

ADM Chemicals Division, Ashland Oil and Refining Company

### A General Synthesis of *as*-Triazines and bis-*as*-Triazines

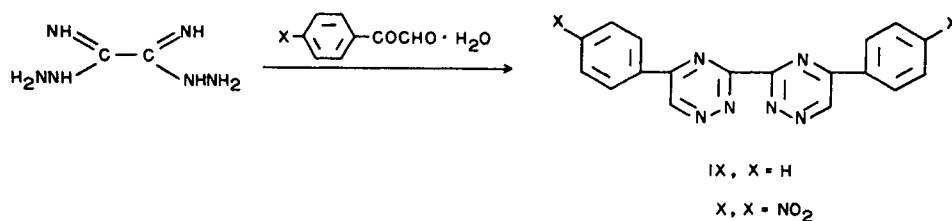
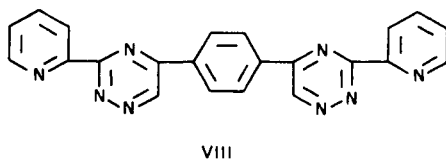
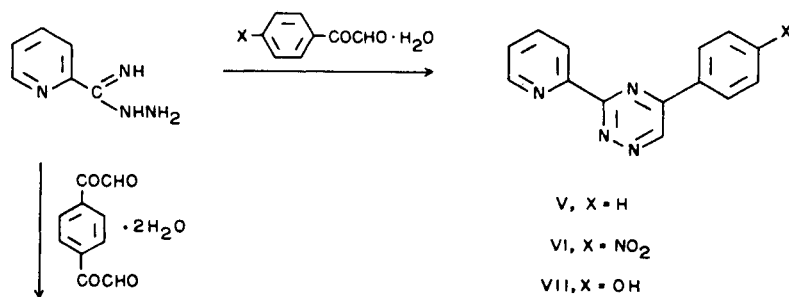
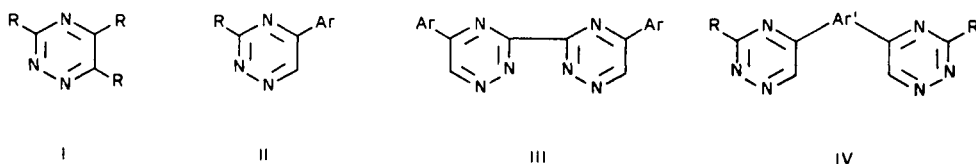
*B. M. Culbertson and G. R. Parr*

The most important syntheses of *as*-triazines have received some amount of systematic study; these include semicarbazide, thiosemicarbazide or aminoguanidine reactions with 1,2-dicarbonyl compounds or their monoximes, with  $\alpha$ -keto acids or their esters or amides, or with  $\alpha$ -hydroxy ketones (1). The parent compound, 1,2,4-triazine, has only recently been prepared for the first time (2).

Recent publications by Case (3,4) report amidrazones (hydrazidines) of the formula  $RC(=NH)NHNH_2$  undergo

cyclocondensation readily with diketones such as benzil and pyridil to form 3,5,6-trisubstituted 1,2,4-triazines (*as*-triazines) of formula I.

We have recently been concerned with the study of various heteroaromatic systems, and now wish to report that amidrazones of the aforesaid formula and bis-amidrazones of the formula  $R'[C(=NH)NHNH_2]_2$  will also undergo cyclocondensation readily with glyoxal ( $Ar-COCHO$ ) and bis-glyoxalyl [ $Ar'(COCHO)_2$ ] compounds to form



3,5-disubstituted *as*-triazines (II), 5,5'-disubstituted 3,3'-bis(*as*-triazines) (III), and 3,3'-disubstituted 5,5'-bis(*as*-triazines) (IV) in excellent yields.

According to available literature, there has been no general method developed for the preparation of the aforesaid classes (II, III and IV) of *as*-triazines. It appears that use of the disclosed reaction for synthesis of a specific compound of type II, III or IV is limited only by the availability of the necessary amidrazone and/or glyoxalyl starting materials.

The synthesis of 3-(2-pyridyl)-5-phenyl-*as*-triazine (V), 3-(2-pyridyl)-5-(*p*-nitrophenyl)-*as*-triazine (VI), 3-(2-pyridyl)-5-(*p*-hydroxyphenyl)-*as*-triazine (VII), 5,5'-(1,4-phenylene)-bis-[3-(2-pyridyl)-*as*-triazine] (VIII), 5,5'-diphenyl-3,3'-bis(*as*-triazine) (IX), and 5,5'-bis(*p*-nitrophenyl)-3,3'-bis(*as*-triazine) (X) demonstrates both the generality and utility of the reaction.

The nmr spectra of compounds V and VII exhibited respectively in each case one-proton multiplets at 9.7 ppm ( $\tau$  0.3) and 10.1 ppm ( $\tau$  -0.1) and these values are consistent with those expected for H<sub>6</sub> on these two 3,5-disubstituted 1,2,4-triazines (2,5). Suitable solutions of the other compounds could not be obtained for nmr analysis.

