Separation from a California Petroleum and Characterization of Geometric Isomers of 3-Ethyl-4-methylcyclopentylacetic Acid[1]

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A monocyclic C_{10} acid has been isolated from a California petroleum by distillation of esters followed by gas chromatography on two partitioning agents. Spectral interpretations (nmr and mass spectra) indicated that the acid is a methylethylcyclopentylacetic acid. By way of α bromination and dehydrohalogenation, the isolated acid was converted to a mixture of three cyclopentylideneacetic acids, separable by gas chromatography. Since each unsaturated acid contained four allylic hydrogens, they were assigned as 3-ethyl-4-methylcyclopentylideneacetic acids. Analysis of the mass spectra allowed assignment of the unsaturated esters with the methoxycarbonyl group *cis* to the side of the cyclopentane ring bearing ethyl or methyl, respectively. The four isomeric 3-ethyl-4-methylcyclopentylideneacetic acids were synthesized from the *erythro* and *threo* isomers of 2-ethyl-3-methylsuccinic acid, by way of the homologous adipic acids, and the *cis*- and *trans*-3-ethyl-4-methylcyclopentanones. Comparison of mass spectra and retention times in gas chromatography allowed assignment of the unsaturated esters from degradation as isomers **3**, **4**, and **5**. Hydrogenation of the two unsaturated esters from *trans*-3-ethyl-4-methylcyclopentanone yielded isomeric saturated esters which could not be separated by gas chromatography, but which had gas chromatographic and mass spectral properties identical with those of the isolated ester. Hydrogenation of unsaturated esters from the *cis* ketone gave separable isomeric saturated esters, one of which (acetic acid side chain *trans* to alkyl groups) had properties in agreement with the isolated ester. Thus, the isolated ester is a mixture of two or three of the stereoisomers of the ester of 3-ethyl-4-methylcyclopentylacetic acid. No optical rotation could be observed in the isolated acid, which is the first nonisoprenoid branched structure which has been established in the naphthenic acids with ten or more carbons.

The application of currently available methods for separation and structure determination have proved capable of effecting the isolation and identification of naphthenic acids with more than ten carbon atoms. Previously reported investigations from this laboratory have resulted in the characterization of acyclic isoprenoid acids at the C_{14}, C_{15}, C_{19}, and C_{20} molecular weights,[2] as well as a monocyclic isoprenoid acid,[3] *trans*-2,2,6-trimethylcyclohexylacetic acid. The present investigation has been directed to a C_{10} monocyclic acid, partly because von Braun reported[4] the occurrence of such an acid in petroleums from such widespread sources as Rumania, Russia, California, Texas, Venezuela, and Japan. After great effort had failed to separate this C_{10} acid in what could be classified as a homogeneous condition,[5] the crude acid was degraded to a C_8 ketone (the "von Braun ketone"), which was compared with large numbers of ketones of established structure. By a process of elimination, the structure of this ketone was assigned as 3,3,4-trimethylcyclopentanone, but this structure was not confirmed by synthesis. In 1942 this ketone was synthesized by two groups[6] (later by others), and found to have properties different from those of the von Braun ketone. Subsequently, Lochte and his students[7] reexamined the data and concluded that the von Braun ketone must be the *cis*-3-ethyl-4-methylcyclopentanone. The *cis* and *trans* isomers of this structure were synthesized, and the properties of the *cis* isomer were in agreement with those of the von Braun ketone. When this ketone was converted to the corresponding cyclopentylacetic acid, however, the properties of this acid were not in agreement with those reported by von Braun and his students for the product obtained by reconversion of their ketone to a cyclopentylacetic acid. The frustration of these investigations was heightened by the fact that Lochte and his students were unable to isolate from a California petroleum a C_{10} acid with the properties reported by von Braun. Thus, application of currently available methods to this recalcitrant problem has been undertaken by us. Results of the gas chromatographic investigations to be reported at this time make clear the nature of the difficulties involved in comparisons with the von Braun work: the German investigators were no doubt dealing with a mixture of at least six acids, probably more than ten, and separation of the mixture by the methods then available was quite impossible.

After considerable exploratory work on the sample of naphthenic acids used in our previously reported work,[3] monocyclic C_{10} acids were located in the ester fraction, bp 97–107° (11.5 mm), which was about 5% of the total methyl naphthenate mixture. Gas chromatography of this fraction on neopentyl glycol succinate (NPGS) yielded the tracing shown in Figure 1. Mass spectrometric analysis showed that the 21-min band in this tracing consists largely of methyl nonanoate, while at least one C_{10} monocyclic acid was included in the 29.5-min band. Rechromatography of fraction III-2 (about 5% of fraction III) on the same partitioning agent[8] yielded a single symmetrical band; however, rechromatography on silicone revealed the presence of at least five components (Figure 2). When the major band (fraction III-2-A) was collected as shown in the figure, the product amounted to about 30% of fraction III-2, and hence was about 0.075% of the naphthenate mixture.

Fraction III-2-A appeared as a single symmetrical band when gas chromatographed on NPGS, silicone, or

(1) This investigation was supported by a grant from the Petroleum Research Fund, administered by the American Chemical Society.

(2) J. Cason and D. W. Graham, *Tetrahedron*, **21**, 471 (1965).

(3) J. Cason and K.-L. Liauw, *J. Org. Chem.*, **30**, 1763 (1965).

(4) J. von Braun, *Ann.*, **490**, 100 (1931).

(5) The prodigious effort directed toward the von Braun acid and ketone has been well described: H. L. Lochte and E. R. Littmann, "The Petroleum Acids and Bases," Chemical Publishing Co., New York, N. Y., 1955.

(6) E. R. Buchman and H. Sargent, *J. Org. Chem.*, **7**, 148 (1942); L. Ruzicka, C. F. Seidel, H. Schinz, and M. Pfeiffer, *Helv. Chim. Acta*, **25**, 188 (1942).

(7) (a) H. Goodman, Doctoral Dissertation, The University of Texas, 1951; (b) J. Berry, Doctoral Dissertation, The University of Texas, 1953. We wish to express our appreciation to Professor Lochte for making copies of these dissertations available to us.

(8) As in our earlier publications, Roman numerals are used to designate distillation fractions, Arabic numerals designate fractions from gas chromatography on NPGS, and letters designate fractions from gas chromatography on silicone.

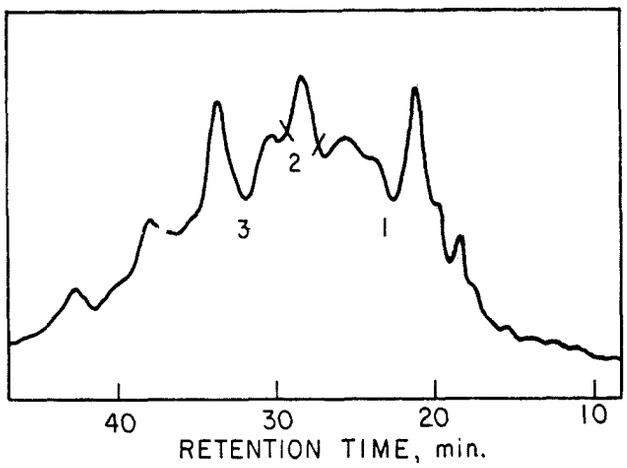


Figure 1.—Tracing from gas chromatography of a 50-μl sample of distillation fraction III of methyl naphthenates, bp 97–107° (11.5 mm). Chromatography was on a 20 ft × $^3/_8$ in. column, packed with 10% NPGS dispersed on 30–60 mesh Chromosorb P; chromatography at 140°, helium flow rate 180 cc/min. Fraction 2 was collected between the cross lines on the tracing.

