enylamine which was characterized by its benzoyl derivative. Lack of time prevented efforts to improve the yields of the amines in this series.

Experimental[4]

2-Nitro-2-ethylbicyclo[2.2.1]heptene-5 (I).—A solution of 37 g. (0.37 mole) of freshly distilled 2-nitro-1-butene[5] and 32 g. (0.55 mole) of cyclopentadiene containing 0.1 g. of hydroquinone was heated in an autoclave at 103–115° for three hours, then allowed to cool overnight. The dark brown reaction product was first distilled from a Claisen flask at reduced pressure. After removal of the forerun containing unreacted starting materials and the dimer of cyclopentadiene, the adduct distilled at 75–78° (5 mm.) as a light yellow liquid; yield 38 g. (61%). Fractionation of this product through a small column yielded a colorless liquid with a camphor-like odor. The physical constants of a center cut were b.p. 79° (5 mm.), $n^{20}\text{D}$ 1.4888.

Anal. Calcd. for $C_9H_{13}NO_2$: C, 64.63; H, 7.83. Found: C, 64.46; H, 7.58.

Reduction of I.—A solution of 19.5 g. (0.12 mole) of I in 50 ml. of methanol was reduced with Raney nickel (3 g.) and hydrogen at slightly more than atmospheric pressure and room temperature. The solvent was removed by distillation and the 2-amino-2-ethylbicyclo[2.2.1]heptane was isolated in the usual manner. The amine distilled as a colorless liquid, b.p. 59–60°, $n^{20}\text{D}$ 1.4825, yield 7 g. (44%).

Anal. Calcd. for $C_9H_{17}NO$: C, 77.62; H, 12.31. Found: C, 77.74; H, 12.56.

The benzoyl derivative of the amine melted at 193–194°.

Anal. Calcd. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70. Found: C, 79.20; H, 8.70.

2-Nitro-2-methylbicyclo[2.2.1]heptene-5 (II).—A solution of 40 g. (0.46 mole) of 2-nitropropene[6] and 65 g. (1 mole) of cyclopentadiene was heated in an autoclave for 90 minutes and allowed to cool overnight. The dark brown liquid yielded a main fraction (24 g., 34%), b.p. 70° (10 mm.), which solidified on cooling. The crude product was purified by vacuum sublimation to yield a waxy, colorless solid m.p. 84–86°. The compound sublimed near the melting point.

Anal. Calcd. for $C_8H_{11}NO_2$: C, 62.72; H, 7.24. Found: C, 62.90; H, 7.40.

Reduction of II.—A solution of 14 g. (0.09 mole) of II in 50 ml. of methanol was reduced as described above. The 2-amino-2-methylbicyclo[2.2.1]heptane distilled as a colorless liquid, b.p. 60° (20 mm.), $n^{20}\text{D}$ 1.4809, yield 5 g. (45%).

Anal. Calcd. for $C_8H_{15}N$: C, 76.73; H, 12.08. Found: C, 76.50; H, 12.25.

The benzoyl derivative of the amine melted at 134–135°.

Anal. Calcd. for $C_{15}H_{19}NO$: C, 78.56; H, 8.35. Found: C, 78.26; H, 8.46.

4-Nitro-4-ethyl-1-cyclohexene (III).—A solution of 15 g. (0.5 mole) of 2-nitro-1-butene, 18 ml. (0.21 mole) of butadiene and 0.1 g. of hydroquinone was heated in a Carius tube at 120–130° for four hours. The adduct distilled at 82–84° (5 mm.), $n^{21}\text{D}$ 1.4810, yield 8.5 g. (37%).

Anal. Calcd. for $C_8H_{13}NO_2$: C, 61.91; H, 8.44. Found: C, 62.24; H, 8.64.

Reduction of III.—A solution of 13 g. of III in 50 ml. of methanol was reduced as described above. The 1-amino-1-ethylcyclohexane distilled at 63.65° (17 mm.), $n^{20}\text{D}$ 1.4603, yield 6.6 g. (62%).

Anal. Calcd. for $C_8H_{17}N$: C, 75.52; H, 13.47. Found: C, 75.39; H, 13.65.

