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THE CARBON ANALOGUE OF THE CLAISEN REARRANGEMENT OF PHENYL ALLYL ETHER

EQUILIBRATION OF BUTENYLBENZENES AND *ortho*-PROPENYLTOLUENES

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Abstract—The elusive carbon analogue of the Claisen rearrangement of phenyl allyl ether has been realized. Under strongly basic conditions in t-butyl alcohol containing potassium t-butylate at 350° for 24 hr, the set of five isomeric 1-phenylbutenes is put into thermodynamic equilibrium with the set of three isomeric 1-(*o*-tolyl)propenes.

EXTENSION of the Claisen rearrangement of phenyl allyl ethers[2,3] to structurally analogous types, in which oxygen has been replaced by other groups or atoms, has met with very limited success. When X is sulfur, for example, it has been reported by Hurd and Greengard that phenyl and *p*-tolyl allyl thioether rearrange in 25% of theory to 2-allyl- and 2-allyl-4-methylthiophenol, respectively.[4] However, more recent reports suggest that the product of thermolysis of phenyl allyl thioether is not *o*-allylthiophenol but mainly propenyl phenyl thiother.[5,6] Under somewhat different conditions 2-methylthiocoumaran[6] and thiochroman[7] are the products. When X is NH, only failures were reported[8–10] until recently when it was discovered that N-allyl-1-naphthylamine rearranges at 260° to 2-allyl-1-naphthylamine.[11]

Search for the carbon analogue in which X is methylene or a substituted methylene begins with the pyrolysis of 4-phenyl-1-butene (I) by Hurd and Bollman.[12] Toluene

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[1] We wish to express our deep gratitude to the Aaron E. Norman Foundation for the award to Robert A. Bragole of two summer research fellowships in 1961 and 1962 and to the National Science Foundation for its support of this work through grant 11378. Present address: Upjohn Company, Carwin Research Laboratories, North Haven, Connecticut.

[2] L. Claisen and O. Eisleb, *Liebigs Ann.* **401**, 21 (1913).

[3] S. J. Rhoads in P. de Mayo (Editor), *Molecular Rearrangements*, Part I; pp. 655–706. Interscience, New York (1963).

[4] C. D. Hurd and H. Greengard, *J. Amer. Chem. Soc.* **52**, 3356 (1930).

[5] E. N. Karaulova, D. Sh. Meilanova and G. D. Gal'pern, *Zh. Obschch. Khim.* **27**, 3034 (1957).

[6] H. Kwart and C. M. Hackett, *J. Amer. Chem. Soc.* **84**, 1754 (1962). Professor Kwart has graciously informed us that an investigation of the possible intermediacy of 2-allylthiophenol will be published shortly.

[7] C. Y. Meyers, C. Rinaldi and L. Bonoli, *J. Org. Chem.* **28**, 2440 (1963).

[8] F. B. Dains, R. Q. Brewster, J. S. Blair and W. C. Thompson, *J. Amer. Chem. Soc.* **44**, 2637 (1922).

[9] F. L. Carnahan and C. D. Hurd, *J. Amer. Chem. Soc.* **52**, 4586 (1930).

[10] C. D. Hurd and W. W. Jenkins, *J. Org. Chem.* **22**, 1418 (1957).

[11] S. Marcinkiewicz, J. Green and P. Mamalis, *Chem. & Ind.* 438 (1961); *Tetrahedron* **14**, 208 (1961).

[12] C. D. Hurd and H. T. Bollman, *J. Amer. Chem. Soc.* **55**, 699 (1933).

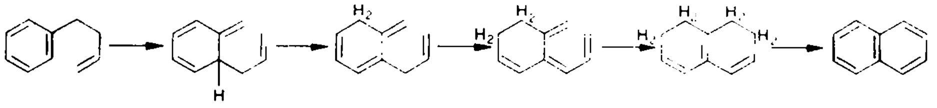
and propylene were major products at 500° while appreciable amounts of naphthalene were formed at 700°.[13] Neither in these experiments nor in a pyrolysis at 400° was any rearranged product formed.[14] That the rearrangement might have failed by reason of unfavorable thermodynamics was excluded by the fact that the expected rearrangement product, *o*-allyltoluene, was unchanged at 400° and suffered extensive decomposition but no rearrangement at 650° and 700°.[14] In both instances oxidation by alkaline permanganate was employed in the analysis of product because benzoic acid and *o*-toluic acid could be isolated quite reliably. But even with this more sensitive probe, no rearrangement in either direction could be detected.