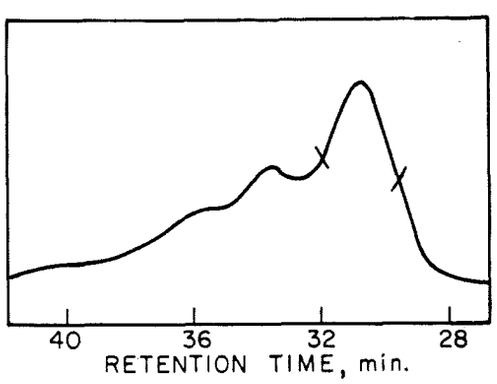


Figure 2.—Tracing from gas chromatography of fraction III-2, collected as shown in Figure 1. Chromatography was on a 10 ft × $^3/_8$ in. column packed with 20% silicone grease dispersed on 30–60 mesh Chromosorb P; chromatography at 145°, helium flow rate 150 cc/min. Fraction III-2-A was collected between the cross lines on the tracing.

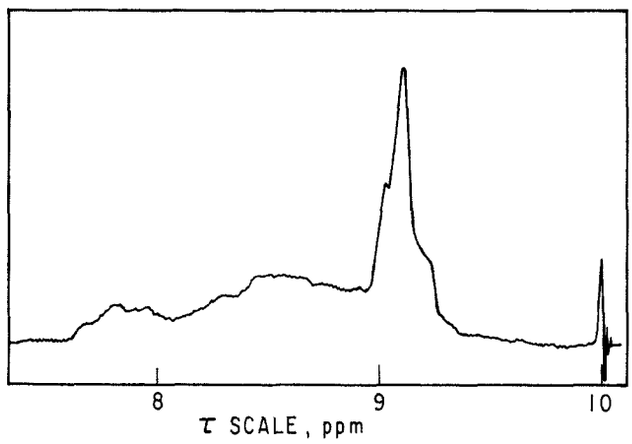


Figure 3.—Partial nmr spectrum of fraction III-2-A, (*cf.* Figure 2), recorded on a Varian Model A-60 spectrometer, in 10% solution in carbon tetrachloride with TMS as internal reference. Not shown is the sharp peak at τ 6.4, the signal from the methoxyl hydrogens, which was used as reference in determining the area corresponding to a proton.

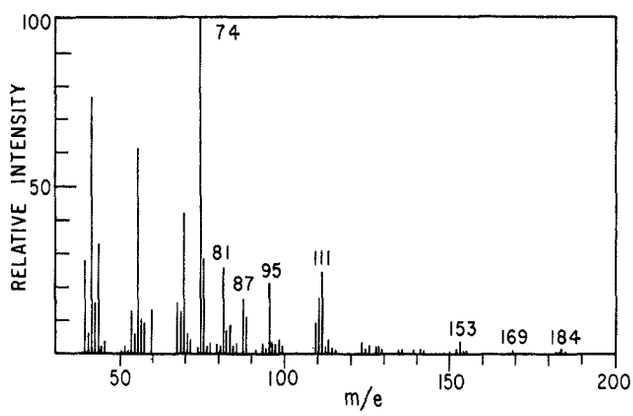


Figure 4.—Mass spectrum of fraction III-2-A, as collected in Figure 2. Data were obtained on a C.E.C. Model No. 21-103C, which was equipped with an ion multiplier detector and otherwise modified to give unit resolution at about 800. The inlet was heated to about 180°, and the ionizing voltage was maintained at 70 ev.

cyanosilicone. The mass spectrum indicated that it consisted mostly of the ester of a monocyclic C_{10} acid [molecular ion (M) at 184]; however, small peaks were recorded for the ester of a monocyclic C_{11} acid (M 198) and of a bicyclic C_{10} acid (M 182). The peak ratios for these ions, in the order just stated, were 100:4:15. Since the bicyclic ester normally gives a considerably more stable molecular ion, this fraction is estimated to be greater than 90% the monocyclic C_{10} acid. A single crystallization of the *p*-phthalimidophenacyl ester of this acid yielded product of mp 135–136.5°, which yielded a single molecular ion (M 433) in the mass spectrometer.

Complete separations in the manner described above were carried out on samples of methyl naphthenates prepared by normal acid-catalyzed esterification, and on samples prepared from the silver salts and methyl iodide. Since no difference could be detected in the products separated, it was concluded that acid-sensitive components were not present in significant quantity in this fraction of naphthenic acids.

The nmr spectrum of the ester in fraction III-2-A, as shown in Figure 3, revealed considerable information about the structure. The broad multiplet centered at about τ 7.85 is in the characteristic location for α hydrogens in esters, and its area is equivalent to two hydrogens, hence there is no α substituent. The major band centered at about τ 9.1 is in the methyl region, and its appearance is that of a doublet methyl superimposed on a methyl adjacent to methylene, although other combinations might well give a similar band. This band is equivalent to 7.5 hydrogens, about midway between two and three methyl groups. Hydrogens on a cyclopropane ring are unlikely to be at this low a field. It has been observed[9] that methylene hydrogens adjacent to a branch tend to overlap the methyl region; *e.g.*, 2-ethyloctadecanoate, which contains two methyl groups, gives an area under the methyl band of nine protons. Thus, the ester in question no doubt contains two methyl groups, and it would not be unexpected if one of these should be part of an ethyl group.

The mass spectrum of fraction III-2-A (Figure 4) confirms and extends structural deductions which could be based on the nmr spectrum. The base peak at *m/e*

(9) J. Cason and G. L. Lange, *J. Org. Chem.*, **29**, 2107 (1964).

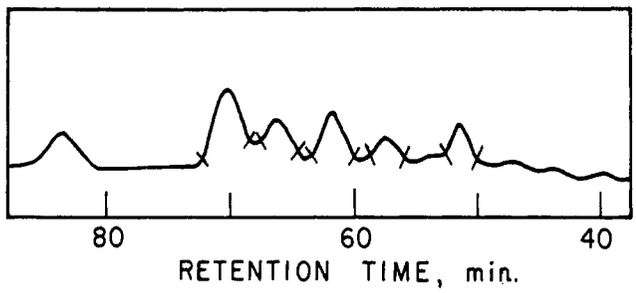
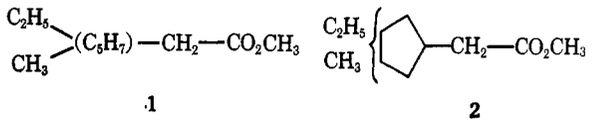


Figure 5.—Tracing from gas chromatography of the product obtained by dehydrohalogenation of the α-bromo ester secured from the ester of fraction III-2-A (*cf.* Figure 2). Chromatography was on a 20 ft × ⅜ in. column packed with 10% NPGS dispersed on 30–60 mesh Chromosorb P; chromatography at 135°, helium flow rate 180 cc/min. The more important bands were collected as shown by the cross marks on the tracings; *cf.* the Experimental Section for data on these fractions.

