NOTES.

983. *An Anthocyanidin of Louro Inamui.*

By ERIC COCKER and WESLEY COCKER.

LOURO INAMUI (*Nectandra eleophora*), a Brazilian hardwood, sometimes used as a substitute for teak, has a high terpene content which has been investigated by Naves (*Bull. Soc. chim.*, 1951, 987). However, extraction of shavings of the wood with hot 1% hydrochloric acid afforded a pink-to-brown solution (A), obviously containing anthocyanin.

Hydrolysis of (A), with boiling 10% hydrochloric acid for 2 minutes, yielded an amber-coloured solution (B) of anthocyanidin which was extracted with amyl alcohol and purified by the methods of Robinson and Robinson (*Biochem. J.*, 1931, **25**, 1687; 1932, **26**, 1647). The colouring matter was investigated (*a*) by the comparative colour reactions employed by Robinson and Robinson (*loc. cit.*), the standards being anthocyanidins (see table) obtained from various flowers and woods (cf. also Robinson and Robinson, *Biochem. J.*, 1933, **27**, 206) or by synthesis, and (*b*) by ascending-front paper chromatography (Bate-Smith, *Nature*, 1948, **161**, 835).

Before hydrolysis, the solution (A) gave a mauve colour with sodium carbonate. Dilution of (A) with alcohol gave a mauve-yellow colour, and the anthocyanin was readily extracted from (A) with amyl alcohol.

The anthocyanidin was easily extracted from (B) with amyl alcohol, which became brown-mauve with sodium acetate. Treatment of the mixture with a drop of ferric chloride solution turned the amyl alcohol layer purple, and the aqueous layer blue. The anthocyanidin was recovered unchanged in the oxidation test; it was not extracted by the cyanidin, and only partly extracted from concentrated solution, but completely extracted on dilution by the delphinidin reagent. Eight volumes of benzene were required to drive the anthocyanidin from amyl alcohol into 1% hydrochloric acid. The above colour reactions and distribution ratios suggest that the wood extract has similarities to malvidin, pelargonidin, and peonidin, but the first two are eliminated by chromatography.

The table gives the chromatographic characteristics of the wood extract (B) and a selection of anthocyanidins run simultaneously on the same paper. Under the conditions employed, the anthocyanidins can be placed in groups (cf. Bate-Smith, *loc. cit.*) but cannot be separately identified.

Anthocyanidin	Source	R_F value: C. & C.*	R_F value: B.-S.†
Wood extract	Louro Inamui	0·37	—
Peonidin	*Paeonia officianalis*	0·37	0·38
Pelargonidin	Strawberries	0·49	—
Cyanidin	(*a*) Synthetic	0·47	—
	(*b*) *Centaurea cyanus* Linn.	0·47	0·24
Malvidin	(*a*) *Malva sylvestris* Linn.	0·49	—
	(*b*) *Epilobium angustifolium* Linn.	0·49	0·54
Delphinidin	(*a*) *Delphinium Lorna.*	0·36	—
	(*b*) *Campanula glomerata* Linn.	0·36	—
Peltogynidin	*Copaiferra pubiflora* (purple heart)	0·44	—

The solvent employed in the tank was butanol–acetic acid–water (40 : 10 : 50) (cf. Bate-Smith, *loc. cit.*).

* We spotted the filter paper with 1% hydrochloric acid solutions of the anthocyanidins; temp. 18° ± 1·5°. Chromatographic runs were made at least 12 times, and R_F values showed variation of only 0·01—0·02.

† Bate-Smith employed 5·5% hydrochloric acid solutions of the anthocyanidins.

The Louro extract falls into the same group as delphinidin and peonidin, but colour reactions and distribution ratio eliminate the former. It is probable, therefore, that the Louro extract contains a new anthocyanidin which, in the majority of its properties, behaves most like peonidin.

The sugars involved have not been investigated, but a leuco-anthocyanin in the wood can be extracted by boiling glacial acetic acid, from which, by heating with 5% hydrochloric acid, a very weak solution of the anthocyanidin may be obtained.

Extraction of Louro Inamui with acetone or methyl alcohol, yields a waxy solid, which gives colour reactions indicative of steroid. This is now being investigated.

We thank the Director of the Botanical Gardens, Dublin, for a gift of flowers, and Professor D. A. Webb for the *Copaiferra pubiflora*.

TRINITY COLLEGE, DUBLIN. [*Received, July 27th*, 1952.]

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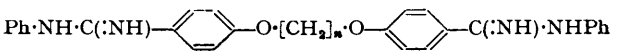
984. *Synthesis of Di-(p-N-phenylamidinophenoxy)methane.*

By F. C. COOPER and M. W. PARTRIDGE.

IN a series of di-(*p-N*-phenylamidinophenoxy)alkanes (I), activity *in vitro* against *Mycobacterium tuberculosis* is considerable when $n = 3$ or 5, but nil when $n = 2$, 4, or 6 (Partridge, *J.*, 1949, 2683). The first member of the series (I; $n = 1$) could not be prepared by the methods then available. We now describe the production of this compound by reaction of the corresponding dinitrile with aniline in the presence of sodamide (Cooper and Partridge, *J.*, in the press) and by a modification of the Pinner reaction; in both cases the yields were small.



(I)

Although the details of the mechanism of the Pinner reaction have not been fully elucidated, it appears that the second stage is facilitated when the equilibrium set up between the reactants,

$$R\cdot C(:\overset{+}{N}H_2)\cdot OEt\}\overset{-}{Cl} + NHR'R'' \rightleftharpoons R\cdot C(:NH)\cdot OEt + \overset{+}{N}H_2R'R''\}\overset{-}{Cl}$$

is displaced in favour of the free ethyl imidate by employing an appropriate excess of a base, NHR'R'', of sufficiently high basic strength (Knorr, *Ber.*, 1917, **50**, 229; Ashley, Barber, Ewins, Newbery, and Self, *J.*, 1942, 113; Delaby, Harispe, and Bonhomme, *Bull. Soc. chim.*, 1945, **12**, 152). In agreement with this, *N*-arylamidines are not obtained in good yield by aminolysis of ethyl imidates by the weakly basic arylamines (Hill and

Rabinowitz, *J. Amer. Chem. Soc.*, 1926, **48**, 732; Delaby *et al.*, *loc. cit.*). By use of a 2-nitroalkyl imidate, which would very probably be a weaker base than an ethyl imidate, two simple *N*-arylamidines have been obtained in satisfactory yield. Thus benzonitrile, brought into reaction with 2-nitrobutanol in the presence of hydrogen chloride, gave 2-nitrobutyl benzimidate hydrochloride in 60% yield. With *p*-anisidine, this afforded *N*-*p*-methoxyphenylbenzamidine (82%); with aniline the yield of *N*-phenylbenzamidine was 46%, whereas by the ethyl benzimidate route under the same conditions the yield was 6%. These results differ from those of Delaby *et al.* (*loc. cit.*), who state that the constitution of the imidic ester has little influence on the yield of amidine. By the nitro-alcohol method, di-(*p*-*N*-phenylamidinophenoxy)methane was obtained in 0·5% yield.

By the method of testing previously employed (Partridge, *loc. cit.*; Crowshaw and Dickinson, *Brit. J. Pharmacol. Chemotherapy*, 1950, **5**, 178), di-(*p*-*N*-phenylamidino-phenoxy)methane was found to be active at a dilution of 1 in 3000 and partially active at 1 in 9000 in the presence of 10% of serum. This further confirms the alternation in anti-tuberculous activity in this homologous series, although the difference in activity between homologues in which $n = 1$ and $n = 3$ is greater than that found between $n = 3$ and $n = 5$.

Experimental.—*2-Nitrobutyl benzimidate hydrochloride.* A mixture of benzonitrile (10·3 g.) and 2-nitrobutanol (11·9 g., 1 mol.) was saturated with dry hydrogen chloride at 0° and kept at 0° for 3 days. The white, crystalline *salt* was washed with dry ether and dried in a vacuum (yield, 15·5 g., 60%; m. p. 140—141°) (Found: C, 51·6; H, 5·7. $C_{11}H_{15}O_3N_2Cl$ requires C, 51·1; H, 5·8%).

N-p-*Methoxyphenylbenzamidine.* A solution of 2-nitrobutyl benzimidate hydrochloride (15 g.) and *p*-anisidine (8·6 g., 1·2 mols.) in dry ethanol (150 c.c.) was kept for 3 days. After evaporation of the solvent, basic material was collected in benzene; an acetate buffer extract (pH 4·5) of the benzene afforded on the addition of ammonia *N*-*p*-methoxyphenylbenzamidine, m. p. and mixed m. p. 114—116° (10·7 g., 82%).

N-*Phenylbenzamidine.* Repetition of the foregoing experiment with aniline (1 mol. and 3 mols.) afforded *N*-phenylbenzamidine in 43% yield in both cases.

When the first stage of the reaction was conducted in dry ether for 2 weeks and aniline (5 ml.) was employed in the second stage, an overall yield of 46% was obtained; the use of ethanol instead of 2-nitrobutanol under the same conditions resulted in a 6% yield of the amidine.

Di-(p-N-*phenylamidinophenoxy*)*methane.* (*a*) A solution of di-*p*-cyanophenoxymethane (Ashley *et al.*, *loc. cit.*) (7·9 g.) and aniline (5·9 g., 2 mols.) in dry benzene (150 c.c.) was refluxed with granular sodamide (2·5 g., 2 mols.) for 5 days. The mixture was washed with water; basic material was extracted with aqueous lactic acid and precipitated by ammonia. On fractional crystallisation from ethanol the crude base (1·25 g.) afforded *di*-(p-N-*phenylamidino-phenoxy*)*methane* (0·5 g., 3·5%) as platelets, m. p. 207·5—208·5° (Found: C, 73·8; H, 5·45; N, 12·8. $C_{27}H_{24}O_2N_4$ requires C, 74·3; H, 5·5; N, 12·85%). The *dipicrate* separated from aqueous ethanol as yellow needles, m. p. 192—194° (Found: C, 52·4; H, 3·05; N, 15·8. $C_{39}H_{30}O_{16}N_{10}$ requires C, 52·35; H, 3·4; N, 15·65%). The concentrated mother liquors from the crystallisation of the diamidine deposited p-(p-*cyanophenoxymethoxy*)-N-*phenylbenzamidine* (0·1 g., 1%), which crystallised from ethanol as plates, m. p. 149—150°, depressed to 125—132° on admixture with the corresponding dinitrile (Found: C, 73·6; H, 5·35; N, 12·2. $C_{21}H_{17}O_2N_3$ requires C, 73·45; H, 5·0; N, 12·25%). Unchanged dinitrile (4·7 g., 60%), m. p. and mixed, m. p. 147·5—148·5°, was recovered from the non-basic fraction. When the reaction was conducted in boiling xylene for 36 hours, the yield of diamidine was 2% but no monoamidine was detected.

(*b*) The dinitrile (10 g.), suspended in a mixture of 2-nitrobutanol (10 g., 2·1 mols.) and dry ether (30 c.c.), was shaken for 14 days. The insoluble solid was collected, washed with ether, and dissolved in ethanol (75 c.c.); aniline (15 g., 4 mols.) was added and the mixture was kept for 7 days. From the basic fraction a crude picrate was prepared; this on treatment with acid afforded basic material (0·25 g.) which on crystallisation from ethanol gave the diamidine (0·07 g., 0·5%), m. p. and mixed m. p. 206—207·5°.

