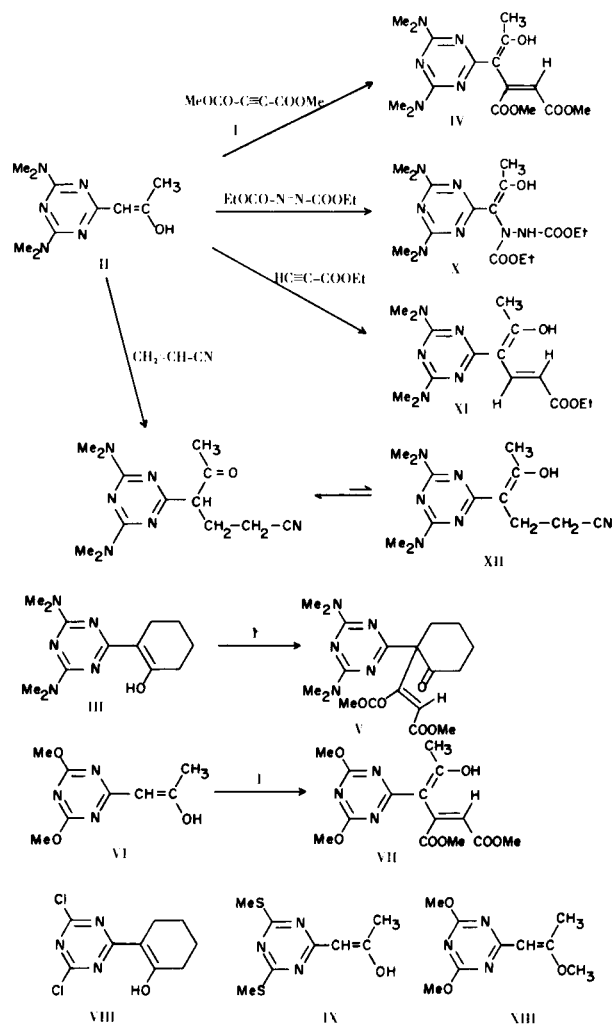
The formation of the various adducts can be explained
by an ene synthesis mechanism (4) with hydrogen transfer
from the enol to a carbon atom of the enophile (if R = H,
return to the enolic form is possible). The same enol hy-
drogen transfer is also found in the thermal cyclizations of

unsaturated ketones (5). It is thus not surprising that the enol ether XIII does not react with dimethyl acetylenedicarboxylate even after 24 hours refluxing in toluene.

The stereochemistry of the product XI obtained with ethyl propiolate and II is in agreement with this cyclic mechanism leading to cis-addition (4) to the multiple bond of the enophile, the two vinyl protons being E to one another (J = 15 Hz) (6). By analogy, Z geometry can be attributed to the two ester functions in IV, V and VII. Although there is no direct proof, the position of the olefinic proton at 6.00 ppm in the unconjugated derivative V would appear to be more compatible with an ester of the maleic type (6.28) than the fumaric type (6.83).

It should be noted that with disymmetric enophiles, only the linear derivatives XI and XII could be isolated, in accord with the principle of preferential orientation in the ene synthesis (4).

Finally, it is known that the electron donating or attracting effects of the substituents at C-2 and C-4 of the triazine ring are exerted at C-6, and if the ene must be an electron-rich olefin, this would explain the lack of reaction of IX, and even more of the dichloro derivative VIII under the conditions used.

EXPERIMENTAL

The melting points were determined with a Büchi (Tottoli) apparatus, and are uncorrected. Ir spectra were recorded in chloroform on a Perkin-Elmer 221 spectrophotometer, and the uv spectra on a Beckman DK2 spectrometer in ethanol. Nmr spectra were measured using a Varian A 60 or a Jeol JNMC 60H, in deuterochloroform with tetramethylsilane (0.00 ppm) as internal reference. Mass spectra were recorded on a Varian MAT type CH-7 or 111 spectrometer using a direct inlet system, source temperature was about 220°.

I. Preparation of the β-Oxo-s-triazines.

Compounds II and VIII were prepared as previously described (2,3), and IX was available according to the method of Eilingsfeld and Scheuermann (7).

2-[2,4-Bis(dimethylamino)-s-triazinyl] cyclohexanone (III).

