1036. *Condensation of Amines with Alloxan: Formation of Uramils (5-Aminobarbituric Acids)*

By J. W. Clark-Lewis and J. A. Edgar

5-Arylaminobarituric acids (anilinobarbituric acids, 7-aryluramils) are obtained as by-products when *p*-substituted aromatic amines are boiled with ethanolic alloxan monohydrate, although the main products are amine salts of alloxanic acid. Reaction of *p*-substituted anilines with alloxan monohydrate in cold methanol yields 5,5-di(arylamino)barbituric acids, analogous to products from aromatic amines and diethyl oxomalonate. Decomposition of the diarylaminobarbituric acids in boiling ethanol gave the same mixture of amine salts of the uramils and alloxanoic acid as was obtained from the amines and boiling ethanolic alloxan.

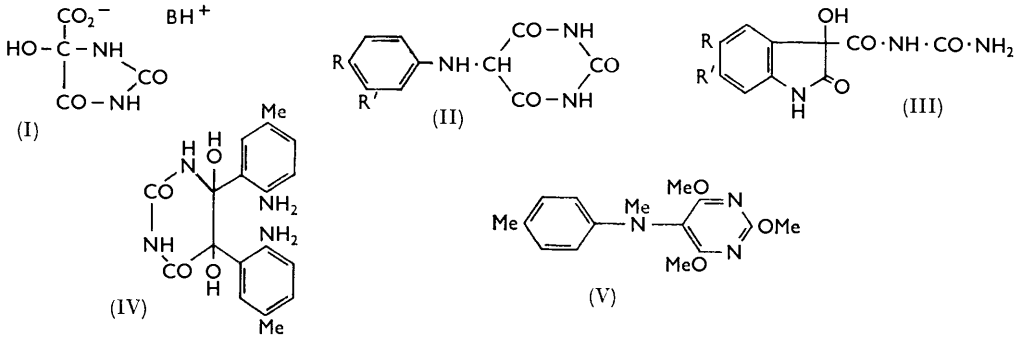
p-Substituted aromatic amines (*p*-toluidine, 3,4-dimethylaniline, and *p*-anisidine) have been found to react with alloxan monohydrate in boiling ethanol to yield mainly the amine salts (I; B = base) of alloxanic acid and smaller quantities of 5-arylaminobarbituric acids (7-aryluramils) (II). The main reaction is thus analogous to formation of salts of alloxanic acid from aliphatic and alicyclic secondary amines and alloxan monohydrate in aqueous or aqueous ethanolic solution.[1] The *p*-substituted aromatic amines and anhydrous alloxan in acetic acid yield dioxindole-3-carboxyureides (III),[2] but electrophilic aromatic substitution by alloxan apparently does not proceed in boiling neutral ethanolic solution, as no ureides were obtained under these conditions. The sparingly soluble amine salts of the uramils (II) (*ca.* 8—15%) separated from the boiling ethanolic solutions, and basification of these salts yielded the primary aromatic amines while acidification of the salts (or the basified solutions) yielded the 5-arylaminobarbituric acids (II). The *p*-toluidine salt of the uramil (II; R = Me, R′ = H) was obtained similarly by Rossi and Scandellari [3] but was assigned a different structure (IV).

5-Aminobarbituric acids (uramils) have received comparatively little attention since the early work summarised by Johnson and Shepard,[4] and their preparation 50 years ago of the first two 5-arylaminobarbituric acids: 5-phenylaminobarbituric acid (II; R = R′ = H) and 5-benzyl-5-phenylamino-2-thiobarbituric acid. Three further representatives (II; R = Me or Cl, R′ = H) and (II; R = R′ = Cl) were synthesised recently,[5]

[1] J. W. Clark-Lewis and J. A. Edgar, *J.*, 1962, 3887.
[2] J. W. Clark-Lewis and J. A. Edgar, preceding Paper.
[3] G. Rossi and G. Scandellari, *Gazzetta*, 1932, **62**, 351.
[4] T. B. Johnson and N. A. Shepard, *J. Amer. Chem. Soc.*, 1913, **35**, 994; *ibid.*, 1914, **36**, 1741.
[5] D. E. O'Brien, F. Baiocchi, R. K. Robins, and C. C. Cheng, *J. Medicin. Pharmaceut. Chem.*, 1962, **5**, 1085.

