References and Notes

(1) Unsaturated Macrocyclic Compounds. 121. For part 120, see L. Lombardo and F. Sondheimer, *Tetrahedron Lett.*, 3841 (1976).
(2) D. Cremer and H. Günther, *Justus Liebigs Ann. Chem.*, **763**, 87 (1972); H. Günther, A. Shyoukh, D. Cremer, and K. H. Frisch, *Tetrahedron Lett.*, 781 (1974).
(3) R. H. Wightman and F. Sondheimer, *Tetrahedron Lett.*, 4179 (1975).
(4) R. T. Weavers and F. Sondheimer, *Angew. Chem.*, **86**, 167 (1974).
(5) A. Yashuhara, T. Satake, M. Iyoda, and M. Nakagawa, *Tetrahedron Lett.*, 895 (1975).
(6) Since this manuscript was prepared, Professor Staab kindly sent us a manuscript describing the synthesis of one of the possible isomers of benz[14]annulene itself [U. E. Meissner, A. Gensler, and H. A. Staab, *Angew. Chem.*, **88**, 374 (1976)].
(7) For short reports of the use of this method for preparing other annelated bisdehydroannulenes, see (a) T. M. Cresp and F. Sondheimer, *J. Am. Chem. Soc.*, **97**, 4412 (1975); (b) R. R. Jones, J. M. Brown, and F. Sondheimer, *Tetrahedron Lett.*, 4183 (1975); (c) R. H. Wightman, T. M. Cresp, and F. Sondheimer, *J. Am. Chem. Soc.*, **98**, 6052 (1976).
(8) T. M. Cresp and F. Sondheimer, *J. Am. Chem. Soc.*, **99**, 194 (1977).
(9) O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, **40**, 1242 (1957).
(10) The conversion **5** → **6** → **7** → **8** has been described by N. Darby, Ph.D. Thesis, University of Alberta, 1972.
(11) T. M. Cresp, M. V. Sargent, and P. Vogel, *J. Chem. Soc., Perkin Trans. 1*, 37 (1974).
(12) M. Gaudemar, *Ann. Chim. (Paris)*, **1**, 161 (1956); see also F. Sondheimer, Y. Amiel, and Y. Gaoni, *J. Am. Chem. Soc.*, **84**, 270 (1962). This derivative, as well as the magnesium derivative of 3-bromo-1-butyne, has been shown to exist in the allenic form [C. Prévost, M. Gaudemar, L. Miginiac, F. Bardone-Gaudemar, and M. Andrac, *Bull. Soc. Chim. Fr.*, 679 (1959)].
(13) See R. L. Crossland and K. L. Servis, *J. Org. Chem.*, **35**, 3195 (1970).
(14) See F. Sondheimer and D. A. Ben-Efraim, *J. Am. Chem. Soc.*, **85**, 52 (1963).
(15) E. Spath, *Sitzungsber. Akad. Wiss. Wien*, **120**, 1117 (1911).
(16) Towards the end of this work it was found that the oxidative coupling of terminal diacetylenes to macrocyclic 1,3-diacetylenes usually proceeds in higher yield when anhydrous cupric acetate instead of the monohydrate is employed (see T. M. Cresp, J. Ojima, and F. Sondheimer, *J. Org. Chem.*, in press).
(17) Various attempts have been made to reduce the acetylenes of **14** in order to obtain a benz[14]annulene (see ref 6). The only significant result was obtained by reduction with diisobutylaluminum hydride,[18] which yielded a monodehydrobenz[14]annulene (N. Darby, unpublished results).
(18) See J. J. Eisch and W. C. Kaska, *J. Am. Chem. Soc.*, **88**, 2213 (1966).
(19) See W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1961); *Org. Synth.*, **45**, 44 (1965); J. Wolinsky and K. L. Erickson, *J. Org. Chem.*, **30**, 2208 (1965).
(20) The ylide **27** was prepared by the reaction of ethyl γ-bromocrotonate with triphenylphosphine, followed by dehydrobromination of the resulting phosphonium salt with aqueous sodium hydroxide, as described for the corresponding methyl ester [E. Buchta and F. Andree, *Naturwissenschaften*, **46**, 74 (1959)].
(21) The trisdehydro compounds were chosen as models in the [18]annulene series, since no unsubstituted bisdehydro[18]annulenes are known.
(22) See P. J. Garratt and K. Grohmann in Houben-Weyl, "Methoden der Organischen Chemie", Vol. 5, Part 1d, Georg Thieme Verlag, Stuttgart, 1972: (a) Table 1; (b) Table 2; (c) Table 4.
(23) Similarly, it has been shown that introduction of six methyl groups into 1,7,13-trisdehydro[18]annulene causes a bathochromic shift of only ~7 nm [F. Sondheimer and D. A. Ben-Efraim, *J. Am. Chem. Soc.*, **85**, 52 (1963)].
(24) See G. Ege and H. Vogler, *Tetrahedron*, **31**, 569 (1975); H. Vogler and G. Ege, *ibid.*, **32**, 1789 (1976).
(25) For a more satisfactory "reactivity" criterion of aromaticity and antiaromaticity in macrocyclic π systems, see ref 7c.
(26) K. Fries and H. Bestian, *Chem. Ber.*, **69**, 715 (1936).
(27) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jensen, and T. Walker, *J. Chem. Soc.*, 1094 (1952).

Acid-Catalyzed Cyclialkylation of Benzene with Isoprene

E. J. Eisenbraun,*[1a] W. M. Harms,[1a-c] J. W. Burnham,[1a,c,d] O. C. Dermer,[1a] R. E. Laramy,[1e] M. C. Hamming,[1e] G. W. Keen,[1e] and P. W. Flanagan

Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma 74074, and Research and Development Department, Continental Oil Company, Ponca City, Oklahoma 74601

Received December 2, 1976

The acid-catalyzed reaction of isoprene with benzene forms a more complex mixture of reaction products than previously observed from alkylbenzenes. The formation of identified products is rationalized through existing carbonium ion theory. These products include 1,1-dimethylindan, the majority of the possible tetramethylhydrindacenes, both hexamethyltrindans, and two isopentyltetramethylhydrindacenes. Synthesis through independent routes provided standards for identification of products and study of intermediates.

The acid-catalyzed cyclialkylation of benzenoid hydrocarbons is well known.[2a] Such reaction with isoprene is a convenient and direct route to substituted 1,1-dimethylindans and tetramethylhydrindacenes. While an array of products are observed with mono- and dialkylbenzenes, the reaction can provide a reasonably clean product or product mixture from which several pure hydrocarbons have been isolated.[2b-e] Hydrocarbons **1**, **2**, and **7** were readily isolated in the current work and appear as major peaks in the GC trace shown in Figure 1.

Cyclialkylation products have been considered to have potential as high-energy fuels[2d,3a] and source materials in medicine[3b] and perfumery.[4] Acetylated and nitrated derivatives show musk properties.[4] Acetylation also yields ketones active as preemergence herbicides.[5]

The cyclialkylation of benzene with isoprene is not a useful reaction for the preparation of 1,1-dimethylindan (**1**)[6] in quantity, since this is rapidly converted to the hydrindacenes as shown in Scheme I. Schmerling[2b] first observed that the yield of **2** exceeds that of **1**.

Despite the low yields of **1** and **2**, we decided to use the cyclialkylation reaction for their preparation and a concomitant study of the cyclialkylation process in which **1** is regarded as an isolable but reacting intermediate.

