113–115° (lit.[10] m.p. 115°) and the 2,4-dinitrophenylhydrazone had m.p. and m.m.p. 120–121° (lit.[11] m.p. 122–123°). Pentan-2-one was shown to be absent by analytical g.l.c.

1-Phenylbutane-1,3-dione.—1-Phenylbutane-1,3-dione was reduced as described above for pentane-2,4-dione and yielded from ether a colorless liquid, b.p. 180–220°. Analytical gas chromatography showed the major product to be 3-phenylbutan-2-one (*ca.* 65% of distillate) together with 2-phenylbutane and two other compounds probably hydrocarbons. 2-Methyl-1-phenylbutan-1-one was shown to be absent. The total distillate yielded 3-phenylbutan-2-one semicarbazone, m.p. and m.m.p. 170–170.5° (lit.[12] m.p. 170–171°) and 2,4-dinitrophenylhydrazone, m.p. and m.m.p. 125–126° (lit.[13] m.p. 125–126°). Authentic 3-phenylbutan-2-one was prepared from 1-phenylpropan-2-one by methylation with methyl iodide and aqueous sodium hydroxide.[13] 2-Phenylbutane was prepared from this by Wolff–Kishner reduction.

3,3-Dimethylpentane-2,4-dione.—3,3-Dimethylpentane-2,4-dione[14] (5 g.) was reduced as described above and yielded, on ether extraction, a colorless liquid, b.p. 130–180° (2.1 g.). Analytical gas chromatography showed that 3,4-dimethylpentan-2-one was the major product together with some starting material and a little low-boiling material, probably a hydrocarbon. 2,4-Dimethylpentan-3-one was shown to be absent. The total product on distillation gave 3,4-dimethylpentan-2-one, b.p. 135–138°. Authentic 3,4-dimethylpentan-2-one, prepared by methylation of 2-methylpent-2-en-4-one and subsequent hydrogenation,[15] had b.p. 136–138°, semicarbazone m.p. 113°.

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Imido Glycols as Stable Polar Liquid Phases in Gas Chromatography*

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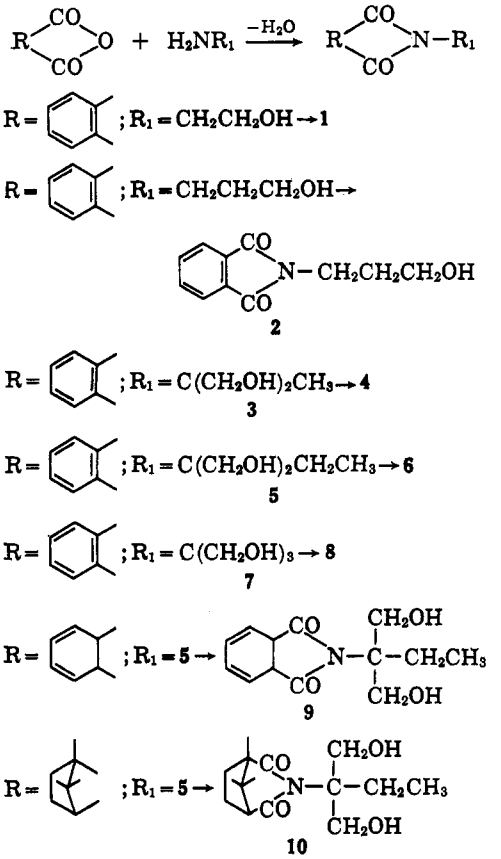
Effective gas chromatographic separation of polar compounds is intimately connected with the availability of high-boiling polar liquid phases. Conventional liquids, like polyethylene glycols and their esters, show considerable deterioration (aging) at useful column temperatures (around 150°). Unfortunately, as a rule, the more polar and suitable the liquids are (that is, the better the separations they permit as long as they are freshly prepared), the faster they deteriorate ("bleed"). In most of the cases the useful life span of such unstable columns is a few weeks or even less, and the specific retention (elution) time, so important for proper identification purposes, is no longer a constant but at best a relative criterion. In the search for temperature-stable high-boiling polar liquids we were guided by earlier observations in the preparation of N-vinyl monomers[1,2] that certain tertiary dicarboximides (**1**) represent compounds of remarkable stability against exposure to high temperatures.

