NOTES.

1 : 9-*Diaminoacridine.* By (Miss) E. R. Klein and F. N. Lahey.

With the appearance of a paper by Albert, Rubbo, Goldacre, Davey, and Stone (*Brit. J. Exp. Path.*, 1945, **26**, 160) and one by Craig (*J.*, 1946, 534), in which reference was made to 1 : 9-diaminoacridine supplied by one of us, it becomes desirable to record the synthesis of this substance, although the work for which it was prepared has not yet been successfully concluded.

The synthesis was accomplished along standard lines. Condensation of 2-bromo-3-nitrobenzoic acid with *o*-nitroaniline in the presence of sodium carbonate without the use of a solvent gave 2 : 2′-dinitrodiphenylamine-6-carboxylic acid. The same product was obtained from 3-nitroanthranilic acid, *o*-bromonitrobenzene, and sodium carbonate with nitrobenzene as a solvent. Ring closure of 2 : 2′-dinitrodiphenylamine-6-carboxylic acid was accomplished with either sulphuric acid or phosphorus oxychloride yielding 1 : 9-dinitroacridone, which was readily reduced to 1 : 9-diaminoacridone by stannous chloride and hydrochloric acid or by sodium hydrosulphite. Reduction of 1 : 9-diaminoacridone with sodium amalgam gave 1 : 9-diaminoacridine directly, apparently without the intermediate formation of the acridan.

1 : 9-Diaminoacridine crystallises in yellow needles, m. p. 177°. It gives a colourless hydrochloride and is further characterised by the formation of an acetyl derivative, m. p. 250—251°.

2 : 2′-*Dinitrodiphenylamine-6-carboxylic Acid.*—(*a*) 2-Bromo-3-nitrobenzoic acid (5·0 g.), *o*-nitroaniline (5·0 g.), sodium carbonate (2·0 g.), and a trace of copper powder were thoroughly mixed and heated at 190—210° for 2 hours with stirring. On cooling, benzene was added, and the sodium salts were filtered off and taken up in hot water. On cooling this solution in ice, the sodium salt of 2 : 2′-dinitrodiphenylamine-6-carboxylic acid separated, and was filtered off and acidified with hydrochloric acid. 2 : 2′-*Dinitrodiphenylamine-6-carboxylic acid* crystallised from ethyl alcohol or xylene in yellow crystals, m. p. 246°. Yield, 1·2 g. (Found : N, 13·84. $C_{13}H_9O_6N_3$ requires N, 13·86%).

(*b*) A mixture of sodium 3-nitroanthranilate (4·1 g.), *o*-bromonitrobenzene (6·0 g.), sodium carbonate (1·06 g.), a trace of copper powder, and nitrobenzene (30 ml.) was refluxed for 4 hours. It was then poured into benzene and the precipitated sodium salts filtered off. The acid obtained on acidification was recrystallised from ethyl alcohol, and was identical with that recorded above. Yield, 1·6 g.

1 : 9-*Dinitroacridone.*—2 : 2′-Dinitrodiphenylamine-6-carboxylic acid (1·0 g.) and concentrated sulphuric acid (7 ml.) were heated on a steam-bath with stirring for 15 minutes. The dark green solution was then poured on ice. The precipitated 1 : 9-*dinitroacridone* was filtered off and heated with sodium carbonate solution and then with water. It crystallised from xylene in fluffy orange crystals, m. p. 257—258°. Yield, 0·7 g. (Found : C, 54·9; H, 2·6. $C_{13}H_7O_5N_3$ requires C, 54·7; H, 2·5%). The same compound was obtained by using phosphorus oxychloride for ring closure.

2 : 2′-Dinitrodiphenylamine-6-carboxylic acid (1·0 g.) was refluxed with phosphorus oxychloride (10 ml.) for 1 hour. The excess of phosphorus oxychloride was removed under reduced pressure and the dark residue treated with water and filtered off. The brown solid was boiled for 15 minutes with 5% hydrochloric acid and again filtered. It was then dissolved in boiling N/5-potassium hydroxide (50% alcohol). From this solution, 1 : 9-dinitroacridone was precipitated with dilute hydrochloric acid. Yield, 0·7 g.

1 : 9-*Diaminoacridone.*—Stannous chloride (2·5 g.) was dissolved in boiling concentrated hydrochloric acid (9 ml.) and the solution saturated with hydrogen chloride. 1 : 9-*Dinitroacridone* (1 g.) was added during 1 hour with stirring, and the boiling continued for half an hour after the addition was complete. The stannic chloride complex (1·8 g.) which settled out was filtered off, washed with ether and dissolved in 50 ml. of hot water. The solution was cooled in ice and a slight excess of ammonia (*d* 0·88) added.

