taken on a Perkin-Elmer Infracord, Model 137. Melting points were determined using a capillary melting point apparatus. Fusions in molten alkali were carried out in a nickel pot of the same design and size as used by Weedon and coworkers.[22] Column chromatography involved the use of either silicic acid (Mallinckrodt, 100 mesh) or Florisil (Floridin Co.) as adsorbent.

(22) R. G. Ackman, R. P. Linstead, B. Wakefield, and B. C. L. Weedon, *Tetrahedron*, **8**, 221 (1960).

Registry No.—*cis*-9-Octadecene, 1779-13-1; deuterioperchloric acid, 19029-50-6; oleyl tosylate, 6110-54-9; 1-octadecanol, 112-92-5.

Acknowledgments.—The authors are indebted to C. J. Dooley for the mass spectrometric analyses. Chlorine, carbon, and hydrogen analyses were carried out by O. Panasiuk, M. Tatomyr, and J. Porta.

Stereochemical Studies in Substituted Cyclopentanecarboxylates

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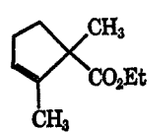
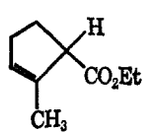
Assignment of stereochemistry is made to the pairs of esters **3–4** and **13–14**, prepared from the hydrogenation of **1** and **2**, respectively. The stereochemical course of the reaction of cyclohexane and acetyl chloride to give 2-methylacetylcyclopentane and of the alkylation of ketone **18** was reinvestigated. Compounds **3–20** exhibit a systematic variation in their nmr spectra, characteristic of each geometric series.

In connection with other stereochemical studies it was desired to have on hand authentic specimens of the stereoisomers of ethyl 1,2-dimethylcyclopentanecarboxylate and ethyl 2-methylcyclopentanecarboxylate. Since the literature assignment of stereochemistry had been made rather arbitrarily to the *trans* isomer **3**[1,2] and since the chemical transformations which related an ethyl 2-methycyclopentanecarboxylate to *trans*-1,2-dimethylcyclopentane[3,4a] were carried out on a sample of unknown stereochemical purity,[4b] the previous assignments were not considered to be unequivocal. For these reasons, the stereoisomeric pairs of esters **3–4** and **13–14** were synthesized and their chemical and spectral properties were probed as more rigorous criteria of stereochemistry. In ancillary studies, a reinvestigation of the sequence of transformations employed in the previous syntheses of **4** and **14** and of the stereochemical assignment made to these products was undertaken.

Preparation of Cyclopentanecarboxylates 3, 4, 13, and 14.—Hydrogenation of the cyclopentencarboxylate **1**[1] led to the formation of a mixture of **3** and **4** in a ratio which was independent of solvent but varied with catalyst (Table I). Our results stand in contrast with those previously reported[1] in which the hydrogenation in acetic acid in the presence of platinum was claimed to give only **3**. Hydrogenation of the cyclopentencarboxylate **2**, prepared from the photochemical rearrangement of ethyl 3-cyclopropyl-2-butenoate,[5] gave a more equal mixture of the stereoisomeric esters **13** and **14** (Table I). In both cases platinum appears to bring about a more stereoselective hydrogenation course.



1



2

TABLE I

STEREOCHEMISTRY OF HYDROGENATION

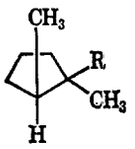
Starting ester	Solvent	Catalyst	Product ratio
1	Ethanol	Pd–C	57:43 (**3**:**4**)
	Acetic acid	Pd–C	57:43 (**3**:**4**)
	Acetic acid	Pt	73:27 (**3**:**4**)
2	Ethanol	Pd–C	50:50 (**13**:**14**)
	Acetic acid	Pt	40:60 (**13**:**14**)

Assignment of Stereochemistry.—Saponification of the isomeric mixture of **3** and **4** obtained from the hydrogenation of **1** took place with a very large difference in reaction rate between the two isomers. Selective hydrolysis thus served as a convenient method for the separation of the two isomers. Under conditions which hydrolyzed the minor isomer almost completely (3 days at room temperature), the predominant isomer could be recovered unchanged. Clearly, the latter isomer possesses the more hindered carboethoxy group and must therefore be **3**.