A trial cyclialkylation reaction (procedure A) gave the expected low yields of **1** (3.5%) and **2** (9–10%). A second run (procedure A) in which the amounts of reagents were increased 20-fold showed a decreased yield of **1**, which results from the increased time necessary for addition of isoprene, and consequent conversion of **1** to other products.

The preparation of **1** in larger quantity was required to determine its role as an intermediate. Since increasing the scale of the preparation was unsatisfactory, we carried out numerous successive small runs (procedure B) involving rapid mixing of reagents, quenching, and workup of the reaction mixture. By this means we were able to accumulate a substantial quantity of **1**.[6] The other products from this preparation were thus also available for study. Distillation of the product mixture afforded the crystalline tetramethylhydrindacene **2** and the crystalline *as*-hexamethyltrindan **7**. Preparative GC was used to isolate **6**,[7a] **9**,[7b] and *tert*-butylbenzene (**11**).[7b] Their structures, along with those of **2** and **7**, were established by spectroscopic studies.

It is assumed that **9** is derived by an isopentenylation of **6**

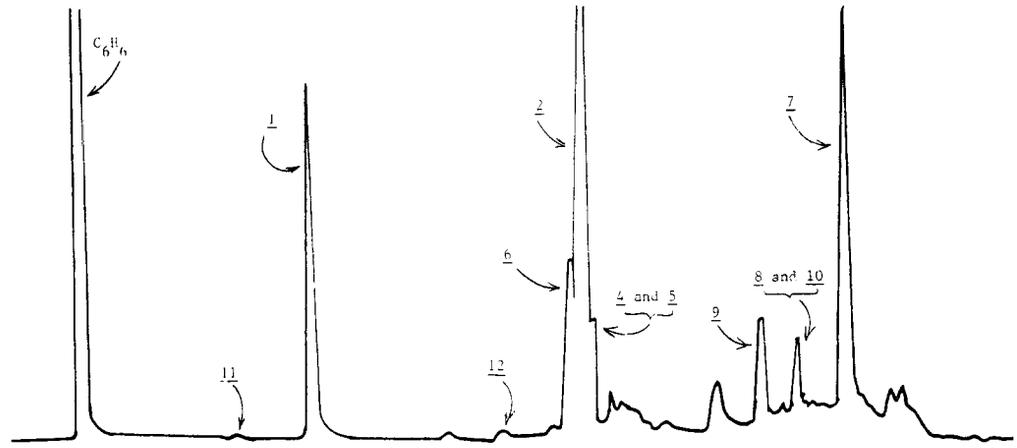
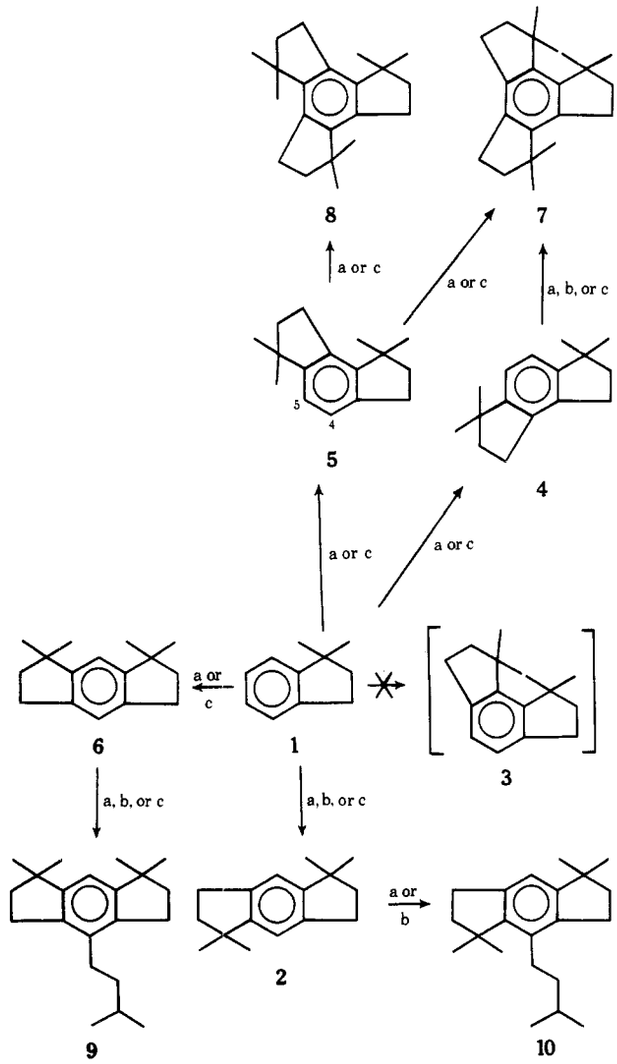


Figure 1. Programmed-temperature GC of distilled cyclialkylation products.

Scheme I



a, benzene, isoprene, sulfuric acid; b, isoprene, trifluoroacetic acid, sulfuric acid in petroleum ether; c, isoprene, sulfuric acid.

with subsequent hydrogenation of the side chain through protonation and hydride acquisition as previously observed.[2c] Once **11** had been identified, it was assumed that 6-*tert*-butyl-1,1-dimethylindan (**12**) would be present.[2c,d] This was confirmed by GC comparison (Figure 1) with authentic material. The formation of *tert*-butylbenzene may be rationalized as due to acid-catalyzed degradation of isoprene to a C_4 moiety.[8a,b]

The GC trace of the reaction product mixture from this cyclialkylation is complex. The trace[9a] shown in Figure 1 is substantially more complicated than that of product mixtures from mono- or dialkylbenzenes.[2c] The complexity of this mixture and the difficulty encountered in isolating pure compounds prompted the synthesis of **4**, **5**, **6**, **8**, and **10** to determine whether these hydrocarbons were represented by GC peaks of Figure 1 and whether **2**, **4**, **5**, and **6** could serve as reaction intermediates.

Syntheses of **2**, **4**, **5**, and **6** involved use of the acid-catalyzed cyclialkylation process applied to specifically prepared intermediates as shown in Scheme II. Amberlyst-15, a sulfonic acid resin, was found to be the most effective and convenient reagent for these cyclizations.[10]

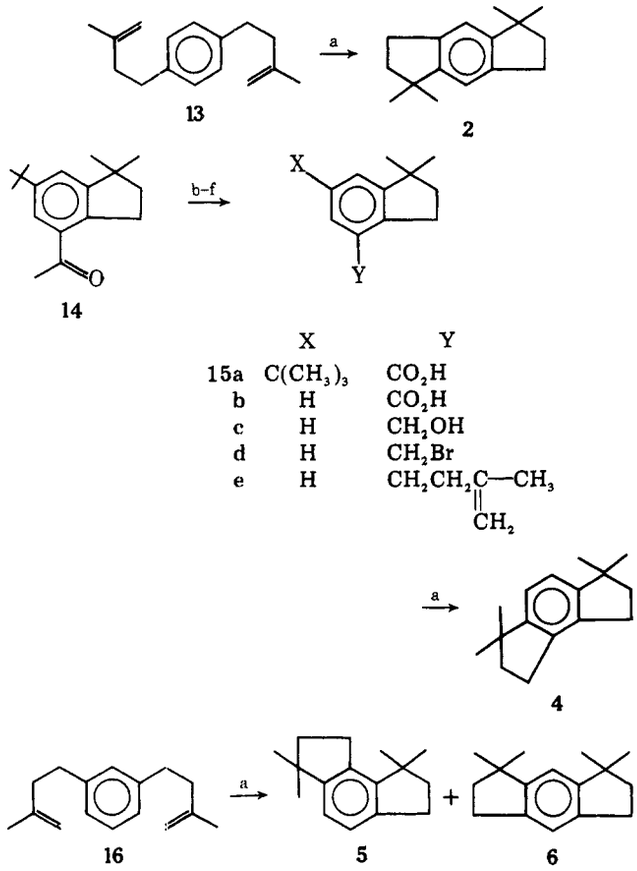
An added reason to synthesize **2** from the diene **13** was to determine whether cyclization would be exclusively to **2** or the less sterically favored **3** would result. The absorptions of the *gem*-methyl groups of **2** appear at δ 1.21 as a singlet. If **3** were present in the reaction mixture, *gem*-methyl absorption should be in the δ 1.3–1.4 range, as it is for the hindered methyl groups of **7**. When NMR data were obtained at intervals during the reaction, these low-field *gem*-methyl absorptions were not observed. Our GC and NMR data also indicate that the pendant double bonds of **13** are first shifted to become trisubstituted. This was established by comparing shift values of vinyl and allylic protons during the course of the reaction with those of 2-methyl-4-phenyl-2-butene.[6] Hence, **3** is probably not formed and therefore not a precursor to **7**.

