mm.), 7 g. (40% based on acid used), ν = 1775 cm.$^{-1}$. A melting point of 56° has been reported[17] for this lactone.

4-(*p*-Tolyl)pentanoic Acid.—The previous lactone was reduced according to the procedure of Martin.[18] After 22 hr. the toluene layer was separated and extracted with dilute sodium hydroxide. The basic layer was acidified with hydrochloric acid and extracted with ether. The ether extracts were dried and the product distilled, b.p. 115° (1.5 mm.), 2.7 g. (38%). Boiling points of 173° (9 mm.)[17] and 180° (14 mm.)[6] have been reported.

4-(*p*-Tolyl)-1-pentanol.—The above acid was esterified with ethanol and hydrochloric acid. The ester, b.p. 144 (9 mm.),[6,17] was obtained as a colorless oil in 78% yield. A solution containing 2.3 g. of the ester in ether was added dropwise to a solution containing 0.47 g. of lithium aluminum hydride and the solution stirred at room temperature for 15 min. Excess hydride was destroyed with moist ether. The product was distilled *in vacuo*, b.p. 72–74° (0.1 mm.), 1.28 g. (62%). Simonsen[4] reports a boiling point of 151° (16 mm.) for this alcohol. Its infrared spectrum was identical with that of II-2 and its 3,5-dinitrobenzoate melts at 78° (reported[6] m.p. 80°).

Infrared Spectra.—Infrared spectra were carried out unless otherwise specified on neat liquids using a Perkin-Elmer Model 21 spectrometer.

Gas Chromatography.—A Model 154C Perkin-Elmer vapor fractometer was used with helium as the carrier gas under the conditions indicated in each case.

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[17] H. Rupe and A. Steinback, *Ber.*, **44**, 584 (1911).

[18] E. L. Martin, *J. Am. Chem. Soc.* **58**, 1438 (1936).

The *meso* and Racemic Forms of 2,4-Pentanediol and Certain of Their Derivatives

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The *meso* and racemic forms of 2,4-pentanediol have been separated from their mixture *via* fractional distillation of their cyclic sulfite esters, and their structures identified through their proton resonance spectra. The separated diols have been converted to diacetates, bis-3,5-dinitrobenzoates, dichlorides, and dibromides of corresponding structural symmetry and the isomeric pairs characterized. The reduction of acetylacetone by sodium–ethanol, nickel–hydrogen, and sodium borohydride yielded the *meso* and racemic 2,4-pentanediols in the ratios 9:11, 11:9, and 2:1, respectively.

The *meso* and racemic forms of 2,4-pentanediol and their derivatives are of topical interest as model systems for spectroscopic and chemical studies relating to polymers.[1–6] This paper discusses a convenient preparation for the isomeric diols, and their conversion to dihalides and other derivatives.

Previously reported separations of *meso* and racemic forms in 2,4-disubstituted pentane systems are as follows. The sodium hydroxide complexes of the diol cyclic borate esters have been separated in aqueous solution by paper ionophoresis[7] and by chromatography on the borate form of an anion-exchange resin[3]; the diol mono-*p*-bromobenzenesulfonate esters have been separated by solution chromatography on alumina.[8] The dichlorides have been separated in the vapor phase on a dioctyl phthalate column[5] and the diamines were separated long ago *via* crystallization of their acetyl derivatives.[9] Apart from the last system, the above separations are suitable only for small quantities unless very large sized equipment is used. It was, therefore, our aim to develop a simple distillation method for large-scale separation of the diol isomers in a pure state (*via* an ester derivative), using chromatography only as a method of analysis for the isomers. Then, the further goal was to study methods for converting each pure form of the diol to some other useful 2,4-disubstituted pentane derivatives, without loss of isomeric purity.

Results and Discussion

Separation and Characterization of *meso* and Racemic 2,4-Pentanediol.—An experimental review of various methods of reduction of acetylacetone—a readily available starting material—showed that a most straightforward procedure for obtaining a high yield of good-quality diol mixture could be worked out using sodium borohydride, which we recommend in preference to other methods even though it gives an isomer ratio somewhat removed from 1:1 (see Experimental).

A separation of the isomeric diols *via* fractional distillation of their cyclic sulfite esters[10] was found to work quite successfully. Thus, the conversion of the diol mixture to a cyclic sulfite mixture through thionyl chloride was straightforward, requiring only the simplest apparatus; and direct fractionation of the reaction mixture without elaborate work-up was satisfactory. The *meso* and racemic cyclic sulfites, the b.p. of which differ by only 10° at 12 mm., apparently form a sufficiently non ideal boiling mixture for a clean separation to be achieved in a modestly efficient fractionating column (see Experimental). The hydrolysis of the individual cyclic sulfite isomers back to diols with aqueous sodium hydroxide was straightforward, and this type of process is known to occur by sulfur–oxygen bond fission, *i.e.*, without the possibility of change of configuration.[11,12] The over-all yields of pure diol

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[1] J. T. Clarke and E. R. Blout, *J. Polymer Sci.*, **1**, 419 (1946). A 2,4-pentanediol mixture having no ultraviolet absorption above 220 mμ had b.p. 201.0 to 201.2° (760 mm.) and $n^{20}\text{D}$ 1.4354.

