Polyazabicyclic Compounds. Part I. Preliminary Experiments on the Bischler and the Bamberger Synthesis of Benzo-1 : 2 : 4-triazines.

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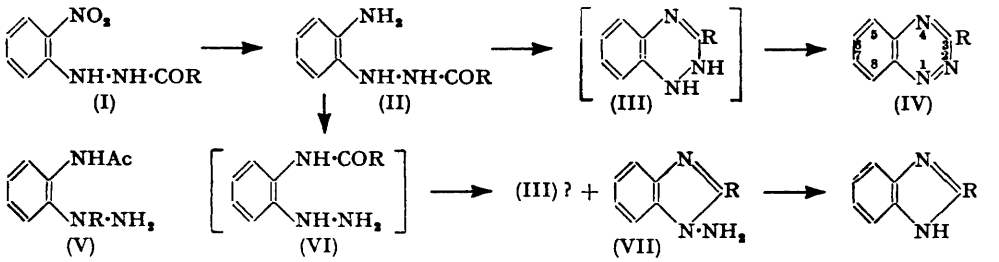
(A) *N*-Acyl-*N'*-*o*-nitrophenylhydrazines have been catalytically reduced to stable *N*-acyl-*N'*-*o*-aminophenylhydrazines. Under acid conditions these amines may cyclise to dihydrobenzo-1 : 2 : 4-triazines (not isolated, but oxidised to benzo-1 : 2 : 4-triazines), or undergo acyl-group migration and subsequent cyclisation to *N*-aminobenziminazoles. The latter form benzylidene derivatives, and are oxidised by ferricyanide to benziminazoles.

(B) The cyclisation of 1 : 5-diphenyl-, 3-methyl-1 : 5-diphenyl-, and 1 : 3 : 5-triphenyl-formazan by sulphuric and acetic acid gave high yields of benzo-1 : 2 : 4-triazine, and its 3-methyl and 3-phenyl analogue, respectively. Except with the 3-phenylformazan, a methoxyl group in the potential triazine 6-position inhibits cyclisation, whilst a potential 8-methoxyl group lowers the yields. Phenazines may arise as by-products from the cyclisation of formazans with or without 3-substituents.

(A) The first synthesis of benzo-1 : 2 : 4-triazine (IV; R = H) and its 3-methyl homologue (IV; R = Me) was described by Bischler (*Ber.*, 1889, **22**, 2801), who reduced the nitrocompounds (I; R = H and Me) with sodium amalgam and alcoholic acetic acid and, without isolating either of the intermediates (II and III), oxidised the product with alkaline ferricyanide. No yields of triazines were reported, and from the reaction with the parent (I; R = H) *o*-phenylenediamine and 2-methylbenziminazole (presumably an artefact) were also obtained. The reaction with the methyl analogue (I; R = Me) also furnished a compound, m. p. 162°, regarded as the amine (II; R = Me). By similar means Bischler and Brodsky (*Ber.*, 1889, **22**, 2809) obtained 6-bromo- and 6-bromo-3-methyl-benzo-1 : 2 : 4-triazine in poor yields. In closely related experiments Hempel (*J. prakt. Chem.*, 1890, **41**,

161) claimed to have isolated benzo-1 : 2 : 4-triazine from the action of cold phosphoric anhydride upon the hydrazine (V; R = Me or Et).



A few attempts which we made to prepare benzo-1 : 2 : 4-triazine by Bischler's method were discouraging, reduction of the nitro-compound being far from complete (reduction must also have been incomplete in Bischler's own experiments, since the reduction product gave in alkali a dark blue-violet colour which disappeared suddenly during subsequent oxidation, and the acylnitrophenylhydrazines all give deeply coloured solutions in alkali, as Bischler himself reported). Accordingly, the catalytic reduction of *N*-formyl-, *N*-acetyl-, and *N*-benzoyl-*N'*-*o*-nitrophenylhydrazine was examined. In warm ethanol, in the presence of palladium–charcoal, reduction was rapid and quantitative. The colourless reduced solutions became yellow in air, and fresh alcohol produced pink or red colorations, but careful concentration retrieved high yields of the amines (II; R = H, Me, or Ph) as colourless crystalline solids. (It is assumed that under the conditions of preparation acyl-group migration would not occur, but at present formal proof of the presence of an amine group is lacking. On treatment with nitrous acid the compounds gave solutions which with alkaline β-naphthol merely formed yellow precipitates.) Unlike the nitro-compounds these amines were, as expected, insoluble in alkali, and it is interesting that *N*-acetyl-*N'*-*o*-aminophenylhydrazine had substantially the same m. p. (164—166°) as the by-product assigned this structure by Bischler (*loc. cit.*).

The amines were quite stable under ordinary conditions and specimens have been kept unchanged for several months. On one occasion only was different behaviour observed; a specimen of *N*-formyl-*N'*-*o*-aminophenylhydrazine, several months old, had changed to a tar from which light petroleum extracted *ca.* 45% of benzo-1 : 2 : 4-triazine. This behaviour has not been observed again despite attempts to stimulate it, and consequently the amines were submitted to various conditions which might be expected to effect cyclisation.

For the formally analogous conversion of acyl derivatives of *o*-phenylenediamine into benziminazoles, 4N-hydrochloric acid is a convenient reagent (Phillips, *J.*, 1928, 172). The colourless solutions of *N*-*o*-aminophenyl-*N'*-formylhydrazine in this acid quickly became deep red when heated. Basification destroyed the colour, and oxidation of the resulting mixture with potassium ferricyanide produced benzo-1 : 2 : 4-triazine. The low yield (10—20%) appeared to decrease slightly if heating of the amine with acid was prolonged, and the triazine appeared to be accompanied by a colourless by-product. Most of the starting material remained unaccounted for. *N*-Acetyl-*N'*-*o*-aminophenylhydrazine behaved similarly, but in this instance oxidation produced good yields of 3-methylbenzo-1 : 2 : 4-triazine, which again fell when the initial step was prolonged. From this reaction 2-methylbenziminazole was also isolated. *N*-*o*-Aminophenyl-*N'*-benzoylhydrazine, treated for a short time with hot hydrochloric acid, behaved similarly to its analogues, and subsequent oxidation led to the formation of 3-phenylbenzo-1 : 2 : 4-triazine (22%); however, on prolonged warming of the amine with acid there separated from the initially deep-red solution a dark oil. This was probably the dihydrobenzotriazine, for it slowly deposited the yellow triazine which was then isolated in improved yield (37%). From both experiments with the benzoyl compound small amounts of a colourless by-product, m. p. 204—205°, were isolated, identical with that discussed below.

