Anal. Calcd. for $C_{15}H_{11}O_2NCl_2$ ($C_9H_6ClN \cdot C_6H_5ClO_2$): Cl, 22.88. Found: Cl, 22.78.

Both salts decompose when treated with a hot mixture of petroleum ether and water, the 4-chlororesorcinol going into solution in the water layer and the freed basic component in the organic layer.

Acknowledgment.—The authors are grateful to Drs. J. Lewis Towle and Velmer A. Fassel, and to Messrs. Marvin Margoshes, Robert K. Ingham and Donald L. Esmay for assistance.

AMES, IOWA

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE FACULTY OF SCIENCES, AND OF THE INSTITUTE "ALONSO BARBA," HIGHER COUNCIL FOR SCIENTIFIC RESEARCH, UNIVERSITY OF BARCELONA (SPAIN)]

The *cis*- and *trans*-2-Hydroxycyclopentanecarboxylic Acids[1]

BY JOSÉ PASCUAL AND JOSÉ CASTELLS[2]

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The 2-hydroxycyclopentanecarboxylic acids, reported previously as liquids, have been isolated in solid form. Derivatives have been prepared. A study of some of their physical constants led to the assignment of *cis*-configuration to the acid melting at 52–53.4° (cor.), and of *trans* to the acid melting at 68.3–69.0° (cor.).

By reduction of 2-ketocyclopentanecarboxylic acid ethyl ester followed by hydrolysis, a liquid mixture containing the *cis*- and *trans*-2-hydroxycyclopentanecarboxylic acids is obtained.[3a,b,c,4] Boeseken, *et al.*,[3b] separated this mixture into two liquid components. One of them formed an isopropylidene derivative and enhanced the electrolytic conductivity of boric acid solutions, and, therefore, was considered to be the *cis*-acid. The other substance was impure *trans*-acid.

We have carried out the reduction of ethyl 2-ketocyclopentanecarboxylate with sodium amalgam, according to Dieckmann,[3a] and also by hydrogenation with the aid of platinum oxide. Both methods gave a mixture of esters of the same physical properties, and of the same chemical composition.

TABLE I

MELTING POINTS (CORRECTED) OF DERIVATIVES

Name	α-Isomer (*cis*)	β-Isomer (*trans*)	a[a]	b
Hydroxy acid	52–3.4°	68.3–9°	....	....
Ethyl ester	B.p. 54–56.5 (0.1–0.2 mm.)	id. 57.5–60 (id.)	....	....
3,5-Dinitrobenzoate of ethyl ester	116–116.8	76.2–77.1	116.0–116.8	76.2–77.1°
Anilide	163.8–164.3	149–150.3	163.8–164.3	131.1–131.7
p-Toluidide	181.8–182.2	150–151.2	181.8–182.2	136–140
Hydrazide	155.8–156.5	135.3–137.2	153–154[b]	124–125[b]
Phenylurethan of ethyl ester	88.9–90.2	[c]	88.6–90	....

[a] a is the main derivative separated from the reaction mixture. [b] We report here the melting points of the hydrazides prepared by Mousseron and Jacquier.[4] [c] The attempted preparation of this derivative gave a liquid substance which we did not study further.

We tried the direct separation of the *cis*- and *trans*-2-hydroxycyclopentanecarboxylic acids from the crude mixture by means of solid derivatives, like the acetates, the phenacyl and *p*-nitrobenzyl esters, and the benzylthiouronium salts, but we did not obtain satisfactory results.

However, from the mixture of ethyl esters prepared by hydrogenation we succeeded in separating the pairs of isomerides, a and b, reported in Table I. The 3,5-dinitrobenzoates were especially important, for by stepwise hydrolysis the pure isomeric 2-hydroxycyclopentanecarboxylic ethyl esters and acids were prepared, the latter in solid form. Thus we were able to prepare other pure derivatives which are listed as α- and β-isomerides in Table I.

