J. Chem. Soc. (C), 1971

Compounds related to 1-Hydroxymethylindane-2-carboxylic Acid

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The preparation of the lactone of *cis*-1-hydroxymethylindane-2-carboxylic acid is described and of some substituted amino-derivatives of 1-methylindene-2-carboxylic acid. Some other reactions of ethyl y-bromo-a-benzylacetoacetate are described.

1-Hydroxymethylindane-2-carboxylic acid (I; $R^1 =$ $R^2 = H$) was required for the preparation of derivatives $(R^1 \text{ or } R^2 = Br, OH \text{ etc.})$ in order to study the changes in configuration on replacement of R^1 or R^2 by another substituent; it was expected that the configuration could be readily ascertained by the ease of formation of



the lactone (II) from the *cis*-form. Since indane is usually regarded as having an almost planar conformation, there should be no ambiguity arising from conformation differences in the cis- or trans-forms. The preparation of the lactone $(R^1 = R^2 = H)$ from 1bromomethylindene-2-carboxylic acid¹ is now described.

Ethyl γ -bromo- α -benzylacetoacetate² is unstable at the ordinary temperature and when dissolved in concentrated sulphuric acid the freshly prepared ester gave a mixture of 1-bromomethylindene-2-carboxylic acid and its ethyl ester (IIIj). The bromo-acid so prepared proved identical with the acid prepared by Roser



(but wrongly formulated), by the bromination of 1methylindene-2-carboxylic acid. By this latter method most of the acid used in this work was prepared.

The bromo-acid reacted with silver acetate in acetic acid to give the acetoxy-acid (IIIc). There was no reaction when ether or acetone was used as a solvent, nor when anhydrous potassium acetate was used in acetic acid. The acid chloride of the acetoxy-acid decomposed when kept in vacuo for two to three days, but when freshly prepared gave a stable p-toluidide and p-bromanilide.

The acetoxy-acid (IIIc) was not reduced by hydrogen at ordinary temperature and pressure in presence of a palladium-carbon catalyst, but at 60° and 50 atm. a

 ⁽a) W. Roser, Annalen, 1888, 247, 157; (b) D. H. Peacock, Chem. Comm., 1966, 518.
 A. K. Macbeth, J. Chem. Soc., 1923, 123, 1122.

reduced product was obtained which after alkaline hydrolysis and acidification gave a mixture of the lactone (II; $R^1 = R^2 = H$) of the *cis*-hydroxymethyl acid, and a methylindane acid isomeric with that prepared by Roser (loc. cit.), and later by Neville.³ In an experiment with a less active palladium catalyst 1methylindene-2-carboxylic acid was isolated from the products and this result supplied a clue to the probable path of formation of the methylindane acid; part of the original acetoxy-acid probably underwent hydrogenolysis to the methylindene acid and this on subsequent reduction gave the methylindane acid. I am indebted to Professor D. W. Cameron for this suggestion. No isomeric methylindane acid was isolated nor any transhydroxymethyl acid. Usually the reduction product contained 40-50% lactone and the rest was methylindane acid.

The same methylindane acid was obtained by hydrogenation of the methylindene acid with palladiumcarbon as catalyst, and here again no isomeric acid was detected. The methylindane acid so obtained had m.p. 134°. According to its method of preparation it would be expected to be the cis-acid (Linstead et al.4). This acid gave a liquid methyl ester which, when boiled with sodium methoxide in methanol solution, isomerised and on hydrolysis gave an isomeric methylindane acid m.p. 90°, probably identical with the acid prepared by Roser (loc. cit.) and resolved by Neville (loc. cit.). This acid is presumably the *trans*-acid.

The bromomethyl acid readily reacted with primary and secondary amines to give the acids (IIId—i), which were somewhat unstable. The methyl esters prepared from the methyl ester of the bromo-acid were more stable and more highly coloured. The product of the action of phenylhydrazine was acetylated with acetic anhydride and gave a colourless, crystalline solid the analysis of which was consistent with it being the acetyl-anhydro-compound. The formation of an anhydro-compound distinguishes this derivative from the p-toluidino-compound, and similar compounds, which give acetyl derivatives of the corresponding acids. No anhydro-compounds, with a five-membered ring involving the carbonyl group were obtained.

