NOTES.

551. *Action of* N-*Bromosuccinimide and* N-*Bromophthalimide on* α-*Amino-acids.*

By A. SCHÖNBERG, R. MOUBASHER, and M. Z. BARAKAT.

THERE seem to have been no reports about the reaction mentioned in the title. *N*-Bromosuccinimide reacts vigorously at room temperature with α-amino-acids (*e.g.*, alanine, leucine, and α-phenylglycine), yielding aldehydes containing one carbon atom less, *e.g.*, acetaldehyde, *iso*valeraldehyde, and benzaldehyde respectively. Evolution of carbon dioxide was proved in the case of alanine.

$$\begin{matrix}CH_2\cdot CO\\CH_2\cdot CO\end{matrix}\!\!>\!NBr + R'\cdot NH\cdot CHR\cdot CO_2H \longrightarrow R'\cdot NBr\cdot CHR\cdot CO_2H \text{ (or } R'\cdot NH\cdot CRBr\cdot CO_2H) + \begin{matrix}CH_2\cdot CO\\CH_2\cdot CO\end{matrix}\!\!>\!NH$$

$$\longrightarrow R'\cdot N{:}CR\cdot CO_2H \xrightarrow{H_2O} CO_2 + NH_2R' + R\cdot CHO$$

Sarcosine (*N*-methyglycine) yields formaldehyde when treated with bromosuccinimide. This distinguishes the reaction from the degradation of α-amino-acids effected by polyketones, *e.g.*, benzoquinone (Schönberg, Moubasher, and Mostafa, *J.*, 1948, 176), where no degradation is effected when one of the hydrogen atoms of the α-amino-acid is substituted.

When *N*-bromophthalimide was used to degrade alanine and α-phenylglycine in an aqueous medium, warming was necessary for rapid degradation.

Experimental.—Action of N-*bromosuccinimide on* α-*amino-acids.* (*a*) *N*-Bromosuccinimide (1 g.) was allowed to react for 10 minutes without cooling (shaking) with alanine (1·5 g.) or leucine (1·3 g.) in water (35 c.c.), a vigorous reaction taking place with the formation of a red-brown colour. The mixture was then cooled and 2 : 4-dinitrophenylhydrazine hydrochloride in aqueous alcohol was added; an orange precipitate which formed was filtered off and crystallised from alcohol, giving the 2 : 4-dinitro-

phenylhydrazone of acetaldehyde or *iso*valeraldehyde respectively (m. p. and mixed m. p.) in about 50% yield.

When the reaction was carried out with α-phenylglycine, the product was filtered off and to the filtrate 2 : 4-dinitrophenylhydrazine hydrochloride (as above) was added. Benzaldehyde 2 : 4-dinitrophenylhydrazone was obtained, crystallised and identified as above, the yield being about 40%.

(*b*) *N*-Bromosuccinimide (1 g.) and sarcosine hydrochloride (0·6 g.) in water (30 c.c.) were refluxed in the apparatus previously described (Schönberg, Moubasher, and Mostafa, *loc. cit.*) in a stream of carbon dioxide for 90 minutes. The receiver contained 2 : 4-dinitrophenylhydrazine (0·6 g.) in alcohol (20 c.c.). At the end of the experiment concentrated hydrochloric acid (5 c.c.) was added, orange crystals (0·08 g.) being obtained and crystallised from ethyl alcohol. They were proved by their m. p. and mixed m. p. to be formaldehyde 2 : 4-dinitrophenylhydrazone.

Formation of carbon dioxide and succinimide in the degradation. *N*-Bromosuccinimide (1 g., 1 mol.) was added to alanine (1 mol.) in water (35 c.c.) and the reaction allowed to proceed as above; the mixture was then concentrated by heat and brought to dryness under reduced pressure. The residue was recrystallised from benzene and proved to be succinimide by its m. p. and mixed m. p. (yield, 0·25 g.). The evolution of carbon dioxide during the degradation was proved (barium hydroxide).