Comparison of the values for the α- and β-derivatives with those listed for the a- and b-compounds shows that the substances in the b-group are not pure in spite of their apparently sharp melting points. In the preparation of the 3,5-dinitrobenzoyl derivatives we also obtained a product melting at about 70°, but it could be resolved by several recrystallizations into the pure components. In this connection we should like to point out that the low-melting hydrazide reported by Mousseron and Jacquier[4] melted about ten degrees below our β-hydrazide.[5]

Of the two methods employed, catalytic reduction gave by far the better yield, and thus we feel that the more reliable configurational inference can be drawn from the yields obtained in that way, *i.e.*,

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(1) This paper includes part of the experimental work presented by J. Castells in partial fulfillment of the requirements for his Doctor's degree, and it was presented at the XIIth International Congress of Pure and Applied Chemistry. A preliminary note has been published in *Anales fís. y quím.*, **46**, 403 (1950).

(2) Research Fellow of the "Patronato Juan de la Cierva de Investigación Técnica," 1948–1950.

(3) (a) W. Dieckmann, *Ann.*, **317**, 64 (1901); (b) J. Boeseken, G. Sloff and J. M. Hoeffelman, H. E. Hirsch, *Rec. trav. chim.*, **52**, 881 (1933); (c) H. Stenz, Fr. Fichter and H. Arni, *Helv. Chim. Acta*, **19**, 392 (1936).

(4) M. Mousseron and R. Jacquier, *Bull. soc. chim. France*, 238 (1950).

(5) Another recent example of confusing mixtures of isomers melting like pure compounds is given by N. R. Campbell and J. H. Hunt, *J. Chem. Soc.*, 1379 (1950).

55.5% of the α- and 29.5% of the β-3.5-dinitrobenzoyl derivative. It is known that catalytic hydrogenation with platinum favors the formation of *cis*-derivatives; for example, this has been shown in the analogous case of the ethyl 2-ketocyclohexanecarboxylates.[6] Therefore, the α-ester of the hydroxy acid obtained from the α-3,5-dinitrobenzoate, as well as the α-hydroxy acid itself, should be the *cis*-isomer.

This conclusion is supported by the properties of the pure esters of the hydroxy acids (see Table II). The Auwers–Skita rule holds. The viscosity should be higher for the *trans*- than the *cis*-ester, similar to the example of the 2-hydroxycyclohexanecarboxylic esters,[6] and such is indeed the case. However, the difference in the viscosity of the isomers is much less pronounced in the present case. The boiling points seem to agree with the assigned configuration. We agree with Mousseron and Jacquier[4] in assigning the *cis* configuration to the hydrazide of higher melting point.

Table II

2-Hydroxy-cyclo-pentane-carboxylic ethyl ester	B.p. (0.1–0.2 mm.), °C.	d^{25}_{25}	$n^{25}\text{D}$	η^{25}	$\frac{n^2 - 1}{n^2 + 1}\frac{M}{d}$
α	54–56.5	1.0723	1.4551	0.075	52.87
β	57.5–60	1.0685	1.4534	.084	52.91

Experimental

Reduction of Ethyl 2-Ketocyclopentanecarboxylate.—The hydrogenation of a 1:1 ketoester–ethanol solution was carried out by means of platinum oxide (10%) at room temperature and a pressure of 3–4 atmospheres. The filtered mixture did not give any color reaction with ferric chloride. The product was distilled in vacuum. (It is better to perform the distillation at 0.1 mm. in order to prevent the formation of unsaturated ester); physical constants: d^{25}_{25} 1.0716; $n^{25}\text{D}$ 1.4559; η^{25} 0.076.

Reaction of the Ethyl 2-Hydroxycyclopentanecarboxylates with Phenyl Isocyanate.—A solution of 0.40 g. of the mixture of catalytic hydrogenation and 0.4 g. of phenyl isocyanate in 12 ml. of purified ligroin (b.p. 75–100°) was refluxed during 5–6 hours in the absence of moisture. The solution was filtered while still warm. On cooling, an oily substance separated, which changed overnight into 0.25 g. of a solid product, m.p. 71–83°. Repeated recrystallization from ligroin gave finally 0.05 g. of solid, m.p. 88.6–90°.

Phenylurethan from Pure *cis*-Hydroxyester.—Operating as before, from 0.20 g. of *cis*-hydroxy ester we obtained directly 0.25 g. of needles, gathered in starry aggregates, m.p. 88.9–90.2°, identical with the substance described above.

Anal. Calcd. for $C_{15}H_{19}O_4N$: N, 5.03. Found: N, 5.00, 5.02.