The authors gratefully acknowledge their indebtedness to Mr. C. E. Coulthard, Dr. L. Dickinson, and Miss B. Croshaw, of Boots Pure Drug Co., Ltd., for the biological tests.

THE UNIVERSITY, NOTTINGHAM. [*Received, September 26th*, 1952.]

985. *Some Compounds related to Hexœstrol.*

By D. A. Forss, W. Freund, and E. R. Stove.

Since the discovery by Dodds, Golberg, Lawson, and Robinson (*Nature*, 1938, **141**, 247; *Proc. Roy. Soc.*, 1939, *B*, **127**, 140) of the synthetic œstrogens hexœstrol and diethylstilbœstrol, numerous attempts have been made to obtain compounds with androgenic or progestational effect by introducing keto- or keto-alcohol groups into their skeleton.

In spite of many failures to prepare ketones of the hexœstrol type with androgenic activity it was considered worth while to prepare compounds which had the ketonic group in the aliphatic chain and not attached to the phenyl group, as in the compounds previously investigated. However, 3-*p*-methoxyphenyl-4-phenylhexan-2-one (Satriana, Loter, and Baizer, *J. Amer. Chem. Soc.*, 1951, **73**, 866) as well as the isomeric 4-*p*-methoxyphenyl-3-phenylhexan-2-one proved inactive.

Experimental

M. p.s are uncorrected.

3 : 4-*Diphenylhexan-2-one.*—αβ-Diphenylvaleronitrile (m. p. 115°; 11·8 g.; Kohler, *Amer. Chem. J.*, 1906, **35**, 386) was added slowly to a boiling solution of methylmagnesium iodide (from 15 g. of methyl iodide) in ether (200 c.c.). After approx. 5 hours' boiling, the same amount of Grignard solution and another 100 c.c. of ether were added. After another 10 hours' boiling, the solution was decomposed with water and dilute hydrochloric acid. The ether was washed with more dilute hydrochloric acid and water, dried (Na_2SO_4), and evaporated. The oily residue was digested with cold alcohol. The solid, after several recrystallisations from alcohol, melted at 127°, and was free from nitrogen. A considerable amount of pure ketone can be obtained from the extracted aqueous solution. Kohler reported m. p. 116°; his compound was probably contaminated with nitrile.

β-p-*Methoxyphenyl-α-phenylvaleronitrile.*—Condensation of *p*-methoxybenzaldehyde with benzyl cyanide gave β-cyano-4-methoxystilbene, m. p. 96° (Frost, *Annalen*, 1880, **250**, 159 reported 93°) after recrystallisation from alcohol. On to this (23·5 g.) in the thimble of a Soxhlet extractor a Grignard solution from ethyl bromide (*ca.* 26 g.), magnesium (5 g.), and ether (300 c.c.) was boiled until all had been dissolved (*ca.* 10 hours), more ether (100 c.c.) being meanwhile added. The Grignard solution was decomposed as above. A yellow solid was collected, washed with water, digested with a small amount of cold alcohol, and dried (tile). After two recrystallisations from alcohol, β-p-*methoxyphenyl-α-phenylvaleronitrile* separated in rods, m. p. 122° (Found: C, 81·5, 81·7; H, 7·3, 7·2; N, 5·3; MeO, 11·7. $C_{18}H_{19}ON$ requires C, 81·5; H, 7·2; N, 5·3; MeO, 11·7%). The ethereal layer was washed with dilute hydrochloric acid and water, dried (Na_2SO_4), and evaporated, leaving an oil which after digestion with alcohol yielded more of the compound of m. p. 122°. The yield of pure material was approx. 50%.

4-p-*Methoxyphenyl-3-phenylhexan-2-one.*—β-*p*-Methoxyphenyl-α-phenylvaleronitrile (13·3 g.) in a Soxhlet thimble was added by extraction to a boiling Grignard solution of methyl iodide (14·5 g.) in ether (200 c.c.). After 36 hours' refluxing, a Grignard solution from another 14·5 g. of methyl iodide was added, and the solution boiled for a further 12 hours, then decomposed as above. The ethereal layer, treated as above, gave a brown residue which on digestion with cold alcohol gave 4·9 g. of solid still giving a positive nitrogen test. After three recrystallisations from alcohol, nitrogen-free material was obtained. 4-p-*Methoxyphenyl-3-phenylhexan-2-one* formed needles, m. p. 109—110° (Found: C, 80·9, 80·9; H, 7·9, 7·9; MeO, 10·8. $C_{19}H_{22}O_2$ requires C, 80·9; H, 7·8; MeO, 11·0%). From the mother liquors of the recrystallisation, an isomeric *ketone*, m. p. 60—61°, was isolated in small quantities (Found: C, 81·0, 80·9; H, 7·9, 7·9%).

αβ-*Di*-p-*hydroxyphenylvaleric Acid.*—α-Cyano-4 : 4′-dimethoxystilbene (m. p. 108—109°; Niederl and Ziering, *J. Amer. Chem. Soc.*, 1942, **64**, 885) was treated with a Grignard solution of ethylmagnesium bromide. αβ-Di-*p*-methoxyphenylvaleronitrile, m. p. 130—131°, was obtained in agreement with Hunter and Korman (*ibid.*, 1948, **70**, 3424). This (7 g.) was heated with concentrated hydrochloric acid (23 c.c.) at 210—215° for 4 hours. The product (partly solid) was dissolved in sodium hydrogen carbonate solution (solution deep red) which after filtration was made nearly neutral with N-hydrochloric acid. A dark brown resin was precipitated, filtered off, and dried (substance A). The filtrate was made strongly acid (pH 1—2) and the

white solid which was precipitated was immediately filtered off (substance B). The filtrate gradually deposited colourless crystalline material (substance C).

Substance A did not yield a uniform compound.

Substance B (0·9 g.; m. p. 221—229°) was recrystallised from 180 c.c. of water, giving 0·4 g. of material, m. p. 234—244°. This (1 g.) was heated with acetyl chloride giving αβ-*di*-p-*acetoxyphenylvaleric acid*, m. p. 215—216° (from alcohol) (Found: C 68·2, 68·2; H, 6·0, 6·1. $C_{21}H_{22}O_6$ requires C, 68·1; H, 6·0%).

Substance C (0·1 g.), recrystallised from water, gave needles, m. p. 188—191°, the lower-melting isomer of αβ-*di*-p-*hydroxyphenylvaleric acid* (Found: C, 71·4, 71·4; H, 6·1, 6·4. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%).

The diacetate of m. p. 216° gave, on hydrolysis, the higher-melting *isomer*, m. p. 243—245° (Found: C, 71·3, 71·3; H, 6·3, 6·3%).

I thank Dr. M. J. Etheridge of the Physiology Department for the biological assays, and Dr. K. F. Tettweiler, formerly of the University of Melbourne, for the microanalyses. This work was supported in part by a grant from the National Council for Health and Medical Research, Canberra.

Department of Physiology, The University, Melbourne. [*Received, November 7th*, 1951.]

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986. *The Infra-red Spectra of Methyl Ximenynate and Ximenynyl Alcohol.*

By N. H. E. Ahlers and S. P. Ligthelm.

The infra-red spectra of methyl ximenynate and ximenynyl alcohol (Ligthelm and Schwartz, *J. Amer. Chem. Soc.*, 1950, **72**, 1868; Ligthelm, Schwartz, and von Holdt, *J.*, 1952, 1088) have been determined by using a Perkin Elmer 12B spectrometer with path lengths of *ca.* 10μ and 50μ to resolve all absorption maxima in the range 2·5—15μ. The compounds were placed undiluted between rocksalt plates.

The spectrum of methyl ximenynate indicated maxima at 3·48μ (C–H stretching vibration of CH_3 and CH_2 groups), 5·74μ (C=O stretching), 6·90 and 7·28μ (C–H bending vibrations of methyl and methylene groups), 4·50μ (acetylenic triple bonds), 8·54 and 9·88μ (ester methyl group), 10·47μ (olefinic double bond), and 13·86μ (deformation vibration of the long aliphatic chain). This is similar to the spectra of long-chain fatty esters in general (Ahlers, *J. Oil Col. Chem. Assoc.*, 1950, **33**, 421) with the addition of a characteristic acetylenic band superimposed. In view of the known absorption near 10·33μ for the vibration of C–H linkages of internal double bonds (RCH=CHR', where R and R' are large) in a *trans*-system, the strong band at 10·47μ may be indicative of a *trans*-configuration at the olefinic double bond in methyl ximenynate, the wave-length shift (0·14μ) involved being due to conjugation with the acetylenic bond. *cis*-Isomers are relatively transparent in this region (Swern, Knight, Schreve, and Heether, *J. Amer. Oil Chem. Soc.*, 1950, **27**, 17).

The spectrum of ximenynyl alcohol resembles that of the methyl ester without the absorption characteristics of the carbomethoxy-group; the presence of the hydroxyl group is shown by bands at 3·04μ (stretching vibration) and 9·48μ (bending vibration).

The authors thank the President and Council of the Research Association of British Paint, Colour, and Varnish Manufacturers, and the South African Council for Scientific and Industrial Research for their permission to publish this note; also Dr. D. A. Sutton of Pretoria for his general advice.

Paint Research Station, Teddington, Middlesex.

National Chemical Research Laboratory,
South African Council for Scientific and Industrial Research,
Pretoria, South Africa. [*Received, May 2nd*, 1952.]

987. *The Chemistry of Western Australian Plants. Part VII.* Oleanolic Acid Acetate from* Eucalyptus calophylla *Bark.*

By D. E. White and L. S. Zampatti.

In view of the occurrence of triterpene acids in the barks of other Myrtaceæ (Part VI *; Ralph and White, *J.*, 1949, 3433) that of *Eucalyptus calophylla* R.Br., the common "red-gum" or "marri" of Western Australia, has now been examined, and oleanolic acid acetate has been isolated.

Oleanolic acid acetate was previously found in birch bark (Ruzicka, Frame, Leicester, Liguori, and Brüngger, *Helv. Chim. Acta*, 1934, **17**, 426) and its weakly acid nature is comparable to that of ursolic acid acetate (Jeger, Borth, and Ruzicka, *ibid.*, 1946, **29**, 1999) which was not extracted from an ethereal solution by sodium carbonate or sodium hydroxide.

Experimental.—M. p.s are corrected. Analyses are by Drs. Weiler and Strauss, Oxford.

Extraction. Dry bark (3·6 kg.) of *E. calophylla*, collected in the University grounds, was powdered and extracted with ether (5 l.) for 2 days. The extract was concentrated, the concentrate treated with 5% sodium hydroxide solution, and the insoluble sodium salt (24 g.) extracted with benzene for 7 hours. The insoluble residue (14 g.), in methanol (800 ml.) (charcoal), was acidified with dry hydrogen chloride. Next morning the solid was collected (10 g.) and after 7 crystallisations from methanol formed needles, m. p. 258° alone and mixed with authentic oleanolic acid acetate, $[\alpha]_D^{17}$ +77° (Found: C, 77·1; H, 9·8. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·1%).

On concentration of the ether extract to 200 ml., an amorphous solid (1·1 g.) separated and was purified by crystallisation from methanol (charcoal) and decantation from a gel which also separated. Seven further crystallisations from methanol gave needles, m. p. 257°, identical (mixed m. p.) with the acid obtained above.