Many years later Cope introduced into the system those substituents (cyano, carboethoxy and phenyl) which had had such a marked accelerating effect in his own Cope rearrangement. But again, no rearrangement of the Claisen type could be detected.[15]

A kinetic explanation for the failure to observe the carbon analogue of the Claisen rearrangement does not survive quantitative scrutiny. A reasonable model for estimation of the upper limit of the activation energy is based on a rate-determining bond cleavage in which a benzyl and an allyl radical are formed. With the activation energy of dissociation of ethylbenzene to a benzyl radical and a methyl radical known to be 63 ± 1·5 kcal/mole,[16] and with the contribution of delocalization in the allyl radical estimated to be 21 kcal/mole,[17] an activation energy of 42 kcal/mole is calculated. This value would be lowered by the energetic advantage of simultaneous bond-making in the transition state of the bond-breaking process. The estimated maximum activation energy may be combined with the assumption of an entropy of activation of −10 to 0 e.u. to lead to the prediction of an appreciable rate in the temperature range 300–350°. This estimated maximum activation energy is not sufficiently larger than the activation energy of 31·6 kcal/mole found for the Claisen rearrangement of phenyl allyl ether[18] to be assigned responsibility for the failure to observe the carbon analogue of the Claisen. Indeed, the formation of toluene and propylene at 500° provides experimental support for the contention that the breaking of the carbon–carbon bond is feasible.[12]

A more likely source of the difficulty is the second step in which the hypothetically intermediate allylic triene must be reconverted to an aromatic system by prototropic rearrangement if the reaction is to complete itself. In the Claisen rearrangement this step is facilitated by the activating effect of the carbonyl group, but even here yields are improved by the action of dimethylaniline or other bases.[19] This felicitous improve-

[13] The formation of naphthalene can be rationalized as the result of a sequence of reactions including the carbon analogue of the Claisen, a pair of 1,5-hydrogen shifts, a triene cyclization and dehydrogenation:



[14] C. D. Hurd and H. T. Bollman, *J. Amer. Chem. Soc.* **56**, 447 (1934).

[15] A. C. Cope, L. Field, D. W. H. MacDowell and M. E. Wright, *J. Amer. Chem. Soc.* **78**, 2547 (1956); A. C. Cope, J. E. Meili and D. W. H. MacDowell, *Ibid.* **78**, 2551 (1956).

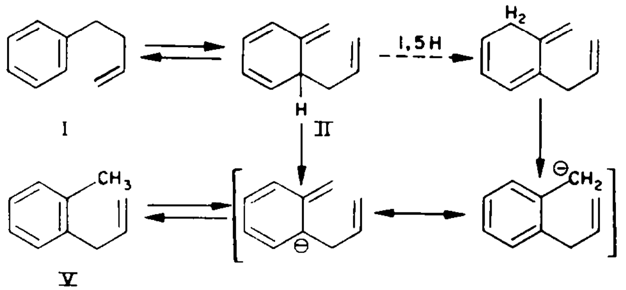
[16] M. Szwarc, *J. Chem. Phys.* **17**, 431 (1949).

[17] W. von E. Doering and W. R. Roth, *Angew. Chem. Inter. Ed.* **2**, 115 (1963).

[18] H. L. Goering and R. R. Jacobson, *J. Amer. Chem. Soc.* **80**, 3277 (1958).

[19] L. Claisen, *Liebigs Ann.* **418**, 69 (1918).

ment, realized without having dimethylaniline appear in the rate-expression,[18,20] is believed to result from the more rapid removal of the sensitive dienone from the jeopardy of accessible but undesirable chemical changes. In the carbon analogue of the Claisen, the only available thermal prototropic rearrangement is a 1,5-hydrogen shift which unfortunately does not lead to aromatization. But even if it did, the addition of its activation energy (29 kcal/mole)[21] to the estimated thermodynamic difference between I and II (36 – 9 kcal/mole) would lead to a rate-determining activation energy of 56 kcal/mole, which is much higher than the estimated activation energy of dissociation into a benzyl and an allyl radical.



Although the crucial hydrogen in II is not nearly so acidic nor so labile as that in the dienone intermediate in the Claisen rearrangement, it must be at least as easily removed by base as is the hydrgoen in a conjugated diene.[22] This thought leads clearly to the hypothesis that the carbon analogue of the Claisen rearrangement might be uncovered if the activation energy of the conversion of II to V might be lowered sufficiently. Strongly basic catalysis might achieve this goal.