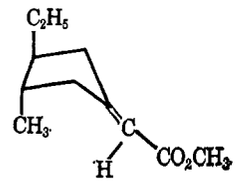
74, ascribed to the rearrangement ion, $CH_2{=}C(^+OH)\text{-}OCH_3$, confirms the absence of any α substituent and shows the presence of at least one hydrogen in a γ position. The significant peak at *m/e* 153 (M − CH_3O) confirms the molecular ion at *m/e* 184. The large size of the peak at *m/e* 111 (M − 73), ascribed to loss of $CH_2CO_2CH_3$, renders the presence of a β substituent extremely probable. This is further supported by the fact that the ion at *m/e* 87, ascribed[10] to $^+CH_2\text{-}CH_2CO_2CH_3$, is of lower intensity than the ion of *m/e* 111. Since there are not significant peaks at *m/e* 101 or 115, a branching methyl or ethyl group at the β position is contraindicated, so it is probable that an acetic acid side chain is attached to a ring. Although the peak at *m/e* 169 (M − 15) is small, it is quite unlikely to be as large as it is unless a methyl group is at a quaternary carbon or substituted in a ring. The presence of the methyl is substantiated by the rather intense peak (21%) at *m/e* 95 [M − (74 + 15)], arising from loss of methyl and the rearrangement ion. The more intense peak at *m/e* 81 [M − (74 + 29)] clearly indicates the presence of an ethyl substituent. Since the ethyl radical is of lower energy than the methyl radical, the ion of *m/e* 81 should be of higher intensity than that at *m/e* 95. According to the evidence described thus far, partial structure **1** may be assigned to the ester in fraction III-2-A. The nature of



1 **2**

the methylene region in the nmr spectrum (Figure 3), the number of methyl groups indicated by this spectrum, and the absence of cyclopropane hydrogens exclude the cyclopropane ring, which is also contraindicated by the absence of acid sensitivity previously mentioned. Since cyclobutane rings are uncommon, and the ethyl and methyl groups must be substituted on the ring to explain the mass spectrum, the evidence seems adequate to assign partial structure **2**.

In order to permit location of the substituents in structure **2**, sufficient (280 mg) fraction III-2-A was accumulated to allow degradation by the sequence involving α bromination of the acid and dehydrohalogenation of the α-bromo ester. The nmr spectrum of the α-bromo ester, collected from gas chromatography on silicone, confirmed the presence of two α hydrogens in the acid brominated, and only one β hydrogen. This spectrum shows two doublets centered at about τ 6 (one for each diastereoisomer) with a total area of one hydrogen. Gas chromatography on silicone revealed only one major band; however, use of NPGS as partitioning agent gave poor resolution of two components, which are assigned as diastereoisomers on the basis of the nmr spectrum. The diastereoisomers (112 mg) collected by chromatography on silicone were used for dehydrohalogenation. Gas chromatography of the unsaturated ester revealed the large number of products shown in Figure 5. Although the 83-min band is due to an aromatic compound always observed after dehydrohalogenation with quinoline, the other bands proved to be due to esters. Since large ratios of β,γ-unsaturated esters could hardly be formed, stereoisomers in the isolated acid involving the methyl and ethyl substituents must be considered. This factor eliminates, tentatively, a geminal-substituted isomer; however, this isomer was definitely eliminated by other work, to be published later, in which there was determined the mass spectrum of methyl 3-ethyl-3-methylcyclopentylacetate. The nmr spectra of two of the α,β-unsaturated esters collected in the chromatography shown in Figure 5 (retention times of 61.5 and 70 min) revealed the presence of *four allylic hydrogens;* therefore, there are only four possible α,β-unsaturated esters, as represented in structures **3**–**6**. The mass spectra of three of the unsaturated ester fractions demonstrated that they have three of the structures represented by structures **3**–**6**. In order to allow comparison of fragmentation patterns and specific assignment of structures, these four α,β-unsaturated esters were synthesized.



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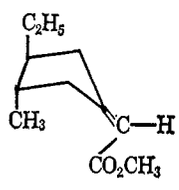

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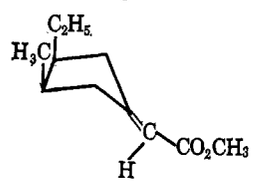

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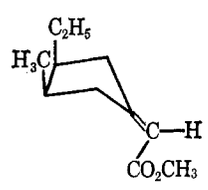
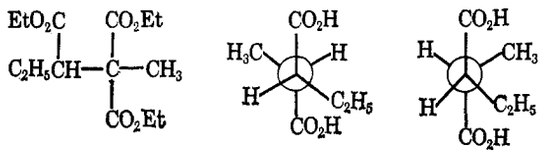


6

Starting material for synthesis of the unsaturated esters was 2-ethyl-3-methylsuccinic acid, which could be obtained in the two diastereoisomeric forms by a procedure similar to that utilized by Golden and Linstead.[11] When the triester **7**, prepared by alkylation of diethyl methylmalonate, was hydrolyzed in hydrochloric acid, cooling the reaction mixture resulted in crystallization of about 40% of the product as pure *erythro*-2-ethyl-3-methylsuccinic acid (**8**). Evapo-

(10) Among the more useful discussions of the mass spectra of carboxylic esters is that of R. Ryhage and E. Stenhagen, "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Acaemic Press Inc., New York, N. Y., 1963, p 399.

(11) J. H. Golden and R. P. Linstead, *J. Chem. Soc.*, 1732 (1958).

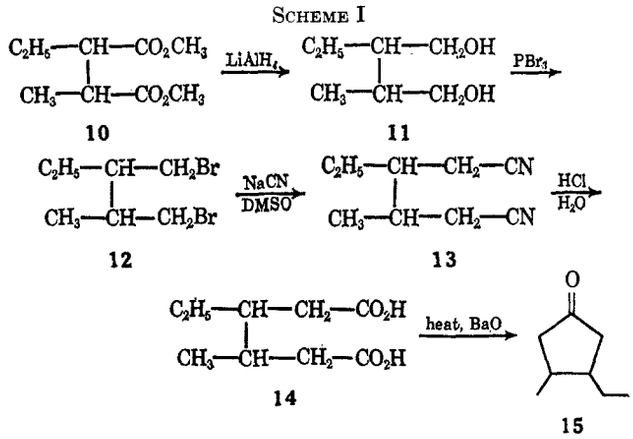


7 8 9

ration of the filtrate and heating the residue at 200°, followed by esterification, yielded a product which was about 90% ester of the *threo* isomer (**9**), 5% of the *erythro* form, and 5% of the anhydride. When the total hydrolysate was heated, without isolation of any *erythro* acid, about 90% of the total product was *threo* isomer; therefore, it is clear that heat equilibration converts the *erythro* isomer to the *threo* isomer. Newman projections indicate that the *erythro* acid (**8**) would be more stable and hence be predominant at equilibrium; however, the *threo* anhydride would be more stable. Previously, heat equilibrium was found[12] to favor the *threo* form of *sym*-dimethylsuccinic acid, and this behavior was attributed to equilibration *via* the anhydride.

