# THE HETERODIENE SYNTHESIS

## II. Condensation of Benzamidine with Aromatic Aldehydes. Addition of Acetylene-Dicarboxylic Ester to sym-Dihydrotriazines*

V. M. Cherkasov, N. A. Kapran, and V. N. Zavatskii

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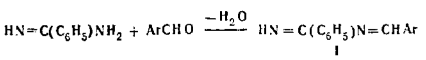
The reaction of benzamidine with aromatic aldehydes gives 2-aryl-4,6-diphenyl-1,2-dihydro-sym-triazines. These compounds react as heterodienes with acetylenedicarboxylic ester. In this process, the triazine ring is cleaved with the splitting out of the imine of an aromatic aldehyde, and the ester of 2,4-diphenyl-5,6-pyrimidinedicarboxylic is formed.

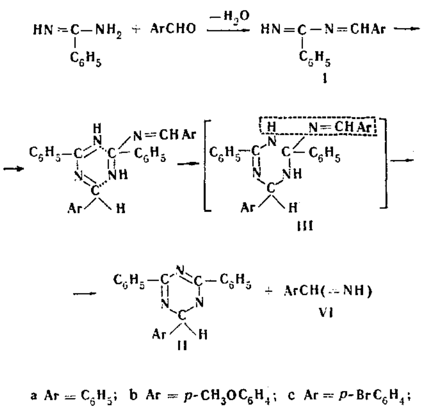
The products of the condensation of benzamidine with aromatic aldehydes were first described by Pinner [1, 2] and Kunckell [3] as benzylidenebenzamidines (I).



$$HN{=}C(C_6H_5)NH_2 + ArCHO \xrightarrow{-H_2O} \underset{I}{HN{=}C(C_6H_5)N{=}CHAr}$$

a $Ar = C_6H_5$; b $Ar = o\text{-}HOC_6H_4$

It has been found that these compounds, and also the products of the condensation of benzamidine with other aldehydes obtained by us under the same conditions have the structure of 2-aryl-4,6-diphenyl-1,2-dihydro-sym-triazines (II) (Table 1). The reaction probably takes place according to the following scheme:



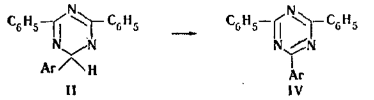
a $Ar = C_6H_5$; b $Ar = p\text{-}CH_3OC_6H_4$; c $Ar = p\text{-}BrC_6H_4$;

d $Ar = p\text{-}(CH_3)_2NC_6H_4$; e $Ar = o\text{-}CH_3OC_6H_4$;

f $Ar = o\text{-}HOC_6H_4$

The compound I formed in the first stage of the reaction reacts by a 1,4-bipolar cycloaddition mechanism as a heterodiene with a second molecule, which is a dienophile, and accordingly adds in the 2,1 position. The intermediate products III were not isolated. It is possible that the splitting out of the aromatic aldehyde (VI) takes place in the formation of the reaction complex in the 1,4-cycloaddition reaction. If compounds III are actually formed, they must be unstable since at $C_6$ they are amides of orthoacids and, moreover, it can be seen from the construction of Stuart-Briegleb atomic models that the aldehyde imine group at $C_6$ is subject to steric hindrance.

Structure II is confirmed by the case of oxidation of the compounds in the cold with tetrachlorobenzoquinone and by their dehydrogenation in acetonic solution (at −10° C) with tetracyanoethylene to the corresponding sym-triazines (IV) (Table 2).



a $Ar = C_6H_5$; b $Ar = p\text{-}CH_3OC_6H_4$; c $Ar = p\text{-}BrC_6H_4$;
d $Ar = p\text{-}(CH_3)_2NC_6H_4$; e $Ar = o\text{-}CH_3OC_6H_4$;
f $Ar = o\text{-}HOC_6H_4$

The structure of compounds (IV) was shown with IVc as an example; on reduction with Raney nickel it is converted into the known triphenyl-sym-triazine (IVa) (Kiafenin). The structure of compound II is also confirmed by the results of analyses of silver salts (Table 1). The silver content is somewhat low because the silver salts could not be purified by recrystallization, with the exception of the salt of IIb.

