68. *Some Addition Reactions of the Azomethinic Group.*

By D. PHILPOTT and W. J. JONES.

The reactivity of the azomethinic group in anils and indolenines has been investigated. It has been found that aldehyde-anils are more reactive than ketone-anils or benzoyleneindolenines, although methyleneaniline stands alone in that it does not combine with acid chlorides or with acetoacetic ester. Of the aldehyde-anils investigated, the most reactive are benzylideneaniline and benzylidene-β-naphthylamine, cinnamylideneaniline having somewhat lower additive power.

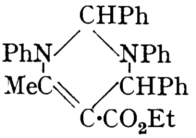
THE addition compound of benzylideneaniline with acetyl chloride has been investigated by Garzarolli-Thurnlackh (*Ber.*, 1899, **32**, 2277), and that of benzylideneaniline with benzoyl chloride by him and by James and Judd (J., 1914, **105**, 1427). On hydrolysis these addition compounds yield the original aldehyde, hydrogen chloride, and the acyl or aroyl derivative of the original amine. Very similar in properties to these addition compounds is that formed by benzylideneaniline with acetic anhydride, which on hydrolysis gives benzaldehyde, acetic acid, and acetanilide. According to Leuchs and Winzer (*Ber.*, 1925, **58**, 1522), Leuchs with Philpott, Sander, Heller, and Köhler (*Annalen*, 1928, **461** 27) and Leuchs, Wulkow, and Gerland (*Ber.*, 1932, **65**, 1586) addition of acid anhydrides and acyl halides to indolenines occurs at the azomethinic group, *viz.*,

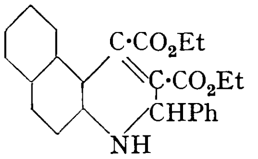
⁚C(O·COR)·N(COR)· and ⁚CCl·N(COR)·.

By the action of benzylideneaniline on acetoacetic ester, Schiff and Bertini (*Ber.*, 1897, **30**, 601; 1898, **31**, 207, 601) obtained the α-(α′-anilinobenzyl)acetoacetic ester,

$$CHPh(NHPh)\cdot CH(CO\cdot CH_3)\cdot CO_2Et.$$

This ester occurs in keto- and enolic forms, and by treating the latter with acetic acid and alcohol Bertini (*Gazzetta*, 1899, **29**, 22) obtained a *m*-diazine derivative (I), containing two benzylideneaniline groups to one of acetoacetic ester. Benzylidene-β-naphthylamine and oxalacetic ester (Simon and Conduche, *Compt. rend.*, 1904, **139**, 297) combine, molecule for molecule, to give α-(α′-2-naphthylaminobenzyl)oxalacetic ester, which on treatment with concentrated sulphuric acid condenses to a cyclic substance (II).


(I.)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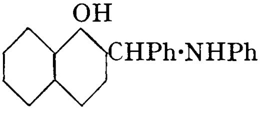
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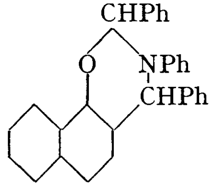
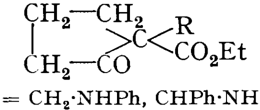

(IV.)

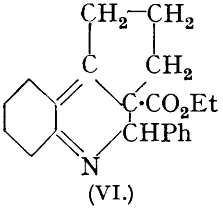
In a similar way, some of the anils combine with naphthols, which potentially contain an enolic group, *e.g.*, benzylideneaniline and α-naphthol form the substance (III) (Betti and Speroni, *Gazzetta*, 1900, **30**, 301). The compounds formed are capable of reacting with aldehydes, and in this way Betti prepared (*ibid.*, 1901, **31**, 377) a naphthoxazine derivative (IV) from the compound of benzylideneaniline and α-naphthol by condensation with benzaldehyde. Betti further found that the addition compounds of anils with naphthols reacted with phenylhydrazine, with substitution of the phenylhydrazine radical for that of aniline.