and we now find that one of these (II; R = Me, R′ = H) arises from alloxan monohydrate and *p*-toluidine in boiling ethanol. This reaction gave the *p*-toluidine salts of *p*-methylphenylaminobarbituric acid (II; R = Me, R′ = H) (15%) and of alloxanic acid (I; B = *p*-toluidine) (56%), and 3,4-dimethylaniline and *p*-anisidine similarly gave analogous amine salts (8%) of the uramils (II; R = R′ = Me) and (II; R = OMe, R′ = H) and of alloxanic acid. The amine salts of the uramils (II) which separated from the boiling reaction mixtures were very sparingly soluble and difficult to purify; their decomposition points were indistinct and depended on the rate of heating. Acidification of the salts gave the uramils which are obtained in better yield, however, from reaction of the aromatic amines in acid solution with 5-hydroxybarbituric acid (dialuric acid) and a trace of alloxan instead of with alloxan alone. The structure of 5-*p*-methylphenylaminobarbituric acid (II; R = Me, R′ = H) was confirmed by three independent syntheses described below. Methylation of this sparingly soluble acid with diazomethane gave the tetramethyl derivative (V), and the n.m.r. spectrum of this derivative showed three three-proton peaks corresponding to the *C*-methyl, *N*-methyl, and 2-methoxyl groups, and a six-proton peak due to the 4- and 6-methoxyl groups.

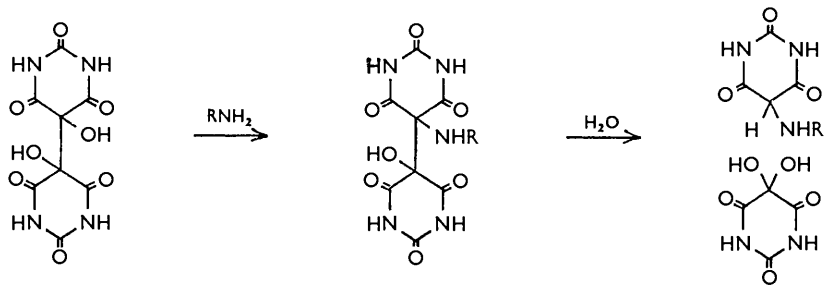
Reduction is clearly involved in the formation of 5-arylaminobarbituric acids from the amines and alloxan, and it seems likely that the uramils result from reaction of the amines with alloxantin, *e.g.*, as shown in Scheme 1. Some alloxantin was formed when an aqueous ethanolic solution of alloxan itself was boiled for several days, and reaction of alloxantin with ammonia and primary aliphatic amines is known to give 5-aminobarbituric acid [6] and 5-alkylaminobarbituric acids.[7] This reaction was formerly supposed [8] to occur by dissociation [9] of alloxantin into dialuric acid and alloxan, but dialuric acid alone yields the amine salts of dialuric acid [10] and the supposed dissociation is rendered improbable by a recent polarographic study.[11] Alloxantin is prepared [12] by mixing equimolecular



quantities of alloxan and dialuric acid, and Davidson and Soloway [13] showed that satisfactory yields of uramils are obtained by reaction of aliphatic amines with dialuric acid in acid solution in the presence of catalytic amounts of alloxan, although the reaction pathway shown in Scheme 1 appears more probable than the suggested participation of 5-iminobarbituric acid.[13] Alloxantin lacks the acidic 5-proton of dialuric acid so that reaction of alloxantin with bases is not impeded by salt formation, and this probably accounts for the smoother formation of uramils from alloxantin than from dialuric acid. Indeed their formation from dialuric acid probably depends on aerial oxidation of the acid to alloxantin.[13]