Methyl oleanolate acetate. Oleanolic acid acetate (300 mg.) (both samples) on treatment with methyl sulphate and potassium hydroxide formed methyl oleanolate acetate (210 mg.), m. p. 222° undepressed by an authentic sample, $[\alpha]_D^{17}$ +68°.

Oleanolic acid. Treatment of oleanolic acid acetate (50 mg.) with boiling 10% alcoholic potassium hydroxide (10 ml.) for 2 hours gave oleanolic acid (30 mg.), m. p. 309° undepressed by an authentic sample, $[\alpha]_D^{17}$ +82°.

The authors are indebted to Mr. W. J. Dunstan for the authentic samples of oleanolic acid and its derivatives.

University of Western Australia, Nedlands. [*Received, July 14th*, 1952.]

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988. *The Preparation of Substituted Quinones by a New Oxidizing Agent.*

By A. G. Brook.

Various oxidizing agents have been used for the oxidation of quinols to quinones, *e.g.*, metallic oxides (Ag_2O, PbO_2, MnO_2) for very sensitive quinones, stronger reagents such as chromic and nitric acids for relatively stable ones (Cason, "Organic Reactions," Vol. IV, p. 305). In many cases, the yields are low, owing to further oxidation or the difficulty of removing the quinone from the acidic medium.

Yields of >90%, without the formation of by-products, are obtained by use of mixed nitrogen oxides, predominantly N_2O_4, prepared from fuming nitric acid, sulphuric acid, and arsenious oxide. Reactions of nitrogen tetroxide with organic compounds have been reviewed by Riebsomer (*Chem. Reviews*, 1945, **36**, 157); its use in the oxidation of tetrachloro- and tetrabromo-catechol under more severe conditions wherein the quinone formed is further oxidized is described by Zincke (*Annalen*, 1924, **435**, 145). The oxides may be kept as a low-boiling liquid (20—30°), and their chief virtue, besides speed and cleanliness of reaction, lies in that they can be completely removed from the quinone at the water-pump. Results are shown in the Table. Nitrogen oxides are not suitable for the oxidation of quinol itself.

* Part VI, *J.*, 1952, 4065.

p-Benzoquinone	Yield (%)	M. p.	Quinone	Yield (%)	M. p.
2 : 3-Dicyano	92	178—180°	Tetrabromo-*o*-benzoquinone	92	148—150°
5-Chloro-2 : 3-dicyano	95	154	Tetrachloro-*o*-benzoquinone	88	131—132
2 : 3-Dichloro-5 : 6-dicyano...	93	203 [a]	3 : 3′ : 5 : 5′-Tetrabromo-diphenoquinone	94	>360
Tetrachloro	97	290 [b]			
2 : 5-Dimethyl	97	124—125			

[a] With decomp. [b] Sealed tube.

Experimental.—Nitrogen oxides were prepared by slow distillation of a mixture of fuming (98%) nitric acid (83 ml.), concentrated sulphuric acid (33 ml.), and arsenious oxide (100 g.), the red vapour boiling in the range 20—30° being condensed by ice–salt (Friend, " Textbook of Inorganic Chemistry," Vol. VI, Pt. 1, p. 167). Cautious heating in the early stages of the reaction is necessary. The nitrogen oxides were kept in a glass-stoppered bottle at 0° and were handled in a pipette as a liquid.

Oxidation of 2 : 3-*dichloro*-5 : 6-*dicyanoquinol.* Into a suspension of the finely ground quinol (20 g.) in carbon tetrachloride (300 ml.) at room temperature, crude nitrogen oxides (6 ml.) were introduced by pipette during 5 minutes, with rapid stirring. Stirring was continued for a further 5 min., and the quinone was filtered off and recrystallized from chloroform–benzene.

The same technique was applied to the other quinols, on scales varying from 0·5 to 50 g. Quinones which were soluble in carbon tetrachloride were isolated by evaporation.

The author is indebted to Professor R. P. Linstead and Dr. E. A. Braude for encouragement and advice, and to the Nuffield Foundation for a Travelling Fellowship in Natural Science, 1951—1952.

Department of Organic Chemistry, Imperial College of Science and Technology, London, S.W.7. [*Received, July 26th*, 1952.]

989. *The Magnetic Susceptibility of Urania–Thoria Solid Solutions.*

By J. K. Dawson and M. W. Lister.

The experimental magnetic moment of quadrivalent uranium in the dioxide, 3·20 Bohr magnetons, lies between the extreme theoretical value of 3·58 for a $5f^2$ electron configuration with L–S coupling and full orbital contribution, and 2·83, the spin-only value. The interpretation of this fact before the results of dilution experiments were available was that the electron configuration was $5f^2$ but that there was partial orbital quenching due to inefficient shielding by the 6*s* and 6*p* electrons (Dawson and Lister, *J.*, 1950, 2181).

Trzebiatowski and Selwood have published magnetic-susceptibility measurements on solid solutions of uranium dioxide in isomorphous, diamagnetic thoria (*J. Amer. Chem. Soc.*, 1950, **72**, 4504), and at about the same time we also obtained results on this system. The two sets of results were in good agreement and the magnetic moment–composition curves have been given previously in a discussion of the corresponding fluoride system (Dawson, *J.*, 1951, 2889), but since the solid solutions were made by a method different from that of Trzebiatowski and Selwood the results are given in more detail below.

Extrapolation of the magnetic moment to infinite dilution does not give the value 3·58 expected for a $5f^2$ configuration, but about 3·0 Bohr magnetons—close to the spin-only value. The extrapolated experimental susceptibility at room temperature is 3350×10^{-6} compared with the spin-only value for two unpaired electrons of 3410×10^{-6} (the theoretical value for two 5*f* electrons effectively shielded from external influence by 6*s* and 6*p* electrons is 5460×10^{-6}). The agreement of the experimental susceptibility at infinite dilution with the spin-only value is similar to that observed in oxides of the transition elements, such as Cr_2O_3 and Fe_2O_3 (Selwood, Lyon, and Ellis, *J. Amer. Chem. Soc.*, 1951, **73**, 2310), and is taken to imply a $6d^2$ electron configuration for quadrivalent uranium.

Experimental.—Uranium dioxide of the same quality as that used in the previous investigation of the intermediate oxide system (Dawson and Lister, *loc. cit.*) was mechanically mixed with diamagnetic thorium dioxide. The mixture was compressed into suitably sized pellets and the solid solutions were then formed by homogenisation at 2400° in a high-vacuum furnace (Alberman, *J. Sci. Inst.*, 1950, **27**, 280). It was found that the outsides of the pellets were dark owing to tantalum impurity from the furnace; the samples for the susceptibility measurements were taken from the insides of the pellets. *X*-Ray powder photographs showed that solid solution had been achieved. It was observed that the colour of the dilute solid solutions was

TABLE 1. *Magnetic susceptibilities of* UO_2–ThO_2 *solid solutions.**

U, %	$T°$, K	$10^6\chi_g$	$10^6\chi_{U(IV)}$	U, %	$T°$, K	$10^6\chi_g$	$10^6\chi_{U(IV)}$	U, %	$T°$, K	$10^6\chi_g$	$10^6\chi_{U(IV)}$
100	90	14·77	4043	70	197	7·98	3125	40	197	5·20	3566
	197·5	10·90	2998		293	6·35	2503		293	3·92	2709
	293	8·74	2416		334	5·87	2318		327	3·64	2525
	375	7·55	2092		401	5·19	2055		353	3·41	2368
	423	7·00	1945	60	197	7·23	3299		397	3·19	2226
	476	6·57	1828		293	5·62	2581		417	3·01	2107
	525	6·04	1686		330·5	5·16	2376		433	2·94	2058
	563	5·73	1607		352·5	4·95	2284	30	197	4·13	3781
90	197	9·81	2994		393	4·58	2116		293	3·05	2826
	293	7·90	2424		417	4·39	2034		337	2·72	2538
	337·5	7·22	2220	50	197	6·11	3350		398	2·38	2232
	402	6·45	1987		293	4·75	2618		405·5	2·15	2032
	493	5·57	1725		335·5	4·30	2382	20	197	2·94	4072
80	197	9·07	3109		398	3·94	2188		293	2·14	3014
	293	7·25	2498		450	3·50	1950		338	1·89	2687
	338	6·59	2277						400	1·64	2351
	398	5·95	2060						452	1·48	2139
	448·5	5·47	1900					10	293	1·05	3100

* χ_g = Gram-susceptibility.
$\chi_{U(IV)}$ = Ionic susceptibility corrected for diamagnetism of cation and anions (calculated by Angus's method, *Proc. Roy. Soc.*, 1932, *A*, **136**, 569).

green—the typical uranous colour, in contrast to the dark brown of the pure oxide. The susceptibility results are given in Table 1, and the Weiss constants and magnetic moments in Table 2 were obtained from the susceptibilities by means of the equation $\mu = 2{\cdot}83\sqrt{\chi(T - \Delta)}$.

TABLE 2. *Magnetic moments and Weiss constants of* UO_2–ThO_2 *solid solutions.*

U, %	100	90	80	70	60	50	40	30	20
Δ	233	205	199	196	160	164	129	99	86
μ	3·20	3·11	3·14	3·13	3·07	3·10	3·03	2·98	3·02

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A.E.R.E., HARWELL, nr. DIDCOT, BERKS.
CHEMISTRY DEPARTMENT, UNIVERSITY OF TORONTO. [*Received, July 26th*, 1952.]

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990. *A Direct Method for the Preparation of Some α-Chloro-carboxylic Esters, and Notes on Other α-Halogeno-carboxylic Esters.*

By A. D. CAMPBELL and D. R. D. SHAW.

IT has been shown by Horn, Miller, and Slater (*J.*, 1950, 2900) that Guest's method (*J. Amer. Chem. Soc.*, 1947, **69**, 300), involving the chlorination of alkyl-substituted malonic acids with sulphuryl chloride followed by decarboxylation of the resulting α-chloro-alkylmalonic acids, and esterification, is a satisfactory general method for the preparation of pure α-chloro-carboxylic esters but because of the large number of steps involved the overall yields are not always high. Dice and Bowden (*ibid.*, 1949, **71**, 3107) prepared α-bromo-carboxylic esters by treating the potassium salt of the monoethyl esters of alkyl-malonic acids with a solution of bromine in carbon tetrachloride but the yields were not high compared with those obtained by direct bromination of the carboxylic acid followed by esterification. Chlorine being used in place of bromine, Dice and Bowden's method has now been applied to the preparation of α-chloro-carboxylic esters (II) :

$$CHR(CO_2Et)_2 \xrightarrow{KOH} \underset{(I)}{CHR(CO_2K)(CO_2Et)} \xrightarrow{Cl_2} \underset{(II)}{CHRCl{\cdot}CO_2Et}$$

The potassium salts of monoethyl esters of alkylmalonic acids (I) were prepared according to Freund (*Ber.*, 1884, **17**, 780) by adding the calculated quantity of ethanolic potassium hydroxide to a solution of diethyl alkylmalonate in absolute ethanol. Very little of the alcohol-insoluble dipotassium salts was obtained. Walker (*J.*, 1892, **61**, 696) used sufficient dilute ethanolic potassium hydroxide to half-hydrolyse only part of the ester in order to prevent the formation of dipotassium salts, but this method was found to be unnecessarily tedious.