[2] M. Matsumoto and K. Imai, *Kobunshi Kagaku*, **15**, 160 (1958).

[3] E. Nagai, S. Kuribayashi, M. Shiraki, and M. Ukita, *J. Polymer Sci.*, **35**, 295 (1959). The melting points reported for the two isomeric forms of 2,4-pentanediol cyclic borate are 85° and 37°. The microanalyses reported for 2,4-pentanediol isomers separated *via* the cyclic borates are incredibly bad.

[4] M. Shiraki and E. Nagai, *Nippon Kagaku Zasshi*, **81**, 976 (1960); R. Chujo, S. Satoh, T. Ozeki, and E. Nagai, *Reports Prog. Polymer Physics, Japan*, **5**, 248 and 251 (1962).

[5] T. Shimanouchi and M. Tasumi, *Spectrochim. Acta*, **17**, 755 (1961).

[6] T. Takata, *et al.*, *Kobunshi Kagaku*, **16**, 693 (1959); **18**, 235 (1961).

[7] J. L. Frahn and J. A. Mills, *Australian J. Chem.*, **12**, 65 (1959).

[8] H. B. Henbest and B. B. Millward, *J. Chem. Soc.*, 3579 (1960).

[9] C. J. Dippel, *Rec. trav. chim.*, **50**, 525 (1931).

[10] *Cf.* F. M. Robertson and A. C. Neish, *Can. J. Res.*, **25B**, 491 (1947). These authors suggested that the *meso* and *laevo*-2,3-butanediols might be easily separated *via* fractional distillation of their cyclic sulfites.

[11] C. A. Bunton, P. B. D. de la Mare, P. M. Greaseley, D. R. Llewellyn, N. H. Pratt, and J. G. Tillett, *J. Chem. Soc.*, 4751 (1958).

[12] C. A. Bunton, P. B. D. de la Mare, A. Lennard, D. R. Llewellyn, R. B. Pearson, J. G. Pritchard, and J. G. Tillett, *ibid.*, 4761 (1958).

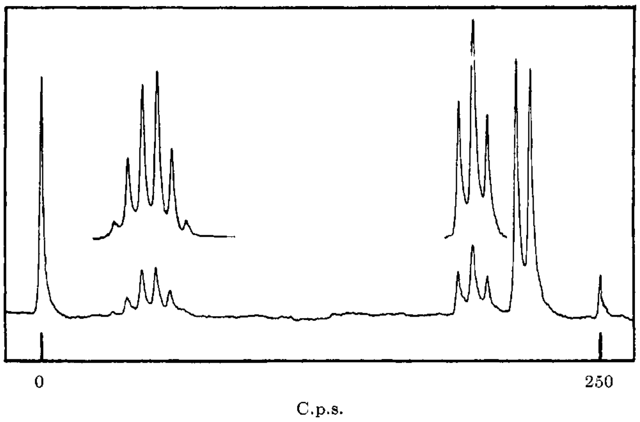

Fig. 1.—Proton resonance spectrum at 60 Mc./sec. of a deuterium oxide solution of the 2,4-pentanediol with m.p. 48–49° and having a bis-3,5-dinitrobenzoate with m.p. 179°. The scale is set arbitrarily at zero for the signal from OH protons and 250 c.p.s. therefrom at a side band.

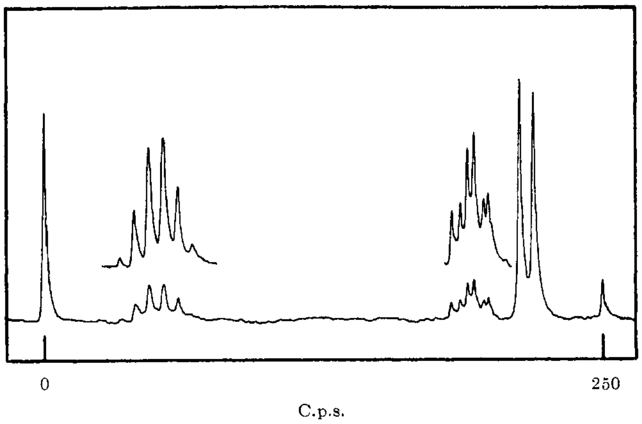

Fig. 2.—Proton resonance spectrum at 60 Mc./sec. of a deuterium oxide solution of the 2,4-pentanediol noncrystallizable at room temperature and having a bis-3,5-dinitrobenzoate with m.p. 190°. (Scale as for Fig. 1.)

isomers separated from the mixture were 30% of *meso* plus 17% of racemic diol.