In fact, heating for several hours at 350° in 0·25N potassium t-butylate in t-butyl alcohol establishes thermodynamic equilibrium between the five double bond isomers of 1-phenylbutene and the three of *o*-tolylpropene-1. Since the predominant isomers are the *trans*-styrene derivatives, to a first approximation equilibrium is established between *trans*-1-phenylbutene-1 (IV) and *trans*-*o*-tolylpropene-1 (VI).

Migration of the double bond in the starting material and the product occurs at temperatures so much lower than those required by the carbon–Claisen rearrangement that the system of five isomeric phenylbutenes represents a preequilibrium, as does the system of three isomeric *o*-tolylpropenes in the reverse rearrangement. Although this aspect of the problem was not developed to the point of finding a gas chromatographic column capable of separating the five phenylbutenes, it was possible to isolate and identify by IR spectra, 4-phenylbutene-1 (I), *trans*-1-phenyl-butene-2 (III) and *trans*-1-phenylbutene-1 (IV). In t-butyl alcohol and potassium t-butylate at 300°, the relative amounts of these isomers at equilibrium were 14, 35 and 51%, respectively, whereas at 200° the relative amounts were 12·5, 12·5 and 75% respectively. At lower temperature (55°) partial equilibration was effected by 1M potassium t-butylate in

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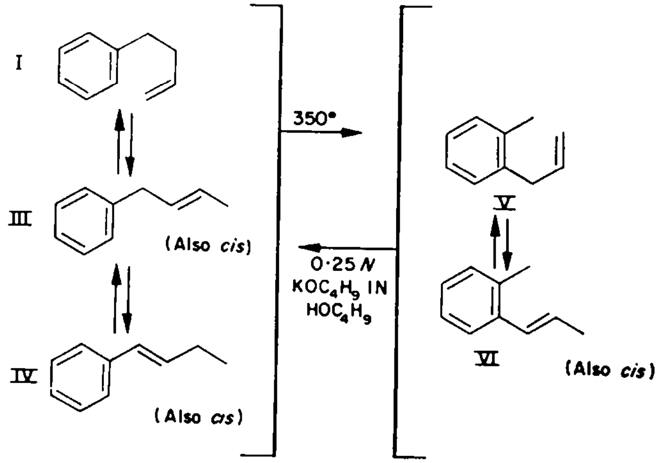
[20] D. S. Tarbell and J. F. Kincaid, *J. Amer. Chem. Soc.* **62**, 728 (1940).

[21] W. R. Roth, *Liebigs Ann.* **671**, 25 (1964) reports this value for the 1,5-hydrogen shift in cycloocta-1,3,6-triene.

[22] W. von E. Doering, G. Schroeder, K. Trautner and S. Staley, *Abstracts of Papers, 144th Meeting, Amer. Chem. Soc.* p. 14M. Los Angeles, Calif. April 2 (1963).



dimethylsulfoxide.[23] Under these conditions the relative amounts of *trans*-1-phenylbutene-2 (III) and *trans*-1-phenylbutene-1 (IV) were 6·6 and 92·2%, respectively, with the small remainder (1·2%) not being positively identified.

Direct analysis of equilibrated olefins could not be carried out by gas chromatography; nor was it possible to find a column to separate 1-*o*-tolylpropane and 1-phenylbutane, the two products of hydrogenation of the mixture of olefins. An effective analytical procedure follows the method of Hurd and Bollman[14] in which the mixture is oxidized with excess potassium permanganate to a mixture of *o*-toluic and benzoic acids. In the present modification these acids are then esterified with diazomethane to a mixture of methyl benzoate and methyl *o*-toluate which can be analyzed quantitatively by gas chromatography. It is important to note that the accuracy depends most critically on the extent to which the yield of acid from each of the olefins is either 100% of theory or at least identical to the yield from each of the other olefins. Our information on this point is not complete but includes oxidation of the two most difficulty oxidizable olefins, *o*-allyltoluene (V) and 4-phenylbutene-1 (I). These olefins afford *o*-toluic and benzoic acid in 81 and 82% of theory, respectively. It is also significant that no other acid, such as phenylacetic, can be detected.