The synthesis of **4** from 4-acetyl-6-*tert*-butyl-1,1-dimethylindan (**14**) via 1,1-dimethyl-4-hydroxymethylindan (**15c**)[4b] was accomplished in 20% overall yield. Gas chromatography comparisons[9b] showed **4** to be one of the minor peaks of the tetramethylhydrindacene fraction shown in Figure 1.

Cyclization[6,10] of 1,3-bis(3-methyl-3-butenyl)benzene (**16**) prepared by the Grignard process of Theimer and Blumenthal[4d] gave a 1:1 mixture of **5** and **6**. These were separated by distillation.[11] Comparison of the NMR spectra of **6** obtained from cyclialkylation and **6** made by synthesis as shown in Scheme II established the identity of the former. The purified **5** and **6** were individually mixed with the tetramethylhydrindacene fraction of the cyclialkylation products, and their presence in this mixture was established by using capillary GC.[9b] The order of elution and the peak ratios on the capillary column were **6:5:4:2** (3:1:2:12).

The synthesis of *s*-hexamethyltrindan (**8**) was accomplished as shown in Scheme III. This allowed a comparison of the GC trace of pure **8** with Figure 1 and thus identification of another of the GC peaks. We also synthesized **10** by acylation of **2**,

Scheme II



	X	Y
15a	$C(CH_3)_3$	CO_2H
b	H	CO_2H
c	H	CH_2OH
d	H	CH_2Br
e	H	$CH_2CH_2C(=CH_2)CH_3$

a, Amberlyst-15, cyclohexane, Δ; b, OBr^-, H_3O^+; c, $AlCl_3$, toluene; d, $(i\text{-}C_4H_9)_2AlH$, C_6H_6; e, HBr; f, methallylmagnesium chloride, ether.

reduction of the resulting ketone, dehydration, and catalytic hydrogenation as shown in Scheme IV.

In Figure 1, **8** and **10** show the same retention time. However, the mixture was resolved to give **8**:**10** (1:3) by using a "Scot" capillary GC column.[9c]

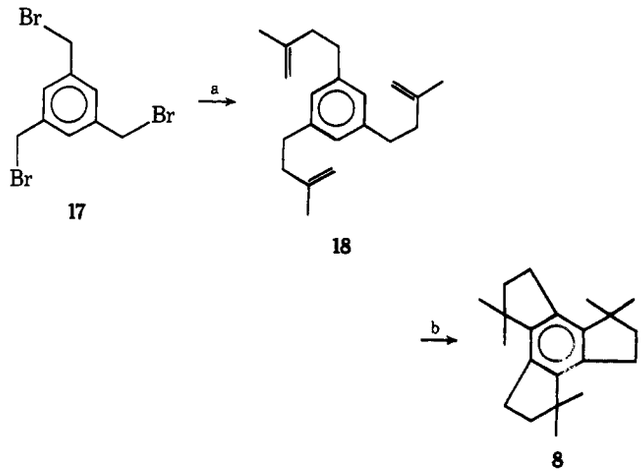
To establish the relationship of **1** and the tetramethylhydrindacenes **2, 4, 5,** and **6** as intermediates to **7, 8, 9,** and **10** shown in Figure 1, we sought reaction conditions not requiring benzene as solvent. Isoprene added to a mixture of trifluoroacetic acid, petroleum ether, and sulfuric acid caused a low-yield conversion of **2** to **10** and **6** to **9.** In addition, it provided **7** from **4** but did not yield **7** or **8** from **5.**

When isoprene was added to sulfuric acid and a solvent (petroleum ether, cyclohexane, chlorobenzene, or methanesulfonic acid) containing **2, 4, 5,** or **6,** no useful products were obtained. However, treatment of isoprene solutions of **2, 4, 5,** and **6** with sulfuric acid at 0 °C resulted in the formation of **7** from **4, 7** and **8** from **5,** and **9** from **6.** Isopentylation of **2** under these conditions did not occur.

Chromic acid oxidation to ketones at the benzylic position[12] was used to obtain supporting evidence for the structures of **4, 7, 8,** and **9.** Of this series, **4** gave one monooxo and one dioxo derivative. Trindan **7** would be expected to give three monooxo, three dioxo, and one trioxo derivatives, whereas trindan **8** would yield one monooxo, one dioxo, and one trioxo derivative. The GC data showed the expected number of products for **7** and **8.** The oxidation of **9** yielded monooxo and dioxo derivatives, mp 84–86 and 194–195 °C, respectively. The ^1H NMR data show that the benzylic protons of the isopentyl group survive the oxidation.

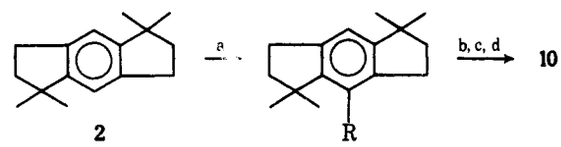
The synthesized hydrocarbon standards **2,**[9b] **4,**[9b] **5,**[9b] **6,**[9b] **8,**[9c] and **10**[9c] were used to identify GC peaks.

Scheme III



a, methallylmagnesium chloride, ether; b, X-15, cyclohexane, Δ.

Scheme IV



19a, R = $(CH_3)_2CHCH_2C(=O)-$
b, R = $(CH_3)_2CHCH_2CH(OH)-$
c, R = $(CH_3)_2CHCH=CH-$

a, $(CH_3)_2CHCH_2C(=O)Cl$, $AlCl_3$, $CH_3CH_2NO_2$; b, $(i\text{-}C_4H_9)_2AlH$, C_6H_6; c, Amberlyst-15, C_6H_6; d, H_2, Pd/C, C_2H_5OH.

Experimental Section[13]

Cyclialkylation of Benzene with Isoprene in the Presence of Sulfuric Acid. Procedure A. To a 1-L, three-necked, round-bottom flask equipped with stirrer and dropping funnel and cooled in an ice bath were added 249 g (3 mol) of benzene and 50 mL (0.51 mol) of 85% sulfuric acid followed by 68 g (1.0 mol) of isoprene in 102 g (1.3 mol) of benzene over 16 min at 15–20 °C. Stirring was continued for 15 min. The red-brown sulfuric acid layer was withdrawn, and the benzene layer was washed with 30 mL of water, with aqueous sodium carbonate, and 2 × 50 ml of water, and dried ($MgSO_4$). Concentration and distillation gave **1** (3.5%).