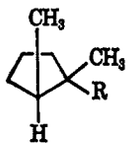
The amides **9** and **10** were prepared from the stereochemically pure acids **7** and **8**, respectively, and their corresponding melting points were found to be 103.5–104.5° and 113–114°. Melting points previously reported for 1,2-dimethylcyclopentanecarboxamide do not closely correspond to either of these values, indicating that no stereochemically pure samples of either of these amides had yet been prepared.[6]

The isomer which predominates on hydrogenation of **2** was found to be at least ten times as reactive as its stereoisomer; it was assigned the *trans* geometry (**14**) on these grounds. The stereochemically pure methyl esters **5** and **6** were prepared by treatment of acids **7** and **8**, with diazomethane. Ketones **11**, **12**, **17**, and **18** were prepared from the reaction of the corresponding carboxylic acids with phenyllithium.

(1) R. Granger and H. Techer, *Compt. Rend.*, **250**, 1282 (1960).
(2) G. Walsh, B. Shive, and H. L. Lochte, *J. Amer. Chem. Soc.*, **63**, 2975 (1941).
(3) H. Pines and N. E. Hoffman, *ibid.*, **76**, 4417 (1954).
(4) (a) C. D. Nenitzescu and G. G. Vanta, *Bull. Soc., Chim. Fr.*, [5] **2**, 2209 (1936); (b) C. D. Nenitzescu and C. N. Ionescu, *Ann.*, **491**, 207 (1931).
(5) M. J. Jorgenson and C. H. Heathcock, *J. Amer. Chem. Soc.*, **87**, 5264 (1965).
(6) The presumed *trans* isomer had been reported to have mp 98[1] and 98.5–99.5°;[2] an isomer of unspecified geometry was reported to have mp 83–84 and 88–89° [L. P. Vinogradova and S. I. Zav'yalov, *Izv. Akad. Nauk. SSSR, Otd. Khim. Nauk*, 2050 (1961); *Chem. Abstr.*, **57**, 12344c (1962)].

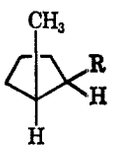


3, R = CO_2Et
5, R = CO_2CH_3
7, R = CO_2H
9, R = $CONH_2$
11, R = COPh

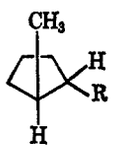


4, R = CO_2Et
6, R = CO_2CH_3
8, R = CO_2H
10, R = $CONH_2$
12, R = COPh

Stereochemistry of Formation of 1-Acetyl-2-methylcyclopentane.—The reaction of acetyl chloride with cyclohexane in the presence of aluminum chloride[3,4a] has been reported to give rise to *trans*-1-acetyl-2-methylcyclopentane. We repeated this prodecure and found that an isomeric mixture of ketones **19** and **20**,



13, R = CO_2Et
15, R = CO_2H
17, R = COPh
19, R = $COCH_3$



14, R = CO_2Et
16, R = CO_2H
18, R = COPh
20, R = $COCH_3$

in a ratio of 17:83, is produced in this reaction. By converting the ketone product into the ethyl ester,[4a] ketones **19** and **20** were related to the two isomeric ethyl 2-methylcyclopentanes derived from the hydrogenation of **2**. The stereochemical results indicate that the reaction of Nenitzescu and Ionescu is not stereospecific, as reported.[3]

Nmr Spectra Properties of Compounds 3 to 20.—The nmr spectra of compounds **3** to **20** were examined for the possibility that they might reveal systematic and characteristic differences which could be employed as criteria of stereochemistry. The data in Table II indicate that distinctive features exist within a stereochemical series. In compounds **4**, **6**, **8**, and **10**, the methyl signal at the 2 carbon appears as a sharp doublet, while, in the *trans* series, compounds **3**, **5**, **7**, and **9**, this signal consists of a broad, unresolved, sometimes complex, doublet.