Action of N-*bromophthalimide on* α-*amino-acids.* *N*-Bromophthalimide (freshly prepared; 1 g.) was heated gently under a reflux condenser to about 90° for 3 minutes with alanine (0·4 g.) or α-phenylglycine (0·33 g.) in water (50 c.c.), whereupon a vigorous reaction took place. The mixture was then allowed to cool with continuous shaking and filtered. The solid yielded phthalimide (m. p. and mixed m. p.). The filtrate was treated with excess of 2 : 4-dinitrophenylhydrazine hydrochloride in aqueous alcohol, whereupon orange crystals were formed; the mixture was kept in ice for 1 hour, and the deposit was crystallised from ethyl alcohol and proved to be the 2 : 4-dinitrophenylhydrazone of acetaldehyde and benzaldehyde respectively; the yield was about 25—35%.

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552. *Ethyl Calcioacetoacetate.*

By R. H. HACKMAN.

ETHYL CALCIOACETOACETATE has been prepared previously by the action of metallic calcium (Erdmann and van de Smissen, *Annalen*, 1908, **361**, 66) or calcium carbide (Packendorff, *Ber.*, 1931, **64**, *B*, 948) on ethyl acetoacetate. Only by the first method was the material isolated. It is now shown that it may be conveniently prepared by the action of calcium oxide on the ester. This calcium compound can be used in the typical condensations of ethyl acetoacetate with alkyl and acyl halides, but the yields with it are less than those obtained by use of the sodium derivative. They are, however, comparable with those obtained by the use of calcium ethoxide (Perkin and Pratt, *J.*, 1909, **95**, 159). The calcium derivative thus provides a useful alternative when metallic sodium is not available; moreover, the calcium compound, unlike that of sodium, is not hydrolysed by cold water.

Experimental.—Preparation. (*a*) To ethyl acetoacetate (20 g.) in dry benzene (200 ml.) freshly calcined calcium oxide (6 g.) was added in small portions so as to prevent the reaction becoming too vigorous. The mixture was heated on a steam-bath until the benzene which distilled was no longer turbid. The solid which separated when the solution cooled was collected and exhaustively extracted with hot benzene. The extract, after concentration, was cooled, whereupon the white calcium compound (16·1 g., 85% on ester consumed) separated; it had m. p. 220—221° (Erdmann and van de Smissen, *loc. cit.*, recorded m. p. 215—220°) (Found: Ca, 13·5. Calc. for $C_{12}H_{18}O_6Ca$: Ca, 13·4%).

(*b*) Ethyl acetoacetate (43 g.), dry benzene (170 ml.), and calcium carbide (14 g.) were heated under reflux for 2 hours. The solution was cooled, and the solid which separated was collected and exhaustively extracted with hot benzene. The benzene extract was concentrated and cooled, and the solid which separated was collected by filtration. The derivative (43 g., 87%) had m. p. 220—221°.

Condensation reactions. (*a*) With ethyl iodide. Ethyl calcioacetoacetate (12 g.), dry ethanol (50 ml.), and ethyl iodide (13 g.) were boiled under reflux for 7 hours. During the first 2 hours all the calcium compound went into solution. After removal of the ethanol and excess of ethyl iodide by distillation, water was added, the esters were extracted in ether, this extract was washed with water and dried ($MgSO_4$), the ether evaporated, and the residue distilled, giving ethyl ethylacetoacetate (5·3 g., 42%), b. p. 189°/743 mm.

(*b*) With acetyl chloride. Ethyl calcioacetoacetate (14·3 g.), dry benzene (100 ml.), and acetyl chloride (8·8 g.) were boiled under reflux for 10 hours. After removal of the benzene and excess of acetyl

chloride the product was worked up as in (*a*), above. The diacetoacetic ester (8·7 g., 53%), b. p. 120°/45 mm., was identified as the copper salt, m. p. 148°.

(*c*) With benzoyl chloride. Prepared as for the acetyl derivative, ethyl benzoylacetoacetate (64%) had b. p. 184°/22 mm.

The author acknowledges the assistance given by Professor J. C. Earl, formerly of the University of Sydney, who suggested the work.