The 2,4-pentanediol isomers have not been well characterized in the past. Both microanalytical and infrared studies have left much to be desired,[1-3,13-17] which may be due in part to the very hygroscopic nature of these diols.

Microanalysis of our diol products, separated by way of the diol cyclic sulfites, shows them to be acceptably pure and they are further characterized by bis-3,5-dinitrobenzoates. As a method of identification of the isomers we have avoided the classical, optical resolution of the suspected racemic form in favor of direct comparison of the proton resonance spectra of the diols in aqueous solution (*cf.* Fig. 1 and 2). The signals given by the hydroxyl and methyl groups and by the methenyl protons in 2- and 4-positions are very similar for both isomers (at 0, *ca.* 220, and *ca.* 50 c.p.s., respectively, on the scale of the figures). The hydroxyl proton signals are single resonance peaks, indicating rapid exchange of protons between the diols and the aqueous solvent.[18] For both compounds, the signal from the methyl groups is a doublet due to splitting by the neighboring methenyl protons in the molecule (coupling constant *ca.* 6.3 c.p.s.); and the methenyl proton signal itself is an approximately symmetrical sextet of bands split by the five nearest neighboring protons on carbon (CH-to-CH_2 coupling constants close to 6.3 c.p.s.). However, the signals from the methylene group, at *ca.* 190 c.p.s., are diagnostically different for the two diols. One isomer is observed to give an almost symmetrical triplet with intensities approximately in the ratio 1:2:1 and separation 6.3 c.p.s., which suggests that this isomer has its two methylene protons in almost identical magnetic environments and that they are coupled almost equally with the methenyl protons (allowing that the chemical shift between these two types of proton is sufficiently great compared to the coupling so that first-order spectra are observed).[19] Both optical forms of the racemic diol give identical spectra and each should exist in a set of staggered conformations, the two most stable of which are probably those illustrated by structures I and II. If facile rotations about the C–C bonds are permitted in aqueous solutions of the diols at room temperature, as is almost certainly the case, the racemic form should have methylene protons formally equivalent and there should also be equivalent coupling between the two methylene protons and each methenyl proton. Therefore, the observed simple triplet in Fig. 1 diagnoses the racemic diol. In all conformations of the *meso*-diol the methylene protons can never formally be exactly equivalent, and the effect of rapid rotation from one conformation to another should yield an observable, averaged chemical shift (barring accidental equality). The signal from the methylene protons in Fig. 2 can be construed as essentially two triplets (with apparent separations of 6.2 and 6.9 c.p.s., respectively) the centers of which appear to be separated by 2.8 c.p.s. This suggests the following approximate interpretation. The coupling constant between protons set at the tetrahedral angle on the same carbon atom is about 12 c.p.s.[20] and, if two such protons are chemically shifted, the general form of the spectrum is a quadruplet. Thus, for example, the quadruplet generated by two protons shifted by 9 c.p.s. with coupling constant 12 c.p.s. would have a central doublet separated by 3 c.p.s., and satellites 12 c.p.s. away having only one-ninth of the intensity of the main doublet. Hence, the spectrum of the methylene protons on Fig. 2 may be interpreted as a doublet separated by *ca.* 3 c.p.s., the members of which are split into triplets through slightly different coupling to the two methenyl protons, while the low-intensity, split satellites which are expected cannot be distinguished above the background noise under our experimental conditions. This spectrum is then quite consistent with the structure of *meso*-2,4-pentanediol, the chemical shift between the methylene protons being probably close to 0.15 p.p.m. (9 c.p.s.). We consider this analysis to constitute plausible identification of the isomeric diols.

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(13) M. Delepine and A. Horeau, *Bull. soc. chim.*, (5) **4**, 31 (1937).

(14) H. Yonemoto, *Yakaguku Zasshi*, **79**, 143 (1959).

(15) J. M. Sprague and H. Adkins, *J. Am. Chem. Soc.*, **56**, 2669 (1934.)

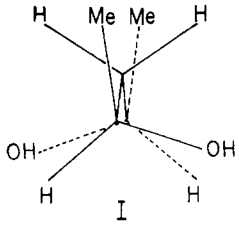
(16) P. S. Stutsman and H. Adkins, *ibid.*, **61**, 3303 (1939).

(17) L. A. Pohoryles, S. Sarel, and R. Ben-Shoshan, *J. Org. Chem.*, **24**, 1878 (1959).