The equilibrations were carried out by heating the olefin for 24 hr in 0·25 M t-butyl alcoholic solution of potassium t-butylate at 350°. Since the analytical procedure involves degradation of the side chain to carboxylic acid, it measures the extent of rearrangement and, when complete, the position of equilibrium between the

TABLE 1. BASED-CATALYZED THERMAL EQUILIBRATION OF PHENYLBUTENES AND *o*-ALLYLTOLUENE AT 350°

Starting material	Methyl *o*-toluate	Methyl benzoate
I	90%	10%
III	95%	5%
IV	90%	10%
V	93%	7%

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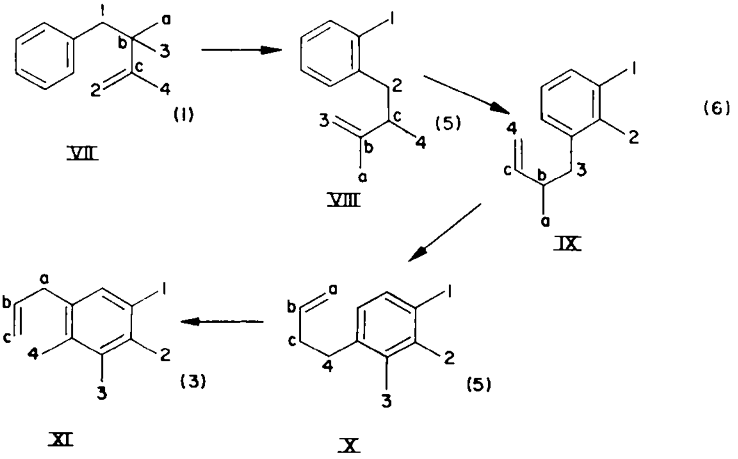
[23] A. Schriesheim, J. E. Hofmann and C. A. Rowe, Jr., *J. Amer. Chem. Soc.* **83**, 3731 (1961); A. Schriesheim, C. A. Rowe, Jr. and L. Naslund, *Ibid.* **85**, 2111 (1963).

phenylbutenes and the *o*-tolylpropylenes. The reaction is quite free of degradation at this temperature, although at 400° appreciable amounts of toluene are produced.

The results are summarized briefly in Table 1. In support of the allegation that equilibrium is reached is the important observation that *o*-allyl toluene leads to the formation of appreciable quantities of phenylbutenes (as benzoic acid). The position of equilibrium (taken as 93:7) at 350° corresponds to a free energy difference between the two sets of olefins of −3·2 ± 0·5 kcal/mole. To a first approximation this free energy difference should correspond closely to that between *trans*-1-phenylbutene-1 (IV) and *trans*-1-(*o*-tolyl)propene (VI). An estimate of this difference can be obtained from the free energies of formation calculated by the Franklin method of group equivalents.[24] The free energies of formation of IV and VI at 600°K (calc. without correction for the conjugative interaction of phenyl and double bond) are +85·94 and +83·48 kcal/mole, respectively. The difference of −2·5 kcal/mole coincides with the experimental value sufficiently well to encourage the calculation thermodynamically of the position of equilibrium prior to the experimental investigation of an unknown example. In connection with these thermodynamic considerations it may be worth noting that the thermodynamic driving force in the oxygen–Claisen rearrangement is fundamentally derived from the difference in the strengths of the carbon–hydrogen and oxygen–hydrogen bonds.[25] By contrast there is no fundamental thermodynamic driving force in the carbon–Claisen rearrangement, a point which must have guided the experiments of Hurd and Bollman.[14] In the projection of further examples of the carbon-Claisen rearrangement, secondary thermodynamic factors will have to be carefully evaluated.

In principle, suitably substituted olefins may be able to suffer more than one carbon–Claisen rearrangement. This point is illustrated by the purely hypothetical example of 4-phenyl-2,3,3-trimethylbutene-1 (VII) which can rearrange to 1-allyl-2,3,4,5,-tetramethylbenzene (XI) (and its two, more stable double-bond isomers) by way of VIII (five isomers), IX (six isomers) and X (five isomers), thereby setting some twenty isomeric olefins into thermodynamic equilibrium.



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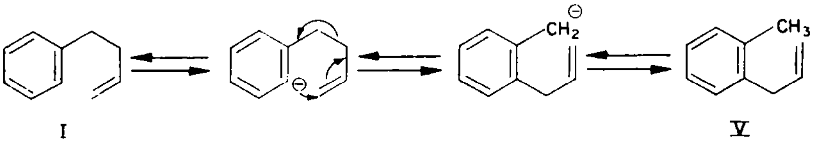
[24] J. L. Franklin, *Ind. Eng. Chem.* **41**, 1070 (1949).