A second run was made with the scale increased 20-fold and the addition time increased from 16 to 135 min. Distilled product consisted of 100 g (2.3%) of **1,** 305 g (9.5%) of crude **2,** a liquid fraction weighing 216 g, and a final fraction (178 g, 6%), bp 160–220 °C (1 mm), of mainly **7.**

Procedure B. A 5-L, indented, round-bottom flask equipped with a dropping funnel, Lightnin XP stirrer, and turbine stirring paddle was cooled to 10 °C in a stirred ice–water–salt bath, and 950 g (12.2 mol) of benzene and 100 mL of 97% sulfuric acid were added. Isoprene (286 g, 4.77 mol) diluted with 492 g (6.3 mol) of benzene was then added as rapidly as the temperature increase permitted (max 20 °C). The total addition time was 3–5 min. The stirrer was stopped and the flask contents were rapidly pumped with a Randolph Model 610 peristaltic pump into a 12-L separatory funnel. After 10 min, the lower "red oil" layer was drained off and the separatory funnel contents were then poured directly onto anhydrous sodium carbonate. The dried material was filtered, combined with that from other runs, and distilled to give **1, 2,** and **7** in 8, 7, and 13% yields, respectively.

1,1-Dimethylindan (**1**)[6] was redistilled: bp 73 °C (3 mm) (lit.[14] 189–191 °C); mass spectrum (70 eV) *m/e* (rel intensity) 146 (M^+, 13) 132 (5), 131 (100), 116 (8), 115 (13), 91 (15); ^1H NMR (CCl_4) δ 7.05 (s, 4, ArH), 2.85 (t, 2, $ArCH_2$–), 1.88 [t, 2, $ArC(CH_3)_2CH_2$–], 1.24 [s, 6, $ArC(CH_3)_2$–].

A higher boiling fraction (bp 120–160 °C at 1 mm) yielded solid 1,1,5,5-tetramethyl-*s*-hydrindacene (**2**) which was filtered out and recrystallized from petroleum ether:[13] mp 95–96 °C (lit.[2a] 91–93 °C); mass spectrum (70 eV) *m/e* (rel intensity) 214 (M^+, 15), 200 (17), 199 (100), 143 (24), 128 (8), 92 (10); ^1H NMR (CCl_4) δ 6.79 (s, 2, ArH), 2.79 (t, 4, $ArCH_2$–), 1.86 [t, 4, $ArC(CH_3)_2CH$–], 1.21 [s, 12, $ArC(CH_3)_2$–].

Anal. Calcd for $C_{16}H_{22}$: C, 89.65; H, 10.35. Found: C, 89.61; H, 10.40.

The second fraction (bp 160–220 °C at 1 mm) yielded crystalline 1,1,4,4,9,9-hexamethyl-*as*-trindan (**7**). Recrystallization from 95% ethanol, acetone, and petroleum ether[13] and chromatography on acidic alumina with petroleum ether[13] gave pure **7**: mp 108–110 °C; mass spectrum (70 eV) *m/e* (rel intensity) 282 (M^+, 20), 268 (76), 267 (100), 211 (24), 181 (9), 126 (11); ^1H NMR (CCl_4) δ 2.81 (t, 2, $ArCH_2$–), 2.69 (t, 4, $ArCH_2$–), 1.81 (t, 6, $ArCH_2CH_2$–), 1.39 [s, 12, $ArC(CH_3)_2$–], 1.29 [s, 6, $ArC(CH_3)_2$–].

Anal. Calcd for $C_{21}H_{30}$: C, 89.29; H, 10.71. Found: C, 89.50; H, 10.70.

Preparative GC Purification of 1,1,7,7-Tetramethyl-*s*-hydrindacene (6) and 4-Isopentyl-1,1,7,7-tetramethyl-*s*-hydrindacene (9). A liquid tetramethylhydrindacene fraction subjected to preparative GC separation[7a] gave crystalline **6**. Recrystallization from acetone and then with cold ether gave pure **6**: mp 60–61 °C (lit.[4d] 45–47 °C); mass spectrum (70 eV) *m/e* (rel intensity) 214 (M^+, 20), 200 (18), 199 (100), 143 (26), 41 (11), 29 (11); ^1H NMR (CCl_4) δ 6.84 (s, 1, ArH), 6.75 (s, 1, ArH), 2.76 (t, 4, $ArCH_2$–), 1.85 [t, 4, $ArC(CH_3)_2CH_2$–], 1.21 [s, 12, $ArC(CH_3)_2$–].

Anal. Calcd for $C_{16}H_{22}$: C, 89.65; H, 10.35. Found: C, 89.56; H, 10.33.

The fraction (bp 120–160 °C, 1 mm) containing the tetramethylhydrindacenes was dissolved in petroleum ether[13] and flushed through layers of silica gel, basic alumina, and acidic alumina until a colorless solution was obtained. Concentration followed by preparative GC[7a] separated **9** from the mixture as a yellow oil with 10% impurity. Hydrocarbon **9** slowly crystallized from the oil. Recrystallization from petroleum ether[13] gave waxy crystals of **9**: mp 46–47 °C; mass spectrum (70 eV) *m/e* (rel intensity) 284 (M^+, 13) 270 (22), 269 (100), 243 (28), 241 (34), 229 (23); ^1H NMR (CCl_4) δ 6.58 (s, 1, ArH), 2.76 (t, 4, $ArCH_2$–), 2.40 (t, 2, $ArCH_2$–), 1.86 [t, 4, $ArC(CH_3)_2CH_2$–], 1.63 [m, 1, $(CH_3)_2CH$–], 1.45 [m, 2, $ArCH_2CH_2CH(CH_3)_2$], 1.20 [s, 12, $ArC(CH_3)_2$–], 0.96 [d, 6, $(CH_3)_2CH$–].

Anal. Calcd for $C_{21}H_{32}$: C, 88.66; H, 11.34. Found: C, 88.71; H, 11.31.

Chromic Acid Oxidation of 1, 2, 6, 7, and 9. Chromic acid oxidation in acetic acid gave the previously described monoketones from **1, 2,** and **6**.[12] Chromic acid oxidation of **7** gave a mixture of ketones which showed seven GC[9a] peaks (three monoketones, three diketones, and one triketone are possible). Preparative GC[7c] and recrystallization from petroleum ether[13] gave a monoketone: mp 136–138 °C; IR (KBr) 1700 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 2.73 (t, 4, $ArCH_2$–), 2.41 (s, 2, $ArCOCH_2$–), 1.92 (t, 4, $ArCH_2CH_2$–), 1.53, 1.45, and 1.40 [3, s, 18, $ArC(CH_3)_2$–].

Oxidation of **9** gave two products (mono- and diketone) separated by preparative GC.[7b] NMR studies showed that the side chain was not attacked in the oxidation. The monoketone from **9** showed mp 84–86 °C; IR (KBr) 1697 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* (rel intensity) 298 (M^+, 20), 256 (20), 255 (100), 242 (50), 227 (53), 43 (16); ^1H NMR (CCl_4) δ 6.91 (s, 1, ArH), 2.96, 2.82 (t, 4, $ArCH_2$–), 2.41 (s, 2, $ArCOCH_2$–), 1.91 (t, 2, $ArCH_2CH_2$–), 1.70 [m, 1, $(CH_3)_2CHCH_2$–], 1.37 [s, 6, $ArC(CH_3)_2$–], 1.35 [t, 2, $(CH_3)_2CHCH_2$–], 1.27 [s, 6, $ArC(CH_3)_2$–], 1.02, 0.92 [d, 6, $(CH_3)_2CH$–].

Anal. Calcd for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.39; H, 10.30.

