[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

The Claisen Rearrangement. III. Benzyl 2-Propenyl-4,6-dimethylphenyl Ether[1]

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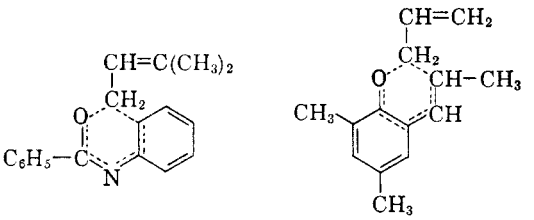
Received August 17, 1959

Benzyl 2-propenyl-4,6-dimethylphenyl ether has been synthesized and its behavior at temperatures up to 210° has been studied. At 135–150° the ether starts to polymerize but shows no tendency to form phenolic products. Between 180–210° the formation of phenolic materials is evident. One liquid phenolic compound was isolated and identified as 2-(2-benzylpropyl)-4,6-dimethylphenol. This identification was confirmed by synthesis.

Since Claisen's discovery[2] of the thermally initiated rearrangement of *O*-allyl ethers to C-allyl derivatives a host of investigators have accumulated a large body of knowledge much of which serves to delineate the scope of the reaction. Claisen thus found[3] that allyl 2-propenyl-4,6-dimethylphenyl ether undergoes thermal conversion to a phenolic compound to which he assigned the structure, 1-(2-hydroxy-3,5-dimethylphenyl)-2-methylpenta-1,4-diene. Recently Lauer and Wujciak[4] proved the structure of the product of this rearrangement and showed further that an appropriately substituted allyl group appears in uninverted form in the product. Schmid, Fahrni, and Schmid,[5] using C^{14}, showed that a small fraction (*circa* 16%) of the product contained the allyl group in inverted form. As they found the process to be strictly intramolecular, they proposed an eight-membered ring transition state to account for the inverted product.

The bulk of the rearrangment product can be nicely accommodated by the widely-accepted double-cycle mechanism for the *para* rearrangement.[6] However, an alternative mechanism involving only the *alpha* carbon of the allyl group was suggested by Lauer[7] to account for the rearrangement of *O*-(γ,γ-dimethylallyl)benzanilide, and reiterated in his discussion of the side chain rearrangement.[4] Although this is indeed a particularly attractive possibility, considering the economy



of atomic motion achieved thereby, it is less attractive geometrically. Thus the bonding of the alpha carbon in the transition state must involve the *p* orbital lobes used by the central carbon in an S_N2 substitution, *i.e.* the oxygen atom, *alpha* carbon of the allyl group, and *beta* carbon of the propenyl side chain should preferentially occupy a linear arrangement.

In light of the above discussion it was advisable to submit the possibility of the single cycle mechanism to experimental test. Unfortunately the most useful test of mechanism devised previously, that of inversion of the allyl group or lack of it, is not applicable in this case. Of the several possible tests we were able to devise, the simplest capitalized upon the fact that in a benzyl ether the *alpha* carbon is completely analogous to the *alpha* carbon of the allyl group but the *gamma* carbon is not. Thus the benzyl ether is not able to undergo the conventional Claisen rearrangement.[8] While benzyl ethers do indeed rearrange under a more drastic thermal impetus[9] or under free radical initiation,[10] it was felt that under the usual conditions a benzyl ether should not undergo the double cycle rearrangement. Conversely if the single cycle process were operable, the rearrangement should proceed normally with the benzyl ether.

The benzyl ether was prepared from the known[3] 2-propenyl-4,6-dimethylphenol using the sodium salt of the phenol in methanol and benzyl chloride. Although the resultant ether, a yellow oil, could not be distilled unchanged under normal vacuum distillation at 0.1–1 mm. pressures, it was distilled readily without decomposition *via* molecular distillation. However, the distilled material was

(1) Published with the approval of the Monographs Publication Committee, Oregon State College, as Research Paper no. 371, School of Science, Department of Chemistry. This work was supported in part by a Grant-in-aid from the General Research Fund of Oregon State College, and in part by a grant from the Cottrell fund of the Research Corporation. One of us, E. N. M., is indebted to the E. I. du Pont de Nemours and Co. for a summer fellowship which aided completion of this work.

(2) L. Claisen, *Ber.* **45**, 3157 (1912).