Reaction of the Ethyl 2-Hydroxycyclopentanecarboxylates with Anilinomagnesium Bromide.—To the ice-cooled solution of ethylmagnesium bromide, prepared from 0.5 g. of magnesium, a cold solution of 1.9 g. of aniline in anhydrous ether was added slowly. A white precipitate formed. The solution was stirred and after 30 minutes 1.0 g. of the mixture of esters was added. The mixture was refluxed for about ten minutes, and, when cold, treated with 2 *N* hydrochloric acid. The bulky precipitate formed between the two layers was separated and washed a few times with a little water. The resulting white substance, recrystallized from ethanol, had m.p. 163.8–164.3°.

Anal. Calcd. for $C_{12}H_{15}O_2N$: N, 6.82. Found: N, 7.08, 7.04.

This substance gave a pronounced melting point depression when mixed with cyclopentene-1-carboxanilide.

The ethereal layer was washed with cold 2 *N* hydrochloric acid, water, and dried. The semisolid residue left after removal of the solvent was drained dry, and after several crystallizations in 1:1 alcohol–water yielded a white solid, m.p. 131.1–131.7°. A mixed melting point with the product described in the preceding section gave no depression.

Anal. Calcd. for $C_{12}H_{15}O_2N$: N, 6.82. Found: N, 7.03, 6.93.

The yield varied widely in the different preparations, increasing with good stirring. The yields were 60% for the high-melting and 15% for the low-melting anilide, based on the mixture of esters employed.

Anilide from Pure *cis*-Hydroxyester.—With the same procedure as used above only one anilide was found, identical to the anilide melting at 163.8–164.3°.

Anilide from Pure *trans*-Hydroxyester.—Recrystallization from aqueous alcohol gave little white leaflets with serrated edges, m.p. 149–150.3°. Its mixture with anilide obtained from the *cis*-hydroxy ester melted at 131–134°.

Anal. Calcd. for $C_{12}H_{15}O_2N$: N, 6.82. Found: N, 7.02, 7.06.

Reaction of the Ethyl 2-Hydroxycyclopentanecarboxylates with *p*-Toluidinomagnesium Bromide.—The procedure is the same as that used with anilinomagnesium bromide. The toluidide formed in larger quantity, the less soluble one, was recrystallized from alcohol. It melted at 181.8–182.2°.

Anal. Calcd. for $C_{13}H_{17}O_2N$: N, 6.38. Found: N, 6.46, 6.46.

The second *p*-toluidide, after very many recrystallizations from somewhat diluted alcohol, melted at 136–140° (uncor.).

Anal. Calcd. for $C_{13}H_{17}O_2N$: N, 6.38. Found: N, 6.12, 6.53.

Toluidide from Pure *cis*-Hydroxyester.—Only the *p*-toluidide, m.p. 181.8–182.2°, was formed.

Toluidide from Pure *trans*-Hydroxyester.—Only one toluidide was formed. Recrystallization from aqueous alcohol gave shiny white sheets, m.p. 150–151.2°.

Anal. Calcd. for $C_{13}H_{17}O_2N$: N, 6.38. Found: N, 6.58, 6.53.

A mixed melting point with the *p*-toluidide from the *cis*-ester melted at 137–149°.

Reaction of the Ethyl 2-Hydroxycyclopentanecarboxylates with 3,5-Dinitrobenzoyl Chloride.—To an ice-cooled solution of 25 g. of ester mixture from the catalytic hydrogenation in 125 g. of dry pyridine was added 41 g. of 3,5-dinitrobenzoyl chloride in portions of 2 g. at a time, with vigorous stirring after each addition, while keeping the temperature low. After the first few additions a precipitate appeared and increased in amount as the reaction progressed. The mixture was left overnight at room temperature; then crushed ice was added, and the solution was made acidic with 4 *N* sulfuric acid. The precipitate, after a water wash, was treated with aqueous 2 *N* sodium carbonate in a mortar until all the dinitrobenzoic acid had been removed. The residue, conveniently washed with water, alcohol, and finally dried, was recrystallized 3–4 times from about 1/2 liter of anhydrous ethanol, and the 3,5-dinitrobenzoate, m.p. 116.0–116.8°, was obtained. The compound formed white, silky needles, gathered in starry aggregates.

Anal. Calcd. for $C_{15}H_{16}O_8N_2$: N, 7.95. Found: N, 7.76, 7.74.