The diketone from **9** showed mp 194–195 °C; IR (KBr) 1695 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* (rel intensity) 312 (M^+, 28), 270 (23), 269 (100), 257 (17), 256 (87), 241 (42); ^1H NMR (CCl_4) δ 7.22 (s, 1, ArH), 3.30 (t, 2, $ArCH_2$–), 2.49 (s, 4, $ArCOCH_2$–), 1.70 [m, 1, $(CH_3)_2CHCH_2$–], 1.42 [s, 12, $ArC(CH_3)_2$–], 1.30 [t, 2, $(CH_3)_2CHCH_2$–], 1.01–0.92 [d, 6, $(CH_3)_2CH$–].

Anal. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.63; H, 9.17.

Synthesis of 1,1,5,5-Tetramethyl-*s*-hydrindacene (2) and Attempted Synthesis of 1,1,8,8-Tetramethyl-*as*-hydrindacene (3). 1,4-Bis(3-methyl-3-butenyl)benzene (**13**) was prepared[3d] from 1,4-bis(chloromethyl)benzene and methallylmagnesium chloride. Distillation of the product gave 20% yield of **13**: bp 85 °C (0.1 mm); mass spectrum (70 eV) *m/e* (rel intensity) 214 (M^+, 5), 159 (100), 104 (30), 91 (20), 55 (32), 29 (19); ^1H NMR (neat) δ 6.97 (s, 4, ArH), 4.71 (s, 4, vinyl), 2.82–2.54 (m, 4, $ArCH_2$), 2.38–2.08 (m, 4, $ArCH_2CH_2$), 1.67 (s, 6, $CH_3C(=CH_2)$–].

Anal. Calcd for $C_{16}H_{22}$: C, 89.65; H, 10.35. Found: C, 89.43; H, 10.50.

The diene **13** (1 g) was cyclized by heating at reflux temperature in 50 mL of cyclohexane containing 1 g of Amberlyst-15. The product was recrystallized and shown by GC, NMR, and melting point of an admixture to be identical with **2** from the cyclialkylation of benzene.

Synthesis of 3,3,6,6-Tetramethyl-*as*-hydrindacene (4). 4-Acetyl-6-*tert*-butyl-1,1-dimethylindan (**14**)[15] was oxidized with NaOBr in dioxane[4b] to the carboxylic acid **15a** in 93% yield: mp 191–192 °C (lit.[4b] 190.5–192 °C); ^1H NMR (CCl_4) δ 11.22 (s, 1, COOH), 7.84, 7.22 (s, 2, ArH), 3.23 (t, 2, $ArCH_2$–), 1.93 (t, 2, $ArCH_2CH_2$–), 1.36 (s, 9, *tert*-butyl), 1.27 [s, 6, $ArC(CH_3)_2$–]. The acid **15a** was de-*tert*-butylated in 92% yield as previously described.[4b] Recrystallization from petroleum ether[13] gave 1,1-dimethylindan-4-carboxylic acid (**15b**): mp 145–146 °C (lit.[4b] 145–147.6 °C); ^1H NMR (CCl_4) δ 12.43 (s, 1, COOH), 7.80 (m, 1, ArH), 7.12 (s, 2, ArH), 3.29 (t, 2, $ArCH_2$–), 1.93 (t, 2, $ArCH_2CH_2$–), 1.26 [s, 6, $ArC(CH_3)_2$–].

A sample of **15b** was esterified with ethanol: mass spectrum (70 eV) *m/e* (rel intensity) 218 (M^+, 32), 203 (100), 131 (33), 129 (30), 128 (29), 15 (29); ^1H NMR δ 7.67 (center of m, 1, ArH), 7.12 (s, 1, ArH), 7.07 (center of m, 1, ArH), 4.23 (q, 2, CH_3CH_2–), 3.20 (t, 2, $ArCH_2$–), 1.88 (t, 2, $ArCH_2CH_2$–), 1.35 (t, 3, CH_3CH_2–), 1.22 [s, 6, $ArC(CH_3)_2$–].

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.89; H, 8.34.

This ester gave a single GC peak.[9a]

Into a 5-L flask equipped with stirrer, thermometer, addition funnel, reflux condenser, heating mantle, and nitrogen flush were placed 700 mL of dry benzene and 260 g (1.9 mol) of diisobutylaluminum hydride. The solution was heated to reflux and a solution of 76 g (0.4 mol) of **15b** in 700 mL of benzene was added over 80 min. The product was cooled and poured onto ice, the mixture stirred, and the pH adjusted to ca. 3 with HCl. Ether extraction, drying ($MgSO_4$), and concentration yielded 65 g (93%) of 4-hydroxymethyl-1,1-dimethylindan (**15c**): bp 100–101 °C (0.5 mm); mass spectrum (70 eV) *m/e* (rel intensity) 176 (M^+, 22), 161 (100), 143 (59), 131 (36), 128 (27), 91 (27); ^1H NMR (CCl_4) δ 6.88 (s, 3, ArH), 4.28 (s, 2, $ArCH_2OH$), 3.84 (s, 1, OH), 2.70 (t, 2, $ArCH_2$–), 1.81 (t, 2, $ArCH_2CH_2$–), 1.18 [s, 6, $ArC(CH_3)_2$–].

In a small flask equipped with a sintered-glass bubbling tube and an exit tube was placed 17.9 g (0.1 mol) of **15c** and the contents were heated to 110 °C. Anhydrous HBr was slowly bubbled through the liquid with periodic shaking over 2 h. The reaction mixture was poured into water, stirred, extracted with ether, dried ($MgSO_4$), and concentrated to give 23 g of crude, lachrymatory brown liquid. Distillation yielded 20 g (84%) of colorless 4-bromomethyl-1,1-dimethylindan (**15d**): bp 110–113 °C (0.4 mm); NMR (CCl_4) δ 6.93 (s, 3, ArH), 4.30 (s, 2, $BrCH_2$–), 2.87 (t, 2, $ArCH_2$–), 1.90 [t, 2, $ArCH_2CH_2$–), 1.21 [s, 6, $ArC(CH_3)_2$–].

A flask equipped with addition funnel, mechanical stirrer, condenser, and nitrogen flask was charged with 5.3 g (0.22 mol) of magnesium turnings and 60 mL of ether. To this was added a crystal of iodine followed by 1 mL of redistilled methallyl chloride. While the mixture was cooled with an ice bath, an additional 18 mL (0.16 mol) of methallyl chloride dissolved in 90 mL of dry ether was added over a 1-h period. The gray slush that resulted was stirred at room temperature for 3 h and then brought to reflux. A solution of 19.8 g (0.083 mol) of **15d** dissolved in 60 mL of ether was added during 1 h. Reflux was continued for 4 h. The reaction mixture was cautiously decomposed with saturated NH_4Cl solution. The resulting mixture was extracted with ether, dried ($MgSO_4$), and concentrated to give 16 g of yellow oil. Distillation yielded 6.6 g (38%) of colorless 4-(3-methyl-3-butenyl)-1,1-dimethylindan (**15e**): bp 80 °C (0.2 mm); mass spectrum (70 eV) *m/e* (rel intensity) 214 (M^+, 10), 199 (35), 159 (100), 158 (77), 143 (36), 129 (34), 128 (31); NMR (CCl_4) δ 6.80 (m, 3, ArH), 4.63 (s, 2, vinylic CH_2), 2.89 (t, 2, $ArCH_2$– of ring), 2.82–2.05 (m, 4, $ArCH_2CH_2$– of chain), 1.86 (t, 2, $ArCH_2CH_2$– of ring), 1.73 (s, 3, CH_3–), 1.21 [s, 6, $Ar(CH_3)_2$–].