Each of the esters (**10**) of the isomeric diacids was reduced with lithium aluminum anhydride to the diol (**11**), and homologation was accomplished *via* the nitrile (**13**), as outlined in Scheme I. Cyclization of the

SCHEME I



glutaric acids (**14**) yielded the isomeric cyclopentanones (**15**). The diols (**11**) cyclized readily to the tetrahydrofurans on heating, so it was necessary to convert the crude glycols to the dibromides (**12**). This conversion went smoothly for the *erythro* diol; however, gas chromatography of the *threo* dibromide showed contamination with two other products. These by-products were not investigated, but they were assumed to be tertiary bromides resulting from carbonium ion rearrangements during reaction with phosphorus tribromide. Such rearrangement is not unexpected in conversion of a *sec*-alkylcarbinol to the bromide; however, a study of models does not make clear why the *threo* isomer is more prone to react by the SN1 route.

The *cis*-2-ethyl-3-methylcyclopentanone (from *erythro* **14**), was readily obtained in a pure condition and was converted by way of the Reformatsky reaction and dehydration to unsaturated esters **5** and **6**. The *trans* isomer of ketone **15**, eventually obtained from the impure *threo* dibromide, was contaminated with a small amount of the *cis* ketone as well as an unidentified component; however, it was separated in a homogeneous condition by gas chromatography. This ketone was converted to unsaturated esters **3** and **4**. All four unsaturated esters (structures **3**–**6**) proved separable by gas chromatography on NPGS, and assignment of structure to the pairs of geometric isomers proved possible by a study of the fragmentation patters in mass spectrometry.

Partial[13] mass spectra of the synthetic unsaturated esters are assembled in Table I, along with the spectra

TABLE I

PARTIAL MASS SPECTRA OF THE ISOLATED AND SYNTHETIC SAMPLES OF THE GEOMETRICAL ISOMERS OF METHYL 3-ETHYL-4-METHYLCYCLOPENTYLIDENEACETATE

	Relative abundance[a]						
m/e[b]	A	B	C	D	E	F	G[c]
67	21	35	12.5	33	12	18	95
69	34	40	12	30	12	17	60
74	1	3.5	0.5	1.4	0.7	1	5
77	16	32	13	34	15	20	65
79	16	32	13	40	15	22	70
81	18	30	13	37	13	19	65
93	21	42	25	76	25	34	81
107	8	23	10	16	7	17.5	20
121	19	21	19	13	19	21	46
135	3.5	19	3.5	14	5	20	24
151	11	7	11	23	11	24	16
153	100	53	100	53	100	54	100
167	8	100	8.5	100	9	100	13
182[d]	8	35	8.5	36	11	39	22[c]

[a] A, isomer **3**; B, isomer **4**; C, isomer **5**; D, isomer **6**; E, 61.5-min band, Figure 5; F, 66-min band; G, 70-min band. [b] All the spectra showed an off-scale peak at *m/e* 28; however, this peak has been neglected for it is due in part to traces of atmospheric nitrogen present in the system. In the spectra of samples A, B, and D, the ion of *m/e* 41 ($C_3H_7 - 2$), which is of diverse origin, was the most abundant; however, it was not taken as the base peak, for this would have tended to obscure the remarkable abundance of the ions of *m/e* 153 and 167. [c] The most abundant ion in this spectrum (five times the abundance of *m/e* 153) is of *m/e* 43 (C_3H_7), another ubiquitously abundant ion; however, it was avoided as the base peak in order not to obscure the comparison with sample C. The abundance of *m/e* 43 in this spectrum is no doubt properly ascribed to the presence of an impurity carried through from the starting ester. A molecular ion of *m/e* 196 (ester of an unsaturated monocyclic C_{11} acid) was of about one-fourth the intensity of the molecular ion at *m/e* 182. [d] The molecular ion.

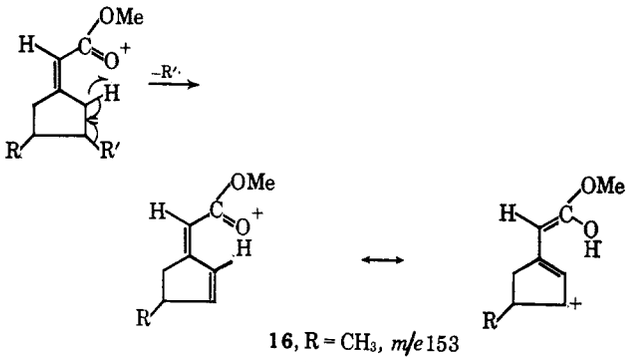
of the three α,β-unsaturated esters obtained by degradation of fraction III-2-A (*cf.* Figure 5). These fragmentation patterns are adequately similar to each other to support the thesis that the compounds are stereoisomers;[14] however, there are striking differences which allow assignment of structure to the geometric isomers. First, it may be noted that the normal rearrangement ion, $CH_2{=}C(^+OH)OCH_3$, *m/e* 74, is virtually absent from all the spectra, as should be the case for these α,β-unsaturated esters. The ions of *m/e* 153 (M − 29) and 167 (M − 15) are remarkably large, and must result from loss of ethyl and methyl groups, respectively, to give highly stabilized ion fragments. A reasonable explanation of this fragmentation is shown in Scheme II, which yields ions **16** and **17**, possessing a highly

(12) J. Cason and F. J. Schmitz, *J. Org. Chem.*, **28**, 555 (1963).

(13) Graphic depiction of the full mass spectra and the nmr spectra, for compounds discussed in this paper, have been recorded in the Ph.D. thesis of Ahmed I. A. Khodair, University of California, Berkeley, Calif., 1965.

(14) K. Biemann, "Mass Spectroscopy, Organic Chemical Applications," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 141.