When cyclisation and oxidation were attempted with nitrobenzene in benzene saturated with hydrogen chloride, *N*-*o*-aminophenyl-*N'*-formylhydrazine gave a low yield of benzo-1 : 2 : 4-triazine, but the same amine boiled with an aqueous solution of *m*-nitrobenzenesulphonic acid (a reagent combining cyclising and oxidising ability) gave, besides a little benzotriazine, a moderately good yield of a colourless product $C_7H_7N_3$, m. p. 156—156·5°. This stable, water-soluble base was clearly not the dihydrobenzotriazine, compounds of the latter type being immediately oxidised to the benzotriazine (Arndt, *Ber.*, 1913, **46**, 3522). The base gave a benzylidene derivative and its ultraviolet absorption was very similar to that of *N*-methylbenziminazole, but with loss of fine structure [see Fig. 1; in the curve for *N*-methylbenziminazole we have not reproduced the fine structure characteristic of this compound (Beaven, Holiday, and Johnson, *Spectrochim. Acta*, 1951, **4**, 338)], facts which prove the compound to be *N*-aminobenziminazole (VII; R = H). This constitution is consistent with the conversion of the compound into benziminazole by alkaline ferricyanide, a reaction analogous to the oxidation of *N*-methyl-*N*-phenylhydrazine to methylaniline by Fehling's solution (Fischer, *Annalen*, 1878, **190**, 167). (The reaction also accounts for the

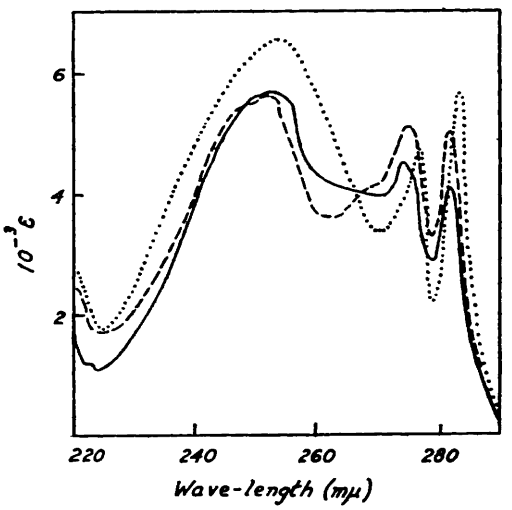


FIG. 1. *Absorption spectra of* (——) 1-*amino-benziminazole* (*in* EtOH), (– – –) 1-*Amino-2-methylbenziminazole* (*in* EtOH), *and* (. . .) N-*methylbenziminazole* (*in hexane*) (Beavan *et al.*, *loc. cit.*).

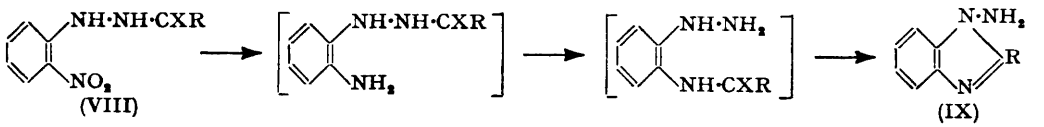
isolation of 2-methylbenziminazole in the experiments discussed above.) That an oxidising agent other than atmospheric oxygen is unnecessary for the formation for benzo-1 : 2 : 4-triazine was shown by the formation of a moderate yield of this compound, together with *N*-aminobenziminazole, when the hydrazide (II; R = H) was heated in benzene solution with a cation-exchange resin.

The acetyl and the benzoyl derivative (II; R = Me and Ph) likewise, with aqueous *m*-nitrobenzenesulphonic acid, gave 1-amino-2-methyl- (VII; R = Me) and 1-amino-2-phenyl-benziminazole (VII; R = Ph) (identical with the compound mentioned above), as well as low yields of the benzotriazines. 1-Amino-2-methylbenziminazole was characterised by its ultra-violet absorption spectrum (Fig. 1), by conversion into a benzylidene derivative, and by oxidation to 2-methylbenziminazole.

The formation of *N*-aminobenziminazoles must involve acyl-group migration from the hydrazine to the amine nitrogen atom (II ⟶ VI), followed by preferential formation of the five-membered ring (VI ⟶ VII). Whether the small concomitant yields of benzo-1 : 2 : 4-triazines arise from the acylamino-compound (VI ⟶ III), or from the acyl-hydrazine (II ⟶ III) is not established. The preferential formation of a five-membered ring recalls the formation of *N*-amino-oxindole from *o*-hydrazinophenylacetic acid (Neber, *Ber.*, 1922, **55**, 826). Acyl-group migrations are not uncommon (see Theilacker, " Isomerisation," in Schwab's " Handbuch der Katalyse," 1943, Vol. VII, 302, Springer, Vienna), but migration from a hydrazino- to an amino-group seems not to have been recognised

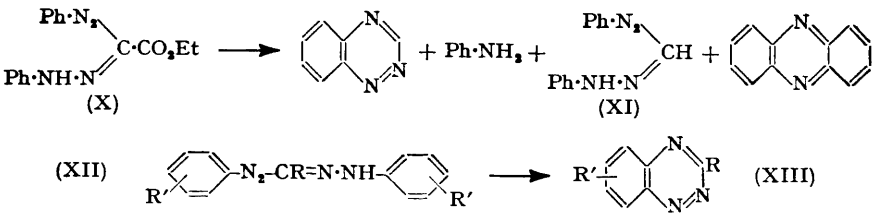
before. Guha and Ghosh (*J. Indian Chem. Soc.*, 1928, **5**, 439) claimed to have obtained stable 3-aminodihydrobenzo-1 : 2 : 4-triazine by reducing *o*-nitrophenylsemicarbazide or *o*-nitrophenylthiosemicarbazide (VIII; R = NH_2, X = O or S) with tin and boiling hydrochloric acid, and similarly to have isolated dihydro-3-methylthiobenzo-1 : 2 : 4-triazine from the thiosemicarbazide (VIII; R = SMe, X = S). Guha and Arndt (*ibid.*, 1931, **8**, 199) subsequently showed that careful reduction of this compound (VIII; R = NH_2, X = S) with stannous chloride gave, instead, 3-aminobenzo-1 : 2 : 4-triazine. It is very probable, therefore, that in the first instance acyl-group migration occurred and that the stable products were the *N*-aminobenziminazoles (IX; R = NH_2 and SMe). Similar remarks are probably applicable to certain other compounds (Guha and Ray, *ibid.*, 1925, **2**, 83).