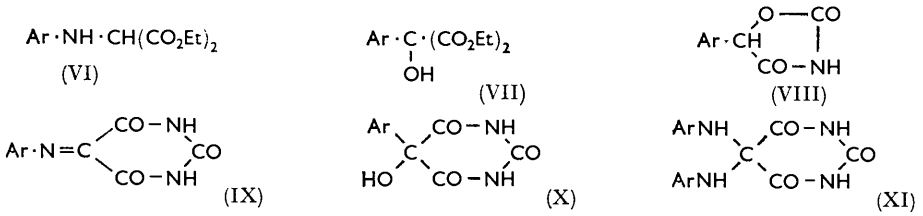
[6] O. Piloty and K. Finckh, *Annalen*, 1904, **333**, 71.
[7] O. Piloty and K. Finckh, *Annalen*, 1904, **333**, 64; R. Möhlau and H. Litter, *J. prakt. Chem.*, [2], 1906, **73**, 472.
[8] H. Biltz and P. Damm, *Ber.*, 1913, **46**, 3662.
[9] E. Biilmann and J. Bentzon, *Ber.*, 1918, **51**, 522.
[10] H. Biltz, K. Marwitzky, and M. Heyn, *Annalen*, 1923, **423**, 147.
[11] W. A. Struck and P. J. Elving, *J. Amer. Chem. Soc.*, 1964, **86**, 1229.
[12] R. S. Tipson, *Org. Synth.*, 1953, **33**, 3.
[13] D. Davidson and H. Soloway, *J. Org. Chem.*, 1939, **3**, 365.

This synthetic method proved to be applicable to the preparation of 7-aryluramils, and *p*-toluidine and dialuric acid in the presence of alloxan gave 5-*p*-methylphenylaminobarbituric acid (II; R = Me, R′ = H) (56%). The second synthesis (83%) of this uramil was achieved by condensation of diethyl *p*-methylphenylaminomalonate (VI; Ar = *p*-C_6H_4·Me) with urea and sodium methoxide,[5] as first used by Johnson and Shepard [4] in the preparation of 5-phenylaminobarbituric acid (II; Ar = Ph). It is noteworthy that this reaction yields the pyrimidine instead of the hydantoin ring system, because the analogous aryltartronic esters (VII) and urea under similar conditions have been shown to yield five-membered oxazolidinediones (VIII) instead of six-membered dialuric acids.[14,15] The third synthesis was achieved virtually quantitatively by reduction of *p*-methylphenyliminobarbituric acid (IX; Ar = *p*-C_6H_4·Me) [2] with sodium borohydride.



Scheme I

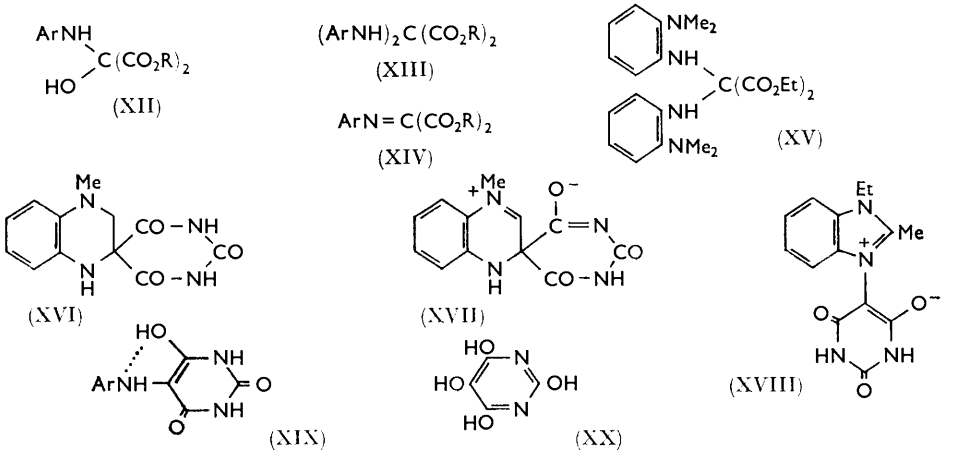
3,4-Dimethylaniline and alloxan in boiling ethanol gave the 3,4-dimethylaniline salt of 5-(3,4-dimethylphenylamino)barbituric acid (II; R = R′ = Me) (8%) and 3,4-dimethylanilinium alloxanate (I; B = 3,4-dimethylaniline) (50%). 5-(3,4-Dimethylphenylamino)-5-hydroxybarbituric acid (X; Ar = 3,4-C_6H_3·Me_2),[2] obtained from anhydrous alloxan and 3,4-dimethylaniline in diglyme, was converted by boiling ethanol into a similar mixture of the amine salts of the uramil (II; R = R′ = Me) and of alloxanic acid, and the latter salt was also prepared (85%) from alloxanic acid and 3,4-dimethylaniline. *p*-Anisidine and alloxan in boiling ethanol similarly gave the *p*-anisidine salt of 5-*p*-methoxyphenylaminobarbituric acid (II; R = OMe, R′ = H) and *p*-anisidine alloxanate.



