seum Nat. Hist. **12**, 1 (1959); H. Winge, *The Interrelationships of the Mammalian Genera* (Reitzels, Copenhagen, 1941), vol. 1, 418 pp.
3. The skeleton is regarded as too beautiful for exposure to risk of change by embedment in plastics; it is said to be a "once-in-a-century" discovery. When the specimen (with matrix, about 19 by 8 by 1.5 cm) is rotated under the microscope, it is often difficult to locate a single small feature quickly and exactly on an opposite side. As an aid to quick identification of structure on both sides, several human hairs of different colors were stuck through holes in the matrix. One such hair equals in diameter (0.1 mm) the middle part of the stylohyal bones (Fig. 2, No. 76). The many thousands of man-hours already expended are insufficient for complete elucidation of the functional characteristics of the bones.
4. The generic name combines "Icarus" (a flyer in Greek mythology) with a common Greek word for bat; the specific nomen directs attention to the clawed forefinger.
5. T. T. Struhsaker, *J. Mammal.* **42**, 152 (1961).
6. L. C. Stegeman, *ibid.* **37**, 58 (1956).
7. P. H. Krutzsch and T. A. Vaughan, *ibid.* **36**, 96 (1955).
8. P. Bloedel, *ibid.*, p. 390; J. Shortt, *Proc. Zool. Soc. London* **1863**, 438 (1863); W. G. Reeder and K. S. Norris, *J. Mammal.* **35**, 81 (1954).
9. Remains of Oligocene, Miocene, and Pliocene bats are extremely rare because of their habitat, erosion, and chance; Eocene types are even rarer. Regarding Eocene bats, see: G. M. Allen, *Bats* (Harvard Univ. Press, Cambridge, Mass., 1939), 368 pp.; C. Dechaseaux, in *Traité de Paléontologie,* J. Piveteau, Ed. (Masson, Paris, 1958), tome 6, vol. 2, pp. 919–944; P. P. Grassé, *Traité de Zoologie* (Masson, Paris, 1955), pp. 1729–1853; C. O. Handley, *J. Mammal.* **36**, 128 (1955); F. Heller, *Nova Acta Leopoldina* No. 2 (1935); P. Revilliod, *Abhandl. Grossherz. Hess. Geol. Landesamtes* **7**, 157 (1917); *Compt. Rend. Soc. Hist. Nat. Genève* **36**, 93 (1919); *Mém. Soc. Paléontol. Suisse* **45**, 131 (1922); P. Robinson, in M. C. McKenna, P. Robinson, D. W. Taylor, *Amer. Museum Novitates No. 2102* (1962), p. 1–33.
10. Univ. of Wyoming No. 2244, found in the Green River shales of Gosiute Lake; available by courtesy of P. McGrew.
11. C. J. Hesse, *Sci. Monthly* **48**, 147 (1939).
12. Six more undescribed mid-Eocene (Bridgerian age) chiropteran fragments merit future attention although they reveal little or nothing of the ancestry or primordial structures of bats: Carnegie Museum No. 13711–14, each a tooth or part of one; Amer. Museum Nat. Hist. No. 55696, a dentary with the second molar; and Yale Peabody Museum No. 16222, part of a dentary, with two incomplete teeth (collected in 1875 but only recently recognized as chiropteran).
13. T. Edinger, *Anat. Record* **138**, 345 (1960); *World Neurol.* **2**, 938 (1961); *Amer. Zoologist* **4**, 5 (1964).
14. E. Gould, *Proc. Am. Phil. Soc.* **109**, 352–360 (1965).
15. Anon., *Proposed Fossil Butte National Monument* (U.S. Nat. Park Serv., Midwest Region, Omaha, Neb., 1964), pp. 1–30 (geology by S. S. Oriel and J. I. Tracey).
16. By the U.S. National Museum and Princeton Univ.
17. C. L. Gazin, *Smithsonian Inst. Misc. Collections* **144**, 1 (1962).
18. W. H. Bradley, *U.S. Geol. Surv. Profess. Papers* **158-E**, 87 (1929).
19. ———, *Bull. Geol. Soc. Amer.* **59**, 635 (1948); in *Paleolimnology,* D. F. Frey, Ed. (Univ. of Wisconsin Press, 1963), pp. 621–52; *U.S. Geol. Surv. Profess. Papers* **496-A**, 1 (1964).
20. J. F. Evernden, D. E. Savage, G. H. Curtis, G. T. James, *Amer. J. Sci.* **262**, 145 (1965).
21. B. Schaeffer and M. Mangus, *Nat. Hist.* **74**, 10 (1965).
22. J. H. D. Hooper, *Animals of Britain No. 2* (1962) (courtesy *Sunday Times,* London).
23. Aided by the W. B. Scott Fund and by NSF grant GB-218. For special help I thank Howard Bott, Wilmot Bradley, Clarence Cushman, David Haddenham, Aline Hansens, Claude Hibbard, Karl Koopman, Giles MacIntyre, Paul McGrew, Robert Rainey, Peter Robinson, Willard Starks, Terry Vaughan, Jack Vernon, and Michael Woodburne.