Finally, the Bischler reaction has been applied to the readily available formyl and acetyl derivatives of 2 : 4-dinitrophenylhydrazine. Reduction of both nitro-groups in the



formyl compound was readily effected with hydrogen and palladium–charcoal, but the colourless reduced solution rapidly became deep orange-red in the atmosphere, and on concentration gave 6-aminobenzo-1 : 2 : 4-triazine in low yield. The acetyl derivative similarly gave 6-amino-3-methylbenzo-1 : 2 : 4-triazine. Various attempts were made to improve the yields of these products: hydrogenation in alcohol containing hydrochloric acid caused no improvement, and in acetic acid saturated with hydrogen chloride was very slow owing to the formation of an insoluble hydrochloride; a cation-exchange resin also failed to improve the process.

(B) An alternative synthesis of benzo-1 : 2 : 4-triazine was reported by Bamberger and Wheelwright (*Ber.*, 1892, **25**, 3201), who obtained it together with aniline, 1 : 5-diphenylformazan (XI), and phenazine by the action of hot concentrated mineral acids on 3-ethoxycarbonyl-1 : 5-diphenylformazan (X), the triazine probably arising from the 1 : 5-diphenylformazan formed by hydrolysis and decarboxylation.



Similarly the formazans (XII; R = Ac and Bz; R′ = H) gave good yields of the corresponding benzotriazines (XIII; R = Ac and Bz; R′ = H), but unaccompanied by phenazines (Bamberger and Lorenzen, *Ber.*, 1892, **25**, 3539; Bamberger and Witter, *Ber.*, 1893, **26**, 2788). The course of the reaction is influenced by the nature of R. Thus benzotriazine formation occurred with the compounds (XII; R = Ph, *o*-C_6H_4·OH, or 3 : 4-CH_2O_2:C_6H_4; R′ = H) (von Pechmann, *Ber.*, 1894, **27**, 1679; Fichter and Fröhlich, *Brit. Abs.*, 1903, **84**, 722), but different products arose from the analogues (XII; R = NO_2, NH_2, or Cl; R′ = H) (Bamberger, Padova, and Ormerod, *Annalen*, 1925, **446**, 260; Fusco and Romani, *Gazzetta*, 1946, **76**, 419). The unsymmetrical 3 : 5-diphenyl-1-*p*-tolyl- (von Pechmann, *loc. cit.*), 3 : 5-diphenyl-1-*p*-sulphonophenyl- (Fichter and Schiess, *Ber.*, 1900, **33**, 747), and 1-α-naphthyl-3 : 5-diphenyl-formazan (*idem*, *loc. cit.*) were cyclised to 6-methyl-3-phenyl- and 3-phenyl-benzo-1 : 2 : 4-triazine and 3-phenylnaphtho(2′ : 1′-5 : 6)-1 : 2 : 4-triazine respectively. Further examples were reported by Massini (*Ann. Chim. farm.*, 1940, 24) and Parkes and Aldis (*J.*, 1938, 1841).

We have examined selected examples of this cyclisation with the aim of establishing its efficiency, and of further defining the effect of substituents in the formazan upon the reaction. The results of heating the nine symmetrical formazans (XII; R = H, Me, or Ph; R′ = H, *o*-OMe, or *p*-OMe) with concentrated sulphuric and glacial acetic acid are summarised below.

Formazan (XII)	Product.
R = R′ = H	Benzo-1 : 2 : 4-triazine (61%), phenazine (3·5%)
R = Me, R′ = H	3-Methylbenzo-1 : 2 : 4-triazine (70%)
R = Ph, R′ = H	3-Phenylbenzo-1 : 2 : 4-triazine (87%) [1]
R = H, R′ = *o*-OMe	8-Methoxybenzo-1 : 2 : 4-triazine (38·5%), 1 : 6-dimethoxyphenazine (3·8%)
R = Me, R′ = *o*-OMe	8-Methoxy-3-methylbenzo-1 : 2 : 4-triazine (39·3%), 1 : 6-dimethoxyphenazine (8·3%)
R = Ph, R′ = *o*-OMe [2]	8-Methoxy-3-phenylbenzo-1 : 2 : 4-triazine (43%)
R = H, R′ = *p*-OMe...	Possibly a trace of 2 : 7-dimethoxyphenazine
R = Me, R′ = *p*-OMe [2]	No product isolated
R = Ph, R′ = *p*-OMe	6-Methoxy-3-phenylbenzo-1 : 2 : 4-triazine (30%)

[1] von Pechmann (*loc. cit.*) did not report his yield. [2] These formazans could not be purified and were used in the crude state.

It is clear that a *C*-phenyl group in the formazan facilitates benzotriazine formation, and also improves the yield. Thus, more drastic conditions (see Experimental) were

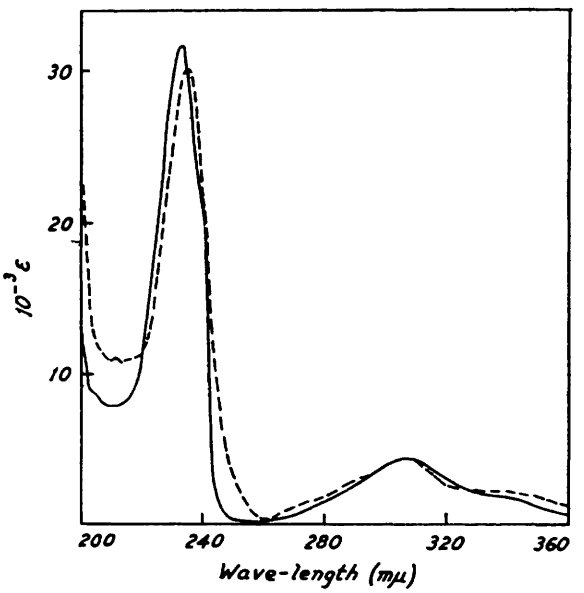


FIG. 2. *Absorption spectra of* (——) *benzo*-1 : 2 : 4-*triazine* (*in* H_2O) *and* (– – –) 3-*methyl*-1 : 2 : 4-*triazine* (*in* H_2O).