These amino-acids when boiled in methanol with hydrochloric acid readily split off the amine function to form a yellow amorphous acid which was soluble in sodium hydroxide to give a colloidal solution. The primary aromatic amines liberated from the p-toluidinoand p-chloranilino-acids were detected by diazotisation and coupling with β -naphthol; the secondary base from the methylanilino-acid was detected by the formation of a nitroso-derivative. The yellow acidic product was probably the polymerised methylene acid (cf. Courtot ⁵

- ³ A. Neville, J. Chem. Soc., 1906, 89, 385.
 ⁴ R. P. Linstead, W. F. Doering, S. B. Davis, P. Levine, and R. R. Whetstone, J. Amer. Chem. Soc., 1942, 64, 1985.
 ⁵ Ch. Courtot, Ann Chim., 1915, [9], 4, 202.
 ⁶ G. R. Clemo, L. H. Groves, L. Munday, and G. A. Swan, J. Chem. Soc. 1051, 862.
- J. Chem. Soc., 1951, 863. ⁷ K. Ziegler and K. Bähr, Ber., 1929, **62**, 1695.

who found that methyleneindene readily polymerised). The reactivity of these amino-acids and esters may be compared with that of 1-bromomethylindene which shows even greater activity, doubtless for similar reasons.6

An acetic acid solution of bromine did not react with 1-bromomethylindene-2-carboxylic acid nor with the 1-acetoxymethylindene acid which is faint support for the view that the original attack of the bromine may involve the 1-methyl group (cf. Ziegler and Bahr 7). Chlorination of certain unsaturated hydrocarbons has been found to give products substituted similarly (cf. ref. 8).

The quinine salt of the acid (IIIa) was repeatedly recrystallised but showed no signs of resolution.

Roser (loc. cit) found that bromination by bromine vapour gave a normal addition product. This result has been to some extent confirmed (see Experimental section). The brominated acid when boiled with an acetic acid solution of hydrogen bromide was partially converted into the 1-bromomethyl acid. The formation of this acid by bromination in acetic acid by preliminary addition is therefore not ruled out. It is noteworthy that indene-2-carboxylic acid when exposed to bromine vapour formed a brownish product insoluble in sodium carbonate and giving no satisfactory analyses (see W. H. Perkin and G. Revay 9).

Ng Buu-Hoi¹⁰ found that N-bromosuccinimide brominated indene in the 1-position. Similarly, methyl 1-methylindene-2-carboxylate gave a bromo-compound which is not brominated in the 1-methyl group and which is probably the 3-bromo-compound (see Experimental section). Other experimenters ¹¹ working with methyl tiglate have found that N-bromosuccinimide brominates in the β -position to the carboxy-group.

EXPERIMENTAL

1-Methylindene-2-carboxylic Acid.—Ethyl a-benzylacetoacetate (37 g.) was added to a mixture of sulphuric acid (98%, 360 g.) and water (15 g.) cooled to -2° during 45 min. at -2° to -4° . The solution, now dark reddish brown, was left in a refrigerator for 2 hr. and then overnight at 15-20°; it was then poured into ice-water (21.). This mixture was heated to $50-60^{\circ}$ to coagulate the sludge and was then filtered and worked up. The acid, as Roser found, readily crystallised from acetic acid with acetic acid of crystallisation. It was readily soluble in acetone, less readily in benzene or ethanol, m.p. 200°; v_{max.} (Nujol) 1100-1300w, 1600m, and 1660m.

The methyl ester, prepared by esterification with sulphuric acid and methanol, readily crystallised from methanol, m.p. 60° (lit.^{1a} 78°); the colourless crystals slowly turned pale yellowish brown in daylight (Found: C, 76.9; H, 6.1. $C_{12}H_{12}O_2$ requires C, 76.6; H, 6.4%). The acid

⁸ (a) P. B. D. de la Mare and K. W. Wong, *Rec. Trav. chim.*, 1968, 87, 824; (b) J. Burgin, W. Engs, M. R. A. Groll, and C. Hearne, *Ind. Eng. Chem.*, 1939, 31, 1413.
⁹ W. H. Perkin and C. Revay, *J. Chem. Soc.*, 1894, 65, 228.
¹⁰ Ng Buu Hoi, *Annalen*, 1944, 556, 1.
¹¹ A. Löffler, R. J. Pratt, H. P. Rüesch, and A. S. Dreiding, *Phys. Rev. Lett.* 1070, 52, 282.