SCHEME II

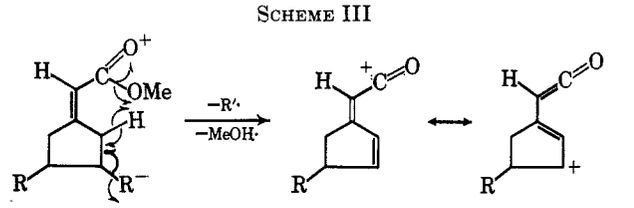


16, R = CH_3, *m/e* 153
17, R = C_2H_5, *m/e* 167

delocalized electron system. If enolization of the ester *via* a cyclic transition state should occur prior to fragmentation, the predicted products would be the same; in any case, the alkyl on the side of the ring *cis* to the methoxycarbonyl group must be lost. It follows that structures **3** and **5** must be assigned to the samples (A and C) giving *m/e* 153 (M − 29) as the dominant ion in fragmentation, whereas structures **4** and **6** must be assigned to samples B and D, wherein the ion of *m/e* 167 (M − 15) is dominant. In further support of this interpretation, it may be noted that the preponderance of the ion of *m/e* 153 is much greater than that of the ion of *m/e* 167, in accord with the greater stability of the ethyl radical.

The ion peaks at *m/e* 121 (M − 29 − MeOH) and at 135 (M − 15 − MeOH) are in accord with the interpretation presented in Scheme II. These ions may occur by loss of methanol from ions **16** and **17** to give the well-known ketene fragments; however, the concerted mechanism presented in Scheme III should be

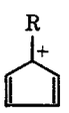
SCHEME III



18, R = CH_3, *m/e* 121
19, R = C_2H_5, *m/e* 135

a lower energy route. In any case, ion **18** should be more abundant in the molecule in which ion **16** is more abundant, as is the fact. Furthermore, differences should be smaller in the cases where the higher energy methyl radical is lost.

The rather abundant ions of *m/e* 79 (M − 74 − 29) and *m/e* 93 (M − 74 − 15) are probably due to the resonance-stabilized ion (**20**) which would result from loss of the rearrangement ion and one alkyl. Formation of this ion would require a multiple rearrangement, however, and there is apparent no simple formulation of the mechanism of its formation. This ion has been observed, however, in the fragmentation of other esters



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of related structure, during investigations in this laboratory which will be published subsequently.

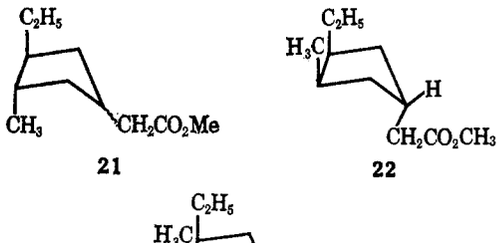
In summary of the structural evidence, for the two cyclopentylideneacetic esters from *trans*-3-ethyl-4-methylcyclopentanone, the one of shorter retention time in gas chromatography has ethyl substituted on the side of the ring which is *cis* to the methoxycarbonyl group (structure **3**). The other isomer from this ketone is structure **4**. The unsaturated ester of shorter retention time from the *cis*-ketone also has ethyl on the side of the ring *cis* to the methoxycarbonyl group (structure **5**), while the isomer of longer retention time has structure **6**. In correlation with the unsaturated esters obtained by degradation of the ester from the naphthenate mixture, isomer **3** proves to have the same retention time in gas chromatography as the 61.5-min band in Figure 5, while isomers **4** and **5** correspond to the 66-min and 70-min bands. The correspondence of the mass spectra according to these pairings will be noted (Table I), especially the ratios between the three molecular ions and the striking differences in the ratios of the ions of *m/e* 153 and 167. The lower abundance of the analytical ions in the spectrum of sample G is no doubt due to the impurity in this unsaturated ester (*cf.* footnote *c*, Table I). For the same reason, the nmr spectrum of sample G did not agree well with that of isomer **5** in the methyl region, whereas the nmr spectra of sample E and of isomer **3** were in excellent agreement. The amount of sample F (2.5 mg) was insufficient for an nmr spectrum with the equipment then available to us; however, for comparison purposes, the nmr spectra were of minor significance. The mass spectra and gc retention times were the definitive factors. The all-important role of the nmr spectra was in establishing the number of allylic hydrogens in the unsaturated esters.

The presence of isomers **3**, **4**, and **5** among the unsaturated esters from degradation shows the presence of naphthenic esters with the alkyls *cis* and with the alkyls *trans;* however, the absence of unsaturated ester **6**, of retention time greater than 70 min (*cf.* Figure 5), is of interest. Since the alkyl groups were *cis* in the naphthenic ester brominated, it is possible that bromination occurred largely from the unhindered side in the most favored conformation for the cyclopentylacetic acid, so that most of the bromo acid would be one diastereoisomer. If that should be the case the base-catalyzed dehydrohalogenation, which is of a concerted nature (E2), would give mostly one of the two possible unsaturated esters.

Catalytic hydrogenation of the unsaturated esters (**3** and **4**) synthesized from the *trans*-cyclopentanone (**15** *trans*) yielded saturated esters which could not be separated by gas chromatography. This was not surprising since these geometric isomers differ only in having the acetic ester side chain *cis* to either the methyl or the ethyl. The saturated ester from hydrogenation had the same retention time, however, as the isolated, ester (fraction III-2-A) on both silicone and NPGS partitioning agents. In addition, the mass spectrum of the synthetic ester was the same as that of the isolated ester as depicted in Figure 4.

When the unsaturated esters from the *cis*-cyclopentanone (**15**, *cis*) were hydrogenated over palladium-on-charcoal catalyst, the two saturated esters could be

separated by gas chromatography, and one ester was obtained in considerably larger amount. As in the previously reported hydrogenation in the cyclohexane series,[3] the isomer obtained in larger amount, and therefore assigned the *cis* geometry, had the longer retention time in gas chromatography. The isomer obtained in smaller amount had the same retention time on two partitioning agents as the isolated naphthenic ester, and showed a very similar mass spectrum. Thus the isolated naphthenic ester consisted of at least one of the geometric isomers represented by formula **21** and the isomer shown in formula **22**. Isomer **23** may be



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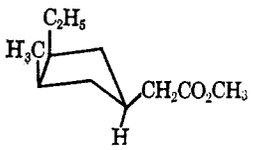

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present in the naphthenic acid mixture, but it was not present in significant amount in fraction III-2-A.

The 3-ethyl-4-methylcyclopentylacetic acid is the first naphthenic acid (other than *n*-alkanoic acids) isolated by us which does not have an isoprenoid structure. There is no reasonable doubt that many other nonisoprenoid structures are present; however, they appear to be of relatively low abundance in the California petroleum which we have examined. In further contrast with the previously reported 2,2,6-trimethylcyclohexylacetic acid,[3] no optical rotation could be observed for the 3-ethyl-4-methylcyclopentylacetic acid, $[\alpha]^{23}D$ 0 ± 0.12°.

Experimental Section

Physical Measurements.—Melting points were determined with a calibrated thermometer in a Büchi Schmelzpunktbestimmungsapparat. Gas chromatography was carried out with an Aerograph A-90-P, under conditions specified in the individual cases. The nmr spectra were determined as defined in the legend to Figure 3, while mass spectra were determined as described in the legend to Figure 4. Ultraviolet spectra were recorded on a Beckman DK-2A ratio recording spectrometer, and infrared spectra were recorded on a Perkin–Elmer Model 137 sodium chloride spectrophotometer. Optical rotations were checked in a Bendix automatic polarimeter, Type 143A, in 0.1-dm cells; limit of detection was about 0.0002° of arc. Microanalyses were by the Microanalytical Division, Department of Chemistry, University of California.