necessary with 3-unsubstituted formazans than with 3-methyl- or 3-phenyl-formazans. Phenazine formation can occur with both 3-unsubstituted and 3-substituted formazans, and the production of 1 : 6-dimethoxyphenazine from 1 : 5-di-*o*-methoxyphenyl-3-methylformazan indicates that only the 1 : 5-substituents in the formazans are involved in phenazine formation. Whilst the effects of substituents accord with the obvious nature of the process of triazine formation as an electrophilic substitution into the benzene ring, the nature of the reaction leading to phenazines is not clear [the scheme outlined by Bamberger and Wheelwright (*loc. cit.*) cannot be seriously considered]. A methoxyl group situated *meta* to the point of cyclisation is detrimental to the reaction, lowering the yield or completely preventing triazine formation. Such an effect is frequently observed in electrophilic cyclisations such as the Combes quinoline synthesis (Roberts and Turner, *J.*, 1927, 1832), the Sandmeyer isatin synthesis (Halberkann, *Ber.*, 1921, **54**, 3079; Theobald, Thesis, London, 1949), and various reactions in the carbocylic series (Hey and Kohn, *J.*, 1949, 3177; Hey and Nagdy, *J.*, 1953, 1894).

Our evaluation of the two methods shows that in general the Bamberger synthesis is superior for the production of benzo-1 : 2 : 4-triazines to the Bischler synthesis, except when the inhibiting effect of a potential 6-methoxyl group is not counterbalanced by a suitable 3-substituent. This conclusion is strengthened by the difficult accessibility of hydrazines suitable for the Bischler reaction.

Attempts to demethylate 8-methoxy-, 8-methoxy-3-methyl-, and 8-methoxy-3-phenyl-benzo-1 : 2 : 4-triazine with aluminium chloride in benzene gave phenolic products which appeared from analysis to contain either benzene of crystallisation or to have been substituted by a phenyl group, the figures favouring the second possibility. The method of purification (vacuum-sublimation) rendered unlikely the retention of solvent of crystallisation, and the tentative formulation of these compounds as phenylated 8-hydroxybenzo-1 : 2 : 4-triazines is further supported by molecular-weight (Rast) determination. We have found no analogy for phenylation under these conditions, and are further examining these compounds.

The benzo-1 : 2 : 4-triazines are all bright yellow, weakly basic compounds, noticeably soluble in water and reprecipitated by alkali. The 6-aminobenzo-1 : 2 : 4-triazines were diazotisable in dilute mineral acid, as shown by a coupling test with β-naphthol. The ultraviolet extinction curves of benzo-1 : 2 : 4-triazine and the 3-methyl derivative are reproduced (Fig. 2).

Experimental

(A) *The Bischler Synthesis*

N-*Acyl*-N′-o-*nitrophenylhydrazines*.—*o*-Nitrophenylhydrazine (7 g.) and 100% formic acid (7 c.c.) were heated at 95° for 1 hr. Removal of the solvent and crystallisation of the residue from alcohol gave mustard-yellow crystals of the product (7·9 g.), m. p. 181—182°. Similarly the hydrazine (5 g.), acetic acid (10 c.c.), and fused sodium acetate (0·5 g.) gave the acetyl derivative which formed golden needles (4·9 g.), m. p. 142—144°, from alcohol. *o*-Nitrophenylhydrazine (5 g.), benzoyl chloride (4·75 g.), and pyridine (30 c.c.), kept overnight at room temperature, and then heated 1½ hr. at 95°, gave when poured into iced dilute hydrochloric acid a gum which slowly solidified. Recrystallisation from alcohol (charcoal) gave bright yellow crystals of the benzoyl derivative (4 g.), m. p. 163—165°. Each of these derivatives dissolved in aqueous sodium hydroxide to give a permanganate-coloured solution.

2 : 4-Dinitrophenylhydrazine (10 g.) and 90% formic acid (50 c.c.), boiled for 18 hr., gave a solution from which water precipitated the product. N-*Formyl*-N′-2 : 4-*dinitrophenylhydrazine* formed yellow needles (9·5 g.), m. p. 187—188° (Found : C, 37·0; H, 2·6. $C_7H_6O_5N_4$ requires C, 37·2; H, 2·7%), from alcohol. *N*-Acetyl-*N*′-2 : 4-dinitrophenylhydrazine was similarly prepared by using 90% acetic acid.

N-o-*Aminophenyl*-N′-*formylhydrazine*.—The nitro-compound (3 g.) and palladium–charcoal (1·2 g. of 5%) in hot alcohol (300 c.c.) were shaken with hydrogen. Reduction was complete in ¼ hr., then the solution was rapidly filtered (it became yellow when exposed to air) and concentrated to a small volume (to ensure good recovery concentration in one stage to as small a volume as possible is essential) in a stream of nitrogen, under reduced pressure. After cooling, the product (1·9 g.) was collected. The *amine* formed soft needles, m. p. 120—121° (Found : C, 55·1; H, 5·6; N, 27·7. $C_7H_9ON_3$ requires C, 55·6; H, 6·0; N, 27·8%). It gave no diazonium reaction and was insoluble in alkali.

N-*Acetyl*-N′-o-*aminophenylhydrazine*.—The nitro-compound (5 g.) in hot alcohol (500 c.c.) was reduced as above. Washing with alcohol produced a pink colour in the initially colourless reduction solution, and the whole became orange before concentration, which, effected as above, gave a white solid (3·6 g.). The *amine* formed crisp rods, m. p. 164—166° (with some bubbling) (Found : C, 58·3; H, 6·7; N, 25·2. $C_8H_{11}ON_3$ requires C, 58·2; H, 6·7; N, 25·4%), from alcohol.

N-o-*Aminophenyl*-N′-*benzoylhydrazine*.—The nitro-compound (3·9 g.), catalyst (1·5 g.), and alcohol (150 c.c.), reduced as above, gave a solution which became burgundy-red when diluted with alcohol. The colour disappeared during concentration, and the *product* (2·5 g.) formed silky needles, m. p. 163—164° (Found : C, 68·9; H, 5·8. $C_{13}H_{13}ON_3$ requires C, 68·7; H, 5·8%), from ethyl acetate.