An excess of a solution of dimethylamine in benzene was added to a solution of 2 g. of VIII in dry benzene at 0°. The mixture was allowed to come to room temperature, 50 ml. of 2% sodium hydroxide was added, and the whole was heated at reflux for 1 hour. After separating, the aqueous layer was extracted with ether, and the combined organic phases were concentrated to obtain 2.05 g. (96%) of a white solid, m.p. 138-139° (from absolute ethanol); molecular weight: 263 (by mass spectroscopy); ir: 1640, 1550, 1500 cm^{-1}; uv max: 230 (ϵ 28,800), 288 (ϵ 14,900), 334 nm (ϵ 4,750); nmr: 1.7 (m, 4, CH_2), 2.4 (m, 4, CH_2), 3.1 (s, 12, N-CH$_3$), 15.2 (s, 1, enol).

(2,4-Dimethoxy-s-triazinyl)acetone (VI).

Sodium (2.3 g.) was added to a mixture of 30 ml. of dry benzene, 9 g. of dry methanol and 10 g. (0.1 mole) of acetylacetone. When the sodium had disappeared, the mixture was cooled to room temperature and 18.5 g. (0.1 mole) of cyanuric chloride in 300 ml. of benzene-ether (2:1) was added rapidly. The mixture was heated for 1 hour at reflux with stirring, stirring being maintained for a further 3 hours. A solution of 9 g. of sodium hydroxide in 200 ml. of methanol was added, stirring being continued overnight. The mixture was heated for 1 hour at reflux, and the solvents removed in vacuum. The residue is taken up in benzene and the solution filtered through sintered glass. Concentration yielded 16.5 g. of a yellow solid, the nmr spectrum of which indicated a mixture of 40% of 2,4,6-trimethoxy-s-triazine and 60% of VI (yield, 50%). Fractional crystallization in benzene gave the title product VI as the more soluble component, m.p. 64-66° (from diisopropyl ether); molecular weight: 197 (by mass spectroscopy); ir: 1715 1640, 1120 cm^{-1}; nmr: 2.1 (s, 3, CH$_3$), 4.1 (s, 6, O-CH$_3$), 5.5 (s, 1, vinyl H), 13.7 (s, 1, enol), 10% of the keto-form can be measured from the methyl signal at 2.3 ppm.

Anal. Calcd. for $C_8H_{11}N_3O_3$: C, 48.72; H, 5.62; N, 21.31; O, 24.34. Found: C, 48.95; H, 5.72; N, 21.53; O, 24.54.

1-(2,4-Dimethoxy-s-triazinyl)-2-methoxy-1-propene (XIII).

A suspension of 5.5 g. of sodium bicarbonate and 9.4 g. (0.05 mole) of 2-propynyl-4,6-dichloro-s-triazine (3,8) in 100 ml. of dry methanol was heated for 6 hours under reflux, then stirred at room temperature for a further 48 hours. After filtration, concentration and recrystallization from diisopropyl ether, 4.2 g. (40%) of a yellow solid was obtained, m.p. 79-81° (from diisopropyl ether); molecular weight: 211 (by mass spectroscopy); ir: 1625, 1560, 1115, 1095, 1070, 835 cm^{-1}; nmr: 2.5 (s, 3, CH$_3$), 3.75 (s, 3, O-CH$_3$), 4.0 (s, 6, O-CH$_3$), 5.6 (s, 1, vinyl H).

II. Ene Syntheses

Except for VII and XII, the following general method was used: 5 or 10 mmoles of the β-oxo-s-triazine and a slight excess of the enophile were heated on reflux for 3-4 hours in 25 or 50 ml. of benzene. Benzene and excess enophile were then evaporated.

Adduct IV.

An almost quantitative yield was obtained, m.p. 149-150.5° (from absolute ethanol); molecular weight: 365 (by mass spectroscopy); ir: 1715, 1630 (shoulder), 1555, 1500 cm^{-1}; uv max: 231 (ϵ 30,500), 325 nm (ϵ 16,900); nmr: 2.0 (s, 3, CH$_3$), 3.05 and 3.1 (two peaks, 12, N-CH$_3$), 3.7 (two peaks, 6, CO-O-CH$_3$), 6.75 (s, 1, vinyl H).