Sulphuryl chloride was initially used as the chlorinating agent but only low yields

(30% or less) of α-chloro-carboxylic esters (II), boiling over a wide range, were obtained. α-Chloro-carboxylic esters were, however, prepared in fair yield by using chlorine in carbon tetrachloride. As shown in the table, the method is particularly suited for the preparation of α-chloro-carboxylic esters of intermediate chain length : the shorter-chain esters are probably more conveniently prepared by direct chlorination of the acid or acid chloride (Wolffenstein and Rolle, *Ber.*, 1908, **41**, 733), and for the longer-chain esters Guest's method (*loc. cit.*) is undoubtedly superior. The low yields of 2-chlorodecanoic * and 2-chlorododecanoic esters are possibly due to hydrolysis of intermediates by traces of water remaining in the potassium salts which, for these higher members, had a soft wax-like consistency and were extremely difficult to dry. This is supported by the identification of non-chlorinated carboxylic esters in the reaction products. Although 2-bromohexanoic acid was obtained in good yield (67%), the same reaction when similarly applied to the synthesis of 2-bromododecanoic acid gave a low yield (11%).

Ethyl α-chloro-ester ...	Butyrate	Hexanoate	Octanoate	Decanoate	Dodecanoate
Yield, %	41	52	54	20	16

α-Iodo-carboxylic esters were prepared directly in the case of ethyl α-iodobutyrate and ethyl 2-iodohexanoate by refluxing the corresponding potassium salt of the ethyl hydrogen alkylmalonate with iodine in dry benzene after the method of Oldham and Ubbelohde (*J.*, 1941, 368) who prepared alkyl iodides from the salts of carboxylic acids. The yields were not high and the method does not appear to be satisfactory for the general preparation of α-iodo-carboxylic esters. Ethyl 2-iodohexanoate and ethyl 2-iodododecanoate were prepared in almost quantitative yield by refluxing gently the corresponding α-bromo-carboxylic esters with an equivalent quantity of sodium iodide in acetone (Finkelstein, *Ber.*, 1910, **43**, 1528).

Experimental.—α-Chloro-carboxylic esters. A typical experiment was as follows. Diethyl butylmalonate (21·6 g., 0·1 mol.) was dissolved in absolute ethanol (100 c.c.), and ethanolic potassium hydroxide (0·1 equiv. in 48 c.c.) was added dropwise (½ hour) with stirring. After 6 hours at room temperature ethanol was removed on a water-bath, finally under reduced pressure for 2 hours. The remaining white solid was dried in a vacuum-desiccator for 48 hours. Chlorine (7·1 g.) in carbon tetrachloride (60 c.c.) was added, during 4 hours with stirring and cooling in ice, to the potassium salt suspended in dry carbon tetrachloride (100 c.c.). After removal of about half the carbon tetrachloride on a water-bath, the residue was cooled, washed with water, dried, and distilled to give ethyl 2-chlorohexanoate (10·6 g.), b. p. 92—93°/15 mm. (Found : Cl, 19·7. Calc. for $C_8H_{15}O_2Cl$: Cl, 19·8%). A portion of the ester was hydrolysed to the acid and converted into the amide, m. p. 58° (Horn, Miller, and Slater, *loc. cit.*, give m. p. 57·8—58·2°).

Ethyl 2-iodohexanoate. (*a*) A solution of sodium iodide (15 g.) in acetone (50 c.c.) was added to ethyl 2-bromohexanoate (11·2 g.), and the mixture was gently refluxed on a water-bath for 1 hour. About two-thirds of the acetone was distilled off, and the residue was washed with water and mercury, dried, and distilled to give *ethyl 2-iodohexanoate* (12 g.), b. p. 111—114°/15 mm. (Found : C, 35·5; H, 5·7; I, 46·7. $C_8H_{15}O_2I$ requires C, 35·5; H, 5·5; I, 47·0%). A portion of the ester was refluxed with sodium hydroxide to give, on acidification, 2-hydroxyhexanoic acid, m. p. 59·5—60·5° (Blaise and Picard, *Ann. Chim.*, 1912, **26**, 282, give m. p. 60—61°).

(*b*) Iodine (25·4 g.) and dry benzene (300 c.c.) were added to the potassium salt of ethyl hydrogen butylmalonate (0·1 mol.; prepared as described above) and the mixture was refluxed for 3 hours. The cooled, filtered solution was washed quickly with dilute sodium hydroxide, dried, and distilled to give the ester (8·2 g.), b. p. 118—120°/20 mm. A portion on hydrolysis gave the hydroxy-acid, m. p. 60°.

Ethyl 2-iodododecanoate, prepared from ethyl 2-bromododecanoate similarly to (*a*) above, had b. p. 167°/5 mm., 122°/1 mm. (Found : C, 47·1; H, 7·3; I, 35·8. $C_{14}H_{27}O_2I$ requires C, 47·5; H, 7·6; I, 35·9%). Refluxing with sodium hydroxide followed by acidification gave the hydroxy-acid, m. p. 73° (Guerin, *Bull. Soc. chim.*, 1903, **29**, 1124, gives m. p. 74°).

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* Geneva nomenclature ($CO_2H = 1$).

991. 2-*Ethylpyridine as a Constituent of Coal-tar Bases.*

By A. B. Densham, D. J. Langston, and A. J. Simpson.

Coulson, Hales, Holt, and Ditcham (*J. Appl. Chem.*, 1952, **2**, 71) have found 3-ethylpyridine in coal-tar bases, and comment on the absence of 2-ethylpyridine. We have now found 2-ethylpyridine in a " commercial β-picoline " fraction which boiled at 144·5° in the plant still.

Experimental.—This fraction was redistilled in a 60-plate laboratory column. The sub-fraction boiling at 147·6—149·5° was analysed for 2-ethylpyridine by infra-red spectroscopy in a paraffin solution (Densham, Langston, and Gough, *J.*, 1952, 2433) by using the 13·42 μ band. It was found to contain approx. 65% of 2-ethylpyridine and 25% of γ-picoline with small amounts of β-picoline and 2 : 6-lutidine. This sub-fraction was treated with picric acid in alcohol in three stages. The picrate from the middle stage, after three recrystallisations from alcohol, had m. p. 106·5° compared with 108° for pure 2-ethylpyridine picrate (Brown and Murphey, *J. Amer. Chem. Soc.*, 1951, **73**, 3308). Further recrystallisation from alcohol and benzene did not alter the m. p. The free base was liberated with sodium hydroxide, steam-distilled, extracted with ether, dried (Na_2SO_4), and distilled. The b. p. was 148·7°, which agrees with Brown and Murphey's figure for 2-ethylpyridine. The infra-red absorption spectrum agreed precisely with that of 2-ethylpyridine except for a small additional band at 8·9 μ possibly due to residual ether.

Pure 2-ethylpyridine of b. p. 148·7°, giving a picrate melting at 108—108·7°, was prepared by Gregg and Craig's method (*J. Amer. Chem. Soc.*, 1948, **70**, 3138). The reduction can be carried out at 25 lb./sq. in. in glass. The infra-red spectrum shows a strong band, useful for analysis, at 13·34 μ in the pure base or a mixture of bases, which shifts to 13·42 μ in CS_2 or paraffin solution.

In order to find how much 2-ethylpyridine is present in coal-tar bases, crude unfractionated pyridine was fractionated in a 60-plate laboratory column. The fraction (3·5%), 144·5—153°, was analysed by infra-red absorption spectroscopy and found to contain 9% of 2-ethylpyridine. Thus the total amount of 2-ethylpyridine present is about 0·3% of the crude pyridine. In the above fractionation 11·5% distilled between 145° and 173°, corresponding to Coulson's broad lutidine–collidine fraction. On this basis the figures reported by Coulson *et al.* for the 3-ethylpyridine content correspond to 0·35% of 3-ethylpyridine in crude unfractionated pyridine, that is, much the same as the content of 2-ethylpyridine.

The authors thank Mr. K. G. Haig of the North Thames Gas Board Products Works for the commercial samples, Mr. W. J. Gooderham for the fractionations, and Dr. E. A. Coulson of the Chemical Research Laboratory for advice. This Note is published by permission of the North Thames Gas Board.

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992. *Bromination of 2-Methylnaphthalene.*

By N. B. Chapman and J. F. A. Williams.

Needing a 2-naphthylmethyl halide for preparative work, we found photochlorination to give mainly tar (cf. Tarbell, Fukushima, and Dam, *J. Amer. Chem. Soc.*, 1945, **67**, 197), whereas catalysed bromination is stated (Hall and Mitchell, *J.*, 1951, 1375) to give 1-bromo-2-methylnaphthalene and photo-bromination at 240—260° (Campbell, Anderson, and Gilmore, *J.*, 1940, 820), to give only a 22% yield of the required product. For the action of *N*-bromosuccinimide on 2-methylnaphthalene in boiling carbon tetrachloride, we found the conditions given by Buu-Hoï unsatisfactory (*Annalen*, 1944, **556**, 1). Early experiments in which larger volumes of carbon tetrachloride were used gave us high yields of 2-naphthylmethyl bromide but repetition of these resulted in high yields of 1-bromo-2-methylnaphthalene, indicating the incidence of adventitious catalysis. Systematic investigation revealed that the critical factor was the purity of the *N*-bromosuccinimide. If this was prepared by the method given by Shirley (" Organic Intermediates," John Wiley and Sons, Inc., New York, 1951, p. 59) and washed free from bromine, it then had to be purified by being kept at 0·5 mm. over phosphoric oxide for 8 hours; immediate use of this pure material gave a 95% yield of crude 2-naphthylmethyl bromide suitable for pre-

parative work. Aged specimens had to be pumped out at 0·5 mm. for 8 hours (phosphoric oxide unnecessary) and used at once if side-chain bromination was to be achieved, indicating that a volatile catalytic impurity, was slowly generated on storage. If this impurity was removed, the course of the reaction was uninfluenced by irradiation with visible light or by the addition of small amounts of water, although washing of *N*-bromosuccinimide purified as above with water just before use was deleterious.

If volatile impurities were not removed, nuclear bromination predominated, even when *N*-bromosuccinimide recrystallised from water was used. Irradiation with visible light or addition of benzoyl peroxide did not inhibit nuclear bromination, whereas addition of water did to some extent, indicating that ionisation and inactivation of the catalytic impurity may have occurred and suggesting that possibly the volatile impurity was unionised hydrogen bromide. With a specimen of *N*-bromosuccinimide purified by pumping, addition of 0·05% (wt.) of hydrogen bromide roughly halved the yield, but with larger amounts (0·5%) no diminution in yield occurred. It therefore seems probable, but not certain, that traces of hydrogen bromide constitute the catalytic impurity.

2-Naphthylmethyl bromide is thermally unstable and prone to decomposition during distillation : we have usually determined yields by determining the " mobile " bromine, but crystalline 2-naphthylmethyl bromide may be isolated, with some 30% loss, by rapid distillation at 16 mm. and crystallisation from ethanol.

The successful photobromination at 20° of toluene mixed with naphthalene in carbon tetrachloride as solvent to give benzyl bromide (Mayo and Hardy, *J. Amer. Chem. Soc.*, 1952, **74**, 911) prompted us to try to improve the yields obtained by Campbell *et al.* (*loc. cit.*). Irradiation with a 500-w bulb of a 1·5M-solution of 2-methylnaphthalene in boiling carbon tetrachloride and dropwise addition of bromine (0·5 mol.) gave crude 2-naphthylmethyl bromide in 75—80% yield. Photolysis of the bromine probably occurred in the mixed vapours, for rapid addition of bromine, with high concentrations in the liquid phase, appeared to cause a fast " dark " side reaction yielding no 2-naphthylmethyl bromide.