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[redacted]

Lupeol chloroacetate. Lupeol (500 mg.) was dissolved in dry benzene (25 c.c.), and chloroacetyl chloride (1·25 c.c.) and diethylaniline (2·5 c.c.) were added. After 24 hours at 20° the solution was decanted from the separated diethylaniline hydrochloride and washed with water, dilute hydrochloric acid, and again with water. The product obtained after the solution had been dried and the solvent evaporated was adsorbed from *n*-pentane–benzene (1 : 2) on to a column of alumina (50 g.; activity I—II). The fraction (565 mg.) eluted with *n*-pentane–benzene (1 : 1; 200 c.c.) was crystallised from chloroform–methanol, giving platelets of *lupeol chloroacetate* (302 mg.), m. p. 177—184° raised by further recrystallisations from the same solvent to 186—188°, $[\alpha]_D^{20}$ +45° (*c*, 1·30) (Found: C, 76·2; H, 10·25; Cl, 7·35. $C_{32}H_{51}O_2Cl$ requires C, 76·4; H, 10·2; Cl, 7·05%).

α-Amyrin chloroacetate. α-Amyrin (4·0 g.) was treated in like manner yielding *α-amyrin chloroacetate* which was crystallised several times from chloroform–methanol; it formed platelets (1·68 g., 36%), m. p. 200—202°, $[\alpha]_D^{20}$ +73° (*c*, 1·93) (Found: C, 76·45; H, 10·15; Cl, 7·35. $C_{32}H_{51}O_2Cl$ requires C, 76·4; H, 10·2; Cl, 7·05%).

β-Amyrin chloroacetate. β-Amyrin (3·0 g.) gave the *chloroacetate*, which, after being crystallised several times from chloroform–methanol, formed platelets (1·95 g., 55%), m. p. 186·5—188°, $[\alpha]_D^{20}$ +81° (*c*, 1·97) (Found: C, 76·15; H, 10·25; Cl, 6·9. $C_{32}H_{51}O_2Cl$ requires C, 76·4; H, 10·2; Cl, 7·05%).

Lupeol iodoacetate. Lupeol chloroacetate (254 mg.) was heated under reflux with potassium iodide (750 mg.) in acetone (150 c.c.) for 4 hours. The solution was concentrated in a vacuum and the product, isolated by ethereal extraction after dilution with water, was crystallised from chloroform–methanol giving platelets of *lupeol iodoacetate* (266 mg.), m. p. 185—195° raised by two recrystallisations from ethyl acetate–methanol to 195—197°, $[\alpha]_D^{20}$ +37° (*c*, 1·34) (Found: C, 65·0; H, 9·0; I, 21·7. $C_{32}H_{51}O_2I$ requires C, 64·65; H, 8·65; I, 21·35%).

α-Amyrin iodoacetate. The chloroacetate (1·50 g.) yielded the *iodoacetate*, which was crystallised several times from chloroform–methanol and formed flat needles (1·05 g., 59%), m. p. 174—175°, $[\alpha]_D^{20}$ +66° (*c*, 1·95) (Found: C, 64·65; H, 8·4; I, 21·2. $C_{32}H_{51}O_2I$ requires C, 64·65; H, 8·65; I, 21·35%).

β-Amyrin iodoacetate. Prepared from the chloroacetate (1·95 g.) the *iodoacetate* crystallised from chloroform–methanol as platelets (1·25 g.), m. p. 166·5—167°, $[\alpha]_D^{20}$ +74° (*c*, 1·50) (Found: C, 64·8; H, 8·65; I, 21·65. $C_{32}H_{51}O_2I$ requires C, 64·65; H, 8·65; I, 21·35%).

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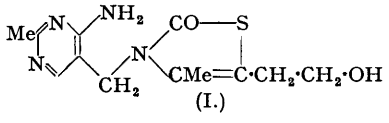
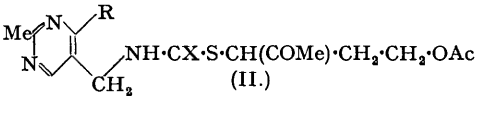
555. *The Synthesis of "Aneurin Thiazolone."*

By PETER SYKES.

IN a recent paper on the mechanism of thiochrome formation from aneurin and aneurin disulphide (Sykes and Todd, *J.*, 1951, 534), much of the argument turned on the structure of an "aneurin thiazolone" obtained by refluxing aneurin disulphide in a number of different solvents. It has now proved possible to confirm that the "thiazolone" has the structure (I) by synthesis and demonstration of the identity of the material with the thiazolone derived from aneurin disulphide.


(I.)


(II.)