Anal. Calcd. for $C_{16}H_{23}N_5O_5$: C, 52.59; H, 6.35; N, 19.17 O, 21.90. Found: C, 52.37; H, 6.37; N, 18.95; O, 21.81.

Adduct V.

A practically quantitative yield was obtained, m.p. 134-135° (from absolute ehtanol); molecular weight: 405 (by mass spectroscopy); ir: 1720, 1630, 1565, 1500 cm^{-1}; uv max: 228 (ϵ 39,700), 281 nm (ϵ 3,850); nmr: 1.7 (m, 4, CH$_2$), 2.5 (m, 4, CH$_2$), 3.1 (s, 12, N-CH$_3$), 3.7 and 3.8 (two peaks, 6, CO-O-CH$_3$), 6.0 (s, 1, vinyl H).

Anal. Calcd. for $C_{19}H_{27}N_5O_5$: C, 56.28; H, 6.71; N, 17.27. Found: C, 56.51; H, 6.71; N, 17.18.

Adduct X.

A practically quantitative yield was obtained, m.p. 127-128° (from absolute ethanol); molecular weight: 397 (by mass spectroscopy); ir: 1720, 1650, 1560, 1505 cm^{-1}; nmr: 1.3 (m, 6, CH$_2$-CH$_3$), 2.3 (s, 3, CH$_3$), 3.1 (s, 12, N-CH$_3$), 4.2 (q, 4, CH_2-CH$_3$),

7.3 (s, 1, N-H), 15.0 (s, 1, enol).

Anal. Calcd. for $C_{16}H_{27}N_7O_5$: C, 48.36; H, 6.85; N, 24.67; O, 20.13. Found: C, 48.56; H, 7.04; N, 24.62; O, 20.09.

Adduct XI.

A 30% yield of this adduct was obtained, (2/3 of II being recovered), m.p. 181-183° (from absolute ethanol, and washing with acetone to remove remaining II); molecular weight: 321 (by mass spectroscopy); ir: 1715, 1610, 1560, 1520 cm^{-1}; nmr: 1.3 (t, 3, CH_2-CH_3), 2.4 (s, 3, CH_3), 3.15 (s, 12, N-CH_3), 4.2 (q, 2, CH_2-CH_3), 6.7 and 8.0 (2d, 2, J = 15 Hz, vinyl H).

Anal. Calcd. for $C_{15}H_{23}N_5O_3$: C, 56.06; H, 7.21; N, 21.79. Found: C, 55.70; H, 7.34; N, 21.80.

Adduct VII.

In this case, the reaction mixture was heated in toluene under reflux for 24 hours, practically quantitative yield, m.p. 110-112° (from diisopropyl ether-absolute ethanol 50:50); molecular weight: 339 (by mass spectroscopy); ir: 1720, 1620, 1560, 1530, 1505 cm^{-1}; nmr: 2.0 (s, 3, CH_3), 3.7 and 3.75 (two peaks, 6, CO-O-CH_3), 3.9 and 4.0 (two peaks, 6, O-CH_3), 7.0 (s, 1, vinyl H), 14.4 (s, 1, enol).

Anal. Calcd. for $C_{14}H_{17}N_3O_7$: C, 49.55; H, 5.05; N, 12.39; O, 33.01. Found: C, 49.30; H, 5.14; N, 12.26; O, 33.28.

Adduct XII.

The reaction mixture was heated for 6 hours at 200° in toluene in the autoclave, almost quantitative yield, m.p. 118-119° (from absolute ethanol); molecular weight: 276 (by mass spectroscopy); ir: 2245, 1710, 1565, 1505 cm^{-1}; nmr: 2.15 and 2.2 (two peaks, 3, CH_3, enol and keto forms), 2.6 (m, 4, CH_2), 3.1 (s, 12, N-CH_3), 3.65 (t, 0.7, J = 6 Hz, CH-CO), 16.5 (s, 0.3, enol).

Anal. Calcd. for $C_{13}H_{20}N_6O$: C, 56.50; H, 7.30; N, 30.41; O, 5.79. Found: C, 56.22; H, 7.12; N, 30.26; O, 5.86.

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