The benzoyl derivative of the amine melted at 101.5–102°.

Anal. Calcd. for $C_{15}H_{21}NO$: C, 77.88; H, 9.15. Found: C, 77.69; H, 9.34.

1,2-Dimethyl-4-nitro-4-ethyl-1-cyclohexene (IV).—A solution of 36 g. (0.35 mole) of 2-nitro-1-butene and 56 g. (0.68 mole) of dimethylbutadiene was heated in an autoclave at 125–130° for two hours. The adduct distilled at 94–94.5° (8 mm.), $n^{20}\text{D}$ 1.4837, yield 17 g. (40%).

Anal. Calcd. for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35. Found: C, 65.40; H, 9.26.

Reduction of IV.—A solution of 20 g. of IV in 50 ml. of methanol was reduced as outlined above. The unsaturated amine, 1,2-dimethyl-4-amino-4-ethyl-1-cyclohexene, distilled at 107–110° (30 mm.), $n^{20}\text{D}$ 1.4811, yield 6 g. (28%).

Anal. Calcd. for $C_{10}H_{19}O$: C, 78.36; H, 12.50. Found: C, 78.19; H, 12.45.

The benzoyl derivative of the amine melted at 103–104°.

Anal. Calcd. for $C_{17}H_{23}NO$: C, 79.33; H, 9.01. Found: C, 97.31; H, 9.20.

4-Nitro-5-(2-thienyl)-1-cyclohexene (V).—ω-Nitro-2-vinylthiophene[7] (5.4 g. 0.35 mole) and 15 ml. of butadiene were heated in a Carius tube at 140° for six hours. The crude adduct was recrystallized from petroleum ether (60–70°) and decolorized with activated charcoal. The white crystals so obtained melted at 69–70°, yield 4.5 g. (61%).

Anal. Calcd. for $C_{10}H_{11}NO_2S$: C, 57.39; H, 5.30. Found: C, 57.42; H, 5.49.

4-Nitro-5-(2-thienyl)-1,2-dimethyl-1-cyclohexene (VI).—Dimethylbutadiene (8.2 g., 0.1 mole) and 7.7 g. (0.05 mole) of ω-nitro-2-vinylthiophene were heated in a Carius tube for six hours at 140°. The adduct was recrystallized from alcohol and melted at 80.5–81°, yield 10 g. (84%).

Anal. Calcd. for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37. Found: C, 60.88; H, 6.62.

Reduction of VI.—A solution of 2.3 g. of VI in absolute ether was reduced with lithium aluminum hydride by the procedure of Gilsdorf and Nord,[8] but not enough of the amine was obtained for purification by distillation. The crude amine was converted to its benzoyl derivative, m.p. 191.5–192°.

Anal. Calcd. for $C_{19}H_{21}NOS$: C, 73.28; H, 6.79. Found: C, 73.54; H, 6.57.

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[4] The carbon and hydrogen analyses were done by K. T. Zilch and J. A. Gallagher.

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[8] R. T. Gilsdorf and F. F. Nord, *ibid.*, **15**, 807 (1950).

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Condensations with Halogenated Aldehydes. IX.[1] β,β,β-Trichloro-α,α-bis-(halogenotolyl)-ethanes, β,β,β-Trichloro-α,α-bis-(hydroxy-(or methoxy)-dichlorophenyl)-ethanes and Related Compounds

BY RANDOLPH RIEMSCHNEIDER[2]

RECEIVED JANUARY 12, 1953

In connection with stereochemical and toxicological[3,4] studies we have prepared several of the highly substituted ethanes named in the title. Table I summarizes the data for the DDT analogs prepared by Baeyer condensation from chloral and the twelve monohalogenotoluenes, 2,4-dichlorophenol or 2,4-dichloroanisole. Their behavior toward alcoholic potassium hydroxide was studied quantitatively (see Table I, last column) and on a preparative scale (Table II). The position of the substituents in the aromatic nuclei was deduced from the mode of formation of the compounds and from their behavior toward alkali, and toward chromic anhydride in acetic acid.