It may be prepared either by cyclisation of the intermediate *S*-(3-acetoxy-1-acetylpropyl) *N*-(4-amino-2-methyl-5-pyrimidylmethyl)thiolcarbamate (II; R = NH_2, X = O) in the presence of dilute hydrochloric acid (the ω-acetyl group being simultaneously removed from the side chain), or from 4-amino-5-aminomethyl-2-methylpyrimidine, carbon oxysulphide, and 3-acetoxy-1-chloropropyl methyl ketone, involving treatment with acid (cf. Matsukawa and Iwatsu, *J. Pharm. Soc. Japan*, 1950, **70**, 28). Dilute hydrochloric acid appears to be a fairly general, if somewhat surprising, reagent for this type of closure for, by its aid, we have been able to cyclise 3-acetoxy-1-acetylpropyl *N*-(4-amino-2-methyl-5-pyrimidylmethyl)dithiocarbamate (II; R = NH_2, X = S), 3-acetoxy-1-acetylpropyl *N*-(4-hydroxy-2-methyl-5-pyrimidylmethyl)dithiocarbamate (II; R = OH, X = S), and phenacyl *N*-benzyldithiocarbamate. Too high a temperature (*e.g.*, refluxing) or too prolonged action of the reagent

result in the decomposition of the cyclic compound first formed. With *S*-phenacyl *N*-benzylthiolcarbamate some ring closure could be made to take place, but the starting material underwent extensive hydrolysis.

Experimental.—3-(4-*Amino*-2-*methyl*-5-*pyrimidylmethyl*)-5-2′-*hydroxyethyl*-4-*methylthiazol*-2-*one* ("*aneurin thiazolone*") (I): (a) *From the thiolcarbamate* (II; R = NH_2, X = O). *S*-(3-Acetoxy-1-acetylpropyl) *N*-(4-amino-2-methyl-5-pyrimidylmethyl)thiolcarbamate (Sykes and Todd, *loc. cit.*) (0·5 g.) was heated in 3N-hydrochloric acid (10 ml.) on a steam-bath for 10 minutes, cooled, made just alkaline with 3N-sodium hydroxide, and set aside till no more solid separated. The thiazolone crystallised as colourless needles (from ethanol), m. p. and mixed m. p. with natural "aneurin thiazolone," 237° (Found: C, 51·7; H, 6·0; N, 19·7. Calc. for $C_{12}H_{16}O_2N_4S$: C, 51·5; H, 5·8; N, 20·0%). The yield was quantitative.

(b) *From* 4-*amino*-5-*aminomethyl*-2-*methylpyrimidine*. 4-Amino-5-aminomethyl-2-methylpyrimidine dihydrochloride (2·1 g.) was treated with a solution of potassium hydroxide (1·1 g.) in methanol (25 ml.), the separated potassium chloride was filtered off, and 3-acetoxy-1-chloropropyl methyl ketone (1·8 g.) added, followed by 20% aqueous ammonia (1 ml.) and an ice-cold saturated solution of carbon oxysulphide in methanol (100 ml.). A stream of dry carbon oxysulphide was passed in for 10 minutes, and the solution then evaporated to dryness *in vacuo*. The residue was washed with water, taken up in hydrochloric acid (10%; 25 ml.), warmed on the steam-bath for 10 minutes, and finally neutralised with 10% sodium hydroxide solution. The product separated as colourless needles (from ethanol), m. p. and mixed m. p. with natural "aneurin thiazolone," 237°.

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556. *Acenaphthene Series. Part VI.* The Three Nuclear-substituted Ethylacenaphthenes.*

By ERIC ILLINGWORTH and ARNOLD T. PETERS.

THE liquid ethylacenaphthene, prepared by the Friedel–Crafts reaction from acenaphthene by means of ethyl bromide and aluminium chloride, was shown by Nürsten and Peters (*J.*, 1950, 2389) to be 2-ethylacenaphthene, whereas solid 3-ethylacenaphthene was obtained by reducing 3-acetylacenaphthene. 1-Ethylacenaphthene has been recorded as both an oil and a solid, and since none of its derivatives has been prepared it was synthesised and its derivatives compared with the isomers obtained from 2- and 3-ethylacenaphthene, respectively.