In the NMR spectrum of IIa there is a single signal with δ 6.15 relating to the C—H protons and a multiplet with δ 7.4 and 8.12 of the protons of the phenyl group. The ratio of the intensities of the C—H protons and the protons of the phenyl groups (1:15) corresponds to the cyclic structure II, since in the case of the linear structure I the ratio should be 1:10. The chemical shift of the C—H protons (δ 6.15), which is unusual for aliphatic protons, is due to the anisotropic influence of the phenyl radical and the electron-accepting action of the two nitrogen atoms. The same chemical shift of the C—H protons (δ 6.06) is found in (IIc).

The erroneous ideas of Pinner and Kunckell on the structure of IIa and IIf, which they took as Ia and Ib, can be explained by the fact that the elementary compositions of IIa and Ia are precisely the same, and IIf and Ib differ in their carbon contents by only 2%. The contents of chlorine and silver in the hydrochlorides and silver salts of compounds with a linear structure, I, differ considerably from the corresponding figures for the cyclic structures II. However, Kunckell [3] gave analytical results for chlorine and silver which were satisfactory for compounds I.

In a preceding paper [4] we described the reaction of "benzylidenebenzamidine" with acetylenedicarboxylic ester (ADCE) as a 1,4-cycloaddition with the formation of the ester of 2,4-diphenylpyrimidine-5,6-dicarboxylic acid (V). In view of the establishment of

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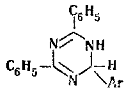
*For part I, see [4].

Table 1

2-Aryl-4, 6-diphenyl-1, 2-dihydro-sym-triazines 

| Compound | Ar | Mp, °C | Empirical formula | Found, % |  |  | Calculated, % |  |  | Yield, % | Silver salts |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | C | H | N | C | H | N |  | Empirical formula | found, % | calculated, % |
| IIa* | $C_6H_5$ | 174—175 | $C_{21}H_{17}N_3$ | 80.17 | 5.41 | 13.95 | 80.98 | 5.50 | 13.49 | 70 | $C_{21}H_{16}N_3Ag$ | 23.12 | 25.79 |
| IIb | $p$-$CH_3OC_6H_4$ | 154—156 | $C_{22}H_{19}N_3O$ | 77.81 | 5.70 | 12.40 | 77.40 | 5.60 | 12.31 | 85 | $C_{22}H_{18}N_3OAg$ | 24.69 | 24.06 |
| IIc** | $p$-Br-$C_6H_4$ | 157—160 | $C_{21}H_{16}N_3Br$ | 64.43 | 4.13 | 10.57 | 64.62 | 4.13 | 10.76 | 90 | $C_{21}H_{15}N_3BrAg$ | 19.65 | 21.70 |
| IId | $p$-$(CH_3)_2NC_6H_4$ | 170—172 | $C_{23}H_{22}N_4$ | 77.75 | 6.19 | 15.65 | 77.94 | 6.25 | 15.80 | 72 | $C_{23}H_{21}N_4Ag$ | 22.50 | 23.38 |
| IIe | $o$-$CH_3OC_6H_4$ | 138—140 | $C_{22}H_{19}N_3O$ | 77.53 | 5.61 | 12.03 | 77.40 | 5.60 | 12.31 | 70 | $C_{22}H_{18}N_3OAg$ | 22.37 | 24.06 |
| IIf | $o$-$HOC_6H_4$ | 181—183 | $C_{21}H_{17}N_3O$ | 76.10 | 5.24 | 12.48 | 77.02 | 5.25 | 12.83 | 75 | $C_{21}H_{16}N_3OAg$ | 22.11 | 24.83 |