[25] To a first approximation the Claisen rearrangement involves the replacement of a C–H and a C–O bond by an O–H and C–C bond. The thermodynamics of this change is −10·9 kcal/mole.[26]

[26] L. Pauling, *The Nature of the Chemical Bond* (3rd Edition) p. 85. Cornell Univ. Press (1960).

In conclusion, it must be emphasized that the success of a mechanistic hypothesis in leading to the realization of a new reaction may be a necessary condition for the acceptance of the mechanism, but it is not a sufficient one. We do not know, for example, that the base does not remove *ortho*-hydrogen to produce a phenide ion which then cyclizes to the product according to a scheme of the following type.



EXPERIMENTAL

Thermal equilibration of phenylbutenes and o-tolylpropenes in the presence of potassium t-butylate. An ampoule containing 1·65 to 2·02 g olefin, 1·0 ml 1·65M potassium t-butylate, 3 ml dry t-butyl alcohol and a small amount of hydroquinone was sealed under N_2 and pyrolyzed at 350° for 24 hr. The ampoule was cooled first to 25° and then at −70° in a Dry-ice bath and opened. Its contents were added to an equal volume of water and extracted with ether. The ethereal extract was washed with cold 5% H_2SO_4aq and water, dried over $MgSO_4$ and concentrated by evaporation of the ether. The yield of olefinic product was quantitative.

Catalytic hydrogenation of an artificial mixture of equal parts of 4-phenyl-1-butene and *o*-allyltoluene in tetrahydrofuran over Pd–C (1%) afforded a mixture of hydrocarbons which appeared as a single, unresolved band on all the GLC columns tested.

Oxidation of the mixture of olefins was effected in a 200-ml, 3-necked, round-bottom, standard taper flask equipped with a Hershberg stirrer and a reflux condenser. The mixture of olefins (0·9–1·8 g), $KMnO_4$ (3·18 times the wt. of the olefin), NaOH (1·4 times the wt. of olefin) and water (ca. 70 times the wt. of olefin) were placed in the flask and allowed to react under stirring for 4 hr at 25°. The aqueous phase was filtered to remove MnO_2, concentrated by evaporation, extracted with ether, cooled and acidified with conc. H_2SO_4 to precipitate organic acid which was collected and washed with water. The crude acid was redissolved in 10% NaOHaq, treated with a small quantity of activated charcoal, filtered and reacidified to give a colorless mixture of acids in 83 ± 3% of theory.

Conversion to the methyl esters was effected by treatment of the mixture of acids in 20 ml ether at 0° with excess ethereal diazomethane. Concentration of the dried ($MgSO_4$) ethereal solution left the mixture of esters in virtually quantitative yield. The esters were analyzed quantitatively by gas chromatography on G. E. Silicone oil SF 96 or Carbowax 20 M (methyl *o*-toluate had a retention time approximately 1·4 times that of methyl benzoate) and identified by collection of pure samples of which the IR spectra were compared with those of authentic samples of methyl benozate and methyl *o*-toluate.

Experimental results are shown in Table 1.

4-Phenyl-1-butene (I). This material was prepared by the method of Bryce-Smith and Turner;[27] b.p. 180–181° (reported[27] b.p. 181·1°); gas chromatographically homogeneous on a 5′, G. E. SF 96 silicone-oil column. Its IR and NMR spectra may be found elsewhere.[28] Oxidation with alkaline permanganate under the conditions described above afforded benzoic acid in 82% of theory, m.p. 121·5–122° alone and in admixture with an authentic sample.

o-Allyltoluene (V). The Grignard reagent from 3·7 g Mg turnings and 26 g *o*-bromotoluene was prepared in a 200-ml flask in the usual way. To the cooled solution 11·8 g allyl chloride in 25 ml ether was added dropwise over a 30 min period. The reaction mixture was poured into 10% H_2SO_4aq. The ether layer was washed with 10% H_2SO_4aq, water and sat. NaClaq, dried over Na_2SO_4 and concentrated by distillation. Vacuum distillation of the residue afforded *o*-allyltoluene (85% of theory); b.p. 93–95°/30 mm (reported[14] b.p. 93–95°/30 mm); gas chromatographically (silicone oil) homogeneous; IR and NMR spectra are reported elsewhere.[28] Oxidation as described above afforded *o*-toluic acid in 81% of theory; m.p. 104–105°, alone and in admixture with authentic *o*-toluic acid.

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[27] D. Bryce-Smith and E. E. Turner, *J. Chem. Soc.* 1975 (1950).