Condensation of *p*-toluidine and *p*-anisidine with alloxan monohydrate in cold methanol gave the 5,5-diarylaminobarbituric acids (XI; Ar = *p*-C_6H_4Me and *p*-C_6H_4OMe) which were decomposed by aqueous sodium hydroxide into the aromatic amines and the alloxanate anion. The 5,5-diarylaminobarbituric acids dissolved readily in cold methanol and ethanol, and the solutions became red when warmed, presumably through anil formation. Boiling ethanolic solutions of these compounds deposited the sparingly soluble amine salts of the uramils, isomeric with the soluble diarylaminobarbituric acids, and the amine salts of alloxanic acid were isolated from the filtrates. The stability of alloxan monohydrate and the existence of 5,5-diarylaminobarbituric acids (XI), 5-(3,4-dimethylphenylamino)-5-hydroxybarbituric acid (X; Ar = 3,4-C_6H_3·Me_2),[2] and its *p*-chloro-analogue

[14] F. E. King and J. W. Clark-Lewis, *J.*, 1951, 3077.
[15] J. L. Riebsomer, H. Burkett, T. Hodgson, and F. Senour, *J. Amer. Chem. Soc.*, 1939, **61**, 3491.

(X; Ar = *p*-C_6H_4Cl) [16] can be attributed to the inductive effects of the carboxyamide groups adjacent to the 5-carbonyl group in alloxan. Similar stabilisation occurs with adducts of oxomalonic esters, and Curtiss and Spencer [17] found that anhydrous dimethyl oxomalonate and primary aromatic amines in dry ether yield dimethyl anilinotartronates, *e.g.*, (XII; Ar = Ph, R = Me), which when treated with water gave mixtures of dimethyl dianilinomalonates, *e.g.*, (XIII; Ar = Ph, R = Me), and dimethyl oxomalonate hydrate. Dehydration of dimethyl anilinotartronate (XII; Ar = Ph, R = Me) was achieved only



by treatment with phosphorus pentoxide,[17] and the C=N bond in the resultant anil (XIV; Ar = Ph, R = Me) proved to be comparable in reactivity to that in phenyl isocyanate. Diethyl oxomalonate and the three toluidines reacted similarly with formation of diethyl toluidino-tartronates, but with aniline the product was diethyl dianilinomalonate (XIII; Ar = Ph, R = Et) and the intermediate tartronate could not be isolated.[18] An excess of *p*-toluidine and diethyl oxomalonate gave diethyl di-(*p*-methylphenylamino)malonate (XIII; Ar = *p*-C_6H_4·Me, R = Et) and a similar reaction with *o*-dimethylaminoaniline gave the analogous ester (XV). The n.m.r. spectrum of this ester (XV) showed the triplet and quartet due to two equivalent ethyl groups and a twelve-proton peak due to the four equivalent *N*-methyl groups.