(3) L. Claisen and E. Tietze, *Ann.* **449**, 81 (1926).

(4) W. Lauer and D. Wujciak, *J. Am. Chem. Soc.* **78**, 5601 (1956).

(5) K. Schmid, P. Fahrni, and H. Schmid, *Helv. Chim. Acta*, **39**, 708 (1956).

(6) *Cf.* S. J. Rhoads, and R. L. Crecelius, *J. Am. Chem. Soc.* **77**, 5057 (1955) and W. Haegele and H. Schmid, *Helv. Chim. Acta*, **40**, 13,255 (1957) for a discussion of this mechanism.

(7) W. Lauer and R. Lockwood, *J. Am. Chem. Soc.* **76**, 3974 (1954).

(8) S. G. Powell and R. Adams, *J. Am. Chem. Soc.* **42**, 646 (1920) L. Claisen, F. Kremers, F. Roth, and E. Tietze, *Ann.* **442**, 210 (1925).

(9) O. Behagel and H. Freiensehner, *Ber.* **67**, 1368 (1934).

(10) M. Kharasch, G. Stampa, and W. Nudenberg, *Science*, **116**, 309 (1952).

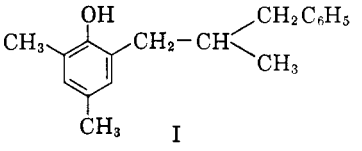
still a light lemon yellow and was therefore carefully chromatographed on alumina. There were obtained thereby two distinct fractions, the first a colorless mobile oil and the second a viscous yellow liquid. The colorless oil was rechromatographed, taken up in petroleum ether and extracted with Claisen's alkali and after removal of the solvent distilled again *via* molecular distillation. This product shows infrared bands at 973 and 1648 cm.$^{-1}$ (disubstituted double bond in *trans* form), 1378 cm.$^{-1}$ (C-CH_3), 1218 cm.$^{-1}$ (Ar—O—CH_2), 856 cm.$^{-1}$ (tetrasubstituted benzene ring) and 732 and 696 cm.$^{-1}$ (monosubstituted benzene ring.) It absorbed exactly two moles of hydrogen and the phenolic product obtained from the reaction mixture showed an infrared spectrum identical with that of an authentic sample of 2-propyl-4,6-dimethylphenol. We believe the structure of the starting material is thoroughly established by this data. The composition of the yellow liquid is now under investigation.

An attempt made to find the mildest possible condition for rearrangement disclosed that at temperatures as low as 135° the ether formed a thick gel, growing a deep yellow in the process. No hydroxyl absorption was noted even after prolonged heating at this temperature. This presumed polymerization has not been further studied.

Not until the temperature reaches 180° does any reaction productive of phenolic material set in. All runs for study of the phenolic products were made at 200–210° where the formation of these materials was rapid enough to provide sufficient base soluble material before polymerization made the product unmanageable. The benzyl ether was free of peroxide as indicated by starch-iodide test and free radical reactions were minimized by carrying out the reaction in the dark under oxygen-free nitrogen.