Separation of Methyl Naphthenates.—The crude naphthenic acids[15] were esterified either with methanol and sulfuric acid as described previously,[3] or by way of the silver salt. For the latter procedure, a 100-g sample of naphthenic acids was stirred with 500 ml of water as the mixture was brought to pH 10 with 6 *N* aqueous potassium hydroxide. To the hot, stirred solution was added 10 *N* silver nitrate solution until precipitation of the silver salt was complete. The silver salt was collected, washed well with water, then stirred well in a flask with 300 ml of methanol. After the salt had again been collected and washed with methanol, it was dried to constant weight at 45° in a vacuum oven. The dried silver salt was stirred in 1 l. of pentane with sufficient sand to act as a dispersing agent, then 170 g of methyl iodide was added to the gelatinous solution. The mixture was stirred vigorously for about 30 min, then allowed to stand overnight. After the sand and precipitated silver iodide had been removed by filtration, solvent and excess methyl iodide were distilled, and the residue was freed of solvent at reduced pressure. Distillation of the ester through a 2-ft Podbielniak-type column with a simple wire spiral yielded about 5 g of ester (designated fraction III) of bp 97–107° (11.5 mm). It is probably more convenient to first distil the naphthenic acid mixture through the column and esterify only the fraction boiling below 165° (5 mm).

Use of thiourea adduction[2] on fraction III failed to improve separation of the desired components, so separation was effected by gas chromatography as illustrated in Figures 1 and 2. The types of acids present in the various fractions were assayed by examination of the mass spectra; the fragmentation pattern of fraction III-2-A is shown in Figure 4. **The *p*-phthalimidophenacyl ester** was prepared, by the method previously described,[2] from 17 mg of the acid obtained by hydrolysis of the ester in fraction III-2-A. A single crystallization from aqueous acetone (65% acetone) yielded 10 mg of the derivative, mp 135–136.5°, showing a single molecular ion, *m/e* 433, in the mass spectrometer. A 1-mg sample of this ester was submitted for analysis.[16]

Anal. Calcd for $C_{28}H_{27}NO_5$: C, 72.0; H, 6.2; N, 3.2. Found: C, 70.8; H, 6.1; N, 3.3.

Degradation of Fraction III-2-A.—A mixture of 257 mg of acid from hydrolysis of fraction III-2-A and 310 μl of phosphorus tribromide was stirred vigorously as 400 μl of bromine was added dropwise from a syringe. After about 1 equiv of bromine had been added and the mixture had turned a deep brown, there was no further heat evolution so the remaining bromine was added rapidly. The reaction mixture was heated for 1 hr in an oil bath at 85–90°, then an additional 135 μl of bromine was added and heating was continued for 20 hr. To the cooled reaction mixture was added, at room temperature, 1 ml of absolute methanol during about 20 min, then the reaction mixture was heated under reflux for 25 min. After the mixture had been cooled again and 7.5 ml of water containing 100 mg of sodium sulfite had been added, the oily product was continuously extracted with hexane. The product received after removal of solvent was gas chromatographed on a 10 ft × 3/8 in. column packed with 20% silicone SE-30 at 166°, helium flow rate 150 cc/min. The α-bromo ester (113 mg) was collected between retention times of 48 and 52 min (band centered at 51 min) in order to remove material in one leading and two trailing bands.

The purified sample of α-bromo ester obtained as described above was heated with 400 μl of synthetic quinoline for 3 hr at 160–170°. The black reaction mixture was cooled and treated with 4 ml of 20% hydrochloric acid, then the product was continuously extracted with hexane. The hexane extract was washed once with 10% hydrochloric acid, then washed with water and dried. Removal of solvent left 68 mg of crude unsaturated esters which were gas chromatographed as described in Figure 5. Collection of the five fractions shown in Figure 5 yielded the data given in Table II. Presumably, the first two fractions are β,γ-unsaturated esters, not investigated because of their small amount and because the α,β-unsaturated esters yielded the desired information.

TABLE II

Retention time, min	Wt, mg	Identity
51	1	Not investigated
57	1	Not investigated
61.5	4	Sample E, Table I
66	2.5	Sample F
70	5	Sample G

(15) The acids were the commercial product, Chevron Grade E, average mol wt 214, which had been extracted prior to cracking from middle distillates of a San Joaquin Valley naphthenic-type crude oil. These acids were generously supplied by the Standard Oil Co. of California.

(16) This analysis was carried out by the method, depending on volumetric determination of combustion products, which has been described by C. W. Koch and E. Jones, *Mikrochem. Acta*, **4**, 734 (1963). Although carbon values are sometimes low, precise values for hydrogen and nitrogen are obtained on the same small sample.

Dimethyl 2-Ethyl-3-methylsuccinate (10).—In a procedure based on that described[17] for synthesis of *sym*-dimethylsuccinic acid, 260 g of diethyl methylmalonate was alkylated with 230 g of ethyl α-bromobutyrate to yield 220 g (65%) of triester **7**, bp 162° (20 mm). The total product was hydrolyzed by heating under reflux for 40 hr with 700 ml of 20% hydrochloric acid. Storage of the reaction mixture overnight at 0° yielded a crystallizate which was washed with 5 *N* hydrochloric acid and then recrystallized from water to yield 48 g of *erythro*-2-ethyl-3-methylsuccinic acid (**8**), mp 183.5–184° (lit.[11] mp 182°). The diester (**10**, *erythro*) obtained by esterification with methanol and sulfuric acid showed only one band on gas chromatography on silicone under conditions described below for the *threo* isomer.

The hydrochloric acid solution obtained as a filtrate from collection of the *erythro* acid was evaporated to dryness, and the residue was heated with stirring for 2 hr at 190–200° (gas evolution had ceased). The crude product was esterified with methanol and sulfuric acid, and the diester was distilled to yield 60 g of the dimethyl *threo*-2-ethyl-3-methylsuccinate (**10**), bp 98° (18 mm) (lit.[11] mp of the acid, 102°). Gas chromatography (10 ft × ⅜ in. column, 20% silicone SE-30 partitioning agent at 151°, helium flow rate 150 cc/min) indicated that this product consists of 90% *threo* diester, 5% *erythro* diester, and 5% of the acid anhydride.

Reduction of Isomeric Dimethyl 2-Ethyl-3-methylsuccinates.—The two isomers were reduced by the same procedure. For the *erythro* isomer, a 15.5-g sample of diester dissolved in 50 ml of ether was added during about 3 hr to a stirred solution of 9.5 g of lithium aluminum hydride in 300 ml of dry ether. Heat of reaction gave gentle reflux during the addition, and after addition had been completed heating under reflux was continued for 4 hr. Excess reducing agent was destroyed by cautious addition of ice–water, then 400 ml of 10% sulfuric acid was added, and the product was continuously extracted with ether for 24 hr. Removal of solvent at reduced pressure yielded 9.5 g of crude glycol **11**.