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[1] Paper VI, *Monatsh.*, **83**, 828 (1952); paper V, *Z. Naturforsch.*, **7b**, 277 (1952). Earlier papers cited there. See also 2nd supplement to the 1st supplementary volume of *Pharmasie*, **99**, 177 (1947), and *Z. Naturforsch.*, **6b**, 179 (1951); **7b**, 251 (1952).

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[3] R. Riemschneider, *Z. angew. Entomol.*, **35**, 2/4 (1953).

[4] *Cf.* paper presented on April 1, 1953, at the Chemists' Meeting in Innsbruck, Austria. *Cf. Angew, Chem.* **65**, 267 (1953).

TABLE I

β,β,β-TRICHLORO-α,α-BIS-[X-PHENYL]-ETHANES

X	M.p., °C.	Yield,[a] %	Solvents[b] of recrystn.	Formula	Carbon, %		Hydrogen, %		Chlorine, %		Mole % HCl evolved in 0.1 *N* methanolic KOH at 15–18° after, hr.,			
					Calcd.	Found	Calcd.	Found	Calcd.	Found	1	5	20	72
2-Methyl-4-chloro	107.5–108[c,d]	90	E	$C_{16}H_{13}Cl_5$	50.2	49.8	3.42	2.99	46.3	46.2		0.50	0.59	0.82
2-Methyl-5-chloro	158[c]	72	E	$C_{16}H_{13}Cl_5$	50.2	50.4	3.42	3.23	46.3	46.1		0.32	0.40	0.69
3-Methyl-4-chloro	70–71[e]	86	P, M[f]	$C_{16}H_{13}Cl_5$	50.2	50.9	3.42	3.90	46.3	46.2	0.85	1.0		
2-Methyl-4-bromo	100–101	90	E	$C_{16}H_{13}Cl_3Br_2$	40.8	41.1	2.78	2.64	22.5	21.9[g]		0.49	0.54	0.82
2-Methyl-5-bromo	182–183	83	E	$C_{16}H_{13}Cl_3Br_2$	40.8	41.2	2.78	3.12	22.5	22.2[h]		0.34	0.48	0.78
3-Methyl-4-bromo	108–109[j]	80	P, M[f]	$C_{16}H_{13}Cl_3Br_2$	40.8	41.6	2.78	2.55	22.5	22.9[i]	0.91	1.0		
2-Methyl-4-iodo	159	83	Pr, E	$C_{16}H_{13}Cl_3I_2$	34.0	34.0	2.30	2.63	18.8	18.9		0.46	0.77	1.0
2-Methyl-5-iodo	170–171	74	Pr, E	$C_{16}H_{13}Cl_3I_2$	34.0	34.0	2.30	2.45	18.8	18.6[k]		.41	0.71	0.84
3-Methyl-4-iodo	112–114[l]	72	Pr[f]	$C_{16}H_{13}Cl_3I_2$	34.0	33.8	2.30	2.01	18.8	19.2	0.60	.90	1.0	
"2-Methyl-4-fluoro"	[m,n]	91		$C_{16}H_{13}Cl_3F_2$	54.9	54.8	3.72	3.70	30.4	30.0				
2-Methyl-5-fluoro	109[n]	84	E	$C_{16}H_{13}Cl_3F_2$	54.9	55.0	3.72	3.58	30.4	31.1		0.60	0.80	1.0
3-Methyl-4-fluoro	58.5–59.5[n]	88	E	$C_{16}H_{13}Cl_3F_2$	54.9	54.7	3.72	3.80	30.4	30.5	1.0			
2-Hydroxy-3,5-dichloro	187[q]	36	E	$C_{14}H_7O_2Cl_7$	36.9	36.8	1.50	1.70	54.5	54.3				
2-Methoxy-3,5-dichloro	160[r,s]	31	E	$C_{16}H_{11}O_2Cl_7$	39.7	39.8	2.20	2.10	51.3	51.4	[t]			
2-Methoxy-3,5-dichloro	154[s]		E	$C_{16}H_{11}O_2Cl_7$	39.7	39.9	2.20	2.80	51.3	51.1	[u]			
4-Chloro[o]	107.5–108.2										0.99			
4-Methyl[o]	89[p]										0.17	0.34	0.65	1.0