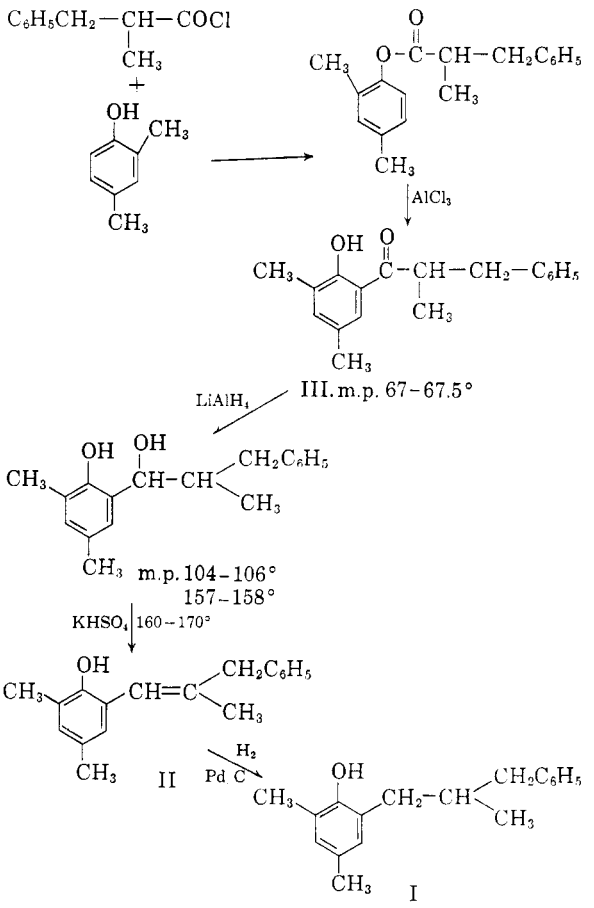
There was obtained by extraction of the heated material with Claisen's alkali about 20% of a phenolic substance, whose hydroxyl group was sufficiently hindered to render it insoluble in 6*N* aqueous alkali. This substance, a viscous clear liquid, b.p. 132–134° (0.15 mm.), n_D^{20} 1.5567, showed a refractive index below that, n_D^{25}, 1.5710, of the starting material and did not add bromine. This evidence which suggested loss of the side chain double bond was confirmed by the infrared spectrum. This latter showed bands at 3600 cm.$^{-1}$ (absorption slowly tapering off on the low frequency side) characteristic of a hindered hydroxyl, 1605 and 1490 cm.$^{-1}$ (an aromatic ring), 1375 cm.$^{-1}$ (C-CH_3 groups), 859 substituted benzene ring) and 738 and 698 cm.$^{-1}$ (a monosubstituted benzene ring). No absorption appeared in the regions from 810–840 cm.$^{-1}$ or 1640–1660 cm.$^{-1}$—characteristic of trisubstituted double bonds.

As the basic skeleton contains both a tetrasubstituted and a monosubstituted benzene ring, the hydroxyl group is present and more heavily hindered than the hydroxyl in 2-propenyl-4,6-dimethylphenol, and as no double bond is present in the side chain, the compound isolated was assigned the structure 2-(2-benzylpropenyl)-4,6-dimethylphenol (I). The correctness of this proposal



I

was verified by a synthesis of this molecule by the route shown in the attached sequence. Thus 2,4-dimethylphenyl α-methyldihydrocinnamate was prepared from the acid chloride of the known[11] α-methyldihydrocinnamic acid. This ester was submitted to the Fries rearrangement to give a



mediocre yield of a solid ketone assigned the structure III. The migratory group was placed in the six position because the product shows strong evidence of chelation, in that a dilute solution in cetane shows no other carbonyl band than one at 1640 cm.$^{-1}$, which can only be attributed to a strongly hydrogen-bonded conjugated carbonyl.[12] The evidence in favor of this interpretation is

(11) F. S. Kipping and A. E. Hunter, *J. Chem. Soc.* **83**, 1005 (1903).

(12) M. Flett, *J. Chem. Soc.* 1441 (1948).

strengthened by the appearance of the hydroxyl band in the region of C–H stretching, 3000–3100 cm.$^{-1}$, indicative of a strong hydrogen bond.

Reduction of the ketone gave a nearly quantitative yield of alcohol, m.p. 105–154°. After separation of the diastereomers *via* chromatography on silicic acid and repeated crystallization from benzene-hexane there were obtained two isomeric alcohols, m.p. 104–106° (27%) and 157–158° (43%). The infrared spectra showed two hydroxyl bands, one at 3480, the other at 3360 cm.$^{-1}$ for the higher melting isomer and 3600 and 3360 cm.$^{-1}$ for the lower. Neither shows absorption near 1640 cm.$^{-1}$. Either isomer on dehydration gave the same olefin, 2-(2-benzylpropenyl)-4,6-dimethylphenol (II). This substance, the expected product of the single cycle rearrangement process, showed infrared bands at 805 cm.$^{-1}$ and 1645 cm.$^{-1}$, characteristic of conjugated trisubstituted double bonds, as well as more complex C-H bending absorption in the 1480–1440 cm.$^{-1}$ region, and a doublet at 1300, 1320 cm.$^{-1}$ which serve to differentiate it effectively from the product actually isolated.