Experimental.

Materials.—Commercial 2-methylnaphthalene was fractionated through a 9" Fenske column with a variable-temperature vapour-jacket. Pure carbon tetrachloride was dried azeotropically and redistilled. *N*-Bromosuccinimide was prepared as stated previously. Pure bromine (May and Baker, Ltd.) was used.

Results.—Selected experiments are summarised in the Table. The reactions were usually carried out by allowing 0·5 equiv. of *N*-bromosuccinimide to react with 4·0 g. of hydrocarbon in 15 c.c. of boiling carbon tetrachloride for 25 hours. Yields were determined by treatment of the reaction product with an excess of standard methanolic silver nitrate and back-titration with ammonium thiocyanate solution.

N-Bromosuccinimide pumped free from volatile impurity		*N*-Bromosuccinimide not exposed to a vacuum	
Conditions	Yield (%) *	Conditions	Yield (%) *
(*a*) Freshly prepared sample, dry, light or dark	~94	(*a*) Freshly prepared sample, dry, light	~ 5
(*b*) As for (*a*); 5 drops of water added	~95	(*b*) As for (*a*); trace of benzoyl peroxide added	~ 0
(*c*) As for (*a*); sample washed with water before use, light or dark	~ 5	(*c*) As for (*a*); 5 drops of water added	~50
(*d*) Aged specimen. In (ii) same sample used as in (*e*)	(i) ~90 (ii) ~70		
(*e*) As for (*d*), (i) 0·05% of HBr added; (ii) 0·5% of HBr added	(i) ~35 (ii) ~70		

* ± 3%.

Typical Preparations.—N-*Bromosuccinimide method.* To 2-methylnaphthalene (64 g., 2 mol.) in carbon tetrachloride (300 c.c.) was added purified *N*-bromosuccinimide (44 g., 1 mol.), and the mixture heated at the b. p. with stirring (25 hours). After cooling, the solid (succinimide) was filtered off, the carbon tetrachloride removed, the residue rapidly fractionated at 16 mm., to remove excess of 2-methylnaphthalene (b. p. 108°/16 mm.), and the product (yield, 95%) rapidly distilled (b. p. 150—170°/160 mm.) and recrystallised from ethanol [m. p. 54° (lit., 54°, 56°); yield 65%].

Photobromination. Bromine (17 g., 1 mol.) in carbon tetrachloride (200 c.c.) was added dropwise during 9 hr. to a stirred solution of 2-methylnaphthalene (64 g., 2 mol.) in carbon tetrachloride (300 c.c.) at the b. p. and irradiated with a 500-w bulb. After the copious evolution of hydrogen bromide had ceased, the mixture was worked up as before, the yield of crude product being 75—80%.

We thank the Medical Research Council for a grant for scientific assistance to one of us (N. B. C.), Imperial Chemical Industries Limited for a grant for microanalyses and materials, and Mr. J. W. James, B.Sc., for some of the early experiments.

THE UNIVERSITY, SOUTHAMPTON. [*Received, August 14th,* 1952.]

993. *The Bromination of Aceto-β-naphthalide.*

By F. BELL.

LELLMANN and SCHMIDT (*Ber.*, 1887, **20**, 3154) and subsequently Morgan (*J.*, 1900, **77**, 819) described the bromination of aceto-β-naphthalide in acetic acid to give aceto-1-bromo-2-naphthalide; however, the main product under the conditions given is the hydrobromide, distinguished from aceto-1-bromo-2-naphthalide by its sparing solubility in cold chloroform. Bromination of aceto-β-naphthalide in chloroform gives this hydrobromide in almost pure condition (Franzen and Eidis, *J. pr. Chem.*, 1913, **88**, 760; Whitehurst, *J.*, 1951, 230).

Mannino and Di Donato (*Gazzetta*, 1908, **38**, ii, 31), by addition of aceto-β-naphthalide to a mixture of hydrobromic and nitric acids, obtained a compound which they regarded as the tribromo-derivative; it was hydrolysed to a base, m. p. 125°, clearly different from 1 : 3 : 6-tribromo-2-naphthylamine, m. p. 143°.

Meldola (*J.*, 1883, **43**, 8) by long warming of an acetic acid solution of aceto-1-bromo-2-naphthalide with bromine (1 mol.) obtained a compound, m. p. 138°, regarded as acetotetrabromo-2-naphthalide, which was unchanged after heating with " syrupy potash " for 3 days.

Neither of these results accords with the well-known difficulty of introducing further substituents into acylated β-naphthylamines already substituted in position 1. On repetition of the experiments we found that in each case the primary product was aceto-1 : 6-dibromo-2-naphthalide hydrobromide. This compound is analytically almost indistinguishable from acetotribromo-2-naphthalide and yields on hydrolysis 1 : 6-dibromo-2-naphthylamine, m. p. 123° (Mannino and Di Donato did not analyse the compound, m. p. 125°, which they assumed to be a tribromo-base). The description of Meldola's acetotetrabromo-2-naphthalide (Calc. : Br, 63·9%) accords closely with that of 1 : 3 : 6-tribromo-2-naphthylamine (Calc. : Br, 63·1%) and it is significant that all known halogenated acetonaphthalides can be easily hydrolysed to the corresponding naphthylamines whereas Meldola's compound was completely resistant.

In unsuccessful attempts to brominate aceto-1 : 6-dibromo-2-naphthalide further it was noticed that up to 13% of bromine was readily taken up to give a product stable in air and only surrendering bromine on being boiled with water, treated with aqueous ammonia or shaken in chloroform with potassium iodide. Similar bromine adsorption products (or loose additive compounds) were formed by aceto-1-chloro-, -1-bromo-, and -6-bromo-1-chloro-2-naphthalides.

It is concluded that the tribromination and tetrabromination of β-acetonaphthalide have not so far been achieved.

Experimental.—Bromination of aceto-1-bromo-2-naphthalide. Bromine (1·6 g.) in chloroform (3 c.c.) was added to the naphthalide (2·6 g.) in chloroform (15 c.c.), and the mixture kept overnight. No change in appearance was noted but when the solution was scratched a bright orange powder separated. This appeared to be the hydrobromide of aceto-1 : 6-dibromo-2-naphthalide with adsorbed, or loosely combined, bromine. The bromine was not removed by shaking with light petroleum, and only very incompletely by boiling water. When the chloroform solution was shaken with potassium iodide, iodine was liberated equivalent to Br, 13·1, 13·2%. Decomposition with dilute potassium hydroxide solution gave pure aceto-1 : 6-dibromo-2-naphthalide; the filtrate with silver nitrate gave silver bromide equivalent to

HBr, 23·7% (Calc. for $C_{12}H_9ONBr_2$,HBr: HBr, 19·1. Calc. for $C_{12}H_9ONBr_2$,HBr,Br_2: Br_2, 27·4%). Use of 2 mols. of bromine in the reaction led to no essential change in the nature of the product, nor did use of acetic acid in place of chloroform as a solvent.

Bromination of aceto-β-naphthalide (method of Mannino and Di Donato). On addition of the naphthalide (9 g.) to a mixture of hydrobromic acid (20 c.c.; *d* 1·48) and nitric acid (6 c.c.; *d* 1·40) there was a brisk reaction. When this had subsided the mixture was heated on a steam-bath for 1 hour, diluted with water, and filtered. The product, after crystallisation from acetic acid to remove resinous material, gave 9—10 g. of the hydrobromide of aceto-1 : 6-dibromo-2-naphthalide, rather indefinite decomp. 220—230°.

Attempted bromination of aceto-1 : 6-dibromo-2-naphthalide. (*a*) Bromine (1 g.) in acetic acid (4 c.c.) was added to the compound (2 g.) in hot acetic acid (25 c.c.), and the solution left on a steam-bath for 5 hours. The deposit was similar to that obtained in (*b*). (*b*) As for (*a*), but chloroform was used as solvent. The deposit (2·2 g.), m. p. 165—195° (decomp.), when warmed with water evolved bromine (9·0, 12·0, 12·8%, with different samples) and with dilute aqueous ammonia gave pure aceto-1 : 6-dibromo-2-naphthalide.

Bromination of aceto-1-chloro-2-naphthalide. (*a*) Bromination of 2·5 g. in cold acetic acid (20 c.c.) yielded *aceto-6-bromo-1-chloro-2-naphthalide hydrobromide* (3·2 g.), coloured yellow by loosely held bromine (Found: HBr, as AgBr: 24·7. $C_{12}H_9ONClBr$,HBr requires HBr, 21·4%). Decomposition with ammonia or by dissolution in pyridine gave pure aceto-6-bromo-1-chloro-2-naphthalide, m. p. 222° (Armstrong and Rossiter, *Chem. News*, 1891, **63**, 137, give 216° and do not mention the intermediate formation of the hydrobromide).

(*b*) Bromine (2·5 g.) in chloroform (4 c.c.) was added to the compound (3 g.) in chloroform (20 c.c.). There was no immediate reaction but after 2 days large, orange-red crystals (3·0 g.), m. p. 200° (decomp.), had separated. This material was similar to that under (*a*) and evolved 2—6·3% of bromine with boiling water. The experiment was repeated but with a two-fold quantity of bromine; the product, in chloroform solution, with potassium iodide gave iodine equivalent to Br, 19·4% (Calc. for $C_{12}H_9ONClBr$,HBr,Br_2: Br, 29·6%). All the products with alkali gave aceto-6-bromo-1-chloro-2-naphthalide.

Chlorination of aceto-2-naphthalide. Clemo and Legg's process (*J.*, 1947, 543) yields variable results. The average yield was 5 g. of the 1 : 4-dichloro-derivative from 20 g. of the starting material (in one experiment the first crop consisted of the hydrochloride of this compound) and it was not possible to recover any of the initial material (cf. Claus and Philipson, *J. pr. Chem.*, 1891, **43**, 58).

The author is indebted to Dr. J. Sandilands for the bromine determinations.

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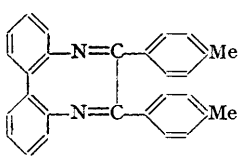
994. *Three Stereochemical Notes.*

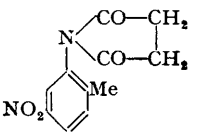
By F. BELL.

(*a*) IT was hoped to resolve an isomer of 6 : 7-diphenyl-5 : 8-diaza-1 : 2-3 : 4-dibenzo-*cyclo*octatetraene-2′ : 2″-dicarboxylic acid (Bell, *J.*, 1952, 1527) with the carboxyl groups external to the diphenyl system. The following observations were made during unsuccessful attempts to prepare such compounds.

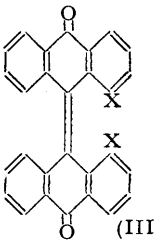
(*b*) Evans and McGookin (*J. Appl. Chem.*, 1951, **1**, 26) reported that 2-amino-4-nitrotoluene yields with succinic anhydride a mixture of two isomers (II), one forming colourless



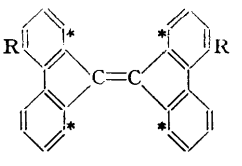
(I)



(II)



(III)



(IV) R = CO_2Et
(V) R = CO_2H

plates, m. p. 227°, and the other more soluble yellow needles, m. p. 176°. A possible explanation appeared to be restricted rotation about the N–phenyl linkage, occasioned by non-planar arrangement of the three valencies of nitrogen. It was decided to examine the succinoylation of some other bases, and it soon became probable, from our experiments

that these compounds were not isomeric and Dr. McGookin (personal communication) confirms this.