Concentration of the mother liquors, preferably with omission of that from the last recrystallization, gave a solid which after at least five recrystallizations, alternately from anhydrous and 95% ethanol, yielded transparent, hard rhombic tablets, m.p. 76.2–77.1°.

Anal. Calcd. for $C_{15}H_{16}O_8N_2$: N, 7.95. Found: N, 7.95, 7.86.

The yields in which the dinitrobenzoates were formed are 30–31 g. of the product, m.p. 116.0–116.8°, and 16–17 g. of the derivative, m.p. 76.2–77.1°. The total of these quantities represents 85% of the theoretical yield based on the mixture from the catalytic hydrogenation.

***cis*-Hydroxy Ester.**—It gave the 3,5-dinitrobenzoate, m.p. 116–116.8°.

***trans*-Hydroxy Ester.**—It gave dinitrobenzoate, m.p. 76.2–77.1°.

Preparation of Pure Ethyl *cis*- and *trans*-2-Hydroxycyclopentanecarboxylates.—To 10 g. of finely pulverized

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[6] J. Pascual, J. Sistaré and A. Regás, *ibid.*, 1943 (1949).

3,5-dinitrobenzoate in a 250-ml. Erlenmeyer flask was added rapidly with vigorous shaking during 15 seconds 75 ml. of 0.5 *N* sodium hydroxide in alcoholic solution. The flask was immersed immediately in a salt–ice cooling mixture. The resulting red solution was acidified as fast as possible (about 30 sec.) with concentrated sulfuric acid, with careful avoidance of any pronounced rise in temperature. The solution became first blue, and colorless when acidic. It was made alkaline again with solid sodium carbonate, regenerating the blue color, and strong cooling was continued in order to separate from the solution most of the salts. The precipitate (P) was filtered and thoroughly washed with cooled anhydrous ethanol. The washings were added to filtrate and concentrated. The resulting mixture of ester and salts was treated with a small amount of water and filtered, giving solid (P′). The filtrate was extracted twice with ether. (If the ethereal solution turns color it is desirable to wash it with a little water.) The ethereal solution (S) contained the ethyl 2-hydroxycyclopentanecarboxylate. The solid (P) was extracted with water, yielding solid (P″). The aqueous extract was extracted twice with ether, and the resulting ethereal solution (S′) was added to (S), and the solvent evaporated. The residue was distilled at 0.1–0.2 mm., and most of the material boiled at about 55°. The distillate did not decolorize a dilute potassium permanganate solution. The esters are fairly hygroscopic. (P′) and (P″) were unchanged 3,5-dinitrobenzoates. The aqueous solution gave 3,5-dinitrobenzoic acid on acidification. From 10 g. of 3,5-dinitrobenzoate, m.p. 116.0–116.8°, we obtained 2.9 g. of ethyl *cis*-2-hydroxyclopentanecarboxylate the constants of which are reported in Table II, and 0.5 g. of non-hydrolyzed product.

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 8.91. Found: C, 61.08, 60.86; H, 8.97, 9.05.

From 7.4 g. of 3,5-dinitrobenzoate, m.p. 76.2–77.1°, we obtained 2.6 g. of ethyl *trans*-2-hydroxycyclopentanecarboxylate (see Table II for the physical constants), and 0.7–0.8 g. of unchanged dinitrobenzoate.

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 8.91. Found: C, 60.38, 60.78; H, 9.01, 9.00.

Preparation of the *cis*- and *trans*-2-Hydroxycyclopentanecarboxylic Acids.—For the hydrolysis of the pure hydroxy esters saturated aqueous barium hydroxide solution may be used, or, more conveniently, 0.5 *N* aqueous sodium hydroxide. The amount of base used was 1.5 equivalents. A few minutes after mixing of the reactants the system became homogeneous, and was then ready to be acidified with concentrated sulfuric acid with cooling. After saturation with ammonium sulfate, the solution was extracted several times with ether. The ethereal solution was dried over sodium sulfate and evaporated. In the case of the *cis*-hydroxy acid, an oily substance resulted which crystallized on rubbing in the cold. After two recrystallizations from ether, in which it is extremely soluble, and from ligroin, the product melted at 52–53.4°. It is deliquescent and for this reason the melting points were determined in sealed capillary tubes. Distillation under atmospheric pressure gave cyclopentene-1-carboxylic acid.

Anal. Calcd. for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.61, 55.31; H, 7.88, 7.72.