(18) For a simple account of n.m.r. spectra of some aliphatic alcohols see J. D. Roberts, "Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp. 48–51 and 64–66.

(19) A slightly similar situation has been found for *trans*-1,3-cyclohexanediol. *Cf.* H. Finegold and H. Kwart, *J. Org. Chem.*, **27**, 2361 (1962).

(20) M. Karplus, D. H. Anderson, T. C. Farrar, and H. S. Gutowsky, *J. Chem. Phys.*, **27**, 597 (1957); H. S. Gutowsky, M. Karplus, and O. M. Grant, *ibid.*, **31**, 1278 (1959).



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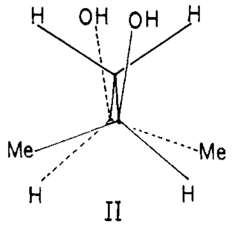
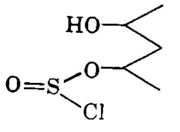


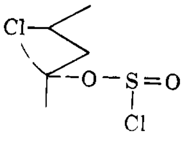
II

2,4-Dihalopentanes.—From some of the classical examples of alcohol–halide conversion in the literature, the outlook for converting the separated 2,4-pentanediols to dihalides, without isomeric equilibration, appeared good. Thus, the conversion of a simple secondary alcohol, 2-octanol, to the corresponding chloride by thionyl chloride in the presence of pyridine has been reported to occur with clean inversion of configuration.[21,22] Furthermore, the racemic-*erythro*- and (+)-*threo*-3-chloro-2-butanols have been converted with clean inversion to pure racemic and *meso*-2,3-dichlorobutanes, respectively, by thionyl chloride in pyridine, demonstrating that the presence of the chlorine substituent, neighboring the hydroxyl group being replaced, does not alter the reaction mechanism for this reagent through "participation."[23]

In accord with the previous results, the reaction of thionyl chloride and pyridine at 0° with each 2,4-pentanediol isomer gave a good yield of a 2,4-dichloropentane, in each case pure except for 2–3% of the alternative isomer, as determined by chromatographic analysis. This reaction would be expected to proceed principally with Walden inversion by the S_N2 mechanism[24–26] at both reaction cites, so that the resulting dihalide should have molecular symmetry identical with that of the 2,4-pentanediol isomer from which it was derived. It is unclear[24] whether or not the production of the few % of alternative isomer was entirely due to competition of unimolecular internal substitution, by the chlorine in the chlorosulfite intermediate III, with the predominant bimolecular substitution by external chloride, since concomitant rearrangement of the product may well contribute (*cf.* bromides col. 2). The results of Lucas and Gould[23] almost certainly preclude the possibility of some form of assisted S_N1 reaction, as in IV for the second stage of our reaction, which could result in retention of the steric configuration at one cite.



III



IV

A previous study has shown that ethyl (−)-lactate can be converted with little or no racemization to ethyl (+)-α-bromopropionate by phosphorus pentabromide and pyridine.[27] The reagents, thionyl bromide and phosphorus tribromide, with or without pyridine, have produced considerable racemization, on the other hand.[21,28] There appears to be no evidence available concerning the effect of these reagents in the presence of neighboring bromine. However, it would be consistent with the foregoing facts to assume that phosphorus pentabromide in pyridine would consistently invert the configuration in hydroxyl–bromide transformations.

Accordingly, phosphorus pentabromide in pyridine with the racemic 2,4-pentanediol produced a reasonable yield of dibromide containing only 2% of the *meso* isomer. With *meso*-2,4-pentanediol, *meso*-2,4-dibromopentane containing much larger amounts of the racemic form was produced (5–20% depending on experimental procedure) essentially because the lower-boiling, racemic form tended to distil out fractionally in preference to the required *meso* product during isolation. Unfortunately, efficient fractionation was required to remove one tenacious impurity from the dibromides (not required for the dichlorides) and prolonged boiling under reduced pressure was observed to induce rearrangement toward a 50–50 *meso* and racemic mixture. Small amounts of the *meso*-dibromide containing 5–6% of the racemic form could nevertheless be obtained consistently.

P.m.r. spectra of these 2,4-dihalopentane isomers, which need not be detailed here,[29] show characteristics, quite analogous to the diol case, which diagnose molecular symmetry confirming the structures designated above. If the 2,4-dihalopentane isomers are required for purposes in which the presence of small amounts of the alternative isomer can be tolerated, it is our conclusion that the processes described earlier are best suitable for the preparation of quantities in the order of tens of grams and more.