[a] Yields of crude, dried products from the *Baeyer* condensation are given. [b] E, ethanol; P, *n*-pentane; M, methanol; Pr, *n*-propyl alcohol. [c] O. Stephenson and W. A. Waters [*J. Chem. Soc.*, 339 (1946)] report 107 and 156°, respectively. [d] P. Müller [*Helv. Chim. Acta*, **29**, 1560 (1946)] reports this compound to melt at 99–100°. [e] B.p. 206.5–208° (1.5 mm.). [f] Recrystallized 2–5 months after vacuum distillation from pentane and then methanol. [g] Calcd.: Br, 33.9. Found: Br, 33.3. [h] Calcd.: Br, 33.9. Found: Br, 33.4. This compound is very sparingly soluble in ethanol. [i] Calcd.: Br, 33.9. Found: Br, 34.0. [j] B.p. 207.5–209° (0.12 mm.). [k] Calcd.: I, 44.9. Found: I, 44.4. [l] B.p. 236–232° (0.7 mm.). [m] B.p. 191–194° (5 mm.), contains the 4-methyl-2-fluoro isomer. [n] R. Riemschneider, ref. 6, pp. 692–693; also *Gazz. chim. ital.*, **78**, 826 (1948). [o] Included for comparison purposes. [p] *Z. Naturforsch.*, **6b**, 181 (1951). [q] R. Riemschneider, *Z. angew. Entomol.*, **35**, 2/4 (1953). The diacetate melts at 178°. Calcd. for $C_{18}H_{11}O_4Cl_7$: C, 40.0; H, 2.00. Found: C, 40.5; H, 2.03. [r] Stereoisomer of the subsequent compound. [s] Unchanged by attempted acetylation. [t] 5–6 hr., 0.99. [u] 5–6 hr., 0.72.

TABLE II

β,β-DICHLORO-α,α-BIS-[X-PHENYL] ETHYLENES

X	M.p., °C.	Solvents[a]	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
2-Methyl-4-chloro	99[d]	M	$C_{16}H_{12}Cl_4$	55.5	55.8	3.46	3.44
2-Methyl-5-chloro	144[b,d]	E	$C_{16}H_{12}Cl_4$	55.5	55.7	3.46	3.09
3-Methyl-4-chloro	92–93.5[c]	M	$C_{16}H_{12}Cl_4$	55.5	56.1	3.46	3.80
2-Methyl-4-bromo	71–72	E	$C_{16}H_{12}Cl_2Br_2$	44.2	44.8	2.78	2.71
2-Methyl-5-bromo	163–164.5	E	$C_{16}H_{12}Cl_2Br_2$	44.2	44.5	2.78	3.02
3-Methyl-4-bromo	73–73.5	M	$C_{16}H_{12}Cl_2Br_2$	44.2	44.8	2.78	2.66
2-Methyl-5-iodo	149–150	E	$C_{16}H_{12}Cl_2I_2$	36.3	36.9	2.28	2.53
2-Methoxy-3,5-dichloro	157[g,i]	E	$C_{16}H_{10}O_2Cl_6$[e]	42.9	42.3	2.20	2.61
2-Methoxy-3,5-dichloro	166[h]	E	$C_{16}H_{10}O_2Cl_6$[f]	42.9	42.9	2.20	2.10

[a] See Table I, ref. *b*. [b] O. Stephenson, *et al.*, (Table I[c]) report m.p. 142°. [c] Oxidized by CrO_3 in boiling acetic acid to 3,3′-dimethyl-4,4′-dichloro-benzophenone, m.p. 141–142°, oxime m.p. 132°. [d] Unchanged on treatment with CrO_3 in boiling acetic acid. [e] Calcd.: Cl, 47.5. Found: Cl, 47.3. [f] Calcd.: Cl, 47.5. Found: Cl, 47.6. [g] Prepared from $C_{16}H_{11}O_2Cl_7$ (I), m.p. 160° (Table I). [h] Prepared from $C_{16}H_{11}O_2Cl_7$ (I), m.p. 154° (Table I). [i] Stereoisomer of the subsequent compound.