Anal. Calcd for $C_{16}H_{22}$: C, 89.65; H, 10.35. Found: C, 89.61; H, 10.33.

Cyclization of 2.7 g (0.012 mol) of **15e** as described for **13** gave 2.6 g of crude **4**. Recrystallization from cold methanol yielded 2.1 g (78%): mp 35–36 °C; mass spectrum (70 eV) *m/e* (rel intensity) 214 (M^+, 15), 200 (18), 199 (100), 143 (26), 128 (11), 41 (10); ^1H NMR (CCl_4) δ 6.75 (s, 2, ArH), 2.72 (t, 4, $ArCH_2$–), 1.89 (t, 4, $ArCH_2CH_2$–), 1.22 [s, 12, $ArC(CH_3)_2$–].

Anal. Calcd for $C_{16}H_{22}$: C, 89.65; H, 10.35. Found: C, 89.40; H, 10.51.

Synthesis of 1,1,6,6-Tetramethyl-*as*-hydrindacene (5) and 1,1,7,7-Tetramethyl-*s*-hydrindacene (6). 1,3-Bis(3-methyl-3-

butenyl)benzene (**16**) was prepared[4d] from 1,3-bis(chloromethyl)-benzene and methallylmagnesium chloride. Distillation of the product gave a 80% yield of **16**: bp 95–99 °C (0.2 mm); ^{1}H NMR (CCl_4) δ 7.17–6.73 (m, 4, ArH), 4.70 (s, 4, vinylic CH_2), 2.82–2.52 (m, 4, $ArCH_2$–), 2.33–2.05 (m, 4, $ArCH_2CH_2$–), 1.67 (s, 6, CH_3–).

Cyclization was accomplished by adding 29 g of **16** to 120 mL of refluxing cyclohexane containing 5 g of dried A-15. Reflux was continued for 30 min and the mixture filtered and concentrated to give 28.3 g of **5** and **6** as a 1:1 mixture. Distillation[11] effected separation of **5** from **6**. An early fraction collected at 42 °C (0.3 mm) was identical in NMR spectrum with **6** obtained from the cyclialkylation reaction. This fraction crystallized upon cooling. A late fraction containing **5** did not crystallize: bp 66 °C (0.3 mm) (lit.[4d] 100–105 °C, 0.5 mm); ^{1}H NMR (CCl_4) δ 6.74 (s, 2, ArH), 2.75 (t, 4, $ArCH_2$–), 1.84 (t, 4, $ArCH_2CH_2$–), 1.27 [s, 6, $ArC(CH_3)_2$–], 1.20 [s, 6, $ArC(CH_3)_2$–].

Synthesis of 1,1,4,4,7,7-Hexamethyltrindan (8). The tribromide **17** was prepared from trimethyl 1,3,5-benzenetricarboxylate using a previously described procedure.[16] The tribromide **17**, mp 99–100 °C (lit.[16] 97–99 °C), NMR (CCl_4) δ 7.22 (s, 3, ArH) and 4.34 (s, 6, $-CH_2$–), was converted to **18** in 18% yield using the procedure for the preparation of **15e**. The 1,3,5-tris(3-methyl-3-butenyl)benzene (**18**) was separated from an accompanying diene by distillation: bp 127 °C (0.2 mm); mass spectrum (70 eV) *m/e* (rel intensity) 282 (M^+, 16), 227 (94), 226 (44), 171 (100), 129 (31), 41 (40), 29 (39); ^{1}H NMR (CCl_4) δ 6.67 (s, 3, ArH), 4.63 (s, 6, vinylic CH_2), 2.78–2.05 (m, 12, $ArCH_2CH_2$–), 1.72 (s, 9, CH_3–).

Anal. Calcd for $C_{21}H_{30}$: C, 89.29; H, 10.71. Found: C, 89.37; H, 10.69.

Cyclization of 2.8 g (0.01 mol) of **18** as described for **15e** gave 2.8 g of solid. Recrystallization from petroleum ether[13] yielded 2.0 g (67%) of **8**: mp 238–239 °C; mass spectrum (70 eV) *m/e* (rel intensity) 282 (M^+, 12), 268 (20), 267 (100), 211 (10), 166 (7); ^{1}H NMR (CCl_4) δ 2.82 (t, 6, $ArCH_2$–), 1.82 (t, 6, $ArCH_2CH_2$–), 1.25 [s, 18, $ArC(CH_3)_2$–].

Anal. Calcd for $C_{21}H_{30}$: C, 89.29; H, 10.71. Found: C, 89.10; H, 10.56.

Synthesis of 4-Isopentyl-1,1,5,5-tetramethyl-*s*-hydrindacene (10) from 2. Friedel–Crafts acylation of **2** using 3-methylbutyryl chloride in nitroethane yielded 4-(3-methylbutyryl)-1,1,5,5-tetramethyl-*s*-hydrindacene (**19a**) as a white solid: mp 62–64 °C; mass spectrum (70 eV) *m/e* (rel intensity) 298 (M^+, 21), 283 (61), 242 (19), 241 (100), 57 (19), 41 (19); ^{1}H NMR ($CDCl_3$) δ 6.92 (s, 1, ArH), 2.65–2.90 [m, 6, $ArCH_2$– and $ArC(=O)CH_2$–], 2.35 [m, 1, $(CH_3)_2CHCH_2$–], 1.9 (t, 2, $ArCH_2CH_2$–), 1.86 (t, 2, $ArCH_2CH_2$–), 1.23 [s, 6, $ArC(CH_3)_2$–], 1.21 [s, 6, $ArC(CH_3)_2$–], 1.02 [d, 6, $(CH_3)_2CH$–].

Anal. Calcd for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.40; H, 9.92.

Reduction of **19a** using diisobutylaluminum hydride as described above provided the alcohol **19b** in 87% yield: mp 83–86 °C; mass spectrum (70 eV) *m/e* (rel intensity) 300 (M^+, 21), 282 (25), 267 (31), 243 (100), 187 (12), 143 (11); ^{1}H NMR ($CDCl_3$) δ 6.82 (s, 1, Ar), 5.25 (d, of d, 1, $ArCHOHCH_2$–), 3.10 (t, 1, $ArCH_2CH_2$–), 3.02 (t, 1, $ArCH_2CH_2$–), 2.75 (t, 2, $ArCH_2CH_2$–), 2.06 [m, 2, $(CH_3)_2CHCH_2CHOH$–], 1.86 (t, 4, $ArCH_2CH_2$–), 1.63 (s, 1, ROH), 1.38 [s, 3, $ArC(CH_3)_2$–], 1.36 [m, 1, $(CH_3)_2CHCH_2$–], 1.34 [s, 3, $ArC(CH_3)(CH_3)$–], 1.19 [s, 6, $ArC(CH_3)(CH_3)$–], 0.99 (d, 3, CH_3CHCH_3–), 0.97 (d, 3, CH_3CHCH_3–).

Anal. Calcd for $C_{21}H_{32}O$: C, 83.94; H, 10.73. Found: C, 83.81; H, 10.90.