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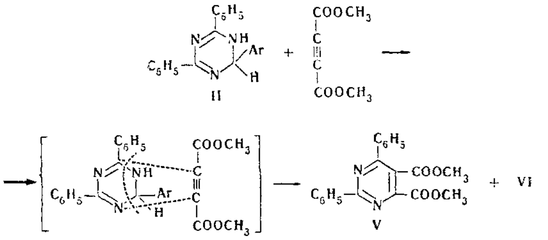
*Described in the literature [5]. **Found, %: Br 20.52. Calculated, %: Br 20.37.

the cyclic structure of the products of the condensation of benzamidine with aromatic aldehydes, it was shown that the heterodiene adding the ADCE is not Ia but **IIa.** It was to be expected that IIb–f should also react with ADCE in the manner of a 1,4-cycloaddition with the formation of V:



a Ar = $C_6H_5$; b Ar = $p$-$CH_3OC_6H_4$; c Ar = $p$-$BrC_6H_4$;

d Ar = $p$-$(CH_3)_2NC_6H_4$; e Ar = $o$-$CH_3OC_6H_4$; f Ar = $o$-$HOC_6H_4$

The reaction takes place on boiling in benzene with yields of compounds V of 60–80%. The splitting out of VI was shown in the cases of the reactions IIa, d, and f.

Instead of compounds VI, which, in the form of the bases, are hydrolyzed immediately, the corresponding aldehydes (benzaldehyde, p-dimethylaminobenzaldehyde, salicylaldehyde) were isolated and identified. D Dienophiles with double bonds—maleic anhydride, fumaric and maleic esters, styrene, acrylonitrile, etc.—do not add to II. As shown above, such strong dienophiles as tetracyanoethylene, and also N-sulfinylbenzenesulfonamide, dehydrogenate compounds II almost quantitatively to the corresponding triazines. In view of the mechanism proposed above for the formation of compounds II in the condensation of benzamidine with aromatic aldehydes, it may be assumed that the corresponding fragments of the dihydro-sym-triazines in positions 3 and 6 react like benzylidenebenzamidine, and 1,4-cycloaddition of acetylenedicarboxylic ester takes place.

The authors express their thanks to E. I. Fedin for recording and interpreting the NMR spectra.

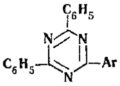
## EXPERIMENTAL

**2-Aryl-4, 6-diphenyl-1, 2-dihydro-sym-triazines (IIa–f).** A solution of 0.05 mole of benzamidine and 0.025 mole of an aromatic aldehyde in 20 ml of chloroform was boiled for 4–5 hr. The solvent was distilled off in vacuum. The residue was triturated with ether and filtered off. Yield 70–90%. The substances were purified by crystallization from ethanol or benzene. Compounds IIa–f are colorless well-crystallized substances which are soluble in acetone and chloroform.

**The silver salts of IIa–f.** An alcoholic solution of 0.002 mole of a compound II was treated with 0.0025 mole of a saturated solution of silver nitrate. The white precipitate that deposited was filtered off and washed with water and ethanol. On being boiled in water, the salts darkened and decomposed. The salt of IIb was recrystallized from ethanol. The other salts were insoluble in ethanol.

**Hydrochloride of IIa.** A current of dry hydrogen chloride was passed into a solution of 0.002 mole of IIa in 300 ml of absolute ether. A fine colorless precipitate of the hydrochloride deposited; yield 90%. Mp 274–275° C (from absolute ethanol). According to Kunckell [3], mp 274° C. Found, %: Cl 10.19. Calculated for $C_{21}H_{17}N_3 \cdot HCl$, %: Cl 10.19.