Experimental

Sodium–Alcohol Reduction of Acetylacetone.—Fifty-six grams of sodium was added in small amounts to a stirred solution of 40 g. of acetylacetone in 750 ml. of ethanol held between 0–10°. After *ca.* 14 hr., methanol was added to destroy residual sodium quickly. The solution was neutralized with concentrated hydrochloric acid, and the product freed from salt and alcohol yielding, after distillation, 12 g. (30% yield) of 2,4-pentanediols, b.p. *ca.* 85° (6 mm.). With 100 g. of acetylacetone in the above procedure, the yield of diols was 21 g., representing a lower yield from the acetylacetone but more efficient use of the sodium and alcohol.

Fractional distillation of the diol mixture obtained by the above procedures through a 4-ft. column (described later) gave, apart from a small forerun, only fractions of constant refractive index, $n^{20}\text{D}$ 1.4342, and b.p. 74° (3 mm.). Vapor phase chromatography on diverse columns also failed to separate the two isomers present.

Nickel–Hydrogen Reduction of Acetylacetone.—Hydrogen at 1000–2000 p.s.i. was passed into a suspension of *ca.* 20 g. of pyrophoric Raney nickel in a solution consisting of 300 ml. of acetylacetone, 400 ml. of dioxane, and 50 ml. of triethylamine, at 135°. After 5 hr., 80% of the theoretical amount of hydrogen was absorbed and the reaction solution remained colorless. Fractionation yielded 196 g. (75% yield) of diols, b.p. 65° (2 mm.), $n^{20}\text{D}$ 1.435. Higher yields were possible by running the reaction longer.

Sodium Borohydride Reduction of Acetylacetone.—A solution of 1 kg. of acetylacetone in 3 kg. of methanol was added slowly to

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(21) A. McKenzie and T. M. A. Tudhope, *J. Biol. Chem.*, **62**, 551 (1924).

(22) *Cf.* W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman, and A. D. Scott, *J. Chem. Soc.*, 1266 (1937).

(23) H. J. Lucas and C. W. Gould, Jr., *J. Am. Chem. Soc.*, **63**, 2541 (1941).

(24) *Cf.* C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 391–395.

(25) *Cf.* E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, Chap. 5 and 8.

(26) *Cf.* J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp. 139–141.

(27) W. Gerrard, J. Kenyon, and H. Phillips, *J. Chem. Soc.*, 153 (1937).

(28) J. Kenyon, H. Phillips, and G. R. Shutt, *ibid.*, 1663 (1935).

(29) See W. C. Tincher, Abstracts of 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962, Polymer Chemistry Section, Appendix, p. 142; and further work to be published.

a stirred solution of 250 g. of sodium borohydride and 5 g. of sodium hydroxide pellets in 2.5 kg. of water, maintained below 20°. The solvents were then removed rapidly at *ca.* 20 mm. pressure. Five kilograms of glycerol was added to the solid residue of sodium hydroxide-coordinated 2,4-pentanediol monoborates and the product was distilled under reduced pressure through a short fractionating column, yielding 885 g. (87% yield) of diols with n^{20}D 1.434.

Separation of 2,4-Pentanediol Mixture.—One equivalent of thionyl chloride (623 ml.) was added slowly to the diol product from the sodium borohydride reduction above (885 g.) dissolved in 400 ml. of ether and contained in a large conical flask equipped with a magnetic stirrer. When the voluminous evolution of hydrogen chloride ceased, the solution was heated to 100° and dry nitrogen bubbled through for 1 hr. Further cleaning up of the reaction mixture by water washing was found to be unnecessary and involved subsequent use of an unwieldy amount of drying agent owing to the high solubility of water in these sulfite esters. Fractional distillation of the product using a 4-ft.-long, vacuum-jacketed column of 0.5-in. i.d., packed loosely with glass helices of 0.25-in. o.d. (which gave a 25-plate separation of benzene–carbon tetrachloride mixtures at atmospheric pressure), gave 70 g. of forerun, b.p. 64–72° (12 mm.), then 545 g. *meso*-2,4-pentanediol cyclic sulfite, b.p. 72° (12 mm.), n^{20}D 1.4403, and 26 g. of cyclic sulfite mixture, b.p. 72–82° (12 mm.), and finally 300 g. of racemic 2,4-pentanediol cyclic sulfite, b.p. 82° (12 mm.), n^{20}D 1.4472. The reflux ratios required were about 100:1 for the forerun, which contained a number of impurities, and about 10:1 for the remainder of the distillation. Chromatography (*cf.* Table I) showed the *meso* isomer to be quite pure. However, the racemic isomer consistently contained a very closely boiling impurity (hence, the poor microanalysis that follows), but this did not seem to affect adversely the purity of the racemic diol finally prepared.