Alloxan reacts differently with *o*-dimethylaminoaniline to give a mixture of the spiran (XVI) and the dihydroquinoxalinium betaine (XVII),[19,20] whereas *o*-diethylaminoaniline and alloxan gives only the benzimidazolium barbiturate (XVIII).[20] Oxidation is clearly involved in the formation of both betaines (XVII) and (XVIII), and, as alloxan is known to be an oxidant, part of it is presumably reduced to alloxantin or dialuric acid in these reactions. The present study was undertaken to see if oxidation–reduction processes occur with simpler amines, and the results support the view that aryluramils may be involved in the formation of the spiran (XVI) and the betaines (XVII) and (XVIII).[21]

The infrared absorption of the aryluramils (II) is very close to that of sodium dialurate in the carbonyl region, with absorption peaks at 6·0 and 6·2 μ, which suggests that the tautomer (XIX) makes a significant contribution to the uramil structure. The completely enolised tautomeric form of the uramils is evidently not significant because the methylated uramil (V) is devoid of absorption in the region 5·5—6·3 μ apart from a very weak band at

[16] R. B. Barlow, H. R. Ing, and I. M. Lewis, *J.*, 1951, 3242.
[17] R. S. Curtiss and F. G. C. Spencer, *J. Amer. Chem. Soc.*, 1909, **31**, 1053; 1911, **33**, 985.
[18] R. S. Curtiss, H. S. Hill, and R. H. Lewis, *J. Amer. Chem. Soc.*, 1911, **33**, 400.
[19] F. E. King and J. W. Clark-Lewis, *J.*, 1951, 3080.
[20] J. W. Clark-Lewis, J. A. Edgar, J. S. Shannon, and M. J. Thompson, *Austral. J. Chem.*, 1964, **17**, 877.
[21] J. W. Clark-Lewis, J. A. Edgar, J. S. Shannon, and M. J. Thompson, *Austral. J. Chem.*, 1965, **18**, 907.

6·0 μ. Moreover, the uramil (V) has an absorption peak at 285 mμ which is not present in the unmethylated uramils. Crystalline dialuric acid shows absorption in the region 5·88—6·25 μ so that the structure (XX) proposed by Tipson and Cretcher [22] seems improbable in view of the absence of similar bands in the methylated uramil (V).

Experimental

Microanalyses were performed by the Australian Microanalytical Service, Melbourne.

Infrared spectra were recorded on an Infracord instrument with Nujol mulls, unless otherwise stated, and ultraviolet spectra with solutions in 95% ethanol. N.m.r. spectra were recorded with a Varian DP 60 instrument at 60 Mc./sec. and calibrated with a Muirhead–Wigan decade oscillator (D-890-A) using side-bands generated from the signal of tetramethylsilane as an internal standard in deuterochloroform solutions, or from the proton signal of HDO when deuterium oxide was used as solvent. Chemical shifts are given as τ-values.

p-*Toluidine Salts of* 5-p-*Methylphenylaminobarbituric Acid* (II; R = Me, R′ = H) *and Alloxanic Acid* (I).—(*a*) *p*-Toluidine (1·1 g.) in ethanol (40 ml.) was added to a solution of alloxan monohydrate (1·6 g.) in water (20 ml.) and the mixture was heated under reflux until the initial red colour of the solution had changed to greenish yellow (*ca.* 2 hr.). The p-*toluidine salt* of 5-p-*methylphenylaminobarbituric acid* (0·5 g., 15%) which had separated as small needles, m. p. *ca.* 230° (decomp.), was collected by filtration (Found: C, 63·0; H, 5·9; N, 16·2. $C_{18}H_{20}N_4O_3$ requires C, 63·5; H, 5·9; N, 16·5%). Carbonyl absorption occurred near 5·95 μ. Dilution of a solution of the salt in concentrated hydrochloric acid with water gave 5-*p*-methylphenylaminobarbituric acid almost quantitatively, and the sparingly soluble product was purified by repeated precipitation with dilute hydrochloric acid from solution in 5% aqueous sodium hydroxide, and by precipitation with water from dimethyl sulphoxide or dimethylformamide, which gave the uramil as a powder, m. p. 330° (decomp.) (lit.,[5] 330°, decomp.) (Found: C, 55·9; H, 5·1; N, 17·4; O, 21·1. Calc. for $C_{11}H_{11}N_3O_3,\frac{1}{4}H_2O$: C, 55·6; H, 4·9; N, 17·7; O, 21·9%). Infrared absorption occurred near 6·0 and 6·2 μ, with a sharp band near 3·15 μ; $\lambda_{max.}$ 250 mμ (ε 18,000); $\lambda_{min.}$ 229 mμ (ε 11,000). Basification of the acidic solution after filtration from the uramil gave *p*-toluidine.