Amberlyst-15[10] in boiling benzene was used in the dehydration of **19b**. The reaction was indicated by GC to be complete after 10 min. The mixture containing **19c** was isolated and hydrogenated at atmospheric pressure in 95% ethanol using 5% Pd/C catalyst. Filtration, extraction, and distillation provided pure **10**: mp 65–67 °C; mass spectrum (70 eV) *m/e* (rel intensity) 284 (M^+, 12), 269 (100), 211 (40), 197 (52), 183 (36), 165 (40); ^{1}H NMR ($CDCl_3$) δ 6.75 (s, 1, ArH), 2.75 (t, 4, $ArCH_2CH_2$–), 2.5–2.65 (m, 2, $ArCH_2CH_2$–), 1.87 (t, 4, $ArCH_2CH_2$–), ~1.5 [m, 3, $(CH_3)_2CHCH_2CH_2$–], 1.33 [s, 6, $ArC(CH_3)_2$–], 1.18 [s, 6, $ArC(CH_3)_2$–], 0.95 [d, 6, $(CH_3)_2CH$–].

Anal. Calcd for $C_{21}H_{32}$: C, 88.66; H, 11.34. Found: C, 88.79; H, 11.25.

Exhaustive Isoprene Treatment of the Tetramethylhydrindacenes. Procedure C. To a 50-mL, indented, three-neck flask equipped with addition funnel, thermometer, and Teflon-coated magnetic stirring bar was added 0.001 mol of hydrocarbon dissolved in 3.4 g (0.05 mol) of isoprene.[13] The mixture was stirred and cooled to 0 °C. Sulfuric acid (1 g) was added dropwise while the temperature was maintained below 10 °C. The flask contents were poured onto anhydrous Na_2CO_3, diluted with petroleum ether,[13] and analyzed by GC.[9a]

Procedure D. Alternatively, trifluoroacetic acid (TFA) and petroleum ether were used as solvents. For this procedure, based on 0.001 mol of hydrocarbon, 40 mL of TFA, 6 g of sulfuric acid, and 6 mL of petroleum ether[13] were mixed and cooled to 10 °C. A solution of 0.7 g (0.01 mol) of isoprene dissolved in 14 mL of petroleum ether[13] was added with stirring. The temperature was maintained below 20 °C during the addition.

A. 1,1-Dimethylindan (1). The above procedures C and D were applied to **1** in order to obtain products for a comparison with those of the benzene–isoprene cyclialkylation carried out in excess benzene. These processes both gave the same array of cyclialkylation products but more polyisoprene resulted from procedure C.

B. 1,1,5,5-Tetramethylhydrindacene (2). The tetramethylhydrindacene **2** was treated with isoprene (procedure C) but this reaction failed to provide detectable amounts of **7**, **8**, or **10**. However, procedure D gave a product with GC retention time[9a] identical with that of **10**. Procedure D also yielded a diisopentylation product believed to be derived from **10**.

C. 3,3,6,6-Tetramethyl-*as*-hydrindacene (4). Procedures C and D applied to **4** caused low conversion to a product having the same retention time[9a] as the hexamethyltrindan (**7**).

D. 1,1,6,6-Tetramethyl-*as*-hydrindacene (5). Procedure C provided the hexamethyltrindans **7** and **8** in the ratio 1:4.

E. 1,1,7,7-Tetramethyl-*s*-hydrindacene (6). Procedures C and D caused conversion of **6** to **9**. Procedure D produced the higher yield.

Acknowledgments. We thank the American Petroleum Institute and the Continental Oil Co. for partial support of this work.

Registry No.—**1**, 4912-92-9; **2**, 17465-54-2; **4**, 61813-30-7; **6**, 6047-64-9; **7**, 55682-87-6; **7** monoketone, 61813-31-8; **8**, 40650-56-4; **9**, 40650-58-6; **9** monoketone, 55712-64-6; **9** diketone, 40650-59-7; **10**, 61813-32-9; **13**, 61813-33-0; **14**, 13171-00-1; **15a**, 61813-34-1; **15b**, 55712-38-4; **15b** Et ester, 55591-12-3; **15c**, 55591-09-8; **15d**, 61813-35-2; **15e**, 55030-58-5; **16**, 6047-59-2; **17**, 18226-42-1; **18**, 55124-94-2; **19a**, 61813-36-3; **19b**, 61813-37-4; benzene, 71-43-2; isoprene, 78-79-5; 1,4-bis(chloromethyl)benzene, 623-25-6; methallyl chloride, 563-47-3; 1,3-bis(chloromethyl)benzene, 626-16-4; trimethyl 1,3,5-benzenetricarboxylate, 2672-58-4; 3-methylbutyryl chloride, 108-12-3.

References and Notes

(1) (a) Oklahoma State University; (b) Ph.D. Thesis, Oklahoma State University, May 1972; (c) American Petroleum Institute Graduate Research Assistant, 1968–1972; (d) Continental Oil Co. Fellowship, 1973; (e) Continental Oil Co.

(2) (a) L. R. C. Barclay, "Cyclialkylation of Aromatics", "Friedel-Crafts and Related Reactions", Vol. 2, Part 2, G. A. Olah, Ed., Interscience, New York, N.Y., 1964, p 785; (b) L. Schmerling, U.S. Patent 2 848 512; (c) E. J. Eisenbraun, J. R. Mattox, R. C. Bansal, M. A. Wilhelm, P. W. K. Flanagan, A. B. Carel, R. E. Laramy, and M. C. Hamming, *J. Org. Chem.*, **33**, 2000 (1968); (d) T. F. Wood and J. T. Angiolini (to Givaudan Corp.), U.S. Patent 3 347 946 (1967); (e) T. F. Wood and J. T. Angiolini, *Tetrahedron Lett.*, 1 (1963).

(3) (a) A. W. Weitkamp, *Adv. Catal.*, **18**, 2 (1968); (b) J. A. Barltrop, R. M. Acheson, P. G. Philpott, K. E. MacPhee, and J. S. Hunt, *J. Chem. Soc.*, 2928 (1956).

(4) (a) R. H. Wright, *Perfum. Essent. Oil Rec.*, **58**, 648 (1967); (b) M. G. J. Beets, H. Van Essen, and W. Meerburg, *Recl. Trav. Chim. Pays-Bas*, **77**, 854 (1958); (c) M. G. J. Beets, W. Meerburg, and H. Van Essen, *ibid.*, **78**, 570 (1959); (d) E. T. Theimer and J. H. Blumenthal (to International Flavors and Fragrances, Inc.), U.S. Patent 3 244 751 (1966); (e) T. F. Wood, "Chemistry of the Aromatic Musks", Givaudan Corp. Clifton, N.J., 1971; (f) T. F. Wood, W. M. Easter, Jr., M. S. Carpenter, and J. Angiolini, *J. Org. Chem.*, **28**, 2248 (1963).

(5) (a) R. Frank, *Can. J. Plant Sci.*, **49**, 209 (1969); (b) T. F. Wood and J. T. Angiolini (to Givaudan Corp.), U.S. Patent 3 283 016 (1966); (c) D. A. Brown and R. D. Hart (to Amchem Products, Inc.), U.S. Patent 3 342 585 (1967); (d) N. E. Achuff and T. F. Wood (to Givaudan Corp.), U.S. Patent 3 393 994 (1968); (e) W. F. Evans and T. F. Wood (to Givaudan Corp.), U.S. Patent 3 393 995 (1968); (f) W. F. Evans and T. F. Woods (to Givaudan Corp.), U.S. Patent 3 399 049 (1968); (g) T. F. Wood and J. T. Angiolini (to Givaudan Corp.), U.S. Patent 3 509 215 (1970).

(6) A more convenient preparation of **1** from 2-methyl-4-phenyl-2-butanol has been described: W. M. Harms and E. J. Eisenbraun, *Org. Prep. Proced. Int.*, **3**, 239 (1971).