According to the mode of preparation of β,β,β-trichloro-α,α-bis-(2-methoxy-3,5-dichlorophenyl)-ethane, two different substances, m.p. 160 and 154°, are obtained, and the same is true for the corresponding ethylene of which we obtained two forms, m.p. 157 and 166°. The reasonable assumption of restricted rotation offers a rational explanation for the isomerism observed; reference to Stuart models will illustrate this phenomenon. In fact, such considerations were part of the incentive to the present investigation.[4] Stuart models of β,β-dichloro-α,α-bis-(2-methoxy-3,5-dichlorophenyl)-ethylene show that the rotation of the benzene rings is restricted, which leads to the prediction of three possible configurations of which two have the relation of object and mirror image (Fig. 1). The situation regarding the corresponding ethane is more complex because here one may

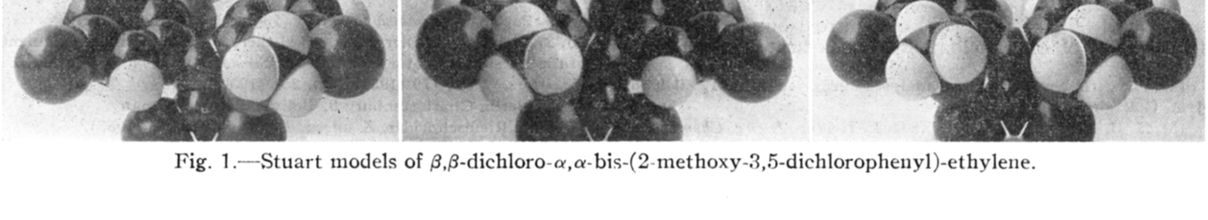

Fig. 1.—Stuart models of β,β-dichloro-α,α-bis-(2-methoxy-3,5-dichlorophenyl)-ethylene.

assume restricted rotation of the benzene rings, of the methoxyl groups, or of both. We are studying this question in greater detail.

Experimental Part[5]

Preparation of the β,β,β-Trichloro-α,α-bis-(halogenotolyl)-ethanes.[6]—To a mixture of 2.2 parts of monohalogenotoluene and 1 part of chloral 98.5% sulfuric acid was added with strong stirring during a period of 30 minutes; quantities of 0.03–0.05 mole of chloral were used, and 6 g. of sulfuric acid was employed for 1 g. of chloral. Ordinarily the reaction temperature was 10°, but in the case of the iodotoluenes it was 1–2°. A reaction period of 2 hours is sufficient for the quantities given.

After completion of the reaction the mixture was poured on ice, the organic layer washed with water, and unchanged starting materials were steam distilled. The products were purified by recrystallization (Table I), preceded by vacuum distillation in the case of *o*-halogenotoluene derivatives (Table I[e,j,l,f]).

Preparation of β,β,β-Trichloro-α,α-bis-(2-methoxy-3,5-dichlorophenyl)-ethane (I). (a) Isomer M.p. 154°.—To a well-stirred mixture of 5 g. (0.03 mole) of chloral hydrate and 80 g. of 96% sulfuric acid was added at 10° 10 g. (0.06 mole) of molten 2,4-dichlorophenol. Two hours later the mixture was poured on ice, washed with water and with pentane and recrystallized from ethanol. One gram of the ethane so obtained was dissolved in a little ether and treated for 2 days at 0° with 100 cc. of a 4% diazomethane solution. The recovered material was recrystallized from ethanol and melted at 154° (see Table I).

(b) Isomer M.p. 160°.—To a stirred mixture of 3.3 g. (0.02 mole) of chloral hydrate and 50 g. of 96% sulfuric acid 7 g. (0.04 mole) of 2,4-dichloroanisole was gradually added at room temperature. After 4 hours the mixture was decomposed as above, washed with water and pentane, and recrystallized from alcohol, yielding the product m.p. 160° (*cf.* Table I). A mixture of the stereoisomeric I melts at ~ 135°.