Experiments with N-o-*Aminophenyl*-N′-*formylhydrazine*.—(i) The amine (0·39 g.) and 4N-

hydrochloric acid (4 c.c.) gave a hydrochloride which quickly dissolved on warming. At 95° the initially colourless solution rapidly became deep red, and after 6 min. at this temperature it was stirred into iced water (16 c.c.) containing potassium hydroxide (3·5 g.). Addition of potassium ferricyanide (1·7 g.) in water (16 c.c.) caused a small rise in temperature and produced a flocculent black precipitate with some effervescence. After 15 min. the mixture was extracted continuously with ether for several hr. Removal of the ether gave a black oil (0·28 g.) which was digested with light petroleum (100 c.c.; b. p. 40—60°). The turbid yellow extract deposited a very small quantity of white needles, m. p. 116—117°, when cool, and the solution, when passed over alumina, gave a yellow band which on elution with benzene provided benzo-1 : 2 : 4-triazine (60 mg.). The pure compound formed deep yellow plates, m. p. 76—77° (Found : C, 64·2; H, 4·1. Calc. for $C_7H_5N_3$: C, 64·1; H, 3·8%) [$\lambda_{max.}$ (in H_2O) 233, 307 mμ; 10^{-3} ε 31·7, 4·25], after sublimation (80°/1 mm.) and recrystallisation from light petroleum. Bischler (*loc. cit.*) gave m. p. 65—66°, whereas Bamberger and Wheelwright (*loc. cit.*) gave m. p. 74—75°. The picrate separated very slowly from alcohol as brown prisms, m. p. 98—99° after sintering at 87°, which decomposed into the components on attempted recrystallisation.

From an experiment precisely similar, except that heating at 95° was continued for ½ hr., a sticky dark brown solid (0·15 g.) was obtained which yielded benzo-1 : 2 : 4-triazine (40 mg.) by chromatography, and a brown, light petroleum-insoluble solid (50 mg.).

(ii) The amine (0·4 g.), nitrobenzene (5 drops), and benzene (20 c.c.) saturated with hydrogen chloride, were refluxed for 2 hr. The colourless liquid became yellow and deposited a dark-red oil. Water was added, the aqueous layer was extracted with benzene, and the combined extracts were concentrated, diluted with light petroleum, and treated with hydrogen chloride. The precipitate was washed with light petroleum saturated with hydrogen chloride, treated with water, and extracted with benzene. Evaporation of the benzene and addition of light petroleum gave benzo-1 : 2 :4-triazine (70 mg.), m. p. 73—74°.

(iii) The amine (0·2 g.) and an aqueous solution of sodium *m*-nitrobenzenesulphonate (0·33 g.) which had been made just acid to litmus with dilute hydrochloric acid were refluxed for 1 hr. The solid dissolved quickly and the solution became deep orange-yellow (or deep red in larger runs). When cool it was strongly basified with sodium hydroxide solution and extracted continuously with benzene. Concentration of the extract and addition of light petroleum (b. p. 60—80°) gave white plates which were repeatedly washed with hot light petroleum. The combined filtrates (A) were preserved. Crystallised from benzene (charcoal) the solid gave shiny plates (110 mg.) of 1-*aminobenziminazole*, m. p. 156—156·5° (Found : C, 63·2; H, 5·2; N, 32·0; *M*, 133. $C_7H_7N_3$ requires C, 63·1; H, 5·3; N, 31·6%; *M*, 131) [$\lambda_{max.}$ (in EtOH) 252, 274, 282 mμ; 10^{-3} ε 5·67, 4·50, 4·10; $\lambda_{min.}$ 224, 270, 279, mμ; 10^{-3} ε 1·09, 3·95, 2·90]. This compound (0·1 g.), benzaldehyde (0·1 c.c.), ethyl alcohol (2 c.c.), and piperidine (1 drop) were refluxed for 1 hr. Dilution with water and trituration of the oil gave a solid (0·12 g.). 1-*Benzylideneaminobenziminazole* formed small needles, m. p. 126—127° (Found : C, 76·2; H, 4·9; N, 18·8. $C_{14}H_{11}N_3$ requires C, 76·0; H, 5·0; N, 19·0%), from ligroin containing a little benzene.

The filtrates (A), when concentrated and passed over alumina, yielded benzo-1 : 2 : 4-triazine (45 mg.), m. p. 73—74°.

(iv) The amine (0·2 g.) in benzene (20 c.c.) was refluxed overnight with Amberlite IR-120(H) (0·2 g.). Filtration, concentration, and addition of light petroleum gave 1-aminobenziminazole (0·04 g.), m. p. 151—152°. Chromatography of the remaining solution over alumina gave benzo-1 : 2 : 4-triazine (0·07 g.), m. p. 73—74°.

Oxidation of 1-*Aminobenziminazole*.—The compound (0·4 g.) in 4N-hydrochloric acid (4 c.c.) was heated at 95° for 6 min. Pouring the solution into iced water (16 c.c.) containing potassium hydroxide (3·5 g.) precipitated starting material (m. p. and mixed m. p.). Addition of an ice-cold solution of potassium ferricyanide (1·7 g.) in water (16 c.c.) produced effervescence and mild frothing, and during 15 min., with occasional shaking, the solid gradually dissolved and the solution darkened. Continuous extraction with benzene, followed by concentration of the extract and addition of light petroleum, gave a colourless precipitate. Recrystallisation from water provided benziminazole (0·18 g.), m. p. and mixed m. p. 170—171° [picrate, m. p. and mixed m. p. 225—226°].

Experiments with N-*Acetyl*-N′-*o*-*aminophenylhydrazine*.—(i) The amine (1 g.) dissolved immediately in 4N-hydrochloric acid (10 c.c.), and the pale yellow solution when warmed at 95° quickly become deep red. After 5 minutes' heating, the solution was poured into iced water (40 c.c.) containing potassium hydroxide (9 g.). Potassium ferricyanide (4 g.) in water (40 c.c.) was added, and after being occasionally shaken during 15 min. at room temperature, the mixture was extracted continuously with benzene. Removal of the solvent gave a brown solid (0·62 g.)

which was extracted with boiling light petroleum (100 c.c.). The extract gave by passage over alumina 3-methylbenzo-1 : 2 : 4-triazine (0·5 g., 56·8%), m. p. 92—94°. This formed bright-yellow rods, m. p. 97—98° (Found : C, 66·2; H, 4·8; N, 28·9. Calc. for $C_8H_7N_3$: C, 66·2; H, 4·9; N, 28·95%) [$\lambda_{max.}$ (in H_2O) : 235, 307 mμ; $10^{-3}\varepsilon$ 30·5, 4·30], from light petroleum. Bischler (*loc. cit.*) gave m. p. 88—89°. The petroleum-insoluble residue (0·13 g.) gave needles of 2-methylbenziminazole, m. p. and mixed m. p. 173—174° (Found : C, 72·4; H, 6·0. Calc. for $C_8H_8N_2$: C, 72·7; H, 6·1%), from benzene.