(*c*) Although it is usually assumed that the groups attached to an olefinic linkage lie in one plane, the ready production of dianthronylidenes (III) and related compounds (Bergmann and Loewenthal, *Bull. Soc. chim.*, 1952, **66**, 266) shows that this is by no means necessarily so. Many molecules of this type must exhibit dissymmetry. Even in difluorenylidenes the interference between the hydrogen atoms marked * in (IV) may suffice to give the molecule permanent non-planarity (cf. Fenimore, *Acta Cryst.*, 1948, **1**, 295), and suitable derivatives might be resolvable. With this in view, 9 : 9′-difluorenylidene-4 : 4′-dicarboxylic acid (V) was prepared but proved too highly coloured for polarimetric observations.

Experimental.—(*a*) *o*-Tolil and 2 : 2′-diaminodiphenyl did not interact at 210° during 20 minutes, although *o*-tolil condensed quite readily with *o*-phenylenediamine in acetic acid to give the *quinoxaline*, almost colourless prisms, m. p. 135° (Found : N, 8·5. $C_{22}H_{18}N_2$ requires N, 9·0%), dissolving in concentrated sulphuric acid with a deep red colour.

p-Tolil and 2 : 2′-diaminodiphenyl were heated together at 210° and the resultant plastic mass crystallised from acetic acid. 6 : 7-*Di*-p-*tolyl*-5 : 8-*diaza*-1 : 2-3 : 4-*dibenzo*cyclo*octatetraene* (I) crystallised from *o*-dichlorobenzene as sulphur-yellow crystals, m. p. 261° (Found : C, 86·3; H, 5·6. $C_{28}H_{22}N_2$ requires C, 87·1; H, 5·7%), yielding, like all the compounds of this type, a pale yellow solution in concentrated sulphuric acid. It was not found possible to oxidise the methyl groups without bringing about total decomposition of the molecule. Attempted resolution by selective adsorption on cellulose or lactose was unsuccessful.

(*b*) 2-Bromo-5-nitroaniline gave a uniform *succinoyl* derivative, needles, m.p. 204°, from acetic acid (Found : N, 9·8. $C_{10}H_7O_4N_2Br$ requires N, 9·4%), but 4-bromo-2-nitroaniline with succinic anhydride (equal weight) at 160° (2 hours) gave a *succinoyl* derivative, sparingly soluble in acetone, and a *hydrogen succinamide*, readily soluble in acetone. The former crystallised from acetic acid in prisms, m. p. 180—182° (Found : N, 9·6. $C_{10}H_7O_4N_2Br$ requires N, 9·4%), the latter in yellow needles, m. p. 164° (Found : N, 8·9. $C_{10}H_9O_5N_2Br$ requires N, 8·8%), easily soluble in cold, aqueous sodium carbonate and reprecipitated by hydrochloric acid.

(*c*) The residue, after removal of excess of thionyl chloride from a solution of fluorenone-4-carboxylic acid in this reagent, was treated with phosphorus pentachloride as described by Graebe and Aubin (*Annalen*, 1888, **247**, 280). The resultant dichloro-derivative, m. p. 103° (Graebe and Aubin give m. p. 95°) with cold absolute ethanol furnished the crystalline ester, m. p. 103° (large depression with acid chloride), in good yield. This ester (6 g.), copper powder (12 g.), and benzene (50 c.c.) were boiled under reflux for 2 hours and filtered hot. Bright red crystals of *ethyl* 9 : 9′-*difluorenylidene*-4 : 4′-*dicarboxylate* (IV), m. p. 248°, separated on cooling (Found : C, 81·3; H, 5·2. $C_{32}H_{24}O_4$ requires C, 81·4; H, 5·1%). This compound is very stable and can be sublimed. 1 G. in alcohol (20 c.c.) was hydrolysed by potassium hydroxide (2 g.) in water (2 c.c.) for 2 hours on a steam bath. Hydrochloric acid precipitated 9 : 9′-*difluorenylidene*-4 : 4′-*dicarboxylic acid*, red needles (from ethanol), m. p. 319° (sinters at 305°) (Found : C, 80·4; H, 4·1. $C_{28}H_{16}O_4$ requires C, 80·8; H, 3·9%), readily soluble in sodium carbonate to give an intense orange-red solution. When this solution was kept for some weeks the acid decomposed completely to fluorenone-4-carboxylic acid.

HERIOT-WATT COLLEGE, EDINBURGH. [*Received, August 28th*, 1952.]

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995. *Some Reactions of 5-Aminoacridine and Related Compounds.*

By E. P. TAYLOR.

DURING an investigation of the synthesis and pharmacological properties of certain bisquaternary ammonium salts, it appeared possible that basically substituted bisacridinium salts might prove of interest. Accordingly, decamethylene di-iodide was heated in solution with (*a*) 5-aminoacridine, (*b*) 5-acetamidoacridine, or (*c*) 5-diacetylaminoacridine. From (*a*), 5-aminoacridine hydriodide was obtained (average yield 83%), together with a small amount of an unidentified substance; (*b*) and (*c*) gave acridone, identified by conversion into 5-*p*-diethylaminophenylacridine (this decomposition occurred in alcohol or dioxan, but not in ethyl methyl ketone). Similarly 5-acetamido-3-methylacridine gave 3-methylacridone. It was found that 5-acetamidoacridine was not decomposed by refluxing it in alcohol alone or in an alcoholic solution of potassium iodide.

The results are summarised in the Table.

Solvent *	Solutes †		Main product	Yield (%) ‡
EtOH	5-Acetamidoacridine	$I\cdot[CH_2]_{10}\cdot I$ (1 mol.)	Acridone	84
,,	,,	Nil	5-Acetamidoacridine	100
,,	,,	KI (2 mols.)	,,	100
,,	5-Acetamido-3-methylacridine	$I\cdot[CH_2]_{10}\cdot I$ (1 mol.)	3-Methylacridone	77
,,	5-Diacetylaminoacridine	,,	Acridone	74
Dioxan	5-Acetamidoacridine	,,	,,	72
COMeEt	,,	,,	5-Acetamidoacridine	100
,,	5-Aminoacridine	,,	5-Aminoacridine hydriodide	83 §
$PhNO_2$	5-Acetamidoacridine	,,	,,	11 §

* 210 hours at the b. p., but at 180° in the last case. † 3 Mols. of acridine derivative.
‡ Average of at least two experiments. § Based on decamethylene di-iodide.

Experimental.—Microanalyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.

5-Acetamidoacridine (1 g., 3 mols.), decamethylene di-iodide (0·55 g., 1 mol.), and anhydrous industrial alcohol (45 ml.) were heated under reflux for 210 hours. After about 30 hours, the solution, which had changed from pale yellow to deep orange, began to deposit yellow needles. After cooling, filtration, and washing with alcohol, the dried residue (0·72 g.) consisted of practically pure acridone, m. p. >330° (lit., *ca.* 350°) (Found, on a recrystallised sample: C, 79·65; H, 4·6; N, 7·2. Calc. for $C_{13}H_9ON$: C, 80·0; H, 4·65; N, 7·2%). Phosphorus oxychloride and diethylamine (Ullmann, Bader, and Labhardt, *Ber.*, 1907, **40**, 4796) gave 5-*p*-diethylaminophenylacridine, m. p. 197° (as recorded) (almost 100%).

Heating 5-acetamido-3-methylacridine (Wilkinson and Finar, *J.*, 1946, 116) with alcoholic decamethylene di-iodide gave 3-methylacridone, m. p. 334° (Gleu and Nitzsche, *J. pr. Chem.*, 1939, **153**, 218, give m. p. 335°) (Found: C, 80·05; H, 5·2; N, 6·8. Calc. for $C_{14}H_{11}ON$: C, 80·4; H, 5·3; N, 6·7%).

5-Aminoacridine (1 g., 3 mols.), decamethylene di-iodide (0·68 g., 1 mol.), and ethyl methyl ketone (25 ml.) were heated under reflux. Orange crystals commenced to separate after an hour. After 210 hours' heating, the mixture was cooled. Filtration, washing with ethyl methyl ketone, drying, and repeated extraction with boiling alcohol gave a deep purple-red, unidentified residue (0·1 g.) (Found: C, 67·0; H, 11·4; N, 4·0; I, 16·8%). This *substance* was also insoluble in boiling water. The alcoholic extract was concentrated to 10 ml. and treated with ether. 5-*Aminoacridine hydriodide* separated as a yellow powder (0·9 g.), forming long yellow needles, m. p. *ca* 340°, from water (Found: C, 48·5; H, 3·4; N, 8·55; I, 39·5. $C_{13}H_{11}N_2I$ requires C, 48·45; H, 3·4; N, 8·7; I, 39·4%).

I thank Mr. W. C. Austin for technical assistance, and the directors of Messrs. Allen and Hanburys Ltd., for permission to publish this work.

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996. *Trifluoroacetaldehyde.*

By F. Brown and W. K. R. Musgrave.

Trifluoroacetaldehyde has been prepared from the nitrile by lithium aluminium hydride (Henne, Pelley, and Alm, *J. Amer. Chem. Soc.*, 1950, **72**, 3370) and from 1 : 1 : 1-trifluoropropane by oxidative nitration (Shechter and Conrad, *ibid.*, p. 3371), both methods involving several stages and unsatisfactory yield. The former authors failed to prepare the aldehyde by routine methods, and we too have failed to make it from trifluoroacetanilide; but we obtained good results in the reduction of the acid chloride by Rosenmund's method using, with slight modifications, Fröschl and Danoff's technique (*J. pr. Chem.*, 1936, **144**, 217). The products were fluoral, fluoral hydrate, a waxy polymer similar to that described by Shechter and Conrad (*loc. cit.*), and a small amount of material, probably polymeric, which distilled unchanged. The fluoral hydrate was probably produced from the small amount of water which is retained in the asbestos used for carrying the catalyst even though this is baked thoroughly before use. No trifluoroethyl alcohol was isolated (cf. Henne *et al.*, *loc. cit.*). The failure of these workers to obtain the aldehyde may have been due to use of slightly impure reagents, a point which is stressed by Fröschl and Danoff (*loc. cit.*) who claim that traces of phosphorus or sulphur compounds

cause an uncontrollable change in the functioning of the catalyst. Other workers (Zetsche and Arnd, *Helv. Chim. Acta*, 1925, **8**, 591; 1926, **9**, 173) state that, in liquid-phase reactions, traces of phosphorus compounds act as inhibitors.

Experimental.—Trifluoroacetyl chloride was prepared from the acid and benzoyl chloride (Henne, Alm, and Smook, *J. Amer. Chem. Soc.*, 1948, **70**, 1968) so as to obtain it free from traces of phosphorus compounds.