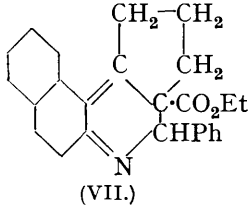
The effect of substituents in the anil on the stability of the acetyl and benzoyl compounds, of the type described by Garzarolli-Thurnlackh and by James and Judd (*loc. cit.*), has now been investigated, and it has been found that the compounds of the anils of benzaldehyde, acetophenone, benzophenone, cinnamaldehyde, and those of benzylidene-β-naphthylamine are readily formed, but that methyleneaniline does not combine with either acetyl or benzoyl chloride. These compounds are insoluble in non-polar solvents and are immediately resolved into their generators, or derivatives thereof, by hydroxylic solvents.

Maleic anhydride has been found to yield with the same anils, including methyleneaniline, the monoanilide of maleic acid and the original aldehyde or ketone. Phthalic anhydride similarly gives the monoanilide of phthalic acid and benzaldehyde in the case of benzylideneaniline.

The initial addition compounds given by methyleneaniline, by benzylideneaniline, and by benzylidene-β-naphthylamine with ethyl*cyclo*pentan-1-one-2-carboxylate, *viz.*, *ethyl 2-anilinomethyl*cyclo*pentan-1-one-2-carboxylate* (V), *ethyl 2-α-anilinobenzyl*cyclo*pentan-1-one-2-carboxylate* (V), and *ethyl 2-α-2′-naphthylaminobenzyl*cyclo*pentan-1-one-2-carboxylate* (V), respectively, have been found to be of the type described by Schiff and Bertini (*loc. cit.*). The structure assigned to this type by these authors is confirmed by the fact that benzylideneaniline and the disubstituted ketonic ester, ethyl 2-methyl*cyclo*pentan-1-one-2-carboxylate, do not react together. It has also been found that the ketone-anils, *e.g.*, those of acetophenone and benzophenone, do not combine with ethyl *cyclo*pentan-1-one-2-carboxylate. The compounds formed by benzylideneaniline and by benzylidene-β-naphthylamine, on treatment with acetic acid and alcohol according to the procedure of Bertini (*loc. cit.*), yield by loss of water, respectively, *ethyl 2-phenyl-3 : 4-trimethylene-2 : 3-dihydroquinoline-3-carboxylate* (VI) and *ethyl 3-phenyl-1 : 2-trimethylene-2 : 3-dihydro-β-naphthaquinoline-2-carboxylate* (VII).

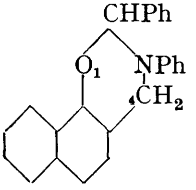

(V; R = CH_2·NHPh, CHPh·NHPh, or CHPh·NH·$C_{10}H_7$.)


(VI.)

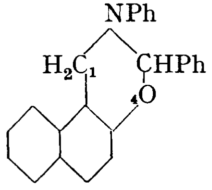

(VII.)

These products are for the most part recovered unchanged after treatment with 50% sulphuric acid, iodine, acetic anhydride, methyl iodide or phenylhydrazine, but with picric acid they give the picrate of the original anil. It has also been found that Bertini's *m*-diazine derivative (I) similarly yields the picrate of benzylideneaniline. Structurally these products resemble the cyclic substance (II) of Simon and Conduche. Ethyl 2-anilinomethyl*cyclo*pentan-1-one-2-carboxylate (V) does not condense on treatment with acetic acid and alcohol, which is reminiscent of the fact that the Doebner synthesis of quinolines frequently fails in the case of formaldehyde and of methylal (Claus and Brandt, *Annalen*, 1894, **282**, 93; Pictet and Misner, *Ber.*, 1912, **45**, 1800).