TABLE II
NMR CHARACTERISTICS OF COMPOUNDS 3 TO 20

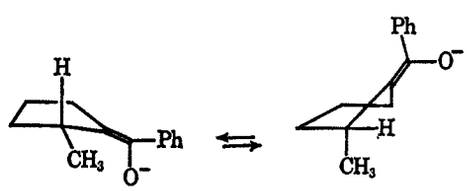
Compound	Chemical shift,[a] τ 1-Methyl[b]	2-Methyl
3	8.82	9.13 (unresolved complex doublet)
4	9.0	9.13[c]
5	8.82	9.14 (broad unresolved doublet)
6	8.98	9.10[c]
7	8.75	9.0 (unresolved complex doublet)
8	8.92	9.03[c]
9[d]	8.78	9.05 (unresolved broad doublet)
10[d]	8.92	9.05[c]
11	8.70	9.19 (nearly resolved doublet)
12	8.82	9.03[c]
13		9.15[c]
14		8.95 (broad complex doublet
15		9.0[c]
16		8.9 (unresolved doublet)
17		9.31[c]
18		9.00[c]
19		9.22[c]
20		9.0[c]

[a] In CCl_4, approximately 10–20%. [b] Sharp singlet in all cases. [c] Sharp doublet. [d] In $CDCl_3$.

The higher chemical shift of the C-1 methyl signal in the *cis* isomers **4**, **6**, **8**, **10**, and **12**, compared with the corresponding *trans* compounds, is a further characteristic feature of this geometric series. The higher shielding in these *cis* isomers is expected, because of diamagnetic shielding by the carbon–carbon bond of the adjacent *cis*-methyl substituent.[7] Alternatively, it is accountable in terms of a deshielding effect operative on the C-1 methyl in the *trans* series. This is likely, since in the *trans* series the adjacent *cis*-methyl group forces the carbonyl substituent into a conformation, probably one in which the plane of the carbonyl bisects the plane of the ring, which produces a deshielding effect on the C-1 methyl. A conformation of this type is also implicated for compounds **13**, **15**, **17**, and **19**, since the adjacent *cis*-methyl is found consistently at higher field (by 0.1–0.3 ppm) than in the corresponding *trans* isomers.

Stereochemistry of Alkylation.—It has previously been reported[2] that methylation of ketone **18** leads to the introduction of the methyl group *trans* to the C-2 methyl, furnishing ketone **11**.[8] We have reinvestigated the methylation of ketone **18** and find that a mixture of ketones results. Independent synthesis of each stereoisomer from acids **7** and **8** established that the mixture consisted of *trans* **11** and *cis* **12** in a ratio of 63:37.

The lack of stereospecificity in the alkylation reaction argues for the absence of any one overwhelming stereochemical directive effect. In particular, the conclusion can be drawn that $A^{1,3}$ strain, similar to that which has been invoked in corresponding cyclohexane enolates,[9,10] if present, does not govern the reaction course. If Ib



Ia Ib

were the dominant conformer of the enolate ion, then alkylation by equatorial approach[11] should give, contrary to experimental results, the *cis*-1,2-dimethyl ketone **12**.

Experimental Section

Hydrogenation of 1.—**1** (1.68 g, 0.01 mol) in 15 ml of ethanol was hydrogenated in the presence of 0.17 g of 20% Pd–C. After 1 hr, the theoretical amount of hydrogen had reacted and hydrogen uptake ceased. Analysis of the product on a 10 ft × 0.25 in. 20M column on Chromosorb W established the composition of

(7) J. I. Musher, *J. Chem. Phys.*, **35**, 1159 (1961).

(8) The ketone obtained was reported to be transformed into an amide of mp 98.5–99.5°, arbitrarily assigned a *trans* stereochemistry. In view of our finding that the melting point of pure **11** is 103.5–104.5°, it is evident that these investigators had in hand a stereoisomeric mixture of amides.

(9) F. Johnson and S. K. Malhotra, *J. Amer. Chem. Soc.*, **87**, 5492 (1965); S. K. Malhotra and F. Johnson, *ibid.*, **87**, 5493 (1965).

(10) Cyclopentane derivatives with an sp^2 ring carbon are more stable in a half-chair conformation (E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw Hill Book Co., 1962, p 251), so that this comparison would seem legitimate.