Trifluoroacetaldehyde. Hydrogen (14 l./hr.) was purified and dried (Fröschl and Danoff, *loc. cit.*) and passed over the surface of liquid trifluoroacetyl chloride (11 g.) in a graduated tube cooled to −78°. By gradually lowering the cooling bath the acid chloride was vapourised during 1 hour, the mixture of hydrogen and vapour being passed through a preheater at 170° and into a Pyrex tube (36″ × 0·7″) packed with palladised asbestos (Pd 2·8%). The temperature of the catalyst was kept at 250° by winding a heating element directly on to the tube, and the exit gases were passed through two traps at −78° and then water containing methyl-orange. After all the acid chloride had vapourised, the stream of hydrogen was continued for 1 hour. A white solid (6 g.) collected in the first trap, and titration of the hydrochloric acid in the water trap showed that 61% had collected there during this stage. The product was allowed to warm to room temperature, at which it liquefied, and a slow stream of nitrogen was bubbled through it. Trifluoroacetaldehyde (1 g., 12·7%) was condensed at −78°, and hydrogen chloride, accounting for a further 30% of the theoretical amount, passed on to a water trap. After redistillation, the fluoral (Found: F, 58·0. Calc. for C_2HOF_3: F, 58·17%) reduced ammoniacal silver nitrate and, when bubled through 2 : 4-dinitrophenylhydrazine in 6N-sulphuric acid, gave the dinitrophenylhydrazone, m. p. 150° (Found: F, 20·4. Calc. for $C_8H_5O_4F_3N_4$: F, 20·5%). On access to damp air, it slowly formed fluoral hydrate (sublimed at 50°).

The residue, after removal of the fluoral from the original product, was a waxy brown solid at room temperature, but when this polymer was heated to 40—45° it slowly decomposed to fluoral (3·1 g.) which had the properties recorded above and formed fluoral hydrate (sublimed at 50°) (Found: F, 49·1. Calc. for $C_2H_3O_2F_3$: F, 49·2%).

Most of the solid residue after removal of the polymer was fluoral hydrate (1·1 g.), which sublimed at 50° (Found: F, 49·2%), gave a 2 : 4-dinitrophenylhydrazone, m. p. 150°, and left a dark liquid (0·2 g.) (Found: F, 49·0%) which distilled unchanged at 110° (bath-temp.).

The overall yield of fluoral and fluoral hydrate was 64%.

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THE UNIVERSITY, SOUTH ROAD, DURHAM. [*Received, August 30th*, 1952.]

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997. *The Reduction of 3-Chlorophthalic Acid and of its Three Methyl Esters.*

By R. F. BIRD and E. E. TURNER.

DURING an investigation for which we required 3-chloro-*o*-xylylene glycol (I), we made a number of observations which may be of general interest. The glycol would be expected to be formed by reducing 3-chlorophthalic acid with lithium aluminium hydride, but, when calculated proportions of reducing agent are used, the product is 7-chlorophthalide (II). Under normal Fischer–Speier conditions, 3-chlorophthalic acid gives the 1-methyl 2-hydrogen ester (III), and reduction of this ester with lithium aluminium hydride gives 7-chlorophthalide.

Methyl 3-chlorophthalate, obtained by the action of methyl iodide on silver 3-chlorophthalate, is reduced by lithium aluminium hydride to 3-chloro-*o*-xylylene glycol, and may be hydrolysed to the 2-methyl 1-hydrogen ester (IV) by the use of the calculated amount of alcoholic potassium hydroxide. This ester readily passes into the neutral ester under

Fischer–Speier conditions, and, when reduced with lithium aluminium hydride, gives 3-chloro-*o*-xylylene glycol.

Phthalide itself is smoothly converted into *o*-xylylene glycol in presence of the calculated amount of lithium aluminium hydride, but 7-chlorophthalide requires a large excess of this reagent to reduce it to 3-chloro-*o*-xylylene glycol.

7-Chlorophthalide dissolves in aqueous alkali to give the ions of 2-chloro-6-hydroxymethylbenzoic acid, but acidification of the solution formed precipitates 7-chlorophthalide. This behaviour is in marked contrast to that of 5-chlorophthalide, from which Levy and Stephen (*J.*, 1931, 867), by dissolution in alkali, followed by acidification, obtained 4-chloro-2-hydroxymethylbenzoic acid which could be sublimed at the ordinary pressure without undergoing cyclisation : this occurred at the melting point.

By reducing 4-aminophthalimide, Levy and Stephen (*loc. cit.*) obtained two (unorientated) aminophthalides, melting at 157° and 120° respectively. From these, by replacing amino by chlorine, they obtained two chlorophthalides, melting at 86° and 143° respectively. The higher-melting chlorophthalide is evidently our 7-chlorophthalide, so that it now becomes possible to say that 4-chlorophthalide melts at 86° and that 4-amino- and 7-aminophthalide melt respectively at 157° and 120°.

Reduction of methyl 4-chlorophthalate with lithium aluminium hydride gives 4-chloro-*o*-xylylene glycol.

Experimental.—M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, of Oxford.

1-*Methyl* 2-*hydrogen* 3-*chlorophthalate*. A solution of 3-chlorophthalic acid (1 part) and concentrated sulphuric acid (1 part) in methyl alcohol (10 parts) was boiled under reflux for 6 hours. Part of the alcohol was distilled off and the residue poured into water. The precipitated *ester* (80%), after being crystallised from water, had m. p. 141° (Found : C, 50·2; H, 3·3; Cl, 16·4. $C_9H_7O_4Cl$ requires C, 50·4; H, 3·3; Cl, 16·5%).

Methyl 3-*chlorophthalate*. A suspension of the silver salt of the acid in dry ethereal methy iodide was boiled for 3 hours. After removal of the silver iodide, the *ester* (65%) crystallised from aqueous methyl alcohol in hexagonal plates, m. p. 67° (Found : C, 52·8; H, 4·0; Cl, 15·6. $C_{10}H_9O_4Cl$ requires C, 52·5; H, 3·9; Cl, 15·5%).

2-*Methyl* 1-*hydrogen* 3-*chlorophthalate*. The neutral ester was gently warmed in one mol. proportion of alcoholic potassium hydroxide until it was neutral to litmus. Acidification precipitated the *ester* (84%), which crystallised from aqueous methyl alcohol in needles, m. p. 170° (Found : C, 50·4; H, 3·3; Cl, 16·4%).

Reductions. The three esters and the free acid were reduced in boiling ethereal solution (the acid by the Soxhlet-extractor procedure), by using 120% of the lithium aluminium hydride which would have been necessary for conversion into glycol. Methyl 3-chlorophthalate gave 3-*chloro*-o-*xylylene glycol* (76%), plates, m. p. 71° (from benzene) (Found : C, 55·4; H, 5·15; Cl, 20·45. $C_8H_9O_2Cl$ requires C, 55·7; H, 5·2; Cl, 20·6%). 1-Methyl 2-hydrogen 3-chlorophthalate gave 7-*chlorophthalide* (80%), colourless needles, m. p. 148°, from aqueous alcohol (Found : C, 56·8; H, 2·9; Cl, 21·3. $C_8H_5O_2Cl$ requires C, 57·0; H, 2·9; Cl, 21·1%). 2-Methyl 1-hydrogen 3-chlorophthalate gave 85% of glycol. 3-Chlorophthalic acid gave 70% of 7-chlorophthalide.

Reduction of phthalide on similar lines gave 90% of *o*-xylylene glycol. Reduction of 7-chlorophthalide with 5 mols. of lithium aluminium hydride gave 3-chloro-*o*-xylylene glycol. Methyl 4-chlorophthalate gave 4-*chloro*-o-*xylylene glycol* (80%), rectangular plates, m. p. 85° (from benzene) (Found : C, 56·4; H, 5·3; Cl, 20·7%).

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BEDFORD COLLEGE, UNIVERSITY OF LONDON. [*Received, September 4th*, 1952.]

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998. *The Isolation of α-Spinasterol from Colocynth.*

By (MRS.) B. HAMILTON and W. O. KERMACK.

POWER and MOORE (*J.* 1910, 99) isolated, from a crude alcoholic extract of *Citrullus colocynthis*, a sterol, m. p. 160—162°, which they did not identify, but claimed to have the molecular formula $C_{27}H_{46}O$. In the present work, a sterol, m. p. 164—165°, corresponding to that described by Power and Moore, has been identified as α-spinasterol by com-

parison of its infra-red spectrum and the m. p.s and rotations of some of its derivatives with those of an authentic sample of α-spinasterol and its derivatives.

Experimental.—A solid colocynth preparation (1 kg.), obtained by extracting the fruit of *Citrullus colocynthis* with 90% alcohol, was steam-distilled to remove a small quantity of yellow oil. After decantation of the brown aqueous phase remaining in the distillation flask, the residue was extracted with warm alcohol in which it was completely soluble, there being no trace of the white, insoluble, crystalline elaterin reported by Power and Moore. After removal of the alcohol, the residue was extracted thoroughly with hot, light petroleum (b. p. 40—60°), and the greenish-yellow solution concentrated and passed through an alumina column. Three bands, pink, green, and yellow, quickly separated at the top of the column, and the first fraction collected on elution with light petroleum (b. p. 40—60°) was colourless. This was followed by a yellow fraction, corresponding to the yellow band, which gave only a very small quantity of yellow oil. The green solution obtained on further elution with ether yielded a green oil which constituted the main fraction of the material. The pink band at the top of the column spread a little on washing the column with various solvents but remained firmly attached to the alumina. Alcohol, ethyl acetate, pyridine, and water failed to elute further material, but the fractions obtained by washing with glacial acetic acid yielded a white solid containing aluminium, suggesting that some compound in the mixture had formed a complex with the alumina of the column.

The first colourless washings from the column contained a white low-melting, waxy solid which, by further chromatography on alumina from light petroleum, was separated into hentriacontane, m. p. 68° (isolated by Power and Moore), and a second white crystalline *compound*, m. p. 58—60° (Found: C, 85·25; H, 14·3%; *M*, 576, 584. $C_{41}H_{84}$ requires C, 85·4; H, 14·6%; *M*, 576). This melting point is definitely lower than would be expected for the straight-chain $C_{41}H_{84}$ and the compound may be a branched-chain isomer.

Both the yellow and the green fraction from the column gave strong Liebermann–Burchard reactions and positive Tortelli–Jaffé tests. Trituration of both these fractions with cold alcohol removed the colours, leaving white solids, which, after several crystallisations from alcohol and light petroleum (b. p. 40—60°), yielded white glistening plates, m. p. 164—165°, $[\alpha]_D$ −2° (Found: C, 83·6; H, 12·0. Calc. for $C_{29}H_{48}O,\frac{1}{4}H_2O$: C, 83·6; H, 11·6%). The infra-red spectrum of this compound agreed very closely with that of α-spinasterol.

The benzoate of this sterol formed white plates, m. p. 193—194°. This material could not be further purified by crystallisation or by chromatography on alumina, but on repeated extraction with limited quantities of hot light petroleum (b. p. 40—60°), or by partition chromatography on a cellulose column using ethyl acetate as the mobile and water as the stationary phase, two products were isolated; one, m. p. 199—200° (alone and mixed with authentic α-spinasteryl benzoate), $[\alpha]_D$ 2° (Found: C, 83·4; H, 9·8. Calc. for $C_{36}H_{52}O_2$: C, 83·7; H, 9·8%), the other, in small amount, m. p. 183—184°, $[\alpha]_D$ 6° (Found: C, 82·7; H, 9·7%). The latter was not further examined. α-Spinasterol melts at 168° and yields a benzoate, m. p. 201°, $[\alpha]_D$ 2°.