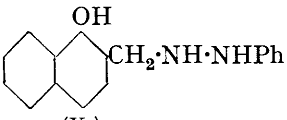
Addition compounds, *2-anilinomethyl-1-naphthol, 1-anilinomethyl-2-naphthol,* and *1-α-anilinocinnamyl-2-naphthol,* of the type of those of Betti and Speroni (III), are formed by methyleneaniline and by cinnamylideneaniline with the naphthols, but not by the anils of acetophenone and benzophenone. Of these, the methyleneaniline addition compounds, but not that of cinnamylideneaniline, condense with benzaldehyde to form *2 : 3-diphenyl-2 : 3-dihydro-1 : 3-α-naphthoxazine* (VIII) and *2 : 3-diphenyl-2 : 3-dihydro-2 : 4-β-naphthoxazine* (IX).



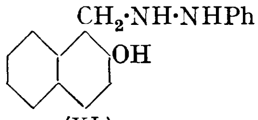
(VIII.)



(IX.)



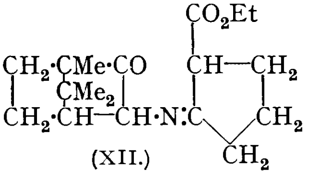
(X.)



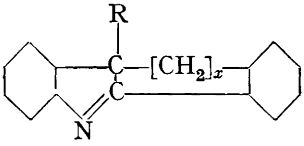
(XI.)

The addition compounds formed by methyleneaniline with the naphthols yield monoacetyl derivatives with acetic anhydride, and with phenylhydrazine they give *2-phenylhydrazinomethyl-1-naphthol* (X) and *1-phenylhydrazinomethyl-2-naphthol* (XI), of the type obtained by Betti (*loc. cit.*).

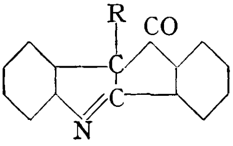
The anilic compound *ethyl 2-camphoryliminocyclopentane-1-carboxylate* (XII), obtained by condensation of α-aminocamphor and ethyl *cyclo*pentan-1-one-2-carboxylate, gives no reaction with acetic anhydride.



(XII.)



(XIII.)



(XIV; R = Me or Ph.)

Leuchs and his co-workers (*loc. cit.*) have found that in indolenines of the general formula (XIII) the azomethinic group, when $x = 1$, *i.e.*, in hydrindenes, adds on acid anhydrides, acid chlorides, and, in some cases, also phenylhydrazine, but that, when $x = 2$, the azomethinic group is inactive. In the present work we have found that, with a hydrindone ring present, *e.g.*, in *3-methyl-2 : 3-o-benzoyleneindolenine* (XIV) and *3-phenyl-2 : 3-o-benzoyleneindolenine* (XIV), the azomethinic group fails to form addition products with acid anhydrides, with acid halides, with phenylhydrazine, or with hydroxylamine.

The low activity of methyleneaniline cannot be entirely attributed to its existence in the polymeric form (von Miller and Plöchl, *Ber.*, 1892, **25**, 2021), since it has here and elsewhere been shown that it is capable of entering into reaction, and that, when it does so, it functions in its monomeric form, even in the cold, *e.g.*, it gives anilinoacetonitrile with hydrogen cyanide (von Miller and Plöchl, *loc. cit.*) and *NN'*-diphenyl-*NN'*-methyleneurea with phenyl *iso*cyanate (Senier and Shepheard, J., 1909, **95**, 504).

EXPERIMENTAL.

Ethyl 2-anilinomethylcyclopentan-1-one-2-carboxylate (V), rectangular plates, m. p. 53° (Found: C, 69·0; H, 7·5; N, 5·7. $C_{15}H_{19}O_3N$ requires C, 68·9; H, 7·3; N, 5·4%), is formed by refluxing (20 mins.) methyleneaniline (10 g.), ethyl *cyclo*pentan-1-one-2-carboxylate (14·9 g.), and alcohol (130 c.c.), concentrating the solution in a vacuum, and recrystallising the product from ligroin (yield, 21 g.). It gives, both in benzene and in alcohol, an orange-yellow coloration, changing to reddish-violet, with ferric chloride.