(11) (a) H. O. House and B. M. Trost, *J. Org. Chem.*, **30**, 2502 (1965); (b) H. O. House and T. M. Bare, *ibid.*, **33**, 943 (1968); (c) H. O. House and C. J. Blankley, *ibid.*, **32**, 1741 (1967); (d) W. S. Johnson, D. S. Allen, Jr., R. R. Hindersinn, G. N. Sausen, and R. Pappo, *J. Amer. Chem. Soc.*, **84**, 2181 (1962), and references therein.

the mixture as 57:43 with the predominant isomer having a lower retention time. In a control reaction the predominant isomers from this hydrogenation showed no isomerization upon further hydrogenation in alcohol with Pd–C. Hydrogenation in acetic acid in the presence of Pd–C proceeded at a comparable rate. Work-up by dilution with water and extraction with ether, followed by treatment of the ether extracts with sodium bicarbonate, furnished a mixture of isomers in the same ratio as was formed from hydrogenation in ethanol.

Hydrogenation in acetic acid in the presence of prereduced platinum oxide proceeded more rapidly to give a mixture of composition 73:27, after work-up as above.

Hydrogenation of 2.—**2** (1.0 g, 0.0065 mol) in 2.1 ml of 95% ethanol was hydrogenated in the presence of 0.1 g of Pd–C. Vapor phase chromatographic analysis of the solution on a 10 ft × 0.25 in. NPGS on Chromosorb W column established the ratio of stereoisomers as 1:1. Hydrogenation in acetic acid in the presence of platinum gave, after work-up as described for **1** above, a 40:60 ratio of isomers.

Hydrolysis of 3 and 4.—A mixture of isomers **3** and **4** (7.4 g) obtained from hydrogenation of **1** was allowed to react at room temperature with 10% potassium hydroxide in a 1:1 ethanol–water medium. After 1 day, 50% of **4** was hydrolyzed. Three days of reaction hydrolyzed over 90% of **4** while the hindered ester **3** gave no carboxylic acid. After dilution with water, extraction of the alkaline medium with ether furnished pure **3** contaminated by less than 5% **4** while acidification of the aqueous solution furnished **8** as a liquid. Conversion of **8** into the amide by way of the acid chloride gave **10**, mp 113–114°,[12] after two recrystallizations and sublimation. *Anal.* Calcd for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 9.92. Found: C, 67.89; H, 10.54; N, 9.85.

Ester **3** was almost completely hydrolyzed after reflux for 3 days in 10% potassium hydroxide in a 1:1 ethanol–water solution. Acid **7** was obtained as a solid (lit.[1] mp 45–46°). Conversion into an amide gave **9**, mp 103.5–104.5°[12] after recrystallization and sublimation (lit.[1,2] mp 98°). *Anal.* Calcd for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 9.92. Found: C, 67.89; H, 10.61; N, 9.70.

Hydrolysis of 13 and 14.—A mixture of **13** and **14**, in a ratio of 85:15 was stirred for 1 hr at room temperature with a 10% solution of potassium hydroxide in a 1:1 mixture of ethanol–water. Extraction of the diluted reaction mixture with ether afforded a small amount of ester whose composition of **13** and **14** was 40:60. The liquid carboxylic acid obtained was pure **16**, as shown by nmr spectroscopy.

Preparation of 5 and 6.—Treatment of an isomeric mixture of **7** and **8** with an ethereal solution of diazomethane afforded the methyl esters **5** and **6**, which could be purified and separated by vapor phase chromatography. The stereochemistry of **5** (*Anal.* Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.44; H, 10.51.) and **6** (*Anal.* Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.91; H, 10.48.) follows from their ratio when related to the known proportion of **7** and **8** present in the starting acids.

Preparation of 11 and 12.—Phenyllithium in benzene–ether (0.00774 mol) was added dropwise to 0.5 g (0.00352 mol) of an isomeric mixture of the acids **7** and **8** in DME at room temperature. The reaction mixture was heated to reflux for 30 min. After cooling, the mixture was poured into a vigorously stirred solution of 0.5 ml of concentrated hydrochloric acid in 50 ml of water. The resulting basic solution was extracted with three portions of ether. Evaporation of the ether produced 0.58 g (82%) of the crude products **11** and **12**. The ketones **11** and **12** could be separated by gas chromatography using a 150-ft capillary column.