Evaporation of the filtrate from the *p*-toluidine salt of the uramil under reduced pressure left an oil which crystallised when treated with ethanol. The p-*toluidine salt* of *alloxanic acid* (1·5 g., 56%) was collected and washed with a little cold ethanol; it crystallised from ethanol as prisms, m. p. 148° (with decarboxylation), alone and when mixed with authentic material described below (Found: C, 49·4; H, 5·1; N, 15·2; O, 30·3. $C_{11}H_{13}N_3O_5$ requires C, 49·4; H, 4·9; N, 15·7; O, 29·9%). Infrared absorption occurred near 2·9, 3·15, 5·65, 5·7, 5·85, and 6·0 μ. An authentic specimen of the salt was prepared by mixing alloxanic acid [1] (0·8 g.) in ethanol (4 ml.) with *p*-toluidine (0·54 g.) in ethanol (4 ml.). The mixture was kept at 2—3° overnight before collection of the *p*-toluidine salt of alloxanic acid (1·2 g., 90%), prisms, m. p. 148° (with decarboxylation), from ethanol, indistinguishable by mixed m. p. and infrared absorption from the sample already described.

(*b*) A solution of *p*-toluidine (0·5 g.) in 5% hydrochloric acid (15 ml.) was mixed with a solution of dialuric acid (0·7 g.) in water (300 ml.) containing alloxan monohydrate (0·05 g.), and the solution was boiled under reflux. The 5-*p*-methylphenylaminobarbituric acid (0·7 g., 56%) was collected after 3 hr. It was indistinguishable from the uramil described under (*a*) by mixed m. p., infrared, and ultraviolet light absorption.

(*c*) Diethyl *p*-toluidinomalonate (1·33 g.),[23] m. p. 55°, b. p. 154°/0·8 mm., was added to a solution of urea (0·45 g.) and sodium methoxide [from sodium (0·46 g.)] in methanol (15 ml.), and the mixture was heated under reflux on a steam-bath for 15 hr. After removal of the solvent at 100° the residue was dissolved in water and filtered. Acidification of the filtrate gave 5-*p*-methylphenylaminobarbituric acid (1·1 g., 83%) identical with that already described. A lower yield (40%) by a similar method has been reported.[5]

(*d*) 5-*p*-Methylphenyliminobarbituric acid (0·5 g.) was added to a solution of sodium borohydride (0·5 g.) in water (15 ml.) at room temperature. The colourless solution obtained was

[22] R. S. Tipson and L. H. Cretcher, *J. Org. Chem.*, 1951, **16**, 1091; cf. A. R. Katritzky and J. M. Lagowski, *Adv. Heterocyclic Chem.*, 1963, **1**, 377.
[23] R. Blank, *Ber.*, 1898, **31**, 1815.

acidified with dilute hydrochloric acid, and the precipitated 5-*p*-methylphenylaminobarbituric acid (0·5 g., 98%) was collected by filtration.

5-(N-*Methyl*-p-*methylphenylamino*)-2,4,6-*trimethoxypyrimidine* (V).—A suspension of 5-*p*-methylphenylaminobarbituric acid (1·0 g.) in methanol (75 ml.) was treated with an excess of ethereal diazomethane and kept at 0° overnight. Evaporation of the filtrate from undissolved material yielded 5-(N-*methyl*-p-*methylphenylamino*)-2,4,6-*trimethoxypyrimidine* (0·4 g., 33%) which crystallised from ethanol as colourless prisms, m. p. 98—99° (Found: C, 62·7; H, 6·9; N, 14·6. $C_{15}H_{19}N_3O_3$ requires C, 62·3; H, 6·6; N, 14·5%). The n.m.r. spectrum (CCl_4) showed the four aromatic protons as two doublets (A_2B_2)(J_{AB} = 8·4 c./sec.) (A = 2′,6′-H, 3·75; B = 3′,5′-H, 3·17) and three-proton peaks at 7·08 (C–Me), 6·99 (N–Me), and 6·09 (2-MeO); the 4- and 6-methoxyl groups absorbed as a single six-proton peak at 6·14. The carbonyl region of the infrared spectrum was devoid of absorption except for a weak band at 6·0 μ; $\lambda_{max.}$ 249 (ε 19,000) and 285 mμ (ε 8000); $\lambda_{min.}$ 229 (ε 12,000) and 272 mμ (ε 7900).