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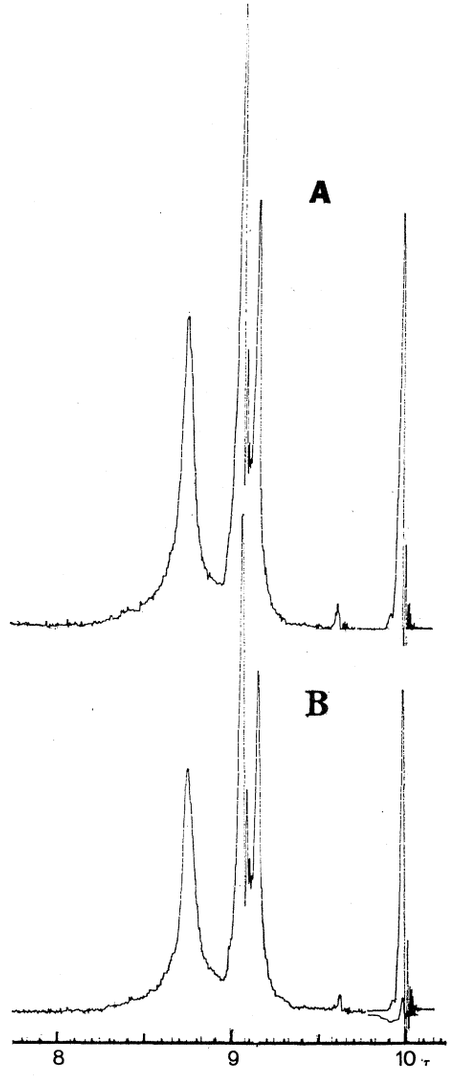
Terpenoid Precursors of Hydrocarbons from the Gasoline Range of Petroleum

Abstract. *2,6-Dimethyloctane and 2-methyl-3-ethylheptane were isolated from petroleum. These hydrocarbons which are present in relatively large amounts appear to be derived from the monoterpenoids.*

The presence in petroleum of hydrocarbons that have skeletal structures or large fragments of the skeletal structures of certain compounds that are also in vegetable and animal products is well established (*1, 2*). Most, if not all, of these hydrocarbons have been isolated from petroleum distillates with a relatively high boiling point.

We have isolated two C_{10}-branched paraffins that appear to be derived from the terpenoids. These hydrocarbons, which are present in relatively large amounts, are 2,6-dimethyloctane and 2-methyl-3-ethylheptane. The finding of a large amount of 2,6-dimethyloctane was not unexpected since higher homologs of this series have previously been shown to be important constituents of petroleum (*1*). This hydrocarbon is probably formed from the acyclic monoterpenoids, though it could also be derived by splitting acyclic terpenoids which have a higher molecular weight. However, the finding, in large amount, of 2-methyl-3-ethylheptane



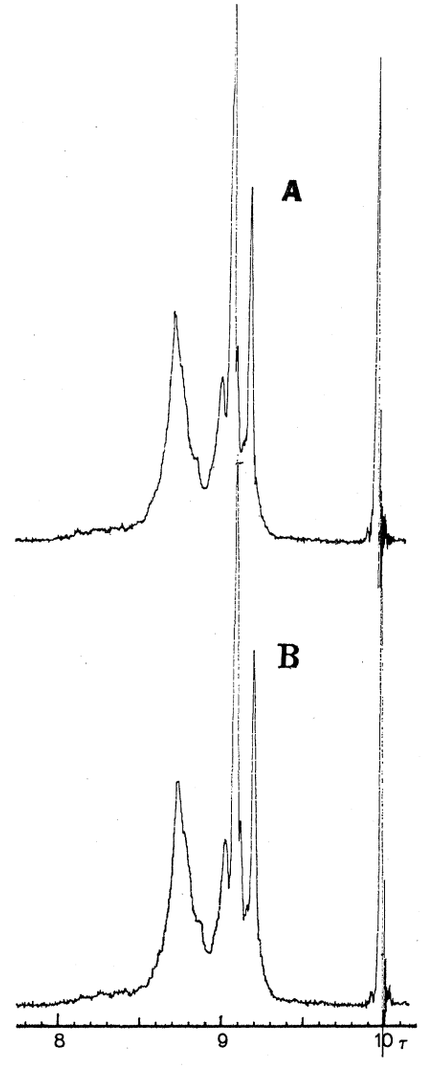
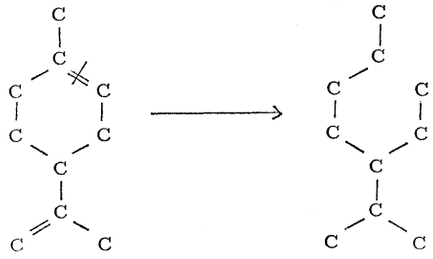