The yellow precipitate was dried and extracted repeatedly with boiling absolute alcohol. Evaporation of the alcohol gave 1 : 9-*diaminoacridone* as greenish-yellow needles which did not melt up to 320°. Yield, 0·4 g. (Found : C, 68·7; H, 4·6. $C_{13}H_{11}ON_3$ requires C, 69·3; H, 4·9%).

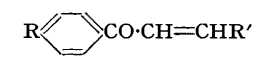
An easier method of reduction involved the use of sodium hydrosulphite. 1 : 9-Diaminoacridone (1·0 g.) was suspended in hot aqueous ethyl alcohol and sodium hydrosulphite added with constant stirring until a clear red solution was produced. A little hydrochloric acid was added and the solution boiled for ½ hour. Ammonia precipitated the 1 : 9-diaminoacridone. Yield, 0·5 g.

1 : 9-*Diaminoacridine*.—1 : 9-Diaminoacridone (0·3 g.) was suspended in 30 ml. of water at 80°. Sodium amalgam (5%; 12·0 g.) was added gradually over 2 hours with stirring, and heating continued for another 2 hours. After cooling, the precipitate was filtered off, washed with water, and crystallised from 30% alcohol. Yield, 0·22 g. 1 : 9-*Diaminoacridine* formed golden-yellow crystals, m. p. 177° (Found : C, 74·5; H, 5·3. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3%). It gave a colourless solution in hydrochloric acid. Treatment with acetic anhydride and working up in the usual way gave a *diacetyl* derivative, m. p. 250—251° (Found : N, 14·5. $C_{17}H_{15}O_2N_3$ requires N, 14·2%).—UNIVERSITY OF MELBOURNE. [*Received, November 28th*, 1946.]

The Preparation and Bacteriostatic Action of Some Aminochalkones and Related Compounds.

By D. H. MARRIAN, P. B. RUSSELL, and A. R. TODD.

KUHN, MÖLLER, WENDT, and BEINERT (*Ber.*, 1942, **75**, 711) prepared a number of analogues of the sulphonamide drugs in which a *p*-aminobenzoyl group was substituted for the *p*-aminobenzenesulphonyl residue and showed that they possessed much weaker bacteriostatic properties than sulphanilamide. Later, however, Kuhn, Möller, and Wendt (*Ber.*, 1943, **76**, 405) showed that 4 : 4′-diaminobenzil has from two to six times the activity of sulphanilamide against *Staph. aureus*, and has accordingly about 30 times the activity of 4 : 4′-diaminobenzophenone. As an aspect of certain other investigations in this laboratory it seemed of interest to prepare and test some aminochalkones and related compounds of type (I), partly in view of the above findings and partly because of the presence of the grouping –C=C–CO– in a number of naturally occurring antibiotics.

(I.) 

4 : 4′-*Diaminochalkone* (I; R = NH_2; R′ = *p*-NH_2·C_6H_4) was prepared by reduction of 4-amino-4′-nitrochalkone, itself obtained by hydrolysing *N* : ω-bis-*p*-nitrobenzylidene-*p*-aminoacetophenone (Scholtz and Huber, *Ber.*, 1904, **37**, 390). 4-Aminochalkone (I; R = H; R′ = *p*-NH_2·C_6H_4) was prepared by reduction of the corresponding nitrochalkone with iron and acetic acid, and 4′-aminochalkone (I; R = NH_2; R′ = Ph) by hydrolysis of *N* : ω-dibenzylidene-*p*-aminoacetophenone. p-*Amino-ω-cinnamylideneacetophenone* (I; R = NH_2; R′ = CH:CH·C_6H_5) and p-*amino-ω-furfurylideneacetophenone* (I; R = NH_2; R′ = α-furyl) were prepared in similar fashion by hydrolysing the corresponding di-compounds.

The above compounds were tested against *Staph. aureus* and *Strept. hæmolyticus* by a serial dilution method in glucose broth and on a synthetic medium. Although all of them showed some activity (cf. Table) it was in no case of a high order. None showed any activity against *Esch. coli* or *Pseudomonas pyocyanea*.

	Maximum dilution inhibiting			
	Staph. aureus.		*Strept. hæmolyticus.*	
	Synthetic medium.	Glucose broth.	Synthetic medium.	Glucose broth.
4 : 4′-Diaminochalkone	1/10,000	—	1/100,000	1/10,000
4-Aminochalkone	1/5,000	—	1/50,000	1/5,000*
4′-Aminochalkone	1/10,000	—	1/10,000	—
I; R=NH_2; R′=CH:CHPh	—	—	1/5,000	1/5,000
I; R=NH_2; R′=α-furyl	1/10,000	1/5,000	1/5,000*	1/5,000

* Partial inhibition.