- Helv. Chim. Acta, 1970, 53, 383.

chloride was prepared by the action of thionyl chloride on the free acid; it was a rather unstable liquid; by reaction with the appropriate amine the following amides were made. Anilide, colourless crystals from ethanol, m.p. 183° (Found: N, 5.55. C₁₇H₁₅NO requires N, 5.6%). Morpholide, very soluble in ethanol and methanol, colourless crystals from aqueous methanol, m.p. 105° (Found: N, 5.8. C₁₅H₁₇NO₂ requires N, 5.75%). p-Bromanilide, readily soluble in ethyl acetate, colourless crystals from ethanol, m.p. 209° (Found: N, 4.7. C₁₇H₁₄BrNO requires N, 4.5%). p-Nitroanilide, pale yellow crystals from acetic acid; sparingly soluble in boiling ethanol, readily soluble in acetone, m.p. 205°. The cinchonine, brucine, strychine, and quinine salts were all prepared in ethanol solution. The cinchonine salt was very soluble in ethanol, slightly soluble in ether; brucine salt sparingly soluble in cold ethanol, m.p. 150-151°; strychine salt, sparingly soluble in hot ethanol; quinine salt soluble in ethanol, acetone, chloroform, and benzene, m.p. 150°. After five crystallisations of this salt from benzene the recovered free acid had doubtful optical activity.

1-Bromomethylindene-2-carboxylic Acid.—(a) From ethyl γ -bromo- α -benzylacetoacetate. Ethyl benzylacetoacetate (44 g.) dissolved in carbon disulphide (90 ml.), was cooled to -2° . Bromine (32 g.), was added during 10-15 min. at -5 to $+3^{\circ}$. The mixture was left in a cold room for 3 hr. and then washed with water and dried (CaCl₂). The carbon disulphide was distilled off under reduced pressure at ca. 15° and the residue was kept in a desiccator under reduced pressure; since the compound was unstable it was used as quickly as possible. The bromo-ester (6.0 g.) was added during 15 min. to concentrated sulphuric acid (15.0 ml.), cooled to $3-5^{\circ}$; the solution changed from deep yellow to dark brown; after being set aside for 3 hr. in ice the solution was brownish purple; it was poured into icewater (200 ml.) and the precipitate was filtered off, washed with water and ether, and dried (2.4 g). This solid was crystallised either from boiling acetic acid or boiling acetone, m.p. 245° (dec.) (Found: C, 52.25; H, 4.0. $C_{11}H_9O_2Br$ requires C, 52.2; H, 3.55%). The ether solution contained impure ethyl 1-bromomethylindene-2-carboxylate.

(b) From 1-methylindene-2-carboxylic acid. The methyl acid (34.8 g.) was added to glacial acetic acid (150 ml.) and cooled to 10°. Bromine (32.0 g.) in acetic acid (50 ml.) was added during 30 min. at 10-15°. The colour of the bromine rapidly disappeared and the suspended methyl acid was all in solution after ca. 80% of the bromine had been added; during the addition of the rest of the bromine the mixture set almost solid and after a few minutes evolution of HBr started. The mixture was left overnight in a cold room, after which it was heated on a water-bath for 0.5 hr., cooled to 10-15° for 3 hr., and filtered. The solid acid was filtered off, washed with ether, and dried (45.0 g.), m.p. 242-245°. Crystallised from boiling acetone it had m.p. 245° (decomp.) (lit., ^{1a} 245°). From the acetic acid mother liquors impure acid (ca. 0.5 g.) was recovered. The bromination was much slower when chloroform was used as a solvent.