(12) A Buchi melting point apparatus was employed.

A sample of pure **11** was prepared in a similar manner by reaction of pure **7** with phenyllithium.

Preparation of 17 and 18.—The ketones **17** and **18** were prepared from a mixture of the acids **15** and **16** present in a ratio of 6:94 by an adaptation of the method described by Bare and House.[13] Fifteen grams (0.117 moles) of a mixture of **15** and **16** in DME was added to a mechanically stirred suspension of 1.09 g of lithium hydride (0.136 mol) in DME under nitrogen. This mixture was refluxed for 2 hr. After the suspension was cooled in an ice bath, phenyllithium[14] in benzene-ether was added dropwise during a 30-min period. After the reaction mixture was stirred at room temperature overnight, it was poured into a vigorously stirred solution of 22.5 ml of concentration hydrochloric acid (0.266 mol) in 400 ml of water. The resulting basic solution was extracted with three portions of ether. The ether layers were combined and extracted with saturated sodium bicarbonate. Acidification of the combined aqueous layers gave 5.24 g (0.041 mol, or 35% of the starting material) of recovered acids **15** and **16**.[14] Distillation of the ether layers at 24 mm gave a 4.0-g fraction boiling at 92–159° that proved to be about 75% **17** and **18** contaminated by 25% some low boiling material. Pure **17** and **18** (7.1 g) distilled at 159–162° (24 mm) [lit.[2] bp 281 (760 mm)]. This fraction contained 6% **17** and 94% **18**. The 10 g of **17** and **18** produced represented a yield of 70% based on reacted acid (45% over-all yield[14]). The ketone mixture contained no alcohol. The recovered acid mixture (**15** and **16**) was not enriched in **15**, so that reaction with phenyllithium had occurred unselectively.

Protonation and Methylation of 17 and 18. Formation of 11 and 12.—The sodium salt of **17** and **18** was generated by refluxing 0.63 g (0.0033 mol) of a mixture containing 6% **17** and 94% **18** with 0.157 g of 56.1% sodium hydride suspension (0.0036 mol) in dimethoxyethane for 20 hr. Half of the reaction mixture was protonated by dropwise addition into cold water. The products were extracted into ether and analyzed by vapor phase chromatography. The proportion of **18** to **17** in the product was found to be 80.5:19.5.

To the remaining reaction mixture was added 0.47 g (0.0033 mol) of methyl iodide. The reaction mixture was refluxed for 1.5 hr. After dilution with water, the product was extracted with ether. Vapor phase chromatographic analysis revealed the presence of a low retention time product, amounting to about 10%, whose ir spectrum was consistent with an enol ether structure, 50% unreacted **18**, a few per cent **17**, and 38% methylated products **11** and **12**. The ratio of **11** to **12**, obtained by vapor phase analysis employing a 150-ft capillary column and by nmr spectral integration was 63:37.

Making a correction for the amount of **17** and **18** which had been converted into the enolate anion, as deduced from the methylation yield, assuming that all the anion reacted with methyl iodide, and making the further assumption that the isomeric ketones **17** and **18** form the enolate at comparable rates, it can be concluded that the ratio of **18**:**17** resulting from the hydrolysis of the anion is 65:35.

Registry No.—**3**, 18964-01-7; **4**, 18964-03-9; **5**, 18964-02-8; **6**, 18964-04-0; **7**, 18964-05-1; **8**, 18964-06-2; **9**, 18964-07-3; **10**, 18964-08-4; **11**, 15775-37-8; **12**, 17359-11-4; **13**, 5222-69-5; **14**, 5222-68-4; **15**, 18335-62-1; **16**, 4541-43-9; **17**, 18964-15-3; **18**, 18964-16-4; **19**, 5183-36-8; **20**, 3664-70-8.

(13) T. Bare and H. O. House, *Org. Syn.*, **49**, in press.

(14) It was subsequently noted that the concentration of phenyllithium solution employed was lower than assumed to be, so that considerably less than the required theoretical amount of phenyllithium was utilized.