Anal. Calcd. for $C_5H_{10}O_3S$: C, 40.0; H, 6.7; S, 21.35. Found: *meso*-sulfite, C, 40.1; H, 6.6; S, 21.2; and racemic sulfite, C, 40.5; H, 6.9; S, 19.6.

Each cyclic sulfite was saponified, while stirring with five times its volume of water, by gradual addition of two equivalents of sodium hydroxide. The water was evaporated under vacuum and the residue extracted with chloroform. Distillation of the extract gave diol in 75% yield for this step: *meso*-diol, b.p. 73° (3 mm.), n^{20}D 1.4327; racemic diol, b.p. 74° (3 mm.), m.p. 48–49°, n^{20}D 1.4378. Both diols are very hygroscopic.

Anal. Calcd. for $C_5H_{12}O_2$: C, 57.7; H, 11.5. Found: *meso*-diol, C, 57.5; H, 11.5; and racemic diol, C, 57.7; H, 11.0.

One gram of each diol isomer was stirred with 5 g. of 3,5-dinitrobenzoyl chloride in 20 ml. of dry pyridine at 0° for 2 hr. The mixture was diluted with water and the crude, insoluble ester washed with aqueous sodium bicarbonate, then with water, and recrystallized from acetone. The melting points were 190 and 179° for the pure *meso* and racemic diesters, respectively. Yields were almost quantitative.

Anal. Calcd. for $C_{19}H_{16}O_{12}N_4$: C, 46.3; H, 3.3; N, 11.4. Found: *meso*-isomer, C, 46.4; H, 3.5; N, 11.4; racemic form, C, 46.6; H, 3.6; N, 11.3.

The diols were identified through their n.m.r. spectra, so identifying also the other derivatives.

2,4-Pentanediol Isomer Ratios and Diacetates.—Samples of the separated diol isomers were esterified to diacetates using, in turn, all three common reagents: acetic acid and anhydride, and acetyl chloride. Analysis of the products by vapor phase chromatography (see p. 1549 and Table I) showed them to be isomerically pure. Physical data are: for *meso*-2,4-pentanediol diacetate, b.p. 70° (4 mm.), 203° (760 mm.), n^{20}D 1.4172; and for the racemic diacetate, b.p. 62° (4 mm.), 201° (760 mm.), n^{20}D 1.4142.[30]

Anal. Calcd. for $C_9H_{16}O_4$: C, 57.4; H, 8.5. Found: *meso*-diacetate, C, 57.0; H, 8.5; and racemic diacetate, C, 57.2; H, 8.5.

Samples of the diol mixtures from the first three preparations above were converted to diacetate mixtures which were shown by vapor phase chromatography to consist of *meso* and racemic forms in the ratios 9:11 (Na/EtOH), 11:9 (Ni/H_2), and 2:1 ($NaBH_4$). Fractional distillation of the diol diacetates was insufficiently efficient in our apparatus to give a good yield of completely separated products, and is not recommended.

2,4-Pentanediol Cyclic Borates.—A previous report has claimed that the reduction of acetylacetone by sodium borohydride in aqueous methanol produces almost entirely the *meso*-2,4-pentanediol (isomer ratio *ca.* 45:1).[31] We have repeated the cyclic borate work-up procedure[31] which led to this erroneous conclusion, as follows. Fifty grams of acetylacetone was reduced with sodium borohydride as described.[31] After evaporation of solvent, the residue was neutralized with 2 *N* aqueous sulfuric acid and the slightly acid solution extracted with chloroform. Distillation of the extract yielded 43 g. of viscous oil, b.p. 136° (1 mm.), the tris-2,4-pentanediol di(cyclic borate). The oil was treated with 5 ml. of water and the resulting partly crystalline mixture of diol and diol (mono) cyclic borate was filtered. The solid material was recrystallized twice from benzene–petroleum ether and yielded 4 g. of large, white prisms, m.p. 83–85° (sealed tube). The infrared spectrum of this product as a Nujol mull was identical with that published for the pure, high-melting 2,4-pentanediol cyclic borate isomer.[3]

Anal. Calcd. for $C_5H_{11}O_3B$: C, 46.2; H, 8.5. Found: C, 45.9; H, 8.5.

The above experience is similar to that previously reported[31] and presumably led to the assumption that the entire product consisted of just the one form of 2,4-pentanediol cyclic borate. Modification of procedure, as follows, shows that the two forms are present. (No configurational rearrangements are suspected in these systems.) Thus, in a similar experiment, the viscous oil was treated with water, as before, then the whole mixture was crystallized from benzene–petroleum ether. The noncrystalline residue was treated with 6 g. of boric acid and fractionally crystallized from hexane. Altogether, there was obtained a series of white, crystalline fractions comprised of 7 g., m.p. *ca.* 80°; 28 g., m.p. *ca.* 75–76°; 1 g., m.p. 65–70°; and some residual oil which could not easily be crystallized.