At first, simple hydroxyalkylphthalimides were tried. The lower members of this series are crystalline sharp-melting compounds, one of them (**2**) not previously encountered in the literature. Unfortunately, the practical usefulness of the lower members as a chromatographic substrate is limited; this is partly due to their relatively high vapor pressure and tendency toward sublimation.

With the commercial availability of higher molecular weight and more polar amino glycols (**3**, **5**, and **7**),[3] certain imides can be prepared which overcome these problems (**4**, **6**, **9**, and **10**). Although these compounds



have been prepared under milder conditions than the one (**4**) described earlier,[4] a proof of homogeneity of the compounds or the identification of their components could not be provided.

Inexplicably, possibly due to its high melting point, the condensation product with tris(hydroxymethyl)-aminomethane (**8**) was useless as a chromatographic liquid phase. Both the 2-methyl- and 2-ethyl-2-aminopropane-1,3-diols have given useful condensation products (**4** and **6**), and for its better resolving power we have preferred the liquid phase obtained with the 2-ethyl compound (**6**).

In gas chromatography of terpenes and terpenoids it is customary to blend a polar with a nonpolar liquid (50:50) in order to make the resulting column capable of resolving the mixture of polar compounds and hydrocarbons as well. With the inclusion of the condensation

* To Professor Louis F. Fieser.

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(2) One of the authors' (R. L. M.) unpublished results.
(3) Courtesy of the Commercial Solvents Corp.
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product of *d*-camphoric anhydride (**10**) in this series we have gained a particularly suitable compound for the separation of terpenes and terpenoids. For instance, a commercial sample of oil of geranium has been readily separated into 31 known and unknown components. Analytical results achieved in resolving complex terpene mixtures will be presented elsewhere.[5]

When used as a liquid chromatographic column phase, compounds **4**, **6**, **9**, and **10** have proved to be perfectly temperature stable over a period of more than a year of constant use, provided that they were "trained" and used at a temperature no higher than 170°. This temperature seems to be the practical limit for this type of columns; raising the temperature by as little as 5° will invariably cause the columns to "bleed," shorten their original retention time, and contaminate the hot wire detector filament to a considerable degree. Thus, properly kept columns have produced matching retention times reproducible in weeks or months within the useful temperature range of 100–170°. In view of a recently presented paper on the subject of retention systems[6] we suggest that this type of column be given some consideration as reference standards, since properly treated columns will not require drift compensation at all.

Experimental

Preparation of N-(3-Hydroxypropyl)phthalimide.—Phthalic anhydride (74 g., 0.5 mole) and 3-aminopropanol (37.5 g., 0.5 mole) were stirred and refluxed with toluene (200 ml). In about 3.5 hr., the theoretical amount of water (9 ml., 0.5 mole) was collected by means of a Dean–Stark phase separator. At this point ice bath cooling of the clear yellow-colored toluene solution caused heavy crystallization. On a Büchner funnel 92.0 g. of light cream-colored solids, m.p. 75–79°, were collected and on concentration the mother liquor afforded an additional 3.8 g. of crystals bringing the yield to 95.4 g. or 93.4%. After three recrystallizations from 80% MeOH, the white crystalline material proved to be gas chromatographically pure, m.p. 78–81°. The infrared spectrum (5% in chloroform) has shown peaks in the λ 2.82, 3.38, *5.62*, *5.83*, *6.08*, *6.20*, 7.12, 7.28, 8.90, 9.28, 10.40, and 10.72 μ areas. The italic peaks are characteristic of the dicarboximide grouping. The n.m.r. spectrum in deuteriochloroform showed a quintet at 1.9 (β-methylene hydrogens), a singlet at 3.00 (hydroxyl hydrogen), and two overlapping triplets centered at 3.65 and 3.84 p.p.m. (α- and γ-methylenes). The aromatic absorption was centered at 7.75 p.p.m. The relative areas of these peaks were 2:1:4:4. Both the infrared spectrum and the n.m.r. data are consistent with formula **2** assigned to this compound.