This olefin absorbs one mole of hydrogen when treated with hydrogen over palladium-on-charcoal at room temperature. The final product and that isolated from the thermal treatment of the benzyl ether show identical physical constants and infrared spectra. This unexpected product does not arise as a result of heating substance II under the rearrangement conditions, for such treatment failed to alter the refractive index of II appreciably and the infrared spectrum also indicated that no serious changes had occurred. It is apparent therefore that this saturated but rearranged material must arise during the thermal treatment of the ether itself.

Of course, this interesting and highly intriguing result negates the possibility of answering the question which prompted this study. Further work is needed before the means by which the benzyl group is transferred from the oxygen to the carbon atom can be made apparent. Published speculation on that process seems unwarranted at present.

EXPERIMENTAL[13]

Benzyl 2-propenyl-4,6-dimethylphenyl ether. A 49% yield of 2-propenyl-4,6-dimethylphenol, m.p. 72–73°, was obtained for the three-step synthesis of Claisen and Tietze[3] from 2,4-dimethylphenol. A freshly prepared solution of sodium methoxide, 7.1 g. (0.31 mole) of sodium in 150 ml. of absolute methanol, was mixed with 50 g. (0.31 mole) of 2-propenyl-4,6-dimethylphenol. To the boiling solution was added 39 g. (0.31 mole) of benzyl chloride over a 20 min. period. The solution was boiled for an additional 3 hr. After being allowed to cool, the solution was mixed with 30–60° petroleum ether and exhaustively extracted with Claisen's alkali. The petroleum ether solution was dried over anhydrous sodium sulfate, the solvent removed initially by distillation at atmospheric pressure, and completed *in vacuo* at 100° for 2 hr. The crude ether, 70.5 g. (78%), was a mobile light yellow liquid, n_D^{20} 1.5711, d_{23}^{25} 1.0395.

The crude ether was distilled in a Hickman molecular still at a bath temperature of 70–80° at 10^{-6} mm. pressure. The distillate was a mobile lemon yellow liquid which was chromatographed on activity II–III alumina (Woelm) using petroleum ether as eluant. The first eluate was a colorless liquid which was taken up in petroleum ether, extracted with Claisen's alkali, dried over anhydrous magnesium sulfate and redistilled in the molecular still. This substance had infrared bands at 696, 732, 856, 973, 1217, 1378, and 1648 cm.$^{-1}$. It showed no absorption in the 1650–1800 or 3100–3600 cm.$^{-1}$ regions. It had an n_D^{25} 1.5710 and λ_{max} 252 mm. ϵ = 11,300.

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.71; H, 7.93. Found: C, 85.64; H, 7.89. A second eluate, a thick deep yellow oil, was obtained but was not further investigated.

The colorless material was hydrogenated over 10% palladium-on-carbon in glacial acetic acid under atmospheric pressure. Absorption ceased after 2 moles of hydrogen were absorbed. Most of the acetic acid was removed *via* evaporation under reduced pressure after removal of the catalyst. The product was taken up in petroleum ether, washed with water, and the resulting phenolic material removed by extraction with 6*N* NaOH. After acidification of the basic extracts the phenol was isolated as usual and distilled in vacuo b.p. 90–95° (1.5 mm.), n_D^{25} 1.5193. The infrared spectrum of this product was identical with that of an authentic sample of 2-propyl-4,6-dimethylphenol prepared from 2-allyl-4,6-dimethylphenol[3] by hydrogenation as above.

Rearrangement. The above ether was heated under reflux (135°) at 0.01 mm. pressure for 8 hr. The very viscous, deep-red resultant material showed no absorption at 3200–3600 cm.$^{-1}$. Another sample (14.59) of the ether was heated in the dark under oxygen-free nitrogen at 200–210° (bath temperature) for 6 hr.

The residual material (12.0 g.) was taken up in petroleum ether and extracted with several portions of 6*N* aqueous sodium hydroxide followed by Claisen's alkali. Each of the combined extracts was acidified and extracted with petroleum ether. Upon evaporation of the solvent, no product was obtained from the 6*N* alkali extract and 2.8 g. (19%) of a clear viscous liquid, b.p. 132–134° (0.15 mm.), n_D^{22} 1.5570 was obtained from the Claisen's alkali extract. This substance showed notable infrared bands at 698 and 738, 859, 1375, 1490, and 1605, and 3600 cm.$^{-1}$.