Fig. 1 (left). NMR spectra of two samples of 2,6-dimethyloctane. (A) Synthetic; (B) from petroleum. Fig. 2 (right). NMR spectra of two samples of 2-methyl-3-ethylheptane. (A) Synthetic; (B) from petroleum.

was unexpected since paraffins with this type of branching have not heretofore been found as major components of petroleum.

Limonene, which is abundant in many essential oils, such as in the rind of citrus fruits, in pine needles, and in turpentine, is the probable, although not necessarily exclusive, precursor. We suggest that 2-methyl-3-ethylheptane is derived from limonene by saturation of the double bond in the side chain and by rupture of the double bond in the ring:



Limonene — 2-Methyl-3-ethylheptane

These hydrocarbons were isolated by preparative scale gas-liquid chromatography of distillate fractions in the boiling range of 159.5° to 161.5°C of the branched paraffin-cycloparaffin portion of the reference petroleum of the API Research Project 6 (*3*). They were tentatively identified from their physical and spectrometric properties. These identifications were subsequently confirmed by direct comparison of their infrared and nuclear magnetic resonance spectra with those of synthetic samples (Figs. 1–4). The amounts were determined by analyzing the distillate fractions in the 159.5° to 161.5°C range by using both capillary and 0.25-inch (0.63-cm) packed columns with polar partitioning liquids (silicon nitrile and diethylene glycol succinate). On these columns the two compounds are well separated, with 2,6-dimethyloctane having the lower retention time. The maximum concentration of 2,6-dimethyloctane occurred in fractions that boiled at 160.4°C; that of 2-methyl-3-ethylheptane in fractions that boiled at 160.9°C. 2,6-dimethyloctane was found to constitute 0.50 volume percent and 2-methyl-3-ethylheptane 0.64 volume percent of the crude petroleum. For comparison, the corresponding value for all other branched paraffins that boiled in the range from 155° to 165°C (a total of 49 are theoretically possible) was 0.44 volume percent.

Because these two hydrocarbons appear to be derived from different precursors, the amounts present and their ratios may be expected to vary from crude to crude depending in part on the content of each precursor in the source materials from which the different crudes were generated. If subsequent investigations establish such a variation, the information may be valuable in several ways. For example, the petroleum industry frequently needs to

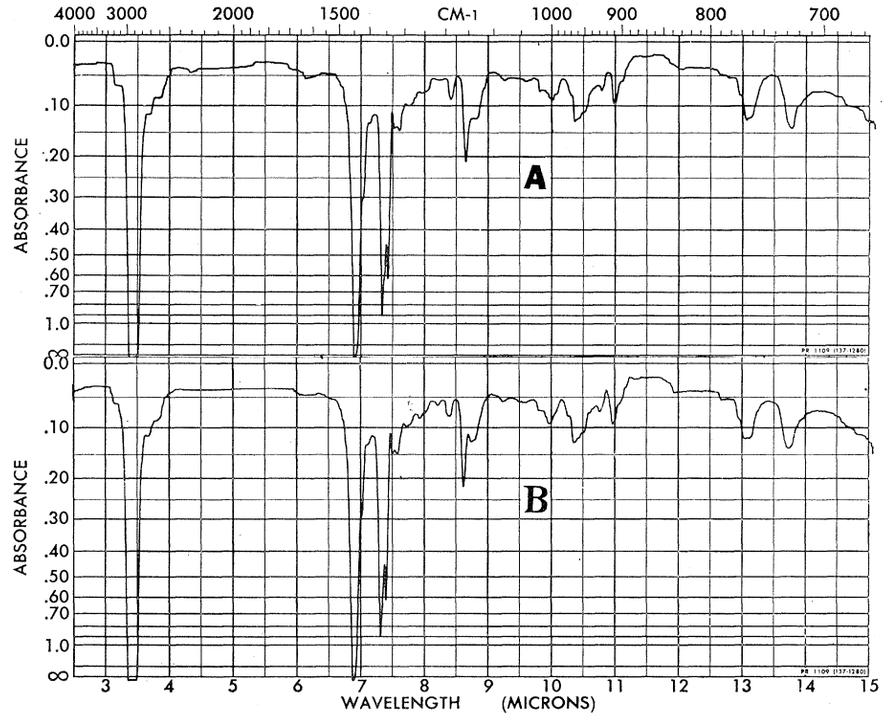


Fig. 3. Infrared spectra of two samples of 2,6-dimethyloctane. (A) Synthetic; (B) from petroleum.