Attempted distillation at reduced pressure of *erythro* glycol yielded only water and a low-boiling compound, which yielded a single band of 6-min retention time on gas chromatography under conditions described for the *threo* diester. Gas chromatography under the same conditions of the crude, unheated product gave two gas chromatography bands of retention times 6 and 23 min. The 6-min band is due to tetrahydrofuran formed so rapidly in the injection port to give the correct retention time, while the 23-min band is the diol surviving the chromatography. The spectral properties of the product collected from the 6-min band showed it to be ***cis*-3-ethyl-4-methyltetrahydrofuran.** There was no significant ultraviolet absorption above 190 mμ, and the nmr spectrum[18] showed two multiplets (4 H) between τ 6 and 7, signals from the four hydrogens α to the ring oxygen; a multiplet (2 H) centered at 7.8, from the two methine hydrogens in the ring; a multiplet (2 H) centered at 8.7, from the methylene hydrogens in the ethyl group; an overlapping doublet and triplet (6 H), from the two methyl groups. An analytical sample[18] was obtained by distillation.

Anal. Calcd for $C_7H_{14}O$: C, 73.7; H, 12.3. Found: C, 72.2, 72.6; H, 10.9, 12.4.

From a 30-g sample of the *threo* diester was obtained 20 g of the crude diol **11**. The *threo* diol was less easily dehydrated to the tretrahydrofuran than was the *erythro* isomer, in that distillation of the *threo* diol gave a mixture of diol and tetrahydrofuran of bp 95–125° (14 mm). Goodman[7] reported a low-boiling fraction [bp 97–103° (13 mm)] from a similar reduction, which was ascribed to starting ester which had escaped reduction.

1,4-Dibromo-2-ethyl-3-methylbutane (12), *erythro* Isomer.—The diol was converted to the dibromide by a procedure which has been described[19] for synthesis of 2-bromodecane. From 9 g of crude diol and 45 g of phosphorus tribromide was obtained 4.36 g of dibromide which showed only a single symmetrical band in gas chromatography (10 ft × ⅜ in. column, 20% silicone SE-30 partitioning agent at 150°, helium flow rate 150 cc/min, retention time 37.5 min). An analytical sample was collected from gas chromatography.

Anal. Calcd for $C_7H_{14}Br_2$: Br, 62.0. Found: Br, 62.1.

threo **Isomer.**—By the procedure described above, a 20-g sample of the *threo* diol yielded 13.6 g of crude dibromide. Gas chromatography under the same conditions used for the isomer showed a major band at 37 min (retention time of the *erythro* isomer, above), but there were minor bands at 25.5 and 43 min. Fractional distillation at 9 mm gave three fractions (3.3 g, bp 94–98°; 4.3 g, bp 99–104°; 5 g, bp >104°), all of which contained (by gas chromatography) all three components. The two higher boiling fractions, which contained a higher ratio of the dibromide, were used for subsequent steps, since no difficulty was expected in purification at a later step. For this dibromide, there has been reported[7a] bp 110° (13 mm).

3-Ethyl-4-methyladipic Acid (14), *erythro* Isomer.—A 4.3-g sample of the *erythro* dibromide was added during 30 min to a stirred mixture, heated at 60°, of 2 g of sodium cyanide and 10 ml of technical dimethyl sulfoxide. After addition had been completed, stirring at 90–92° was continued for an additional 15 min. The cooled reaction mixture was diluted with 35 ml of water and extracted with three 15-ml portions of ether. The extract was washed with 6 *N* hydrochloric acid and water, then dried. Dinitrile **13**, obtained by removal of solvent, gave a single symmetrical band in gas chromatography and showed infrared absorption at 4.52 μ.

Hydrolysis of the nitrile (2 g) was accomplished by heating under reflux with 25 ml of concentrated hydrochloric acid until a homogeneous solution resulted (about 3 days). The resultant solution was concentrated to about 4 ml, and the cooled residue was triturated with several small portions of ether. After ammonium chloride had been removed from the ether extract by filtration, the solvent was evaporated to yield 1.9 g of solid acid which showed characteristic carboxylic absorption in the infrared above 3 and carbonyl absorption at 5.82 μ. A sample recrystallized from water had mp 95–95.5°.

threo **Isomer.**—The two fractions of *threo* dibromide **12** of bp >98° (9.3 g) were converted to the nitrile in the manner described for the *erythro* isomer, and the crude nitrile was hydrolyzed as also described for that isomer. After a small amount of insoluble organic material had been separated from the solution of hydrolysis products, the diacid (**14**, *threo*) was continuously extracted with ether for 24 hr. The crude product so obtained amounted to 3.52 g, and was not purified at this stage. This acid has been reported[7a] as melting at 65–70°.

3-Ethyl-4-methylcyclopentanone (15), *cis* Isomer.—A mixture of 1.8 g of the *erythro* isomer of **14** and 115 mg of barium oxide was heated under a 2-ft simple Podbielniak-type column, with the bath temperature at about 300° and the column jacket at no more than 180°. The ketone, distilled quite slowly, was complete after about 7 hr. The temperature in the head of the column was at 174–184° during distillation of the ketone–water mixture. The ketone was extracted from the water with three 2-ml portions of ether. Solvent was removed from the dried solution by distillation through the same column, to leave a residue of 750 mg of ketone **15**. Gas chromatography under the same conditions used for the dibromide gave a single symmetrical band of retention time 11 min; infrared absorption was at 5.77 μ. Reported[7b] bp for this ketone was 172–174°.

trans **Isomer.**—The crude *threo* acid **14** (3.52 g) was converted to ketone in the manner described above, and the product was gas chromatographed under the same conditions described for the dibromide, to give the products and data shown in Table III. The *trans* ketone gave infrared absorption at 5.77 μ and gave a single symmetrical band in gas chromatography. This ketone has been reported[7] as having bp 180 or 184°.

TABLE III

Retention time, min	Wt, mg	Identity
7.5	270	Unknown
9.5	650	*trans*-**15**
11	102	*cis*-**15**

Methyl *cis*-3-Ethyl-4-methylcyclopentylideneacetates 5 and 6.—A Reformatsky reaction was carried out with 700 mg of *cis* ketone (**15**) 4 g of zinc foil, and 9 g of methyl bromoacetate, following approximately the procedure which has been described

(17) J. Cason, G. Sumrell, and R. S. Mitchell, *J. Org. Chem.*, **15**, 857 (1950).

(18) As was our previous experience [J. Cason and F. J. Schmitz, *ibid.* **28**, 552 (1963)] with a similar type of structure, low values were obtained in combustion analysis. Highest values were obtained (second values reported) on slow combustion at abnormally high furnace temperatures.