5-(3,4-*Dimethylphenylamino*)*barbituric Acid* (II; R = R′ = Me) *and the* 3,4-*Dimethylaniline Salt of Alloxanic Acid* (I).—(*a*) Alloxan monohydrate (1·6 g.) and 3,4-dimethylaniline (1·21 g.) were boiled in 80% aqueous ethanol until the solution became yellow (*ca.* 2½ hr.) and then filtered from the amine salt of the uramil which, after acidification, yielded 5-(3,4-dimethylphenylamino)barbituric acid (8%), m. p. 235—240° (decomp.). Evaporation of the filtrate from the salt of the uramil under reduced pressure left an oil which slowly solidified. Crystallisation of the solid from ethanol gave 3,4-*dimethylanilinium alloxanate* as prisms (1·4 g., 50%), m. p. 148° (decarboxylation) (Found: C, 51·5; H, 5·4; N, 14·9. $C_{12}H_{15}N_3O_5$ requires C, 51·2; H, 5·4; N, 14·9%). Infrared absorption occurred near 5·65, 5·8, 6·0, and 6·15 μ. The salt prepared (85%) by neutralising an ethanolic solution of alloxanic acid [1] with 3,4-dimethylaniline was indistinguishable from that already described.

(*b*) 5-(3,4-Dimethylphenylamino)-5-hydroxybarbituric acid [2] was converted by boiling aqueous ethanol into a mixture of the *p*-toluidine salts of the uramil and of alloxanic acid, identical with those described above, and the products were separated as described under (*a*).

5-p-*Methoxyphenylaminobarbituric Acid* (II; R = OMe, R′ = H) *and the* p-*Anisidine Salt of Alloxanic Acid* (I).—*p*-Anisidine (1·23 g.) in ethanol (40 ml.) was mixed with alloxan monohydrate (1·6 g.) in water (20 ml.) and the solution was boiled under reflux for 3 hr.; during this time the initially red solution became yellow. The *p*-anisidine salt of the uramil was collected and dissolved in concentrated hydrochloric acid and the solution was diluted with water. The 5-p-*methoxyphenylaminobarbituric acid* (0·2 g., 8%) was collected; it melted at *ca.* 180° (decomp.) after crystallisation from aqueous dimethylformamide (Found: C, 52·1; H, 4·7; N, 16·5. $C_{11}H_{11}N_3O_4,\frac{1}{4}H_2O$ requires C, 52·1; H, 4·6; N, 16·6%). Carbonyl absorption occurred near 6·0 and 6·2 μ, and a sharp band occurred at 3·15 μ.

Evaporation of the filtrate from the amine salt of the uramil left the *p*-anisidine salt of alloxanic acid (1·1 g., 38%) which crystallised from ethanol as colourless prisms, m. p. 148° (decarboxylation). Infrared absorption occurred near 2·95, 5·65, 5·75, 5·85, 6·0, and 6·15 μ. The *p*-anisidine salt was also prepared by neutralisation of alloxanic acid.