Table 2

2-Aryl-4, 6-diphenyl-sym-triazines 

| Compound | Ar | Mp, °C | Empirical formula | Found, % |  |  | Calculated, % |  |  | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | C | H | N | C | H | N |  |
| IVb | $n$-$CH_3OC_6H_4$ | 158—160 | $C_{22}H_{17}N_3O$ | 77.40 | 5.24 | 12.17 | 77.88 | 5.04 | 12.38 | 76.5 |
| IVc* | $n$-$BrC_6H_4$ | 198—200 | $C_{21}H_{14}N_3Br$ | 65.01 | 3.73 | 10.87 | 64.65 | 3.63 | 10.82 | 88.5 |
| IVd | $n$-$(CH_3)_2NC_6H_4$ | 217—219 | $C_{23}H_{20}N_4$ | 78.76 | 5.77 | 15.85 | 78.38 | 5.71 | 15.89 | 91 |
| IVe | $o$-$CH_3OC_6H_4$ | 91—93 | $C_{22}H_{17}N_3O$ | 77.55 | 4.99 | 11.96 | 77.88 | 5.04 | 12.38 | 70 |
| IVf | $o$-$HOC_6H_4$ | 246—248 | $C_{21}H_{15}N_3O$ | 76.94 | 4.66 | 12.68 | 77.52 | 4.64 | 12.91 | 69 |

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*Found, %: Br 21.08. Calculated, %: Br 20.57.

**The hydrochloride of IIf** was obtained in the same way as the preceding compound from anhydrousbenzene solution. The hydrochloride was purified by precipitation with absolute ether from a solution in absolute ethanol. Yield 80%; mp 198–200° C. According to Kunckell [3], mp 155° C. Found, %: Cl 9.65. Calculated for $C_{21}H_{17}N_3O \cdot HCl$, %: Cl 9.74.

**2-Aryl-4, 6-diphenyl-sym-triazines (IVa–f).** A solution of 0.001 mole of II and 0.001 mole of tetrachlorobenzoquinone in 15 ml of acetone was stirred in the cold. After some minutes, a precipitate of IV began to deposit, and 2–3 hours later the crystals were filtered off and washed with a small amount of acetone. Yields 70–90%. The reaction with tetracyanoethylene took place similarly. The compounds IV were purified by recrystallization from acetone or ethanol. Compound IVa gave no depression of the melting point in admixture with 2, 4, 6-triphenyl-sym-triazine (Kiafenin).

**Reduction of 2-(p-bromophenyl)-4, 6-diphenyl-sym-triazine (IVc).** A suspension of 0.5 g (0.001 mole) of IVc in 20 ml of methanol was treated with 5 ml of 0.1N caustic soda solution in methanol and 2.5 g of Raney nickel and boiled for 6 hr. After cooling, the precipitate and the catalyst were filtered off, treated with 60 ml of benzene, and filtered off again. The benzene was evaporated to small bulk and cooled, and the crystals were filtered off. Yield 0.32 g (80%), mp 229–230° C. The substance was shown by a mixed-melting point test to be identical with IVa.

**Dimethyl 2, 4-diphenylpyrimidine-5, 6-dicarboxylate (V).** A hot solution of 0.003 mole of II in 20 ml of absolute ether was treated with 0.003 mole of the dimethyl ester of ADC. There was an immediate change in the color of the solution, which was then boiled for 3–4 hr, after which the benzene was distilled off in vacuum. On trituration with a small amount of ethanol, the resinous residue crystallized. The crystals were filtered off and washed with ethanol. The yield of V was 60–80%. Mp 126–127° C (from ethanol). The substance gave no depression of the melting point in admixture with V [4].

**Isolation and identification of the aldehydes.** In the reaction of IIa, IIf, and IId with the dimethyl ester of ADC, after the separation of the V the aldehydes were distilled off with steam and extracted from the distillate with ether. The benzaldehyde and salicylaldehyde were identified in the form of the semicarbazones (yields, melting points): benzaldehyde semicarbazone–58%, 221–222° C; salicylaldehyde semicarbazone–50%, 230–231° C; p-dimethylaminobenzaldehyde–53%, 70–72° C.

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Institute of Organic Chemistry
AS UkrSSR, Kiev