Methyl Ester.—(a) From the bromomethyl acid. The acid was boiled with methanol and concentrated sulphuric acid, cooled, and the crystalline ester filtered off, m.p. 95° (lit.,^{1a} 98°) (from MeOH) (Found: C, 53.6; H, 4.4. C₁₂H₁₁BrO₂ requires C, 53.1; H, 4.1%).

(b) Bromination of the methyl ester of the 1-methyl acid.

J. Chem. Soc. (C), 1971

Methyl 1-methylindene-2-carboxylate (9.4 g.) dissolved in chloroform (40 ml.) was cooled to 5°. A solution of bromine (8 g.) in chloroform (40 ml.) were then added during 5-10min. at $ca. 5^{\circ}$. The solution was left at this temperature for 2 hr., after which the chloroform was distilled off under reduced pressure, with evolution of hydrogen bromide. Light petroleum and methanol were added to the mixture which after being set aside overnight in a cold room was filtered; the crystalline acid was washed with light petroleum (b.p. 40-60°). The crystals (13.0 g.) had m.p. 95°; mixed m.p. with the previous product 95°. From the mother liquors a further 2.5 g. of crystalline ester were obtained. The bromination was much slower when carried out in acetic acid. Both specimens had identical i.r. spectra. Recrystallisation from light petroleum raised the m.p. to 97°. The ester was readily soluble in boiling ether, and in boiling methanol and very soluble in chloroform.

p-Bromanilide of 1-Bromomethylindene-2-carboxylic Acid. -1-Methylindene-2-carboxylic acid p-bromoanilide in acetic acid was mixed with an acetic acid solution of bromine at 20°; the mixture was heated to 60-70°, and then cooled and filtered. The crude product crystallised well from ethanolacetone or benzene-toluene mixture to give colourless needles, m.p. 204°; these were readily soluble in acetone, sparingly soluble in ethanol. This compound is tentatively assigned the 1-bromomethyl structure (Found: C, 50.4; H, 4.3; N, 3.6. C₁₇H₁₃Br₂NO requires C, 50.1; H, 3.1; N, 3.4%). The compound reacted with silver acetate in acetic acid and with p-bromaniline but in neither case did the product crystallise. When boiled for 2-3 min. in methanol with p-toluidine it reacted to give a crystalline product; this, recrystallised from ethanol-acetone, gave pale yellow needles, m.p. 165° [The p-bromoanilide of 1-p-toluidinomethylindene-2-carboxylic acid (C24H21BrN2O) requires C, 66.5; H, 4.8; N, 6.45. Found: C, 66.2; H, 4.8; N, 6.59]. The hydrochloride, from ethanol, had m.p. 274-282° (decomp.).

The 1-bromomethyl acid when mixed with two molecular equivalents of base in ethanol and heated until all dissolved readily reacted. In some cases the mixture had to be boiled to bring about complete dissolution but the compound decomposed if boiling was continued for longer than min. 1-p-toluidinomethylindene-2-carboxylic 1 - 2acid (sparingly soluble hot ethanol more soluble hot acetone) formed pale yellow crystals, m.p. 155° (Found: C, 76.9; H, 6.7. C₁₈H₁₇NO₂ requires C, 77.4; H, 6.1). The acetyl compound had m.p. 223° (Found: C, 75.1; H, 5.9; N, 4.3. C₂₀H₁₉NO₃ requires C, 74.8; H, 5.9; N, 4.35%). The amino-acid boiled with acetic acid decomposed and gave a dirty greenish yellow solid which was filtered off; the filtrate was diazotised and coupled with β -naphthol to give a bright red azo-compound. p-Chloranilino-acid formed pale yellow needles which sintered and decomposed at 175° (Found: C, 68.05; H, 6.05. C17H14CINO2 requires C, 68.1; H, 4.6%). The acetyl derivative formed colourless crystals from hot acetic acid which were sparingly soluble in hot ethanol, m.p. 211° (Found: N, 4.3. C19H16CINO3 requires N, 4.1%). The m-nitranilino-acid formed yellow needles which were readily soluble in boiling acetic acid and in boiling ethanol, readily soluble in cold acetone, but sparingly soluble in boiling benzene (Found: N, 8.85. $C_{17}H_{14}N_2O_4$ requires N, 9.03%). The acetyl derivative, from acetic acid, sintered at 245°, m.p. 255° (decomp.). The Nmethylanilino-acid formed pale yellow crystals from ethanol;