4-*Nitro-4′-aminochalkone*.—*N* : ω-bis-*p*-nitrobenzylidene-*p*-aminoacetophenone (3 g.; Scholtz and Huber, *loc. cit.*) was dissolved in ethanol (250 c.c.) and the solution acidified with dilute sulphuric acid. The precipitated sulphate was collected and dissolved in water, and the solution was made alkaline with sodium hydroxide. 4-*Nitro-4′-aminochalkone* (2·5 g.) separated as an orange-red microcrystalline powder; recrystallised from aqueous ethylene glycol monomethyl ether it had m. p. 220—221° (Found : C, 66·6; H, 4·6; N, 10·4. $C_{15}H_{12}O_3N_2$ requires C, 67·0; H, 4·5; N, 10·4%).

4 : 4′-*Diaminochalkone*.—4-Nitro-4′-aminochalkone (0·5 g.) was dissolved in acetic acid (6 c.c.) and the hot solution poured into a suspension of iron filings (2 g.) in dilute acetic acid (30 c.c. of 5%). The mixture was refluxed until all the nitro-compound had gone into solution, and then filtered hot. The filtrate, on cooling, deposited 4 : 4′-*diaminochalkone* as a crystalline powder. Recrystallised from ethanol the product formed orange needles (0·35 g.), m. p. 183—184° (Found : C, 75·5; H, 6·4; N, 11·5. $C_{15}H_{14}ON_2$ requires C, 75·5; H, 6·2; N, 11·8%); in pyridine solution it showed the blue fluorescence in ultra-violet light characteristic of 4-aminochalkones (Pfeiffer *et al.*, *Annalen*, 1925, **441**, 228), and on treatment with benzaldehyde it gave a *dibenzylidene* derivative, m. p. 180—181° (Found : N, 7·0. $C_{29}H_{22}ON_2$ requires N, 6·8%).

4′-*Aminochalkone*.—Prepared by treatment of *N* : ω-dibenzylidene-*p*-aminocetophenone with dilute sulphuric acid, 4-aminochalkone had m. p. 105—106°. Dilthey, Neuhaus, Reis, and Schommer (*J. pr. Chem.*, 1930, **124**, 81) give m. p. 108°.

4-Aminochalkone.—4-Nitrochalkone (Sorge, *Ber.*, 1902, **35**, 1068) (1 g.) was dissolved in hot acetic acid (3 c.c.) and added to a suspension of iron filings (2 g.) in dilute acetic acid (30 c.c. of 5%). The mixture was heated for 2 hours on the steam-bath, filtered, and cooled. The 4-aminochalkone which separated was recrystallised from aqueous ethanol, and thus obtained as deep yellow plates, m. p. 151—152°. Rupe and Porai-Koschitz (*Chem. Zentr.*, 1906, II, 1761), who prepared the substance by a different route, give m. p. 151°.

p-*Amino-ω-cinnamylideneacetophenone.*—*N* : ω-Dicinnamylidene-*p*-aminoacetophenone (Scholtz and Huber, *loc. cit.*) (3·6 g.) was dissolved in a mixture of ethanol (20 c.c.) and dilute sulphuric acid (5 c.c. of 2N), and the solution was heated on the steam-bath for 10 minutes and then cooled. The precipitated sulphate was collected and dissolved in water, and the solution was made alkaline with sodium hydroxide. The free *base* which separated was recrystallised from aqueous ethanol; it formed long yellow needles (2·1 g.; 83%), m. p. 159—160° (Found : C, 81·6; H, 6·3; N, 5·9. $C_{17}H_{15}ON$ requires C, 81·9; H, 6·2; N, 5·8%).

N : *ω-Difurfurylidene*-p-*aminoacetophenone.*—*p*-Aminoacetophenone (2·7 g.) and furfuraldehyde (3·85 g.) were dissolved in ethanol (25 c.c.), and cooled to 0°, a solution of potassium hydroxide (1·08 g.) in ethanol (20 c.c.) was added, and the mixture was allowed to stand overnight. The crystalline material which separated was recrystallised from ethanol. The *compound* formed yellow needles (4 g.), m. p. 103—104° (Found : C, 74·6; H, 4·4; N, 5·1. $C_{18}H_{13}O_3N$ requires C, 74·2; H, 4·5; N, 4·8%).

p-*Amino-ω-furfurylideneacetophenone.*—*N* : ω-Difurfurylidene-*p*-aminoacetophenone was hydrolysed with sulphuric acid in the normal manner (see above). Recrystallised from water, the *compound* formed yellow needles, m. p. 113—114° (Found : C, 72·9; H, 5·3; N, 6·6. $C_{13}H_{11}O_2N$ requires C, 73·2; H, 5·2; N, 6·7%).

The microbiological assays were carried out in the laboratories of Glaxo Laboratories Ltd., to whom our thanks are due. Grants from the Agricultural Research Council are gratefully acknowledged — University Chemical Laboratory, Cambridge. [*Received, December 19th*, 1946.]