The β,β-Dichloro-α,α-bis-(X-phenyl)-ethylenes.—The ethanes were boiled, in 1-g. portions, in methanol with 50–100 cc. of 0.5 N methanolic potassium hydroxide for 2–3 hours. The cooled mixtures were diluted, extracted with ether if required, and the products were recrystallized from ethanol (see Table II).

Quantitative Dehydrohalogenation of β,β,β-trichloro-α,α-bis-(X-phenyl)-ethanes.—Samples of from 75–200 mg. (±0.1 mg.) of this substance were treated at 15–18° with 25 ml. of 1 N methanolic potassium hydroxide. After intervals of 0.1, 5, 20 and 72 hours the samples were diluted with 25 ml. of water and the residual alkali was titrated with 0.25 N hydrochloric acid against phenolphthalein. The results are listed in the last column of Table I.

It was observed that the low-melting isomer of structure I is more stable toward alkali than the high-melting one; *cf.* Table I, footnotes *t*, *u*.

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(5) All melting points are uncorrected.

(6) *Cf.* R. Riemschneider, 9th supplement to the 1st supplementary volume of *Pharmazie*, 673 (1949). There references to the earlier literature are given.

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Reaction between Glycine and the Hexose Phosphates

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Some of the browning which occurs in foodstuffs during concentration, or dehydration, or during the storage of concentrated or dehydrated products, can be attributed to reactions between reducing sugars and amino compounds (the Maillard reaction).[1] Enders[2] showed that monoses became brown in the presence of glycine at different rates, with xylose the most rapid, followed by arabinose, mannose, galactose, fructose and glucose. He also found that glucose browned about 4 to 6 times as fast as "hexose diphosphate." Neuberg and Kobel[3] studied the reaction of hexose phosphates with glycine polarimetrically. However, no information has been recorded on the relative rates of browning of the now well-characterized hexose phosphates of the glycolytic cycle. Inasmuch as these may account for a considerable proportion of the reducing sugars in certain vegetables,[4] it was pertinent to determine what role they may play in "browning."

The potassium salts of the hexose phosphates in aqueous solution (0.33 M) (see Table I) were allowed to react with 0.33 M glycine at 70° for 18 hours. The free sugars were allowed to react under the same conditions in the presence and absence of 0.33 M phosphate buffer *p*H 6.5. After diluting the reaction mixture 133-fold, *p*H and color were measured. The intensity of the color was determined in an Evelyn colorimeter at 420 mμ. In Table I, degree of browning is expressed in terms of percentage of the increase in the optical density (0.296) of the diluted reaction mixture of glucose, glycine and phosphate buffer. The data show that esterification of the aldehyde group of the glucose resulted in complete inhibition of browning. On the other hand, the presence of a phosphate ester at the primary alcohol group of both glucose and fructose increases the rate of browning. The extent of browning of these phosphate esters was roughly in proportion to their reducing action toward some of the common sugar reagents.[5,6] In the absence of phosphate buffer, the extent of browning of fructose and glucose was

TABLE I

REACTION OF THE HEXOSE PHOSPHATES WITH GLYCINE[a]

Substance	*p*H Initial	*p*H Final	Brown color	Relative reducing values[b] A	Relative reducing values[b] B	Relative reducing values[b] C
Glucose, phosphate	6.5	6.1	100	100	100	100
Fructose, phosphate	6.5	6.3	28	...	...	...
Glucose-1-phosphate	7.7	7.7	0	0	0	0
Glucose-6-phosphate	6.6	5.9	146	19	80	100
Fructose-6-phosphate	6.6	6.6	82	46	80	4
Fructose-1,6-diphosphate	6.5	6.5	21	18	40	2
Glucose[c]	5.4	5.1	8	...	...	...
Fructose[c]	5.4	4.8	16	...	...	...

[a] Concentration of reactants and buffer, 0.33 M, 70°, 18 hours. [b] On a molar basis: Reagent A, Folin–Malmrose[5]; B, Hagedorn–Jensen[6]; C, Hypoiodite.[6] [c] No buffer present.

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(2) C. Enders, *Biochem. Z.*, **312**, 339 (1942).

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(6) R. Robinson and M. G. Macfarlane, *Methoden der Fermentforschung*, **1**, 312 (1940).