it decomposed when boiled with acetic acid and the filtrate after treatment with sodium nitrite solution, extraction with ether, washing *etc.* gave a positive nitrosamine reaction. Phenylhydrazine gave an unstable derivative, m.p. *ca.* 162°, which on treatment with acetic anhydride gave an acetyl derivative, m.p. 165°, as colourless crystals from methanol. This compound was insoluble in aqueous sodium hydrogen carbonate. (The anhydro-compound, $C_{17}H_{14}N_2O$, requires N, 10·6. Found N, 10·6%).

Methyl 1-Anilinomethylindene-2-carboxylate.—Aniline and the 1-bromomethyl ester were heated at 50—60° for 1 or 2 min. in methanol. The product crystallised on cooling the mixture; it formed pale yellow needles from methanolacetone, m.p. 111° (Found: N, 4.95%. $C_{18}H_{17}NO_2$ requires N, 5.0%). The 1-p-toluidino-ester was similarly prepared; it formed bright pale yellow needles from methanol-acetone, m.p. 136° (Found: C, 77.9; H, 6.8; N, 4.8. $C_{19}H_{19}NO_2$ requires C, 77.8; H, 6.4; N, 4.75%).

The 1- α -naphthylamino-ester formed pale yellow needles from methanol, m.p. 168° (Found: N, 4·15. $C_{22}H_{19}NO_2$ requires N, 4·25%). The 1-amino-azobenzene ester formed dark, metallic-looking prisms from ethanol or acetone, m.p. 146° (Found: N, 10·4. $C_{24}H_{21}N_3O_2$ requires N, 10·9%).

Methyl 1-Methyl-3-bromoindene-2-carboxylate.—Methyl 1methylindene-2-carboxylate (5.6 g.), N-bromosuccinimide (5.3 g.), benzyl peroxide (0.2 g.), and carbon tetrachloride (10 ml.) were mixed and heated for 2 hr. on a boiling waterbath. The mixture was filtered, and the solid was washed with carbon tetrachloride; and the combined solutions were concentrated under reduced pressure to give the crude product (9.1 g.); it formed colourless needles from methanol, m.p. 83° (Found: C, 53.5; H, 4.3. $C_{12}H_{11}BrO_2$ requires C, 53.9; H, 4.1%). The bromo-substituent is tentatively assigned the 3-position.

Methyl 1-Methyl-3-anilinoindene-2-carboxylate.—This compound was formed by the action of aniline on the above bromo-compound in ethanol or methanol at $50-60^{\circ}$; it formed colourless needles from methanol which were soluble in ether, m.p. 134°.

1-Acetoxymethylindene-2-carboxylic Acid.-The 1-bromomethyl acid (25 g.) and silver acetate (18.0 g.) in glacial acetic acid (200 ml.) were shaken at 18-22° in the dark for 3 days. The mixture was then heated on a boiling waterbath and filtered whilst hot; the precipitate of silver bromide was washed with ethanol and the mixed washings and filtrate were concentrated under reduced pressure; the mixture was poured into water and the crude acid was filtered off and dried (20-21 g.), m.p. 145-155°; it formed colourless needles from light petroleum-benzene, m.p. 168-169° (Found: C, 67.5; H, 5.5. C13H12O4 requires C, 67.2; H, 5.1%). The compound was very soluble in ethanol, methanol and ethyl acetate, but sparingly soluble in boiling benzene. Silver acetate in ether had no action on it neither did potassium acetate alone or with 5% silver acetate in glacial acetic acid. The same acetoxyacid was formed from the bromomethyl acid prepared by bromination of the methyl acid and from the bromomethyl acid prepared from ethyl 1-benzyl-3-bromoacetoacetate. The acid was readily soluble in aqueous sodium hydrogen carbonate at 40-50° and was reprecipitated unchanged if the solution was acidified after a few minutes. The solution in sodium hydroxide, decomposed after 23 hr. and acidification produced an amorphous acid which was insoluble in organic solvents. When boiled with 25% sulphuric acid it decomposed and gave a mixture of amorphous products.