Compounds V-VIII, by virtue of "ferroin" (=N=C=C=N=) moieties, give very sensitive tests for Fe (II) (see Table I).

TABLE I

## 3,5-Disubstituted 1,2,4-Triazine Fe (II) Test (a)

Compound	Color
V	Very Deep Purple
VI	Purple
VII	Magenta
VIII	Deep Blue

(a) Ferrous chloride (0.1 g.) was dissolved in 1-l. of deionized water. The noted colors were obtained when one drop of a 0.1 *N* DMF solution of the respective compounds were added to 10 ml. of the Fe (II) solutions.

Further aspects of this reaction, *i.e.*, the cyclocondensation polymerization of bis-amidrazones and bis-glyoxalyl compounds to produce poly(*as*-triazines), will be reported elsewhere at a later date.

## EXPERIMENTAL (6)

## Preparation of Hydrazidines.

The compounds 2-pyridylhydrazidine and oxamide-dihydrazone were prepared by treatment of 2-cyanopyridine and dithiooxamide with hydrazine according to the procedure used by Case (3).

## Preparation of Glyoxalyl Compounds.

Phenylglyoxal (7), *p*-nitrophenylglyoxal (8), *p*-hydroxyphenylglyoxal (9), and 1,4-diglyoxalylbenzene (10) were prepared by oxidation of the appropriate ketones with selenium dioxide (11).

Synthesis of 3-(2-Pyridyl)-5-phenyl-*as*-triazine (V).

Phenylglyoxal hydrate, 1.52 g. (0.01 mole), and 2-pyridylhydrazidine, 1.36 g. (0.01 mole), were each dissolved in 25 ml. absolute ethanol. The two solutions were mixed, refluxed for 2 hours, treated with Norit-A (decolorizing charcoal) filtered, and diluted with water to effect crystallization of the product. The yellow precipitate was collected by suction filtration, washed on the filter several times with water, air dried overnight, and dried *in vacuo* (0.01 mm. of Hg.) for 4 hours at 100° to obtain a 1.8 g. (theory, 2.3 g.) yield of yellow crystalline V, m.p. 140-141°. The infrared spectrum of the material had a strong absorption band at 1545 cm<sup>-1</sup>, attributable to the *as*-triazine ring system (12). An analytical sample was recrystallized from very dilute ethanol and dried *in vacuo* (0.01 mm. of Hg.) overnight at 100°, m.p. 140.5-141.0°.

*Anal.* Calcd. for C<sub>14</sub>H<sub>10</sub>N<sub>4</sub>: C, 71.79; H, 4.27; N, 23.93. Found: C, 71.61; H, 4.37; N, 23.94.

Synthesis of 3-(2-Pyridyl)-5-(*p*-nitrophenyl)-*as*-triazine (VI).

According to the procedure used for the preparation of V, 2.4 g. (0.0177 mole) of 2-pyridylhydrazidine was treated with 3.45 g. (0.0177 mole) of *p*-nitrophenylglyoxal hydrate in 60 ml. of absolute ethanol. After 10 minutes reflux, a copious amount of bright yellow precipitate started to form. After refluxing for an additional 20 minutes and allowing the solution to cool, the precipitate was collected by suction filtration, washed on the filter with cold ethanol, and dried *in vacuo* (0.01 mm. of Hg.) for 4 hours at 100° to obtain a 4.4 g. (theory, 5.1 g.) yield of yellow crystalline VI, m.p. 246-248°. The product exhibited in its infrared spectrum strong absorption bands at 1538, 1355, 1550 cm<sup>-1</sup> (strong shoulder on 1538), attributable to the nitro and *as*-triazine moieties (12). Without further purification, the compound was submitted for elemental analysis.

*Anal.* Calcd. for C<sub>14</sub>H<sub>9</sub>N<sub>5</sub>O<sub>2</sub>: C, 60.21; H, 3.23; N, 25.09. Found: C, 60.31; H, 3.21; N, 25.14.

Synthesis of 3-(2-Pyridyl)-5-(*p*-hydroxyphenyl)-*as*-triazine (VII).

Analogous to the procedure used for the preparation of V, 2.72 g. (0.02 mole) of 2-pyridylhydrazidine was treated with 3.36 g. (0.02 mole) of *p*-hydroxyphenylglyoxal hydrate in 60 ml. of absolute ethanol. The solution, which had been refluxed for 1 hour and allowed to set overnight, was flash evaporated to obtain the desired crude product. The crude material was recrystallized from very dilute ethanol and dried *in vacuo* (0.01 mm. of Hg.) for 12 hours at 65° to obtain a 4.0 g. (theory, 5.0 g.) yield of yellow crystalline VII, m.p. 211-213°. The product exhibited in its infrared spectrum the expected strong absorption band at 1550 cm<sup>-1</sup>.

*Anal.* Calcd. for C<sub>14</sub>H<sub>10</sub>N<sub>4</sub>O: C, 67.20; H, 4.00; N, 22.40. Found: C, 66.98; H, 3.92; N, 22.17.