In the case of the *trans*-hydroxy acid, the oily substance resulting after the removal of the solvent crystallized easily. Recrystallization from ether and from ligroin gave transparent tablets melting at 68.3–69.0°. It is very soluble in water but not deliquescent, and is somewhat less soluble in ether than its isomer. It eliminated water on distillation at atmospheric pressure, similar to the *cis*-hydroxy acid.

Anal. Calcd. for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.43, 55.68; H, 7.76, 7.89.

The Hydrazides of the *cis*- and *trans*-2-Hydroxycyclopentanecarboxylic Acids. *cis*-Hydrazide.—To a mixture of 1 g. of *cis*-hydroxy ester and 0.5 g. of hydrazine hydrate a little more ethanol than the amount required for complete dissolution was added. The mixture was refluxed for three hours. After removal of the solvent the residue gave, on cooling, 0.2 g. of white product, which, recrystallized from methanol, melted at 155.8–156.5°.

***trans*-Hydrazide.**—The foregoing procedure was followed, but a much more extended heating was required (16 hours). The derivative crystallized somewhat less easily on being left overnight in a desiccator. The product was dried on a porous plate. The product was recrystallized from methanol–ether. It is very soluble in water, but practically insoluble in anhydrous ether. The amount of this derivative which we obtained was too small for a good analysis. For the same reason it was not possible to get a good melting point; needles, m.p. 135.3–137.2°. A mixed melting point with the *cis*-hydrazide gave a depression.

Anal. Calcd. for $C_6H_{12}O_2N_2$: N, 19.43. Found: N, 18.72, 18.65.

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[Contribution from the Department of Chemistry, Columbia University]

Stereochemistry of the Reaction of Benzoin and Related Compounds with the Grignard Reagent[1]

By David Y. Curtin,[2] Elbert E. Harris and Estelle K. Meislich

cis- and *trans*-1-*p*-anisyl-1,2-diphenylethylene have been prepared by a route which leads to their configurational assignment. The two olefins have been oxidized with osmium tetroxide to *dl-erythro*- and *dl-threo*-1-*p*-anisyl-1,2-diphenylethylene glycol, respectively. This determination of the configuration of the glycols has made possible the elucidation of the stereochemical course of the reaction of benzoin with anisylmagnesium bromide and the reaction of 4-methoxybenzoin with phenylmagnesium bromide. Similarly, the reaction of benzoin methyl ether with anisylmagnesium bromide and the reaction of 4-methoxybenzoin methyl ether with phenylmagnesium bromide have been shown to be stereospecific and to follow the same stereochemical course as the reactions of the benzoins. The steric course of these reactions has been compared with that of a number of Grignard reactions with desylamines.

Benzoin has been shown to react with *p*-anisylmagnesium bromide to give a *dl*-1,2-diphenyl-1-*p*-anisylethylene glycol (I) which was designated "α," while 4-methoxybenzoin reacted with phenylmagnesium bromide to give the "β" racemate.[3] However, the configurations of "α"- and "β"-I were unknown. It has now been possible to establish the configurations of "α"- and "β"- I as *erythro*- and *threo*,[4] respectively, by the method described below.

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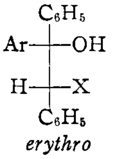
[1] Abstracted in part from the Ph.D. Thesis submitted by Elbert E. Harris to Columbia University.

[2] Department of Chemistry, University of Illinois, Urbana, Illinois.

[3] A. Orekoff and M. Tiffeneau, *Bull. soc. chim.*, [4] **29**, 445 (1921); A. McKenzie, E. M. Luis, M. Tiffeneau and P. Weill, *ibid.*, [4] **45**, 414 (1929).

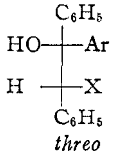
[4] In this work the designations "*erythro*" and "*threo*" will be used as



$$\begin{array}{c} C_6H_5 \\ Ar\text{—}\!\!\!+\!\!\!\text{—}OH \\ H\text{—}\!\!\!+\!\!\!\text{—}X \\ C_6H_5 \end{array}$$

and mirror image

erythro



$$\begin{array}{c} C_6H_5 \\ HO\text{—}\!\!\!+\!\!\!\text{—}Ar \\ H\text{—}\!\!\!+\!\!\!\text{—}X \\ C_6H_5 \end{array}$$

and mirror image

threo