3509

The acid was not reduced by zinc dust and acetic acid on a water-bath and was not brominated by bromine in acetic acid. Thionyl chloride gave a not very stable crystalline acid chloride; p-toluidide, colourless prisms from ethanol, m.p. 152° (Found: N, 4.3. C₂₀H₁₉NO₃ requires N, 4.35%); p-bromanilide, colourless prisms from ethyl acetate, m.p. 154°, mixed m.p. with p-toluidide, 145-148°. The acid was not reduced in acetic acid solution by hydrogen and a palladium-carbon catalyst but was reduced in ethanol solution at 50-60°, 50 atm. pressure, with the same catalyst. The acetoxy-acid (11.0 g.), ethanol (200 ml.), and palladiumcarbon 1.0 (g.) were heated at 60° and 50 atm. for 2 hr. The mixture was filtered and the ethanol was distilled off. The crude product was mixed with sodium hydroxide (15 ml.; 33%) and heated on a water-bath; the dark brown solution was mixed with water (100 ml.) and the ethanol was distilled off. The hot alkaline solution was acidified and an oily mass formed which crystallised when seeded. The solution deposited colourless crystals when set aside. The products (8.5 g.) were extracted with sodium hydrogen carbonate solution, filtered, and the filtrate acidified; this acid, soluble in benzene, was crystallised from water. The hydrogen carbonate-insoluble product crystallised from light petroleum-acetone and had m.p. 121°. The lactone of 1-hydroxymethylindane-2-carboxylic acid (C₁₁H₁₀O₂) requires C, 75.9; H, 5.7. Found: C, 76.1; H, 6.0%. The acid, cis-1-methylindane-2-carboxylic acid was crystallised from acetone-light petroleum and had m.p. 128° (Found: C, 75.15; H, 6.8. C₁₁H₁₂O₂ requires C, 75.0; H, 6.8%). Recrystallised from benzene-light petroleum, it had m.p. 130°. The p-toluidide from ethanol, rather sparingly soluble, had m.p. 188° (Found: N, 4.95. C₁₈H₁₉NO requires N, 5.3%). 1-Methylindene-2-carboxylic acid reduced with palladium-carbon, in ethanol (4 hr., 50 atm., 60-65°) gave the indane acid, m.p. from light petroleum 128—129° (unchanged on mixture with the acid from the reduction of the acetoxymethyl acid). The crude reduction mixture from the acetoxy-methyl acid was very dark; this colour remained in the sodium hydrogen carbonate solution of the acid but the lactone was readily decolourized by crystallisation. The dark coloured solution of the acid in ethanol was not decolourized by passage through an alumina column, although considerable improvement in colour was effected by dissolving the acid in ammonia, adding ferric chloride, and filtering; the cis-acid precipitated from the filtrate was almost colourless.

trans-1-Methylindane-2-carboxylic acid. The cis-acid was esterified with methanol and sulphuric acid; the methyl ester (2 ml.), was added to a solution of sodium (0.15 g.) in methanol (15 ml.) and boiled under reflux for 7 hr. The recovered ester was hydrolysed with 2n-sodium hydroxide (9 ml.). Hydrochloric acid precipitated a pasty acid which was crystallised from aqueous methanol and then from light petroleum, m.p. 90-91° (Found: C, 74.65; H, 6.8. $C_{11}H_{12}O_2$ requires, C, 75.0; H, 6.8%). The p-toluidide was sparingly soluble in boiling ethanol, m.p. 200° (Found: N, 5.45. $C_{18}H_{19}NO$ requires N, 5.3%). The lactone of the cis-1-hydroxymethyl-2-carboxylic acid was not further reduced in ethanol (6 hr., 80°, and 80 atm.); the cismethylindane acid was thus probably not formed by further reduction of this lactone. N-Bromosuccinimide and benzoyl peroxide in boiling carbon tetrachloride reacted very slowly and gave a small yield of a bromo-compound, m.p. 80-82° from boiling, light petroleum.