A similar experiment with heating for ½ hr. gave 34 mg. of 3-methylbenzo-1 : 2 : 4-triazine and 60 mg. of by-product. Heating for 10 min. gave 40% of the triazine.

(ii) The amine (0·2 g.), nitrobenzene (5 drops), and toluene (20 c.c.) saturated with hydrogen chloride were refluxed for 1 hr. (In the absence of acid no cyclisation occurred.) Worked up as in the experiment with the formyl compound the solution yielded 3-methylbenzo-1 : 2 : 4-triazine (80 mg.), m. p. 97—98°.

(iii) The amine (0·2 g.) and a slightly acidified solution of sodium *m*-nitrobenzenesulphonate (0·33 g.) in water (10 c.c.) were refluxed for 2 hr. Basification and continuous extraction of the solution with benzene, concentration, and addition of light petroleum, gave *1-amino-2-methylbenziminazole* (0·11 g.) which formed leaflets, m. p. 164—165° (Found : C, 57·3; H, 6·55; N, 28·5%; *M*, 159. $C_8H_9N_3,H_2O$ requires C, 58·2; H, 6·7; N, 25·4%; *M*, 165) [$\lambda_{max.}$ (in EtOH) 252, 275, 282 mμ; $10^{-3}\varepsilon$ 5·60, 5·10, 5·00; $\lambda_{min.}$ 224, 263, 279 mμ; $10^{-3}\varepsilon$ 1·70, 3·59, 3·30], from benzene (the m. p. was depressed on admixture with starting material). The *benzylidene* derivative, formed as in the previous case, gave needles, m. p. 133·5—134·5° (Found : C, 76·1; H, 5·5; N, 17·9. $C_{15}H_{13}N_3$ requires C, 76·6; H, 5·6; N, 17·9%), from benzene–ligroin.

Chromatography of the filtrate remaining after removal of the aminobenziminazole gave 3-methylbenzo-1 : 2 : 4-triazine (40 mg.), m. p. 94—95°.

Oxidation of 1-Amino-2-methylbenziminazole.—The amine (0·6 g.), suspended in water (32 c.c.) containing potassium hydroxide (7 g.), was treated at 0° with potassium ferricyanide (3·4 g.) in water (32 c.c.). Evolution of nitrogen was slow and a flocculent precipitate was formed as the amine dissolved. After 1 hr. the dark suspension was extracted continuously with benzene. Evaporation of the solvent and crystallisation of the residue from water gave 2-methylbenziminazole (0·28 g.), m. p. and mixed m. p. 174—176°.

Experiments with N-o-*Aminophenyl*-N′-*benzoylhydrazine.*—(i) The amine (0·5 g.) and 4N-hydrochloric acid (5 c.c.) were heated at 95° for 6 min. The resulting clear red solution was poured into iced water (200 c.c.) containing potassium hydroxide (4·1 g.). The addition of potassium ferricyanide (1·41 g.) in water (15 c.c.) immediately produced a dull red colour, and a dark brown precipitate was slowly formed. After 15 min. the mixture was extracted continuously with benzene. The concentrated (5 c.c.) extract deposited crystals (60 mg.), m. p. 198—200°, identical with the aminobenziminazole described below, and the remaining solution gave, by passage over alumina, 3-phenylbenzo-1 : 2 : 4-triazine (100 mg.), which formed yellow prisms, m. p. 126—127° (Found : C, 75·6; H, 4·4. Calc. for $C_{13}H_9N_3$: C, 75·3 : H, 4·4%), from benzene–light petroleum. von Pechmann (*loc. cit.*) gave m. p. 123°.

(ii) When the amine (0·2 g.) was refluxed for 2 hr. with nitrobenzene (6 drops) and toluene (20 c.c.) saturated with dry hydrogen chloride, and the solution was decanted from the oily hydrochloride which was then treated as before, finally by passage of the benzene extract over alumina and elution with benzene–ether (1 : 1), 3-phenylbenzo-1 : 2 : 4-triazine (70 mg.), m. p. 126—127°, was obtained.

(iii) Treatment of the amine (0·2 g.) as before with a slightly acidified solution of sodium *m*-nitrobenzenesulphonate (0·4 g.) in water (10 c.c.) and addition of light petroleum to the final extract gave *1-amino-2-phenylbenziminazole* (100 mg.), m. p. 204—205° (Found : C, 74·7; H, 5·35. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3%), after fractional crystallisation from benzene to remove a trace of a colourless powder.

The initial filtrate afforded by chromatography 3-phenylbenzo-1 : 2 : 4-triazine (50 mg.), m. p. 123—124°.

6-Aminobenzo-1 : 2 : 4-triazine.—Hydrogenation of *N*-2 : 4-dinitrophenyl-*N*′-formylhydrazine (2 g.) in hot ethanol (300 c.c.) in the presence of palladium–charcoal (2 g. of 5%) was complete in 20 min. After filtration, the combined filtrate and washings, which gradually became orange-red, were evaporated to small bulk, brown crystals (220 mg.) separating. After sublimation (200°/1 mm.) and recrystallisation from ethanol, this gave shiny golden platelets of *6-aminobenzo-1 : 2 : 4-triazine*, m. p. 298—299° (decomp.) (Found : C, 57·9; H, 4·1; N, 38·0. $C_7H_6N_4$ requires C, 57·5; H, 4·1; N, 38·4%). In a diazonium coupling test with alkaline β-naphthol this gave a deep violet dye.

6-*Amino*-3-*methylbenzo*-1 : 2 : 4-*triazine*.—In the same way *N*-acetyl-*N'*-2 : 4-dinitrophenylhydrazine (2 g.) gave golden-yellow needles (200 mg.) of **6-*amino*-3-*methylbenzo*-1 : 2 : 4-*triazine***, m. p. 265—266° (decomp.) (Found : C, 59·4; H, 5·4. $C_8H_8N_4$ requires C, 60·0; H, 5·0%).