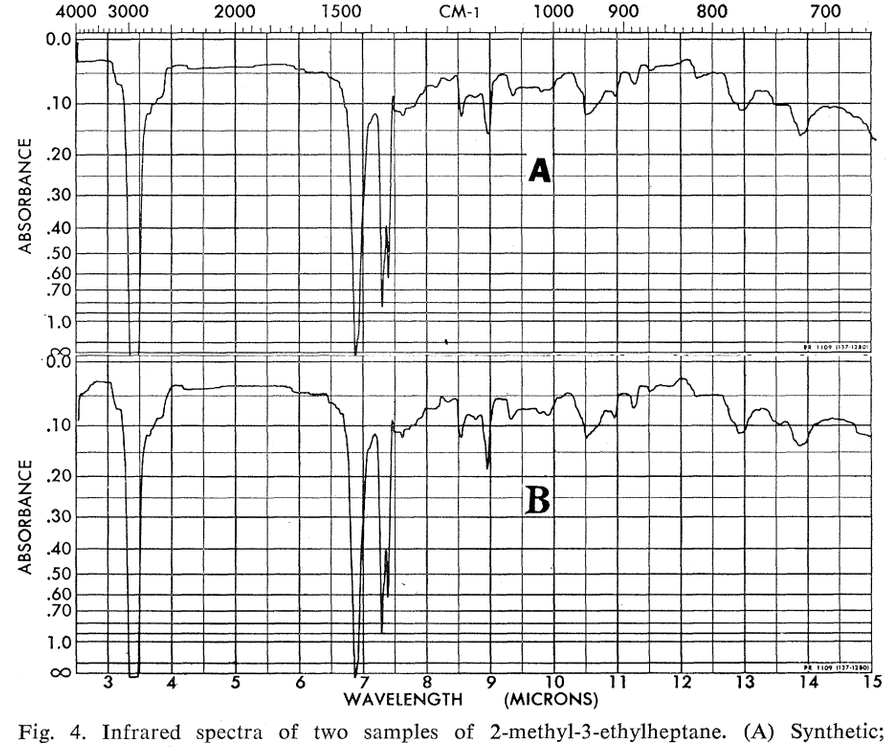


Fig. 4. Infrared spectra of two samples of 2-methyl-3-ethylheptane. (A) Synthetic; (B) from petroleum.

know whether petroleum from wells separated by several miles comes from the same or from different sources. A knowledge of the content of these two hydrocarbons in the given wells may aid in solving this problem. With the information now available an analysis for these two compounds can be made by gas-liquid chromatography, using only retention times for identification provided samples of the pure hydrocarbons are available for calibration.

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References and Notes

1. J. G. Bendoraitis, B. L. Brown, L. S. Hepner, *Anal. Chem.* **34**, 49 (1962); *Proc. World Petrol. Congr., 6th Frankfurt 1963* Sect. V, Paper 15; R. A. Dean and E. V. Whitehead, *Tetrahedron Letters*, No. 21, 768 (1961); B. J. Mair, N. C. Krouskop, T. J. Mayer, *J. Chem. Eng. Data* **7**, 420 (1962).
2. B. J. Mair and José L. Martinéz-Picó, *Proc. Am. Petrol. Inst.* **42**, 173 (1962); R. L. Martin, J. C. Winters, J. A. Williams, *Proc. World Petrol. Congr. 6th Frankfurt 1963* Sect. V, Paper 13.
3. F. D. Rossini, B. J. Mair, A. J. Streiff, *Hydrocarbons from Petroleum.* (Reinhold, New York, 1953).
4. Support by the American Petroleum Institute Research Project 6 is gratefully acknowledged.