5,5-*Di*(*methylphenylamino*)*barbituric Acid Hydrate* (XI; Ar = *p*-C_6H_4Me).—A cold solution of alloxan monohydrate (1·6 g.) in methanol (10 ml.) was added to a cold solution of *p*-toluidine (2·14 g.) in methanol (15 ml.) and the mixture was diluted with water (15 ml.). After cooling to 2—3° for 10 hr. the precipitated 5,5-*di*-(p-*methylphenylamino*)*barbituric acid monohydrate* (3·1 g., 87%) was collected by filtration. It crystallised from aqueous methanol as plates, m. p. *ca.* 256° (decomp.), which readily turned red (Found: C, 60·3; H, 5·6; N, 15·7. $C_{18}H_{18}N_4O_3,H_2O$ requires C, 60·7; H, 5·7; N, 15·7%). Hydrolysis of the salt with 5% aqueous sodium hydroxide gave *p*-toluidine, and addition of aqueous barium hydroxide to the hydrolysate gave an immediate precipitate of barium alloxanate (identified by comparison of its infrared absorption with that of an authentic specimen). A solution of 5,5-di-(*p*-methylphenylamino)barbituric acid in boiling aqueous ethenol turned red initially and was then converted during *ca.* 2 hr. into the mixture of the *p*-toluidine salts of 5-*p*-methylphenylaminobarbituric acid and alloxanic acid already described.

5,5-*Di*-(*p*-*methoxyphenylamino*)*barbituric Acid Hydrate* (XI; Ar = *p*-C_6H_4OMe).—A cold solution of *p*-anisidine (2·46 g.) in methanol (10 ml.) was added to a cold solution of alloxan monohydrate (1·6 g.) in methanol (5 ml.). The mixture was diluted with water (15 ml.) and kept at 2—3° overnight before collection of the product (3·0 g., 77%). 5,5-*Di*-(*p*-*methoxyphenylamino*)*barbituric acid monohydrate* crystallised from aqueous methanol as plates, m. p.

ca. 140° (decomp.) (Found: C, 55·4; H, 4·7; N, 14·2. $C_{18}H_{18}N_4O_5,\frac{1}{4}H_2O$ requires C, 55·7; H, 5·2; N, 14·4%). Boiling aqueous ethanol converted the product into the *p*-anisidine salt of the uramil and of alloxanic acid already described, and 5% aqueous sodium hydroxide gave *p*-anisidine and the alloxanate anion (identified as the barium salt).

Diethyl Di-(p-*methylphenylamino*)*malonate* (XIII; Ar = *p*-C_6H_4Me, R = Et).—A solution of *p*-toluidine (1·07 g.) and diethyl oxomalonate (1·78 g.) [24] in 75% aqueous ethanol (20 ml.) was kept at room temperature for 4 days and then filtered from *diethyl di-*(p-*methylphenylamino*)*malonate* (0·6 g., 32%), which crystallised from aqueous ethanol as needles, m. p. 94° (Found: C, 68·1; H, 7·1; N, 7·5. $C_{21}H_{26}N_2O_4$ requires C, 68·1; H, 7·1; N, 7·6%). Carbonyl absorption occurred near 5·8 μ and N–H stretching absorption near 2·95 μ.

Diethyl Di-(o-*dimethylaminophenylamino*)*malonate* (XV).—*o*-Dimethylaminoaniline (1·4 g.) in ethanol (5 ml.) was mixed with diethyl oxomalonate (1·78 g.) in ethanol (10 ml.) and filtered after 2 days from *diethyl di-*(o-*dimethylaminophenylamino*)*malonate* (0·6 g.); a further quantity (0·75 g.) was isolated from the reaction mixture 2 days later, and crystallisation of the combined product (1·35 g., 61%) from ethanol gave large rectangular plates, m. p. 118° (Found: C, 64·3; H, 7·4; N, 12·9. $C_{23}H_{32}N_4O_4$ requires C, 64·5; H, 7·5; N, 13·1%). The n.m.r. spectrum ($CDCl_3$ containing 10% CCl_4) showed the four equivalent *N*-methyl groups as a twelve-proton peak at 7·29; the triplet and quartet of the ethyl groups appeared at 9·01 and 5·93; and the aromatic and *N*-protons formed a ten-proton multiplet centred at 3·09 which was not analysed. Carbonyl absorption occurred near 5·8 μ and N–H stretching absorption near 3·0 μ.

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA. [*Received, April 21st*, 1965.]

[24] A. W. Dox, *Org. Synth.*, Coll. Vol. I, 1932, p. 261.