(B) *The Bamberger Synthesis*

***Benzo*-1 : 2 : 4-*triazine*.**—A solution of 1 : 5-diphenylformazan (5 g.) (von Pechmann, *loc. cit.*) in acetic acid (75 c.c.) was treated slowly at 0° with concentrated sulphuric acid (20 c.c.). The violet solution was unchanged by heating for 4 min. at 95° and more sulphuric acid (10 c.c.) was then added. After a further ½ hr. at 95° the colour had changed to yellowish-brown, and after dilution with water (200 c.c.) the mixture was extracted continuously with benzene. Concentration of the extract to a small volume, addition of light petroleum, passage over alumina (6″ × 1″), and elution with benzene–light petroleum (1 : 1) gave, first, phenazine (0·14 g.) [yellow prisms, m. p. and mixed m. p. with a specimen prepared by the method of Waterman and Vivian (*J. Org. Chem.*, 1949, **14**, 289), 176—177° (Found : C, 80·2; H, 4·5. Calc. for $C_{12}H_8N_2$: C, 80·0; H, 4·5%), from alcohol], and then benzo-1 : 2 : 4-triazine (1·65 g.), m. p. 76—77° after recrystallisation from light petroleum.

3-*Methylbenzo*-1 : 2 : 4-*triazine*.—The mauve solution of 3-methyl-1 : 5-diphenylformazan (0·4 g.) (Bamberger and Müller, *J. prakt. Chem.*, 1901, **64**, 213) in acetic acid (6 c.c.) became deep blue on the addition at 0° of concentrated sulphuric acid (1·6 c.c.), and then dark greenish-brown after 2 min. at 95°. Diluted and worked up as before this solution yielded 3-methylbenzo-1 : 2 : 4-triazine (0·17 g.).

3-*Phenylbenzo*-1 : 2 : 4-*triazine*.—1 : 3 : 5-Triphenylformazan (2 g.) (Ashley, Davis, Nineham, and Stock, *J.*, 1953, 3881) with glacial acetic acid (30 c.c.) and concentrated sulphuric acid (8 c.c.) (10 minutes' heating; the colour changed in 1 min.) behaved similarly to the methyl compound, and chromatography followed by sublimation afforded 3-phenylbenzo-1 : 2 : 4-triazine (1·2 g.).

1 : 5-*Di*-o-*methoxyphenylformazan*.—A diazonium solution prepared from *o*-anisidine (31 g.), concentrated hydrochloric acid (48 c.c.), and water (30 c.c.), and sodium nitrite (18 g.) in water (30 c.c.) was added to a solution of malonic acid (26 g.) and sodium acetate (50 g.; hydrated) in water (400 c.c.), stirred at 0°. After 10 min. sodium acetate (50 g.) was added and the solution was kept at 0° overnight (considerable frothing occurred). The precipitate was washed with water and a little methanol, and finally crystallised from ethanol. **1 : 5-*Di*-o-*methoxyphenylformazan*** (24 g.) was obtained as maroon blades, m. p. 151—152° (Found : C, 63·1; H, 5·5. $C_{15}H_{16}O_2N_4$ requires C, 63·4; H, 5·7%).

8-*Methoxybenzo*-1 : 2 : 4-*triazine*.—The deep blue solution of 1 : 5-di-*o*-methoxyphenylformazan (10 g.), acetic acid (150 c.c.), and concentrated sulphuric acid (60 c.c.) became dark brown in 15 min. at 95°. After a total of 45 minutes' heating it was diluted with water (300 c.c.) and worked up as before. Elution from the alumina column with benzene gave a mixture from which **8-*methoxybenzo*-1 : 2 : 4-*triazine*** (2·20 g.) [deep-yellow plates, m. p. 149—150° (Found : 60·2; H, 4·5. $C_8H_7ON_3$ requires C, 59·6; H, 4·4%), from benzene–light petroleum] sublimed at 150°/1 mm., leaving a residue which on crystallisation from alcohol provided yellow needles of 1 : 6-dimethoxyphenazine, m. p. 253—254° (Found : C, 69·7; H, 4·8. Calc. for $C_{14}H_{12}O_2N_2$: C, 70·0; H, 5·0%). Yoshioka and Kidani (*J. Pharm. Soc. Japan*, 1952, **72**, 847) gave m. p. 251°. The phenazine exhibits a characteristic green fluorescence in dilute alcoholic solution.

1 : 5-*Di*-o-*methoxyphenyl*-3-*methylformazan*.—The diazonium solution from *o*-anisidine (1·5 g.), concentrated hydrochloric acid (2·6 c.c.), water (4 c.c.), and sodium nitrite (0·9 g.) in water (2 c.c.) was added to potassium hydroxide (5·5 g.) in water (55 c.c.) at 0°. This solution was added portionwise to a vigorously stirred solution of pyruvic acid *o*-methoxyphenylhydrazone (5·2 g.) [prepared from pyruvic acid and *o*-methoxyphenylhydrazine hydrochloride in water, this ***hydrazone*** formed yellow prisms, m. p. 119—121° (Found : C, 57·9; H, 5·9; $C_{10}H_{12}O_3N_2$ requires C, 57·7; H, 5·8%), from dilute ethanol], potassium hydroxide (4 g.), and water (40 c.c.) maintained below −4°. When carbon dioxide evolution had ceased, the precipitate was collected and washed with ice-cold water and cold methanol, giving almost pure product (3·6 g.). **1 : 5-*Di*-o-*methoxyphenyl*-3-*methylformazan*** formed red plates (showing a blue reflex), m. p. 142—143° (Found : C, 64·3; H, 6·4. $C_{16}H_{18}O_2N_4$ requires C, 64·4; H, 6·1%), from dilute alcohol.

8-*Methoxy*-3-*methylbenzo*-1 : 2 : 4-*triazine*.—The formazan (1 g.), acetic acid (15 c.c.) and concentrated sulphuric acid (4 c.c.) at 0° gave an indigo solution which became brown after 1 min. at 95°. Heating was continued for 10 min., and there was then isolated in the usual way

(elution with benzene–ether) a mixture (0·35 g.) from which 8-*methoxy*-3-*methylbenzo*-1 : 2 : 4-*triazine* (0·23 g.) [bright yellow plates, m. p. 124—125° (Found : C, 61·8; H, 5·1. $C_9H_9ON_3$ requires C, 61·7; H, 5·1%), from benzene–light petroleum] was sublimed (135—145°/1 mm.). The residue gave 1 : 6-dimethoxyphenazine (65 mg.), m. p. 253—254°, when crystallised from ethanol.