Dibromo-acids.—1-Methylindene-2-carboxylic acid (3.5

g.) was set aside in a desiccator over an excess of bromine for four days in the dark; the brownish product was then kept over sodium hydroxide *in vacuo* for two days; the weight fell (to 7.0 g.) and was then constant. This solid was extracted with boiling ether; the insoluble residue, crystallised from boiling acetone had m.p. 249° and was identical with the I-bromomethyl acid already described (Found: Br, 29.4. $C_{11}H_9BrO_2$ requires Br 31.6%). From the ether solution an acid crystallised, m.p. 225—226° (Found: Br, 50.4. $C_{11}H_{10}Br_2O_2$ requires Br, 47.9%). Under these conditions the I-bromomethyl acid in varying amounts was always formed.

2,3-Dibromo-1-methylindane-2',4',6'-tribromanilide. 1-Methylindene-2-carboxylic acid p-bromanilide (1.0 g.) treated as above gave 2.2 gm. of crude product, m.p. 180-188°; this was sparingly soluble in boiling ethyl acetate and in boiling carbon tetrachloride. Crystals from boiling benzene-ethyl acetate had m.p. 224° (decomp.) (Found: Br, 61.7. $C_{17}H_{12}Br_5NO$ requires Br, 61.9%).

cis-1-Methylindane-2-carboxylic acid (0.5 g.) was placed in a desiccator in the dark with bromine (ca. 2.0 g.). After 12 days the product, black and sticky, was put over calcium chloride-potassium hydroxide until the excess of bromine had volatilized. The product was then extracted with light petroleum, benzene, and acetone, to leave a black brittle mass, insoluble in ammonium hydroxide, which did not melt when heated. From the solvents no crystalline products were obtained.

trans-1-Methylindane-2-carboxylic acid (0.1 g.) when treated as above gave a light yellow solid, soluble in boiling benzene and precipitated by light petroleum. This melted over the range 185—205° and was not further investigated.

Methyl 1-Chloromethylindene-2-carboxylate.—The bromoethyl acid (1.0 g.) and methanol saturated with hydrogen chloride (10 ml.) was heated on a boiling water-bath for 2

J. Chem. Soc. (C), 1971

hr. in a stream of hydrogen chloride; the mixture was left overnight to give a mass of colourless needles; these were collected and crystallised from hot methanol m.p. 91° (Found: C, 64.0; H, 5.25. $C_{12}H_{11}ClO_2$ requires C, 64.7; H, 4.9%).

Other Reactions of Ethyl y-Bromo-a-benzylacetoacetate.— Benzyltetronic acid (3-benzyl-2,4-dioxotetrahydrofuran), (colourless crystals from aqueous ethanol m.p. 167°) was readily obtained when ethyl 3-bromo-1-benzylacetoacetate was heated for 1 hr. on a boiling water-bath or left for 24 hr. at 15-20°. It is sparingly soluble in cyclohexane, soluble in boiling acetone and in boiling ethyl acetate. This acid (0.5 g.) and aniline (0.5 g.) were boiled for 5 min. (or heated in an oil bath at 80° rising to 160° in 1 hr.) to give the anilide. The product was cooled to give a semisolid mass; excess of aniline was removed by dilute hydrochloric acid and the solid residue was crystallised from aqueous ethanol. The colourless needles were readily soluble in ethanol and in this solution gave no colour with ferric chloride; m.p. 115° (Found: C, 76·1; H, 5·9. C₁₇H₁₅NO₂ requires C, 76.9; H, 5.6%).

Ethyl 2-Aminothiazolyl-4-benzylacetate.—Thiourea (2 g.), ethyl γ -benzyl- α -bromoacetoacetate (5 g.), and water (20 ml.) were mixed and shaken at 10°, rising to 15° after 15 min.; the mixture was acid to litmus and soon became acid to Congo Red. It was left overnight in a cold room; the crystalline solid (A) was filtered off and the filtrate was mixed with an excess of ammonia: an emulsion formed which soon turned to a mass of crystals; these crystals were filtered off (m.p. 154—156°); the first crop (A) had the same melting point. Recrystallised from ethanol-water, m.p. 167°, the compound formed colourless needles (Found: N, 9·6. C₁₄H₁₆N₂O₂S requires N, 10·1%).

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