1-Chloromethyl-2-ethylnaphthalene, recorded as an oil by Buu-Hoï and Cagniant (*Rev. Sci.*, 1942, **80**, 271) and by Bachmann and Sheehan (*J. Amer. Chem. Soc.*, 1941, **63**, 2599), was isolated by the present authors in colourless plates, m. p. 69—70°, and converted by a modification of the published methods (*locc. cit.*) into 1-ethylacenaphthenone, and thence into 1-ethylacenaphthene, m. p. 29—30° (picrate, m. p. 104—105°). Oxidation then gave 2-ethylnaphthalic anhydride, which afforded an imide and a *N*-methylimide which differed from the isomers obtained similarly from 3- and 4-ethylnaphthalic anhydride. Moreover, the scarlet vat dye prepared from 1-ethylacenaphthenequinone by condensation with 2-hydroxythionaphthen, differed from the analogous thioindigoid dyes obtained from 2- and 3-ethylacenaphthenequinone. The previous Table (*J.*, 1950, p. 2389) is now complete.

Experimental.—M. p.s are corrected. Micro-analyses were carried out by Drs. Weiler and Strauss, of Oxford.

2-*Ethylnaphthalic anhydride*. 1-Ethylacenaphthenone (3 g.) was dissolved in boiling acetic acid (140 c.c.), the flame removed, and powdered sodium dichromate (12 g.) added at such a rate as to keep the mixture boiling gently. The mixture was then refluxed for 3 hours and added to water, the precipitate was collected and extracted with boiling 5% aqueous sodium carbonate, and the cooled extracts were acidified. 2-*Ethylnaphthalic anhydride* crystallised from alcohol in colourless needles, m. p. 165—166° (2·5 g., 73%) (Found: C, 73·9; H, 4·2. $C_{14}H_{10}O_3$ requires C, 74·3; H, 4·4%). On admixture with 3-, m. p. 192—193°, and 4-ethylnaphthalic anhydride, m. p. 164—164·5°, it melted at 140—150° and 128—132°, respectively.

2-*Ethylnaphthalimide*. The anhydride (1 g.), alcohol (4 c.c.), and aqueous ammonia (*d* 0·88; 4 c.c.) were heated at 100° for 4 hours in a sealed tube. The *imide* crystallised from alcohol in prismatic needles, m. p. 221·5—222·5° (Found: C, 74·4; H, 4·9; N, 6·1. $C_{14}H_{11}O_2N$ requires C, 74·3; H, 5·1; N, 6·2%). It depressed the m. p. of the 3-, m. p. 217—218·5°, and 4-isomer, m. p. 195—196°, to 180—186° and 175—180°, respectively.

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* Part V, *J.*, 1951, 1602.

2-*Ethyl*-N-*methylnaphthalimide*. The anhydride (1 g.), 33% aqueous methylamine (4 c.c.), and alcohol (4 c.c.) at 100° (1 hour) gave the N-*methylimide*, which crystallised from alcohol in prismatic needles, m. p. 117—118° (Found: C, 75·5; H, 5·5; N, 6·0. $C_{15}H_{13}O_2N$ requires C, 75·3; H, 5·4; N, 5·9%). Admixture with the 3-, m. p. 113—114°, and 4-isomer, m. p. 140°, gave m. p.s 84—95° and 85—97° respectively.

1′-*Ethyl*-1-*thionaphthen*-7′(or -6′)-*acenaphthenylindigo*.—1-Ethylacenaphthenequinone (1 g.) in boiling acetic acid (20 c.c.) was mixed with 2-hydroxythionaphthen (2 g.) in acetic and hydrochloric acids (5 : 1; 20 c.c.); during several minutes' boiling, a red precipitate was formed progressively. Crystallisation of this from toluene gave bright scarlet prismatic needles, m. p. 206·5—207°, of the *dye* (Found: C, 77·2; H, 4·1; S, 9·4. $C_{22}H_{14}O_2S$ requires C, 76·9; H, 4·1; S, 9·4%), which dissolved in concentrated sulphuric acid with a green colour, becoming pink on dilution. Cotton is dyed salmon-pink from a violet alkaline dithionite (hydrosulphite) vat. On admixture with the 2′(or 5′)-, m. p. 204—206°, or the 3′(or 4′)-isomeric dye, m. p. 216—217°, the m. p. was depressed to 170—185° and 174—190°, respectively.

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