The acetate of the sterol formed white glistening plates, m. p. 173—174°, which could not be further purified by crystallisation or chromatography on alumina, but when the benzoate, m. p. 199—200°, was hydrolysed and the sterol acetylated, a product was isolated having m. p. 184° (alone or admixed with authentic α-spinasteryl acetate) (Found: C, 81·7; H, 11·2%; *M*, 428. Calc. for $C_{31}H_{50}O_2$: C, 81·9; H, 11·0%; *M*, 454). The infra-red spectrum of the acetate also agreed very closely with that of α-spinasteryl acetate. It would appear that in the crude sterol fraction there is a second sterol, possibly β-spinasterol, but the evidence is inconclusive.

We are grateful to Dr. W. C. Price and Dr. R. N. Jones for carrying out the infra-red observations and to the latter for comparing the spectra with those in his library of steroid data; and to Dr. D. H. R. Barton for providing us with specimens of α-spinasteryl acetate and benzoate. We also thank Messrs. T. & H. Smith of Edinburgh for supplies of the crude colocynth extract, and the Carnegie Trust for a Scholarship to one of us (B. H.), which made this work possible.

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999. *Condensation Products of Rhodanine and Keto-acids.*

By G. G. Allan, Duncan Maclean, and G. T. Newbold.

This communication records the condensation of rhodanine with lævulic acid (I; R = Me, n = 2), β-benzoylpropionic acid (I; R = Ph, n = 2), and γ-benzoylbutyric acid (I; R = Ph, n = 3) to give respectively 5-(1′-2″-carboxyethylethylidene)- (II; R = Me, n = 2), 5-(α-2′-carboxyethylbenzylidene)- (II; R = Ph, n = 2), and 5-(α-3′-carboxy-*n*-propylbenzylidene)-rhodanine (II; R = Ph, n = 3). The conditions necessary are

(I) $CO_2H\cdot[CH_2]_n\cdot COR$ $CO_2H\cdot[CH_2]_n\cdot CR{:}C\cdot CO\cdot NH\cdot CS\cdot S$ (II)

(III) $CO_2H\cdot[CH_2]_2\cdot CHR\cdot CS\cdot CO_2H$ $CO_2H\cdot[CH_2]_2\cdot CHR\cdot CH_2\cdot CO_2H$ (IV)

critical, ammonia–ammonium chloride being used as condensing agent (cf. Brown, Bradsher, McCallum, and Potter, *J. Org. Chem.*, 1950, **15**, 174; Girard, *Ann. Chim.*, 1941, **16**, 326). No reaction between the keto-acids and rhodanine occurred when sodium acetate–acetic acid were used (Dijksman and Newbold, *J.*, 1951, 1213).

Hydrolysis of (II; R = Ph, n = 2) gives β-phenyl-α-thioadipic acid (III; R = Ph) which on reductive desulphurisation with Raney nickel gives β-phenyladipic acid (IV; R = Ph). Similar treatment of (II; R = Me, n = 2) but without isolation of the pure intermediate thio-acid gave β-methyladipic acid (IV; R = Me).

Condensation products of rhodanine with aldehydes and ketones exhibit mildew prevention activity (Brown and Bradsher, *Nature*, 1951, **168**, 171); an examination for such properties in (II; R = Ph, n = 2) and (II; R = Me, n = 2) was kindly made by Mrs. M. Hamlin in the laboratories of the British Cotton Industry Research Association by the courtesy of the Director. The compounds showed slight fungistatic activity against *Stachybotris atra* and *Memnoniella echinata* but none against *Chaetomium globosum*, *Alternaria tenuis*, *Myrothecium verrucaria*, *A. versicolor*, *Rhizopus arrhizus*, or *A. niger*. Tested against *Mycobacterium tuberculosis in vitro*, the two products showed a minimum inhibitory concentration of *ca.* 1 mg./100 c.c. medium (we are indebted to Mr. D. E. Seymour and Dr. D. J. Drain of Messrs. Herts Pharmaceuticals Ltd., for making available this result).

Experimental.—*5-(α-2′-Carboxyethylbenzylidene)rhodanine.* β-Benzoylpropionic acid (1·78 g.) and rhodanine (1·33 g.), suspended in water (10 c.c.), were treated with aqueous ammonia (0·87 c.c.; *d*, 0·88), followed by a solution of ammonium chloride (0·6 g.) in hot water (5 c.c.), and heated on the steam-bath for 1 hour. Dissolution was rapid and crystals separated which were collected after 4 hours at 0°. The solid (1·8 g.) which evolved ammonia on treatment with cold alkali was dissolved in boiling water (600 c.c.), and the solution made acid (Congo-red) and allowed to cool. Crystallisation of the precipitate from aqueous ethanol gave *5-(α-2′-carboxyethylbenzylidene)rhodanine* (1·65 g.) as yellow needles, m. p. 176—178° (Found: C, 53·3; H, 4·0; S, 21·4%; equiv., 144, 148. $C_{13}H_{11}O_3NS_2$ requires C, 53·2; H, 3·8; S, 21·8%; equiv., 146·5). Light absorption in ethanol: Max. at 276 (ε = 8600) and 346 mμ (ε = 28,600).

Under identical conditions lævulic acid gave *5-(1-2′-carboxyethylethylidene)rhodanine* (30%) as yellow needles, m. p. 189·5—190°, from water (Found: C, 42·0; H, 4·1%; equiv., 116. $C_8H_9O_3NS_2$ requires C, 41·6; H, 3·9%; equiv., 115·5). Light absorption in ethanol: Max. at 270 (ε = 10,800) and 343 mμ (ε = 29,900). γ-Benzoylbutyric acid gave *5-(α-3′-carboxy-*n*-propylbenzylidene)rhodanine* (11%) as yellow needles, m. p. 161—162°, from water (Found: C, 55·0; H, 3·9; N, 4·8; S, 21·2. $C_{14}H_{13}O_3NS_2$ requires C, 54·7; H, 4·3; N, 4·6; S, 20·8%).

β-Phenyl-α-thioadipic acid. 5-(α-2′-Carboxyethylbenzylidene)rhodanine (200 mg.) was heated on the steam-bath under nitrogen for 1 hour with aqueous sodium hydroxide (5 c.c.; 15%). The resulting solution was cooled and poured slowly into an excess of ice-cold 3N-hydrochloric acid with stirring. The precipitated solid was separated, washed with water, and dried. Crystallisation from benzene gave *β-phenyl-α-thioadipic acid* (80 mg.) as plates, m. p. 140° (Found: C, 56·9; H, 5·0%; equiv., by titration, 92·5. $C_{12}H_{12}O_4S$ requires C, 57·1; H, 4·8%; equiv., 84·0).

β-Phenyladipic acid. β-Phenyl-α-thioadipic acid (0·5 g.) in a mixture of sodium hydroxide (10 c.c.; 2N), water (15 c.c.), and ethanol (25 c.c.) was heated under reflux for 7 hours with Raney nickel (6 g.; W6, prepared according to *Org. Synth.*, **29**, 25). The filtered mixture was

evaporated under reduced pressure to 15 c.c. and made acid (Congo-red). After a day the precipitate was collected and crystallised from ether–benzene from which β-phenyladipic acid (310 mg.) separated as flat rectangular prisms, m. p. 148—150° (Found : C, 64·85; H, 6·25%; equiv., 111, 113. Calc. for $C_{12}H_{14}O_4$: C, 64·85; H, 6·35%; equiv., 111). Manske (*J. Amer. Chem. Soc.*, 1931, **53**, 1104) gives m. p. 146°, and von Braun and Weissbach (*Ber.*, 1931, **64**, 1785) give m. p. 148°. The foregoing yield, 32% from (II; R = Ph, n = 2), can be increased to 40% by starting from the ammonium salt of (II; R = Ph, n = 2) and proceeding without isolation of pure (III; R = Ph), the method of Bradsher, Brown, and Grantham (*J. Amer. Chem. Soc.*, 1951, **73**, 5377) being used.

β-*Methyladipic acid.* 5-(1-2′-Carboxyethylethylidene)rhodanine (1·5 g.) was heated under reflux in sodium hydroxide solution (30 c.c.; 15%) for 2 hours under nitrogen. The mixture was acidified (Congo-red) and the crude thio-acid isolated by ether as an oil (1·0 g.). The latter was heated with Raney nickel as in the preceding experiment. The mixture on concentration, acidification, and ether-extraction gave β-methyladipic acid (300 mg.), needles, m. p. 95—97° (from benzene) (Found : C, 52·8; H, 7·7%; equiv., 82. Calc. for $C_7H_{12}O_4$: C, 52·5; H, 7·55%; equiv., 80). Ruzicka and van Veen (*Annalen*, 1929, **468**, 143) give m. p. 93—94°.

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1000. *The Friedel–Crafts Acetylation of* p-tert.-*Butyltoluene.*

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WHEREAS Friedel–Crafts acetylation of *p*-ethyl-, *p*-*n*-propyl-, and *p*-*iso*propyl-toluene under carefully controlled conditions yielded the corresponding 5-alkyl-2-methylacetophenones, the product of acetylation of *p*-*tert.*-butyltoluene was not the expected 5-*tert.*-butyl-2-methylacetophenone (*J.*, 1952, 1123). This substance is now shown to be 4-*tert.*-butyl-2-methylacetophenone, the *tert.*-butyl group having migrated from the *para*- to the *meta*-position relative to the methyl group.

The product of hypobromite oxidation of this ketone (*loc. cit.*) has been identified as 4-*tert.*-butyl-2-methylbenzoic acid. This was first prepared by Effront (*Ber.*, 1884, **17**, 2317) by hydrolysis of the nitrile derived from 2-amino-5-*tert.*-butyltoluene, the constitution of which was established by Baur (*Ber.*, 1891, **24**, 2839). The present authors converted this amine into the corresponding 2-iodo-derivative, and obtained the required acid by carboxylation of the Grignard reagent, using a modification of Hussey's general method (*J. Amer. Chem. Soc.*, 1951, **73**, 1364).

Baur-Thurgau (*Ber.*, 1898, **31**, 1345) described 4-*tert.*-butyl-2-methylacetophenone obtained by Friedel–Crafts acetylation of *m*-*tert.*-butyltoluene, and established its constitution (*Ber.*, 1900, **33**, 2569) by oxidation with dilute nitric acid to 4-*tert.*-butyl-2-methylbenzoic acid.

Experimental.—2-Amino-5-*tert.*-butyltoluene (Dubinin and Kozhevnikova, *Zhur. Obshcheĭ Khim.*, 1951, **21**, 662; *Chem. Abs.*, 1951, **45**, 9500) was purified through its acetyl derivative, m. p. 162° (Effront, *loc. cit.*, gives m. p. 162°; Dubinin and Kozhevnikova, *loc. cit.*, give 161—162°). Hydrolysis of this derivative was difficult, but was effected by refluxing a 10% solution in a mixture of equal volumes of absolute alcohol and fuming hydrochloric acid for 30 hours. On diazotisation of the resulting amine and treatment with potassium iodide, 5-*tert.*-butyl-2-iodotoluene was obtained as a colourless oil, b. p. 135—137°/11 mm., which crystallised in needles (Effront, *loc. cit.*, gives b. p. 264—265°, m. p. *ca.* 34—35°). Treatment of the derived Grignard reagent with solid carbon dioxide yielded 4-*tert.*-butyl-2-methylbenzoic acid, which after distillation in steam separated from diluted alcohol as plates, m. p. 143—144° alone or mixed with the acid obtained by hypobromite oxidation of the product of Friedel–Crafts acetylation of *p*-*tert.*-butyltoluene. Effront (*loc. cit.*) describes the acid as needles, m. p. 140°.

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