Synthesis of 5,5'-(1,4-phenylene)-bis-[3-(2-pyridyl)-*as*-triazine] (VIII).

Analogous to the procedure used for the preparation of VI, 2.26 g. (0.01 mole) of 1,4-diglyoxalylbenzene dihydrate and 2.72 g. (0.02 mole) of 2-pyridylhydrazidine were reacted in 100 ml. refluxing absolute ethanol. The solution, which produced a yellow precipitate after 10 minutes of reflux, was refluxed for 1 hour and allowed to cool to room temperature. The precipitate was collected by suction filtration, washed on the filter with absolute ethanol, and dried *in vacuo* (0.01 mm. of Hg.) for 4 hours at 100° to obtain a 3.3 g. (theory, 3.9 g.) yield of crude VIII, m.p. 321-323° (dec.). The product exhibited in its infrared spectrum the expected strong absorption band at 1550 cm<sup>-1</sup>. The analytical sample was prepared

by recrystallization from a 50% aqueous pyridine solution.

*Anal.* Calcd. for  $C_{22}H_{14}N_8$ : C, 67.69; H, 3.59; N, 28.71.  
Found: C, 67.74; H, 3.56; N, 28.63.

Synthesis of 5,5'-Diphenyl-3,3'-bis-*as*-triazine (IX).

According to the procedure used for the preparation of VIII, 1.7 g. (0.0145 mole) of oxamide dihydrazone was treated with 4.4 g. (0.029 mole) of phenylglyoxal hydrate in dilute ethanol (70%) to obtain a 4.0 g. (theory, 4.5 g.) yield of crude light brown colored IX, m.p. 242-247°. For infrared and elemental analysis, the product was recrystallized from *N,N*-dimethylacetamide to obtain, after drying *in vacuo* (0.01 mm. of Hg.) for 4 hours at 100°, yellow crystalline IX, m.p. 244-246°. The product exhibited in the infrared spectrum the expected strong absorption band at  $1550\text{ cm}^{-1}$ .

*Anal.* Calcd. for  $C_{18}H_{12}N_6$ : C, 69.22; H, 3.87; N, 26.91.  
Found: C, 69.18; H, 3.86; N, 26.85.

Synthesis of 5,5'-bis(*p*-Nitrophenyl)-3,3'-bis-*as*-triazine (X).

Oxamide dihydrazone, 2.32 g. (0.02 mole) and *p*-nitrophenylglyoxal hydrate, 7.88 g. (0.04 mole) were each dissolved in 50 ml. of warm dimethylformamide. The two solutions were combined and brought to reflux, whereupon, a large amount of precipitate started to form. After refluxing for 5 minutes and allowing the solution to cool to room temperature, the product was collected by suction filtration, washed on the filter several times with absolute ethanol, and dried *in vacuo* (0.01 mm. of Hg.) for 4 hours at 100° to obtain at 7.0 g. (theory, 8.04 g.) yield of crude X. For analysis, crude X was recrystallized from pyridine and dried *in vacuo*, m.p. 342-344° (dec.). Compound X also exhibited in its infrared spectrum strong absorption bands at 1550, 1538 and  $1355\text{ cm}^{-1}$ .

*Anal.* Calcd. for  $C_{18}H_{10}N_8O_4$ : C, 53.73; H, 2.49; N, 27.86.  
Found: C, 53.64; H, 2.47; N, 27.81.

## REFERENCES

- (1) J. G. Erickson, P. F. Wiley and V. P. Wytroch, "The Chemistry of Heterocyclic Compounds," Vol. 10, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1956, p. 44.
- (2) W. W. Paudler and J. M. Barton, *J. Org. Chem.*, **31**, 1720 (1966).
- (3) F. H. Case, *ibid.*, **30**, 931 (1965).
- (4) F. H. Case, *ibid.*, **31**, 2398 (1966).
- (5) J. H. Reynolds (Ph.D. Thesis, University of Washington, Seattle, Washington, 1964) discusses nmr considerations in great detail for other azines.
- (6) Melting points were determined with a calibrated Thomas-Hoover Unimelt and are uncorrected. The infrared spectra (Nujol mulls) were obtained with Perkin-Elmer Infracord Spectrophotometer. Micro-analysis were carried out in this laboratory by M. C. Glowacki. The nmr spectra were determined on a Varian A-60 spectrometer using deuteriochloroform as solvent with tetramethylsilane as the internal standard.
- (7) H. A. Riley and A. R. Gray, "Organic Syntheses," Col. Vol. II, John Wiley and Sons, New York, N. Y., 1961, p. 509.
- (8) L. Steinback and E. I. Becker, *J. Am. Chem. Soc.*, **76**, 5809 (1954).
- (9) G. Fodor and O. Kovacs, *ibid.*, **71**, 1046 (1949).
- (10) J. K. Stille and J. R. Williamson, *J. Polymer Sci.*, **A2**, 3867 (1964).
- (11) G. R. Waitkins and C. W. Clark, *Chem. Rev.*, **36**, 235 (1945).
- (12) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 270.

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Minneapolis, Minnesota 55420