General Method of Preparation of the Substrates.—An equimolar mixture of the reagents (anhydride and amino glycol) is stirred and refluxed in the presence of an equal volume of toluene. A Dean–Stark phase separator will indicate when the theoretical amount of water has separated. At this point toluene is evaporated *in vacuo*. The remaining buff-colored viscous residue may then be used directly for coating of column supports. Molecular weight determinations, by the melting point depression of camphor solutions according to Rast,[7] have not indicated significant differences from the calculated figures. For some of the compounds the following results were obtained (compound: mol. wt. calcd., found): **4**: 235, 208; **6**: 249, 222; **9**: 255, 252; **10**: 283, 268.

Infrared Spectra.—Solutions (5% in $CHCl_3$) of compounds **4**, **6**, **9**, and **10** have shown characteristic absorption in the λ 2.77–2.95 (OH), 5.62, 5.82, 6.00–6.08 (CO–N–CO), and 9.33–9.60 μ (OH) areas in agreement with the formulas assigned to them. There is good reason to believe that tertiary imides as indicated in formulas **4**, **6**, **9**, and **10** are the major components.[8] At any rate, if condensation polymers were also present as contaminants, they would be of the linear and not of the cross-linked variety since the compounds are clearly soluble in an appropriate solvent (*i.e.*, chloroform).

Polarity of N-[2-(2-Ethyl-1,3-dihydroxy)propyl]-D-camphorimide.—For comparison of polarities two 5 ft. × 1/8 in. o.d. columns were prepared; in both columns −80 to +100 mesh Chromosorb P served as a solid support.

n-Hexyl alcohol, *n*-heptaldehyde, and *n*-hexyl chloride were analyzed in both columns under identical conditions (10%, 100°, 20 cc./min. He flow rate) giving the following retention times on Carbowax 20M: 7.34, 3.2, and 1.76 min.; on **10**: 5.36, 2.48, and 1.52 min. Analyzing the straight-chain saturated hydrocarbons C_{12}, C_{10}, C_8, and C_6 on both columns, under above identical conditions, the following retention times were found on Carbowax 20M: 5.5, 1.7, 0.6, and 0.36 min.; and on **10**: 6.8, 1.96, 0.66, and 0.4 min. The retention indices[6] at 100°, I_{100}, for *n*-hexyl chloride, *n*-heptaldehyde, and *n*-hexyl alcohol on Carbowax 20M are: 1006, 1108, and 1249; on **10** they are: 954, 1049, and 1162. Thus **10** is a comparable though somewhat less polar substrate than Carbowax 20M; on the other hand, it retains hydrocarbons longer than the latter. This is understandable since a monoterpenoid structure represents the nonpolar moiety of this particular hybrid molecule.

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Synthesis of Analogs of δ-Aminolevulinic Acid*[1]

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We have reported earlier on efforts to prepare certain sulfur analogs[3] of the key intermediate in porphyrin biosynthesis, δ-aminolevulinic acid (δ-ALA).[4] We wish now to report on the synthesis of a number of methylated analogs of δ-ALA synthesized by procedures patterned after the successful synthesis of δ-aminolevulinic acid.[5] These compounds will be evaluated for their effect on the biosynthesis of porphyrins.

Discussion

The necessary methyl hydrogen methylsuccinates for the synthetic pathway outlined in Scheme I were pre-

* To Professor Louis F. Fieser.
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