9 September 1966

Cystinuria: Genetic Heterogeneity and Allelism

Abstract. *Studies of four stone-forming cystinuric subjects from three unrelated pedigrees indicated that each was heterozygous for two of the three described mutant genes producing cystinuria (I, II, III). Their genotypes were I–II, II–III, I–III, and I–III, respectively. These doubly heterozygous patients were phenotypically indistinguishable from cystinuric homozygotes of genotype I–I, II–II, or III–III. The data provide the first direct evidence that all of the known mutations responsible for the genetic heterogeneity in cystinuria are allelic.*

Results of definitive studies (*1, 2*) on the genetics of cystinuria from 27 pedigrees indicated that the occurrence of cystinuria followed classical Mendelian laws for autosomal recessive inheritance. Homozygous affected subjects excreted large quantities of cystine, lysine, arginine, and ornithine in their urine. Renal, ureteral, and vesical calculi composed of cystine were formed because of the very limited solubility of cystine. The findings in heterozygous individuals were heterogeneous. In some families urinary dibasic amino acid excretion among heterozygous individuals (parents and children of affected subjects) was normal, whereas in other families, modest to marked excesses of cystine and lysine were excreted by all heterozygotes. Thus Harris suggested that cystinuria was, in fact, more than one disease entity. We have reported that there are three types of cystinuria (*3*). Type I was characterized by the absence of mediated intestinal transport mechanisms for dibasic amino acids in homozygotes and by normal urinary cystine values in heterozygotes. Type II differed most significantly in that heterozygotes excreted markedly increased quantities of cystine. In type III cystinuria, intestinal transport of all dibasic amino acids was retained by homozygotes, and heterozygotes excreted cystine in slight excess. Quantitative determinations of lysine, arginine, and ornithine in these heterozygotes have confirmed the differences noted in cystine excretion. Thus we have demonstrated statistically significant differences among type I, II, and III heterozygotes for each of the four dibasic amino acids measured (*4*).

In the first nine pedigrees studied, our results were in agreement with those of Harris (*1*), Crawhall (*5*), and their co-workers in that all heterozygotes within a single pedigree showed remarkably similar values for the aforementioned urinary amino acids. That is, there was no example in these nine pedigrees of more than a single type of heterozygote within a single family. Recently, however, we have found three unrelated families in which two types of heterozygotes have been demonstrated in a single pedigree. These results form the basis of this report.

Three individuals, G.F. (31-year-old male), J.P. (25-year-old male), and B.B. (35-year-old female), showed recurrent renal or ureteral cystine stone formation. Each excreted in the urine great excesses of cystine, lysine, ornithine, and arginine, the values being in the range noted for cystinuric homozygotes. However investigation of their families revealed (Figs. 1 and 2) that G.F.'s father (F.F.) showed a urinary amino acid pattern typical for a type III heterozygote (Fig. 1) while his mother (M.F.) and son showed a normal urine pattern characteristic of type I heterozygotes. These results were confirmed by analysis of three separate urine samples from each subject, and were strengthened by finding other type I and type III heterozygotes within the pedigree (Fig. 2). These data represent the first unequivocal demonstration of heterogeneity within a single cystinuric family. Similar, but not identical, results were encountered in the other two families (Fig. 2). J.P.'s father (H.P.) was a type II heterozygote (Fig. 1) while his mother (T.P.) was a type I heterozygote. Analyses for the four amino acids in urine samples from each of B.B.'s five children revealed that three were type II heterozygotes and two were type III heterozygotes (Fig. 2). Representative results from this pedigree also appear in Fig. 1. These findings suggested that J.P., B.B., and G.F. were not homozygous for one of the mutations producing cystinuria but, rather, were each heterozygous for two of the three mutant genes, their genotypes being I–II, II–III, and I–III, respectively.

These findings necessitated additional studies (Table 1) of intestinal amino acid transport in the affected probands —G.F., J.P., B.B., and E.M. (a paternal first cousin of G.F., once removed, with cystinuria and renal lithiasis). None of the patients from the three pedigrees were able to transport significant quantities of lysine, arginine, or cystine. The results were identical to those noted for type I homozygotes (*3*). However, oral tolerance studies with cystine did reveal subtle differences in both G.F. and E.M. in that there were small, but perceptible rises in plasma cystine (Fig. 3), results which were midway between those of type III homozygotes and type I homozygotes (*3*).

Such results indicate that the genetic heterogeneity in human cystinuria is even more complex than supposed. The pedigrees (Fig. 2) indicate that subjects heterozygous for two different mutations causing cystinuria are phenotypically indistinguishable from documented homozygotes, and thus the question of allelism must be considered.

Let us assume that cystinuria, like other disorders characterized by autosomal recessive inheritance, results from defective synthesis of a specific membrane polypeptide which catalyzes transport of the dibasic amino acids in gut and kidney. We can make certain pre-