Anal. (*cf.* preceding). Found for the 75–76° material: C, 45.9; H, 8.4.

Some of the 75–76° melting material was distilled with glycerol to recover diol, and this was converted to diacetate. Chromatography showed a mixture of 20% racemic with 80% *meso*-diacetate.

2,4-Dichloropentane Isomers.—One hundred and sixteen grams of thionyl chloride was run slowly into a mixture of 26 g. of *meso*-2,4-pentanediol and 3 ml. of dry pyridine kept at *ca.* 0° by means of an ice–salt bath. After refluxing for 3 hr., the mixture was worked up by addition of iced water, then ether extraction. The ether layer was washed with aqueous sodium bicarbonate solution and water, dried over anhydrous magnesium sulfate, and fractionated yielding 21 g. of *meso*-2,4-dichloropentane, b.p. 40° (12 mm.), n^{20}D 1.4423. Vapor phase chromatography showed this product to be quite pure apart from *ca.* 2% of its isomer. Pure racemic 2,4-pentanediol treated likewise gave racemic 2,4-dichloropentane of b.p. 36° (12 mm.), n^{20}D 1.4390, which likewise contained a few per cent of its isomer.[32] (If the amount of pyridine is increased this does not alter the final result; it merely complicates the work-up.)

Anal. Calcd. for $C_5H_{10}Cl_2$: C, 42.6; H, 7.1; Cl, 50.3. Found: *meso* isomer, C, 42.4; H, 7.2; Cl, 50.2; racemic form, C, 42.4; H, 6.9; Cl, 50.2.

2,4-Dibromopentane Isomers.—A slurry of phosphorus pentabromide was prepared by allowing 45.6 ml. of bromine to run very slowly on to 97.8 ml. of phosphorus tribromide dissolved in 30 ml. of dry benzene and stirred at 0° under a current of dry nitrogen. Fifty grams of racemic 2,4-pentanediol dissolved in 45 ml. of dry pyridine was run in slowly over a period of 5 hr. attended by vigorous evolution of hydrogen bromide and heat. Passage of dry nitrogen and stirring was then continued overnight while the reaction mixture warmed to room temperature. Iced water was then added and the mixture extracted with benzene. The benzene extract was washed with aqueous sodium carbonate, then by water, dried (Na_2SO_4), and evaporated under vacuum at room temperature. The residue was distilled rapidly at 4 mm. yielding *ca.* 52 g. of at least 96% pure 2,4-dibromopentane. Rapid fractionation of this material yielded racemic 2,4-

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[30] *Cf.* R. L. Frank, R. D. Emmick, and R. S. Johnson, *J. Am. Chem. Soc.*, **69**, 2313 (1947). Data reported for a mixture were b.p. 88–91° (11 mm.), n^{20}D 1.4160.

[31] J. Dale, *J. Chem. Soc.*, 910 (1961). Note that the reduction of the very similar system 1,3-diphenyl-1,3-propanedione by the same reagent is reported in this reference to have given a diol isomer ratio of *ca.* 3:2, a more authentic result quite similar to that obtained in the present work for acetylacetone (2:1) under parallel reaction conditions.

[32] *Cf.* D. V. Tischenko, *J. Gen. Chem. USSR*, **9**, 1380 (1939). Data reported for a mixture were b.p. 142–147° (761 mm.), n^{16}D 1.4339.

dibromopentane, b.p. 40° (4 mm.), n^{20}_D 1.4968, containing only 2% of the *meso* isomer.

The same procedure repeated for the *meso*-diol gave *meso*-dibromide containing substantial quantities of the alternative isomer, 5–20% depending on reaction conditions and the method of isolation. However, fractional distillation of such material through the column described above usually resulted in 25% recovery of a pure dibromide mixture, b.p. 45° (5 mm.), n^{20}_D 1.5015, containing not less than *ca.* 95% of the *meso*-dibromide.[33] Isomeric equlibration was noted on prolonged boiling of the product at 4 mm., so setting a limit to the degree of separation of the higher boiling (*meso*) product attainable by fractional distillation.

Anal. Calcd. for $C_5H_{10}Br_2$: C, 26.1; H, 4.35; Br, 69.5. Found: *meso*-isomer, C, 26.1; H, 4.15; Br, 69.6; racemic form, C, 26.1; H, 4.6; Br, 69.4.