Ethyl 2-α-*anilinobenzyl*cyclo*pentan*-1-*one*-2-*carboxylate* (V), needles, m. p. 88° (Found: C, 74·7; H, 6·9; N, 4·0. $C_{21}H_{23}O_3N$ requires C, 74·8; H, 6·8; N, 4·2%), and *ethyl* 2-α-2′-*naphthylaminobenzyl*cyclo*pentan*-1-*one*-2-*carboxylate* (V), needles, m. p. 111° (Found: C, 77·7; H, 6·5. $C_{25}H_{25}O_3N$ requires C, 77·5; H, 6·5%), are obtained similarly, the former from benzylideneaniline (18·1 g.) and alcohol (75 c.c.) (yield, 27 g.), the latter from benzylidene-β-naphthylamine (23·1 g.) and benzene (80 c.c.) (yield 17 g.), with, in each case, ethyl *cyclo*pentan-1-one-2-carboxylate (15·6 g.). Both give a reddish-violet coloration with ferric chloride.

Ethyl 2-*phenyl*-3 : 4-*trimethylene*-2 : 3-*dihydroquinoline*-3-*carboxylate* (VI), bright yellow needles, m. p. 102° (Found: C, 79·0, 78·8; H, 6·7, 6·6; N, 4·4, 4·3; *M*, cryoscopic in benzene, 291. $C_{21}H_{21}O_2N$ requires C, 79·0; H, 6·6; N, 4·4%; *M*, 319) (yield, 7 g.), and *ethyl* 3-*phenyl*-1 : 2-*trimethylene*-2 : 3-*dihydro*-β-*naphthaquinoline*-2-*carboxylate* (VII), bright yellow needles, m. p. 130° (Found: C, 81·2; H, 6·3; N, 4·0; *M*, in benzene, 354. $C_{25}H_{23}O_2N$ requires C, 81·3; H, 6·2; N, 3·8%; *M*, 369) (yield, 8 g.), are obtained by refluxing (15 mins.), with glacial acetic acid (70 c.c.), and absolute alcohol (70 c.c.), ethyl 2-α-anilinobenzyl*cyclo*pentan-1-one-2-carboxylate (14 g.) and ethyl 2-α-2′-naphthylaminobenzyl*cyclo*pentan-1-one-2-carboxylate (16 g.), respectively. These two substances are also obtained, in even better yield, by refluxing ethyl *cyclo*pentan-1-one-2-carboxylate (1 mol.), glacial acetic acid, absolute alcohol, and either benzylideneaniline (1 mol.) or benzylidene-β-naphthylamine (1 mol.), without isolation of the intermediate addition compounds. Further, it has been found that Bertini's *m*-diazine derivative (I) can be obtained in good yield by the direct action of glacial acetic acid and absolute alcohol on a mixture of benzylideneaniline and acetoacetic ester.

2-*Anilinomethyl*-1-*naphthol*, rhombic prisms, m. p. 117° (Found: C, 81·8; H, 6·3; N, 5·6%), and 1-*anilinomethyl*-2-*naphthol*, needles, m. p. 132° (Found: C, 81·6; H, 6·3; N, 5·7. $C_{17}H_{15}ON$ requires C, 81·9; H, 6·0; N, 5·6%), are formed by allowing a solution of methyleneaniline (2·3 g.) and either α- or β-naphthol (3·1 g.) in benzene (16 c.c.) to stand (2 days), diluting it, after concentration, with ligroin, and recrystallising the product from ligroin–benzene. Their benzene solutions give a reddish-violet coloration with ethereal ferric chloride. Similarly obtained, from cinnamylideneaniline (4·3 g.) and β-naphthol (3·1 g.) after a week, the oily solid precipitated on dilution with ligroin being pressed on porous earthenware and recrystallised from benzene, 1-α-*anilinocinnamyl*-2-*naphthol*, needles, m. p. 218° (Found: C, 85·5; H, 6·1; N, 4·1. $C_{25}H_{21}ON$ requires C, 85·5; H, 6·0; N, 4·0%), gives no coloration with ferric chloride. The *monoacetyl* derivative of 2-anilinomethyl-1-naphthol, needles, m. p. 127° (Found: C, 78·1; H, 6·0; N, 5·0%), and the *monoacetyl* derivative of 1-anilinomethyl-2-naphthol, rectangular plates, m. p. 176° (Found: C, 78·2; H, 6·0; N, 4·8. $C_{19}H_{17}O_2N$ requires C, 78·3; H, 5·8; N, 4·8%), give no coloration with ferric chloride.