Some New Condensation Products of Ethyl cyclo*Pentanone-2-carboxylate with Aromatic Amines.*

By H. C. Barany and M. Pianka.

For the formation of substituted anilides of *cyclo*pentanone-2-carboxylic acid a slight modification of the method of Blount, Perkin, and Plant (*J.*, 1929, 1983) was employed. 0·025 Mole of the amine was gradually added to 0·1 mole of boiling keto-ester containing 0·5 c.c. of pyridine. The mixture was boiled for 2 minutes, cooled, and allowed to crystallise. In some cases crystallisation set in only after some days. Crystals were filtered off, washed with cold ethanol, and treated with a 4% sodium hydroxide solution to free them from any anil formed. The solution was filtered and acidified with dilute acetic acid. The precipitate was filtered off, dried, and recrystallised from ethanol or amyl alcohol. The condensation *products* prepared are shown in the table opposite.

The condensation products were coupled in alkaline solution with phenyldiazonium chloride, yielding dyes insoluble in water, but soluble in lower alcohols, acetone, and ether, and ranging in colour from lemon-yellow to orange-red.

On application of the film strip test (Weissberger and Porter, *J. Amer. Chem. Soc.*, 1943, **65**, 1502), consisting of immersing an exposed strip of photographic film in a 3% sodium carbonate solution of equal weights of the anilide to be tested and *NN*-diethyl-*p*-phenylenediamine hydrochloride for 5 minutes, rinsing with water, and bleaching out the silver and silver halide, coloured strips ranging from greenish-yellow to light brown were obtained.

Mr. Edgerton and the Directors of Dufay-Chromex Limited are thanked for permission to publish this note and Mr. H. D. Murray and Mr. B. Gluck for suggesting the use of the anilides in colour photography.—Research Laboratories, Dufay-Chromex Limited, Elstree, Herts. [*Received, December 9th*, 1946.]

Amine.	M.p. of condensation product.	Formula.	Analysis. Found (%). C.	H.	N.	X.	Required (%). C.	H.	N.	X.
Aniline	104° *		—	—	—	—	—	—	—	—
Benzidine	charring >270 †		—	—	—	—	—	—	—	—
o-Toluidine	95— 96	$C_{13}H_{15}O_2N$	71·79	6·93	6·45	—	71·88	6·91	6·45	—
m-Toluidine	98— 99		71·83	6·98	6·45	—				
p-Toluidine	118—119		71·81	7·01	6·43	—				
p-Chloroaniline	115	$C_{12}H_{12}O_2NCl$	60·59	5·09	5·90	15·00	60·64	5·05	5·89	14·95
p-Bromoaniline	132	$C_{12}H_{12}O_2NBr$	50·96	4·31	4·98	28·71	51·09	4·26	4·96	28·34
2 : 4-Dichloroaniline	156	$C_{12}H_{11}O_2NCl_2$	52·90	4·06	5·12	25·97	52·94	4·04	5·15	26·10
2 : 5-Dichloroaniline	104		52·92	4·04	5·10	26·15				
o-Anisidine	155–156	$C_{13}H_{15}O_3N$	67·02	6·50	6·05	—	66·94	6·44	6·01	—
p-Anisidine	136–137		67·05	6·48	6·10	—				
2 : 5-Diethoxyaniline	95	$C_{16}H_{21}O_4N$	66·10	7·18	4·92	—	65·98	7·22	4·81	—
p-Aminoethyl benzoate	273—274	$C_{15}H_{17}O_4N$	65·56	6·09	5·14	—	65·46	6·18	5·09	—
α-Naphthylamine	162	$C_{16}H_{15}O_2N$	75·84	5·97	5·60	—	75·90	5·93	5·53	—
β-Naphthylamine	172		75·82	6·02	5·58	—				
NN-Diethyl-*p*-phenylenediamine	210—211	$C_{16}H_{22}O_2N_2$	70·02	8·07	10·32	—	70·06	8·05	10·22	—
o-Phenylenediamine	158—159	$C_{18}H_{20}O_4N_2$	65·69	6·10	8·63	—	65·86	6·09	8·54	—
m-Phenylenediamine	217—218 (decomp.)		65·76	6·11	8·65	—				
p-Phenylenediamine	200 (decomp.)		65·81	6·13	8·62	—				

Except for the condensation products of ethyl *cyclo*pentanone-2-carboxylate with *o*-, *m*-, and *p*-phenylenediamine, which were recrystallised from amyl alcohol, all the anilides were recrystallised from ethanol.

Melting points are uncorrected. X = halogen.

* Blount, Perkin, and Plant, *loc. cit.* † Linstead and Wang, *J.*, 1937, 807.