(19) F. S. Prout, J. Cason, and A. W. Ingersoll, *J. Am. Chem. Soc.*, **70**, 298 (1948).

in detail,[20] except that the benzene solvent was replaced with 1:1 benzene–ether.[21] The crude hydroxy ester (1.9 g) was dehydrated with 2.2 g of phosphorus oxychloride in 10 g of pyridine, also following the published procedure.[20] Isolation of the product by continuous extraction yielded 670 mg of unsaturated esters which yielded three bands in gas chromatography (20 ft × 3/8 in. column, 10% NPGS at 138°, helium flow rate 180 cc/min) with respective retention times of 36, 61.7, and 65.5 min. The first band represents the ring-unsaturated isomers, while the latter two bands are the α,β-unsaturated isomers [λ_{max} 220 mμ (ε 12,000)]. The nmr spectra[13] of the compounds collected in these two bands are those expected for the structures, and the mass spectra (*cf.* Table I) show that the band of 61.7-min retention time is isomer **5**, while the compound from the band of longer retention time is isomer **6**. Further, the mass spectrum of isomer **5** is identical with that of the compound from the 70-min band in Figure 5.

Methyl *trans*-3-Ethyl-4-methylcyclopentylideneacetates 3 and 4.—The entire sample (650 mg) of gas chromatographed *trans* ketone **15** was subjected to the Reformatsky reaction and dehydrated as described for the *cis* isomer. The unsaturated esters (700 mg) were gas chromatographed under the same conditions specified for the isomer above, and gave bands of retention times 29, 53.5, and 57.5 min. The components in the band of shortest retention time are the ring-unsaturated isomers, while the bands of longer retention time are due to the α,β-unsaturated isomers [λ_{max} 220 mμ (ε 13,500)]. The nmr spectra[13] are those expected for the structures, and the mass spectra (*cf.* Table I) show that the component of the 53.5-min band is isomer **3**, while the other compound is isomer **4**. Further, the spectra demonstrate that these isomers are identical with the unsaturated esters from degradation which are responsible for the 61.5- and 66-min bands in Figure 5.

Hydrogenation of unsaturated esters 5 and 6, using 10% palladium-on-charcoal catalyst and 95% ethanol as solvent, yielded saturated ester whose gas chromatography (10 ft × 3/8 in. column, 20% silicone SE-30 at 156°, helium flow rate 150 cc/min) showed two bands of retention time 24.5 and 28.7 min. A following chromatography of fraction III-2-A gave a retention time of 24.5 min. Chromatography on NPGS also gave the same retention times for fraction III-2-A and the band of shorter retention time. Since this band is much the smaller of the two it is assigned the *trans* geometry of structure **22**. Full mass spectra and nmr spectra were recorded.[13]

Hydrogenation of unsaturated esters 3 and 4, as described for the isomers, yielded saturated ester which gave only one band in gas chromatography (10 ft × 3/8 in. 20% silicone column at 152°, helium flow rate 150 cc/min, retention time 30 min; 20 ft × 3/8 in. 10% NPGS column at 137°, helium flow rate 180 cc/min, retention time 32 min). Following chromatography of fraction III-2-A showed the same retention times on both columns. Further, mass spectra were the same. Full mass spectra and nmr spectra were recorded.[13]

(20) K. L. Rinehart, Jr., and E. G. Perkins, "Organic Syntheses," Coll. Vol. **4**, John Wiley and Sons, Inc., New York, N. Y., 1963, p 444.

(21) J. Cason and R. J. Fessenden, *J. Org. Chem.*, **22**, 1326 (1957).

Pseudo-Halogens. VII. Scope and Mechanism of Addition of N,N-Dichlorourethan to Monoolefinic Compounds[1,2]

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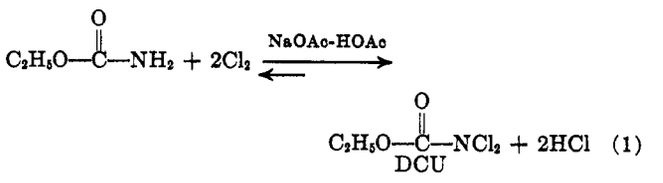
N,N-Dichlorourethan (DCU), a stable, distillable, but reactive pseudo-halogen has been prepared in excellent yield by an improved procedure from chlorine and urethan in buffered aqueous acid solution. DCU adds almost quantitatively to the double bonds of styrene and *trans*-stilbene to yield β-chloro-N-chlorocarbamates which are reduced with aqueous sodium bisulfite to β-chlorocarbamates. With straight-chain terminal olefins (C_6, C_{10}, C_{12}, C_{18}) and 2-methyl-1-pentene, yields of β-chlorocarbamates are about 60%. Nonterminal olefins with allylic hydrogens give 30–40% yields of β-chlorocarbamates, the predominant reaction involving allylic attack. Norbornene yields 3-chloronortricyclene by homoallylic attack; reaction of norbornene with DCU is a convenient route to this three-ring compound. Reaction of DCU with olefins is a free-radical chain reaction proceeding in an anti-Markovnikov manner as shown by physical and chemical proof. Mechanisms are proposed for the various reactions.

Considerable attention is being given in our laboratory to the preparation and reactivity of pseudo-halogens containing nitrogen. The major objectives of the program are (a) to develop single-step and, hopefully, stereospecific syntheses of compounds containing the carbon–nitrogen bond directly from unsaturated systems, and (b) to study the scope and mechanisms of these double-bond addition reactions. In previous papers we have reported our results with iodine isocyanate[3] and with nitrosyl acylates.[4]

In this paper we are reporting (a) an improved high-yield preparation of N,N-dichlorourethan (DCU), a stable, distillable yet highly reactive pseudo-halogen, and (b) the scope, limitations, and mechanism of its addition to monoolefinic compounds.

Preparation of DCU.—DCU was first prepared by Datta and Gupta[5] and subsequently by Houben[6] and by Chabrier,[7] but explicit details concerning yields, methods of isolation, and purity and physical characteristics of product were not reported. We have improved Chabrier's[7] procedure and can obtain DCU of analytical purity in excellent yield (80%) by reaction of the calculated quantity of chlorine with urethan in buffered aqueous solution (eq 1). Neutralization of



(1)

(1) Work to be submitted by T. A. Foglia in partial fulfillment of the requirements for the Ph.D. degree. Presented at the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966.

(2) The authors acknowledge with thanks support of this investigation by Public Health Service Research Grants No. CA-07803 and CA-07174 from the National Cancer Institute.

(3) (a) C. G. Gebelein and D. Swern, *Chem. Ind.* (London), 462 (1965); (b) C. G. Gebelein and D. Swern, Abstract of paper presented at 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965; (c) S. Rosen and D. Swern, *Anal. Chem.*, **38**, 1392 (1966); (d) C. Gebelein, G. Swift, and D. Swern, paper presented at Middle Atlantic Regional Meeting of the American Chemical Society, Philadelphia, Pa., Feb 1966.

(4) H. C. Hamann and D. Swern, *Tetrahedron Letters*, 3303 (1966).

(5) R. L. Datta and S. D. Gupta, *J. Am. Chem. Soc.*, **37**, 569 (1915).

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(7) P. Charbrier, French Patent 56,285 (1952).