[28] R. A. Bragole, Ph.D. Dissertation Yale University, May 1965.

trans-1-*Phenyl-2-butene* (III). Obtained from Aldrich Chemical Company, this material was gas chromatographically homogeneous on both silicone oil and Carbowax 20 columns (IR spectrum reported elsewhere[28]). Ozonolysis of 1·6 g *trans*-1-phenyl-2-butene in 20 ml ethyl acetate was effected in a 100-ml flask cooled to −70°. Ethyl acetate was removed in vacuum; a mixture of 15 ml 30% H_2O_2 and 35 ml glacial acetic acid was added and boiled under reflux for 3 hr. The hot solution was filtered and concentrated to give crude phenylacetic acid which was purified by sublimation in vacuum; m.p. 75–76°.

trans-1-*Phenyl-1-butene* (IV). Under the conditions described above for the equilibration of phenylbutene but at lower temp (210–220°) for 7 hr, *trans*-1-phenyl-2-butene was converted to a mixture of olefins which was separated by gas chromatography on a 5-ft silicone oil column at 130° under 5 lb He into 3 fractions. That fraction with the longest retention time (17·5 min) comprised 70% of the mixture and was collected as *trans*-1-phenyl-1-butene; UV spectrum (EtOH): λ_{max} 251 mμ (ϵ = 17,670), 284 mμ (ϵ = 1,230), 293 mμ (ϵ = 960) [reported[29] λ_{max} 251 mμ (ϵ = 17,780), 284 mμ (ϵ = 1,120), 293 mμ (ϵ = 724)]; IR and NMR spectra are reported elsewhere.[28]

Ozonolysis was effected in the same manner as described under *trans*-1-phenyl-2-butene above and led to the formation of benzoic acid, m.p. 119–120° after sublimation *in vacuo*.

Attempted equilibrations at higher and lower temperatures. Under the conditions descirbed above (potassium t-butylate in t-butyl alcohol), 4-phenyl-1-butene was heated for 8 hr at 200°. Analysis by gas chromatography on the 5-ft silicone column at 130° showed 3 bands. These were identified by retention time, isolation and comparison of IR spectra with those of authentic samples as I(12%), III(12%) and IV(76%).

Under the same conditions at 300° for 8 hr, the same substances were identified in amounts corresponding to 14, 35 and 51%, respectively. (9-ft Dow-Corning 550 silicone column at 135°.)

At the higher temp, a small amount of toluene was added initially to serve as a reference and was determined quantitatively by gas chromatography. At 400° for 8 hr with or without added hydroquinone there was noticeable charring inside the tube. Gas chromatographic analysis indicated the formation of more products than had been observed at 350° and a significant increase in the relative amount of toluene.

At 364° for 24 hr, decomposition products were still detectable, whereas at 350° for 8 hr, the amount of toluene did not increase.

Thermolysis in the absence of potassium t-butylate. 4-Phenyl-1-butene (1·76 g) was heated in a sealed ampoule with 3 ml t-butyl alcohol and a trace of hydroquinone at 350° for 24 hr. Worked in the same manner employed in the equilibrations, this reaction yielded starting material in virtually quantitative yield having an IR spectrum (neat) identical with that of authentic 4-phenyl-1-butene. This olefin was oxidized with alkaline permanganate to give benzoic acid, m.p. 121·5–122°, in 82% of theory. Treated with ethereal diazomethane, this acid afforded gas chromatographically homogeneous methyl benzoate (IR spectrum identical with that of authentic methyl benzoate).

Isomerization of trans-1-*phenyl-2-butene at* 55°. A mixture of 0·52 g *trans*-1-phenyl-2-butene, 0·5 ml 1M potassium t-butylate in dimethyl sulfoxide and 3 ml dimethylsulfoxide was sealed under N_2 and kept at 55° for 24 hr. The cooled contents were poured into water and extracted with pentane. The pentane solution was dried over $MgSO_4$ and concentrated to a residue which was analyzed by GLC (16 ft, ¼″ Dow Corning 550 silicone [15% on beads] at 130° and 10 lb He), and separated into three products of retention times 5·9 min (1·2%), 7·5 min (6·6%) and 10·2 min (92·2%). The latter two products were isolated and identified as *trans*-1-phenyl-2-butene and *trans*-1-phenyl-1-butene, respectively, by IR spectrum. The minor product was not identified.

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[29] C. D. Overberger and D. Tanner, *J. Amer. Chem. Soc.* **77**, 369 (1955).