From the original petroleum ether solution there was recovered, after the base extractions, 9.2 g. (63%) of a neutral polymer. This was not further investigated.

2,4-Dimethylphenyl α-methyldihydrocinnamate. α-Methyldihydrocinnamic acid was prepared by conventional alkylation of diethyl methylmalonate with benzyl chloride followed by basic hydrolysis in 80% aqueous ethanol and decarboxylation at 180–200°. The yield of acid, b.p. 150–152° (8 mm.), n_D^{21} 1.5142, d_4^{22} 1.0644, M_D calcd. 46.54, found 46.32 was 62% from methyl malonate. The literature[11] gives b.p. 160° (12 mm.) for this acid.

A 44-g. (0.27 mole) sample of this acid was treated at 40° with 64 g. (0.54 mole) of thionyl chloride. After 14 hr. the mixture was heated to reflux for 2 hr. The acid chloride was isolated by distillation, b.p. 116–117° (10 mm.), n_D^{22} 1.5162, yield 47.2 g. (96%).

To a solution containing 85.5 g. (0.70 mole) of 2,4-dimethylphenol in 1 l. of dry benzene, 118 g. (0.65 mole) of the acid chloride was added dropwise over a period of 1 hr. The mixture was heated under reflux for 3 hr. The reaction mixture was washed with water and dilute sodium bicarbonate and then dried. The ester was isolated by distillation, b.p. 146–147° (0.5 mm.), n_D^{23} 1.5372, d_{23}^{26} 1.0437, 148.5 g. (86%) as a clear oily liquid.

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.59; H 7.46. Found: C, 80.65; H, 7.44. M_D Calcd. 79.79; found 80.16.

(13) Analyses by Drs. Weiler and Strauss, Oxford, England. The authors are indebted also to Baird Atomic, Inc. and the Shell Oil Company for infrared spectra.

This ester shows strong absorption at 1760 cm.$^{-1}$, the high frequency being characteristic of phenolic esters.[14]

2-(1-Oxo-2-benzylpropyl)-4,6-dimethylphenol. A mixture of 107 g. (0.4 mole) of the above ester and 160 g. (1.21 moles) of anhydrous aluminum chloride was allowed to stand 20 hr. at room temperature. It was then heated on a steam bath for 2 hr. with vigorous stirring. After hydrolysis of the complex with cold conc. hydrochloric acid, the desired ketone was isolated by filtration and recrystallized from 90% ethanol, m.p. 67–67.5°, yield 43 g. (40%).

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.59; H, 7.46. Found: C, 80.37; H, 7.37. An infrared band at 1640 cm.$^{-1}$ characteristic of a strongly hydrogen-bonded conjugated ketone[12] was exhibited by this material in cetane solution.

2-(1-Hydroxy-2-benzylpropyl)-4,6-dimethylphenol. The ketone prepared above, 11.0 g. (0.041 mole), was added dropwise to a solution containing 0.9 g. (0.024 mole) of lithium aluminum hydride in 200 ml. of dry ether. After destruction of excess lithium aluminum hydride the mixture was poured on iced 10% sulfuric acid. The ether layer was separated and the aqueous layer was extracted twice with 100-ml. portions of ether. The combined extracts were washed with dilute ammonia, then with water until neutral, and dried. Evaporation of the ether left 10.8 g. (98%) of a crystalline alcohol, m.p. 105–154°. The mixture of diastereomers was separated by crystallization from a 50-50 benzene-hexane mixture. The pure high-melting isomer was obtained from a chloroform eluate from a silicic acid column. It crystallized as fine silky needles, m.p. 157–158°, 4.7 g. (43%).

Anal. Calcd. for $C_{18}H_{22}O_2$: C, 80.00; H, 8.15. Found: C, 80.20; H, 8.12.

This isomer showed two partly overlapping bands in the OH stretching region at 3360 and 3480 cm.$^{-1}$. No band in the region around 1640 cm.$^{-1}$ was observed.

The low melting isomer crystallized as compact crystals, m.p. 104–106°, 3.1 g. (28%) after repeated crystallization from benzene. It showed two well resolved bands in the infrared at 3600 and 3360 cm.$^{-1}$.

Anal. Calcd. for $C_{18}H_{22}O_2$: C, 80.00; H, 8.15. Found: C, 80.05; H, 8.21.