(7) (a) Preparative GC separations were obtained with a 10 ft × 4 in. column containing 25% Carbowax 20M on 60–70 mesh Gas Pack W; (b) A 10 ft × 0.375 in. column containing 25% Carbowax 20M on 80–100 mesh, acid-washed Gas Pack was used in a F & M Model 700 GC apparatus equipped with dual thermal conductivity detectors; (c) 25 ft × 0.375 in. column containing 10% UC W-98 on 60–80 mesh, acid-washed Gas Pack.

(8) (a) B. S. Friedman and F. L. Morritz, *J. Am. Chem. Soc.*, **78**, 3430 (1956); (b) D. E. Boone, E. J. Eisenbraun, P. W. Flanagan, and R. D. Grigsby, *J. Org. Chem.*, **36**, 2042 (1971).

(9) (a) GC analyses were carried out on a 11 ft × 0.25 in. column of 80–100 mesh Chromosorb G, DMCS-treated and coated with 5% UC W-98, and

a Hewlett-Packard Model 5750 apparatus fitted with dual thermal conductivity and hydrogen flame detectors; (b) 150 ft × 0.02 in. stainless steel capillary column lined with DC-550 oil at 110 °C; (c) 50 ft × 0.02 in. capillary support coated open tubular (SCOT) column lined with Carbowax 20M mounted in a Perkin-Elmer Mark II flame ionization gas chromatograph.

(10) Amberlyst-15 resin and literature describing it were obtained from Rohm and Haas Co. This reagent shows considerable promise in effecting acid-catalyzed conversions.

(11) A Nester/Faust (NFA-100) autoannular spinning band column was used.

(12) W. M. Harms and E. J. Eisenbraun, *Org. Prep. Proced. Int.*, **4**, 67 (1972).

(13) Mass spectra were obtained with a Consolidated Electrodynamics Corp. Model 21-110B high-resolution mass spectrometer operated under low-resolution conditions at 70 eV. NMR spectra were obtained with a Varian Associates HR-60 or HR-100 spectrometer. Peak positions are reported in terms of δ (pPM) downfield from internal standard tetramethylsilane (δ 0). IR spectra were obtained with a Beckman IR-5A spectrometer as films on NaCl plates or as KBr pellets. Melting points were taken in capillary melting point tubes using a Thomas-Hoover apparatus and are corrected. Boiling points are uncorrected. Cyclohexane used in the reactions was "Baker Analyzed" reagent, spectrophotometric quality. The benzene used was Fisher Certified reagent (thiophene free). Phillips pure grade isoprene was used in all cyclialkylation reactions. The sulfuric acid used was reagent grade. The petroleum ether, bp 60–68 °C, was redistilled before use.

(14) A. A. Khalaf and R. M. Roberts, *J. Org. Chem.*, **34**, 3571 (1969).

(15) The ketone **14** (Celestolide) was purchased from International Flavors and Fragrances, New York, N.Y.

(16) W. Reppe and W. J. Schweckendiek, *Justus Liebigs Ann. Chem.* **560**, 104 (1948).

Internal Acid Catalysis in the Formation of Imines from Isobutyraldehyde and Monoprotonated Diamines[1]

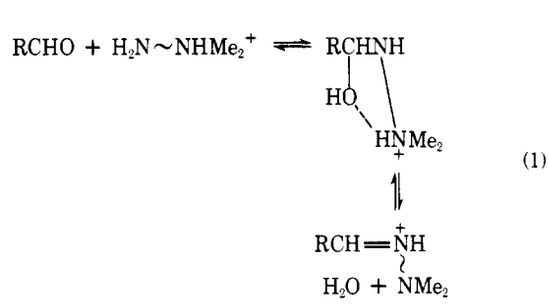
Jack Hine* and Francis A. Via

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

Received November 19, 1976

The reactions of isobutyraldehyde with diamines of the type $Me_2N(CH_2)_nNH_2$ where n = 2, 3, 4, and 5 have been studied at various pHs by stopped-flow spectrophotometry. A small amount of aldehyde disappears in an equilibrium process whose rate is too fast to measure. Rough equilibrium constants for this rapid reaction (K_r) are determined in the various runs. The K_r values at various pHs are resolved into K_{Ca}, the equilibrium constant for formation of the carbinolamine i-$PrCH(OH)NH(CH_2)_nNMe_2$, and K_{Cah}, the equilibrium constant for formation of the protonated carbinolamine i-$PrCH(OH)NH(CH_2)_nNHMe_2^+$. Also determined in the various runs are the equilibrium constants for a slower reaction (K_s), in which equilibrium is not established until about 5–50 s. These are resolved into values of K_{ic}, the equilibrium constants for formation of carbinolamine and imine, and K_{ich}. In all cases K_{ich} covers the formation of protonated carbinolamine and the protonated imine i-$PrCH{=}N(CH_2)_nNHMe_2^+$. However, when monoprotonated 2-dimethylaminoethylamine is the reactant much of the product is probably the 1,1-dimethyl-2-isopropylimidazolidinium ion, and when monoprotonated 3-dimethylaminopropylamine is the reactant an analogous six-membered ring heterocyclic cation is probably formed to a significant extent. Approximate first-order rate constants for dehydration of the carbinolamine mixtures are determined in individual runs. The rate constants obtained at various pHs are resolved into k_{co}, the rate constant for dehydration of the unprotonated carbinolamine, and k_{ch}, the rate constant for dehydration of the protonated carbinolamine. In the case of 2-dimethylaminoethylamine there is also a significant term for catalysis of dehydration of the protonated carbinolamine by the unprotonated diamine. The products $K_{Ca}k_{co}$ and $K_{Cah}k_{ch}$ are reliable second-order rate constants for imination of the aldehyde by the unprotonated and monoprotonated diamine, respectively. The former values give a satisfactory fit to a logarithmic plot against the pK_as of the protonated primary amino groups that includes data on a number of primary monoamines. The values of $K_{Cah}k_{ch}$ for 2-dimethylaminoethylamine and 3-dimethylaminopropylamine are too large by about 7000-fold and 100-fold, respectively, to fit the plot. These deviations are attributed to internal acid catalysis of the dehydration of the intermediate protonated carbinolamine by the dimethylammonio substituent group.

The formation of an imine from an aldehyde or ketone and a primary amine in neutral or basic solution ordinarily involves the reversible formation of a carbinolamine, which, in the rate-controlling step, loses a hydroxide ion to give an iminium ion, whose equilibration with the corresponding imine is established very rapidly.[2,3] This loss of hydroxide ion is uncatalyzed in strongly basic solution but becomes acid catalyzed as the pH is lowered. Nevertheless, increases in the acidity of the reaction solution do not necessarily increase the rate of iminium ion formation, because they decrease the fraction of the amine present in the reactive (unprotonated) form. We thought that relatively rapid iminium ion formation under mild conditions, which is desirable in bifunctional catalysts that are being investigated in this laboratory,[4] could be achieved by internal acid catalysis. We have therefore investigated imine formation from isobutyraldehyde and ω-dimethylaminoalkylamines and learned that with monoprotonated forms of such diamines there may be internal acid catalysis of the dehydration of the intermediate carbinolamine (eq 1). After this work was completed, similar internal acid



(1)

catalysis in iminium ion formation from acetone and various monoprotonated diamines was discovered.[5,6]

Results

Equilibrium Constants for Carbinolamine and Imine Formation. Stopped-flow mixing of aqueous solutions of isobutyraldehyde and amines of the type $Me_2N(CH_2)_nNH_2$ where n = 2, 3, 4, and 5 showed that a small but significant amount of the aldehyde was used up in an equilibrium process that was too fast to measure and that a larger amount of al-