8-*Methoxy*-3-*phenylbenzo*-1 : 2 : 4-*triazine*.—*Benzaldehyde* o-*methoxyphenylhydrazone* (4·5 g.) [from benzaldehyde and *o*-methoxyphenylhydrazine in alcohol; needles, m. p. 88—90° (Found : C, 74·2; H, 6·6. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2%) from ethanol] in pyridine (36 c.c.) was stirred at 0° and treated with the diazonium solution from *o*-anisidine (2·5 g.), acetic acid (7 c.c.), concentrated sulphuric acid (2 c.c.), and sodium nitrite (1·4) g. in water (3 c.c.). After being stirred for 1 hr. at 0° and kept for 4 hr. at this temperature, the deep violet solution was diluted with water and extracted with chloroform. The washed and dried ($MgSO_4$) extract was concentrated, finally in a vacuum and the resulting permanganate-coloured oil was passed in benzene over alumina. The formazan (5·2 g.) was obtained as an oil which could not be crystallised.

The deep blue solution of this oil (4·8 g.) in acetic acid (70 c.c.) and concentrated sulphuric acid (20 c.c.) became brown after 2 min. at 95°; then the usual processing (elution with benzene) gave 8-*methoxy*-3-*phenylbenzo*-1 : 2 : 4-*triazine* (1·3 g.) which formed yellow needles, m. p. 155—156° (Found : C, 70·2; H, 4·9; N, 17·9. $C_{14}H_{11}ON_3$ requires C, 70·8; H, 4·7; N, 17·7%), after sublimation (140°/1 mm.) and crystallisation from benzene–light petroleum.

The Action of Benzene and Aluminium Chloride on 8-*Methoxybenzo*-1 : 2 : 4-*triazines*.—(i) 8-Methoxybenzo-1 : 2 : 4-triazine (0·2 g.), benzene (10 c.c.), and anhydrous aluminium chloride (0·8 g.) were refluxed for 4 hr. Water was added, the aqueous layer was extracted with benzene, and the combined benzene solutions were extracted with dilute sodium hydroxide solution. The alkaline extract was washed with benzene, acidified with acetic acid, and extracted with benzene. Concentration of the benzene solution to a small volume gave a solid (110 mg.; m. p. 206—210°) which was sublimed (180—190°/1 mm.). The yellow sublimate formed from acetone glistening yellow platelets of a *product*, m. p. 238—239° (Found : C, 70·3; H, 4·0%; *M*, 209. $C_{13}H_9ON_3$ requires C, 69·9; H, 4·0%; *M*, 223. $C_7H_5ON_3,C_6H_6$ requires C, 69·3; H, 4·9%).

(ii) 8-Methoxy-3-methylbenzo-1 : 2 : 4-triazine (0·2 g.), treated with aluminium chloride and benzene, gave, in the way described above, a product which on sublimation (180—190°/1 mm.) provided a yellow solid (110 mg.). From acetone this *substance* formed shiny yellow plates, m. p. 177—178° (Found : C, 71·2; H, 4·9%; *M*, 211. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4·7%; *M*, 237. $C_8H_7ON_3,C_6H_6$ requires C, 70·3; H, 5·5%).

(iii) 8-Methoxy-3-phenylbenzo-1 : 2 : 4-triazine (0·2 g.) demethylated in the same way gave, after sublimation (180°/1 mm.) of the solid, a *product* (60 mg.) which formed woolly yellow needles, m. p. 213—214° (Found : C, 75·9; H, 4·3; N, 14·3. $C_{12}H_{13}ON_3$ requires C, 76·2; H, 4·4; N, 14·0. $C_{13}H_9ON_3,C_6H_6$ requires C, 75·7; H, 5·0; N, 13·95%), from benzene.

Attempted Cyclisation of 1 : 5-*Di*-p-*methoxyphenylformazans*.—1 : 5-Di-*p*-methoxyphenylformazan (2·75 g.; von Pechmann and Wedekind, *Ber.*, 1895, **28**, 1695), treated as described for the preparation of 8-methoxybenzo-1 : 2 : 4-triazine, gave, after chromatography, a pale yellow solid (20 mg.) (the colour and physical properties proved it not to be a triazine). Twice sublimed it had m. p. 109—113° (Found : C, 69·3; H, 5·7. Calc. for $C_{14}H_{12}O_2N_2$: C, 70·0; H, 5·0%). Tomlinson (*J.*, 1939, 161) gave m. p. 163° for 2 : 7-dimethoxyphenazine.

Pyruvic acid p-*methoxyphenylhydrazone* [needles, m. p. 142—143° (Found : C, 57·3; H, 5·8. $C_{10}H_{12}O_3N_2$ requires C, 57·7; H, 5·8%), from 30% ethanol], treated in the way described for the *o*-isomer, gave a solid red formazan which became tarry when collected. Application of cyclising conditions to this material produced no recognisable product.

1 : 5-*Di*-p-*methoxyphenyl*-3-*phenylformazan*.—The diazonium solution from *p*-anisidine (2·5 g.), acetic acid (7 c.c.), concentrated sulphuric acid (2 c.c.), and sodium nitrite (1·4 g.) in water (3 c.c.) was stirred into a solution of *benzaldehyde* p-*methoxyphenylhydrazone* (4·5 g.) [needles, m. p. 121—122° (Found : C, 74·2; H, 5·9. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2%), from alcohol] in pyridine (36 c.c.) at 0°. After being kept overnight at 0° the solution was diluted with water (200 c.c.), and the precipitate was washed with hot water and a little methyl alcohol. 1 : 5-*Di*-p-*methoxyphenyl*-3-*phenylformazan* (4·3 g.) formed permanganate-coloured needles (olive-green reflex), m. p. 165—166° (Found : C, 70·0; H, 5·7. $C_{21}H_{20}O_2N_4$ requires C, 70·0; H, 5·6%), from ethanol.

6-*Methoxy*-3-*phenylbenzo*-1 : 2 : 4-*triazine*.—The formazan (1 g.) solution in acetic acid (15 c.c.) and concentrated sulphuric acid (4 c.c.) was heated at 95° until the colour changed from

deep blue to brown. The usual method (elution with benzene) gave **6-*methoxy*-3-*phenylbenzo*-1 : 2 : 4-*triazine*** (200 mg.) which formed shiny yellow plates, m. p. 197—198° (Found : C, 70·7; H, 4·8. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4%), from benzene.

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