2-(2-Benzylpropenyl)-4,6-dimethylphenol. A mixture of 1.2 g. (0.0044 mole) of 2-(1-hydroxy-2-benzylpropyl)-4,6-dimethylphenol, m.p. 157–158°, and 1.5 g. of freshly fused potassium acid sulfate was heated at 160–170° for 30 min. The product was isolated by ether extraction and purified by distillation, b.p. 124–125° (0.15 mm.), n_D^{21} 1.5795, d_{23}^{25} 1.0267, 0.96 g. (86%).

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.71; H, 7.93. Found: C, 86.09; H, 8.12.

M_D: Calcd.: 79.18. Found: 80.21.

Similar dehydration of the alcohol, m.p. 104–106°, gave 96% yield of a product with identical physical properties and infrared spectrum. Both samples showed absorption at 805 cm.$^{-1}$ and 1645 cm.$^{-1}$ characteristic of a double bond and lacked the doublet in the O—H stretching region.

2-(2-Benzylpropyl)-4,6-dimethylphenol. A solution of olefin in glacial acetic acid was reduced at room temperature and atmospheric pressure over palladium-on-charcoal. One mole of hydrogen was absorbed. The solution was poured into water and the product extracted with petroleum ether. The reduced material was isolated in high yield by distillation under reduced pressure. Both the physical properties and infrared spectra were identical with those of the phenolic product from the reaction of the benzyl ether.

Anal. Calcd. for $C_{18}H_{22}O$: C, 84.99; H, 8.70. Found: C, 85.2; H, 8.84.

CORVALLIS, ORE.

(14) J. F. Grove and H. A. Willis, *J. Chem. Soc.* 877 (1951).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF OREGON]

Polarographic Reduction of Some Biaryls and Arylalkenes[1,2]

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Received July 10, 1959

Polarographic half-wave reduction potentials of twenty-seven aromatic hydrocarbons (including fifteen conjugated alkenylnaphthalenes, the phenylnaphthalenes, the phenylanthracenes, and the binaphthyls) were obtained under comparable conditions in a solvent-electrolyte mixture of 0.1*M* tetra-*n*-butylammonium iodide in 75% dioxane-water. In general, among isomeric compounds, the facility of reduction is found to increase with lessened steric restriction to the attainment of coplanarity in the molecule. Notable exceptions to this rule are found in the cases of the vinyl- and cyclopentenylnaphthalenes, where the 1-naphthyl isomers are reduced at slightly less negative potentials than the sterically less-hindered 2-isomers. Results are interpreted in terms of angles of twist present in the substrate molecules at the time of electron addition (transition state) and inherent conjugative powers of the alkenyl and aryl moieties. Coulometric data are reported for seven compounds.

The polarographic reducibilities of styrene[4] and biphenyl[5] are considered manifestations of the general phenomenon of conjugation inasmuch as the π-electronic systems, as present in benzene and ethylene,[6] are not similarly reducible. In general, one might anticipate that the electroreducibility of any biaryl or arylalkene would depend on at least three inherently different (but closely associated) factors, *viz.* (a) the conjugative powers

(1) Abstracted (in part) from the Ph.D. dissertation of C. D. Lind, University of Oregon, June, 1956. This research was supported in part by a grant from The Petroleum Research Fund administered by the AMERICAN CHEMICAL SOCIETY and in part through sponsorship by the Office of Ordnance Research, U. S. Army, contract no. DA-04-200-ORD-176. Grateful acknowledgment is hereby made to these donors.

(2) Presented (in part) at the Northwest Regional Meeting of the AMERICAN CHEMICAL SOCIETY, Spokane, Washington, June, 1957. Paper XI in the series on Chemical Reactivities of Arylcycloalkenes. For paper X see ref. 15.

(3) Research Associate, 1957–1958.

(4) H. A. Laitinen and S. Wawzonek, *J. Am. Chem. Soc.*, **64**, 1765 (1942).

(5) S. Wawzonek and H. A. Laitinen, *J. Am. Chem. Soc.*, **64**, 2365 (1942).

(6) M. v. Stackelberg, *Polarographische Arbeitsmethoden*, W. de Gruyter and Co., Berlin, 1950, pp. 210–211.