Vapor Phase Chromatography.—The retention times given in Table I were obtained with a column 10 ft. long and 0.4-in. i.d., packed with 8% by weight of Carbowax (mol. wt., 9000) on 30/60-mesh firebrick, and with an inlet pressure of 40 p.s.i. of helium gas to an F. and M. Scientific Corporation Model 500 instrument. The retention times quoted in the table were for 1-μl. samples and a flow rate of 570 ml./min. The table also shows the maximum quantities of material in μl. which could be separated under the conditions described, indicating the degree of spreading of the various samples on the column.

N.m.r. Spectroscopy.—Samples of each isomeric form of 2,4-pentanediol with four times their volume of deuterium oxide were degassed and sealed under vacuum in thin-walled tubes, 6 × 0.5 in. in diameter. Spectra were run at room temperature on a Varian machine operating at 60 Mc./sec., equipped with a Varian 12-in. electromagnet, flux stabilizer, and field-homogeneity stabilizer. A side band of 250 c.p.s. was set off at high field from the signal due to the hydroxyl protons. Hence, the arbitrary scale on Fig. 1 and 2 is set at zero for the exchanging hydroxyl protons in an alcohol–water–HDO–deuterium oxide mixture containing *ca.* 4% H and 96% D.

TABLE I

RETENTION TIMES IN MINUTES FOR 2,4-DISUBSTITUTED PENTANE DERIVATIVES UNDER CONDITIONS SPECIFIED IN THE TEXT

Derivative	Temp., °C.	Retention time *meso*	Retention time Racemic	Max. quant. (μl.)
Diacetates	130	6.25	5.1	1
Cyclic sulfites	130	4.7	6.45	50
Dichlorides	80	3.8	3.15	1
Dibromides	100	6.7	5.5	10

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[33] R. G. Kelso, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Am. Chem. Soc.*, **77**, 1751 (1955). Data reported for a mixture were b.p. 70° (17 mm.), n^{20}_D 1.4960.

The Acetylation of Some Substituted Ferrocenes[1]

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A number of mono- and disubstituted ferrocenes have been acetylated. It has been found that iodine is lost from iodoferrocene under the acetylation conditions employed. Contrary to another report, bromo- and chloroferrocenes are acetylated to give 1′-acetylbromo- and chloroferrocenes in good yield. Acetylation of acetamido- and urethanoferrocenes gives predominantly the heteroannularly substituted isomers, and these substituents are deactivating.

In recent years a number of reports have appeared on the electrophilic substitution reactions of ferrocene derivatives.[3] Rosenblum[4] has reported some studies of this type and has used a molecular orbital calculation to predict the effect of substituent groups. Recently Morrison and Pauson[5] have shown that Friedel–Crafts acetylation of chloro-, methylthio- and methoxyferrocenes leads to the replacement of the substituent by hydrogen. Thus chloroferrocene yields ferrocene and methoxyferrocene yields acetylferrocene. In connection with our work on metallocenyl carbonium ions and for other reasons it was desirable to have in hand substituted ferrocenes. This led to a study of the acetylation reactions of iodo-, bromo-, chloro-, acetamido-, methoxycarbonylamino-, ethoxycarbonylamino-, 1,1′-diethoxycarbonylamino-, and cyanoferrocenes.

Results and Discussion

The results are summarized in Table I.

Structural assignments were made chiefly on the basis of infrared spectral correlations. The pertinent data are summarized in Table II. It can be seen that all disubstituted compounds assigned the 1,2-homoannular structure possess bands near 9 and 10 μ (1111 and 1000 cm.$^{-1}$) in accordance with the 9–10 rule set forth by Rosenblum.[6] In addition the 1,2-disubstituted compounds clearly show hydrogen bonding between the amide hydrogen and the oxygen atom of the acetyl group.[7] 2-Acetyl-1,1′-di(ethoxycarbonylamino)ferrocene also possesses a spectrum indicative of hydrogen bonding whereas 3-acetyl-1,1′-di(ethoxycarbonylamino) ferrocene does not. The compounds assigned the 1,1′-disubstituted structure lack the bands near 9 and 10 μ but do show absorption near 8.95 μ (1117 cm.$^{-1}$) which is known to be indicative of a ferrocene possessing a cyclopentadienyl ring substituted only with an acetyl group.[6]

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[2] (a) This paper is based on the Ph.D. thesis of D. W. Hall, December, 1962; (b) the Denver Research Center of the Marathon Oil Company.

[3] For a review see K. Plesske, *Angew. Chem.*, **74**, 301, 347 (1962).

[4] M. Rosenblum and W. G. Howells, *J. Am. Chem. Soc.*, **84**, 1167 (1962).

[5] J. G. Morrison and P. L. Pauson, *Proc. Chem. Soc.* (London), 177 (1962).

[6] M. Rosenblum, *Chem. Ind.* (London), 953 (1958).

[7] R. E. Richards and H. W. Thompson, *J. Chem. Soc.*, 1248 (1947).