2-*Phenylhydrazinomethyl*-1-*naphthol* (X), yellow needles, m. p. 106° (Found: N, 10·7%), and 1-*phenylhydrazinomethyl*-2-*naphthol* (XI), yellow needles, m. p. 206° (decomp.) (Found: N, 9·8. $C_{17}H_{16}ON_2$ requires N, 10·6%), separate when hot mixtures of the corresponding anilinomethyl compounds with phenylhydrazine in alcohol are cooled; they are recrystallised from alcohol.

2 : 3-*Diphenyl*-2 : 3-*dihydro*-1 : 3-α-*naphthoxazine* (VIII), prisms, m. p. 150° (Found: C, 85·5; H, 5·8; N, 4·2%), and 2 : 3-*diphenyl*-2 : 3-*dihydro*-2 : 4-β-*naphthoxazine* (IX), prisms, m. p. 140° (Found: C, 85·6; H, 5·8; N, 4·1. $C_{24}H_{19}ON$ requires C, 85·5; H, 5·6; N, 4·2%), are best obtained by heating together at 110° (5 mins.) the parent anilinomethyl compounds (1 mol.) with benzaldehyde (1 mol.), washing the products with absolute alcohol, and recrystallising them from ligroin–benzene. They may also be prepared directly by keeping an alcoholic solution of methyleneaniline (1 mol.), the corresponding naphthol (1 mol.), and benzaldehyde (2 mols.) for a week. In benzene these oxazines give a reddish-brown coloration with ethereal ferric chloride.

Ethyl 2-*camphoryliminocyclopentane*-1-*carboxylate* (XII), needles, m. p. 129° (Found: C, 70·8; H, 9·0; N, 4·6. $C_{18}H_{27}O_3N$ requires C, 70·8; H, 8·9; N, 4·6%), is obtained by refluxing (2 hours) a solution of α-aminocamphor (6·0 g.), ethyl *cyclo*pentan-1-one-2-carboxylate (5·6 g.), and sodium acetate (5·0 g.) in 75% aqueous acetic acid (36 g.), diluting the solution with water, taking up the precipitated oil in ether, separating, drying, and concentrating the ethereal solution, and recrystallising the product from alcohol (yield, 3·1 g.). It gives yellow colorations in alcohol both with ferric chloride and with sodium ethoxide.

3-*Methyl*-2 : 3-o-*benzoyleneindolenine* (XIV), yellow rhombic prisms, m. p. 175° (Found : C, 82·4; H, 4·8; N, 6·2; *M*, in benzene, 241. $C_{16}H_{11}ON$ requires C, 82·4; H, 4·7; N, 6·0%; *M*, 233), and 3-*phenyl*-2 : 3-o-*benzoyleneindolenine* (XIV), fine yellow needles, m. p. 225° (Found : C, 85·3; H, 4·6; N, 4·8; *M*, in benzene, 307. $C_{21}H_{13}ON$ requires C, 85·4; H, 4·4; N, 4·7%; *M*, 295), are obtained by refluxing (3 hours) the parent monophenylhydrazone of 1 : 3-diketo-2-methylhydrindene (4 g.) (Wislicenus and Kötze, *Annalen*, 1889, **252**, 81) and the monophenylhydrazone of 1 : 3-diketo-2-phenylhydrindene (5 g.) (Nathanson, *Ber.*, 1893, **26**, 2576), respectively, anhydrous zinc chloride (32 g.), and absolute alcohol (20 c.c.), twice washing the product with cold dilute N-hydrochloric acid, drying, extracting impurities with warm alcohol, and recrystallising the residual benzoyleneindolenine from ligroin–benzene (yields, 1·5 g. and 1·7 g.).

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[*Received, January 4th,* 1938.]