3- and 4-substituted bases. Where the steric requirements of the ordinate reaction are *less* than those of the abscissa reaction, the *ortho* substituted bases lie *below* the line. When the steric requirements of the two reactions are similar (Figs. 8, 12), all of the points lie on a single line.

Strains in the Transition State.—From the available data the steric requirements of a borane group in an addition compound must be quite similar to the steric requirements of a methyl group in a hydrocarbon. However, in the transition state (I) the geometry of the methyl group must be quite different from that of the borane group (II). It is therefore pertinent to inquire into the relative strains observed in an addition compound with the strains in the corresponding transition state.

In the reaction of methyl iodide with 2-*t*-butylpyridine the activation energy is 3.8–3.9 kcal./mole greater than in the corresponding reactions of 4-alkylpyridines. Consequently, it is considered that strain of this magnitude must be present in the transition state. The strain in the homomorphs of *o*-*t*-butyltoluene is considerably larger, 6.0 kcal./mole (Table II).

Similarly, from the activation energy for the reaction of pyridine and 4-picoline with methyl iodide, an activation energy of 13.3 kcal. is estimated for 2,6-lutidine. In view of the observed value, 15.1 kcal./mole, a strain of 1.8 kcal./mole is calculated for the transition state in the reaction of methyl iodide with 2,6-lutidine. An identical value is obtained for 2,4,6-collidine. The strain in homomorphs of hemimellitene is estimated to be 2.7 kcal./mole (Table II).

Thus, both in the transition state involving 2-*t*-butylpyridine and that involving 2,6-lutidine the strain estimated is approximately two-thirds the value of the strains present in the homomorphic addition compounds. If this simple relationship proves to hold in other, more hindered systems, it should provide a valuable insight into the geometry and structure of the transition state.

In conclusion, it appears that the results support the proposal that molecular addition compounds of the pyridine bases may serve as reasonably good models for transition states involving these bases and alkyl halides. Consequently, it may be hoped that the study of selected series of addition compounds may contribute to a better understanding of the precise nature of the transition states in related chemical reactions.

Lafayette, Indiana

[Contribution from the Institute of Rubber Research, University of Akron]

The Branching Reaction. I. Chain Transfer of Styrene with Thiol, Alcohol and Nitrile[1]

By Maurice Morton, J. A. Cala and Irja Piirma

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The chain transfer activity of 2-methyl-2-propanethiol, 2-methylpropionitrile, 2-propanol and 2-methyl-2-propanol in the polymerization of styrene was measured. This work was intended to measure the relative ease of formation of certain sulfur-, oxygen- or carbon-headed free radicals and thus to establish the relative activity of these radicals in abstracting hydrogen from a given compound, as it may apply to the formation of branches on a polymer chain. The following values were obtained for the rate expressions for the transfer reaction between a styrene radical and each respective compound: 2-methyl-2-propanethiol, $1.0 \times 10^6 \exp(4400/RT)$; 2-methylpropionitrile, $2.0 \times 10^6 \exp(10400/RT)$; 2-propanol, $2.3 \times 10^6 \exp(12500/RT)$; 2-methyl-2-propanol, $4.2 \times 10^6 \exp(13800/RT)$. Furthermore, measurements of the isotope effect with deuterium indicate that it is the hydroxyl hydrogen in the tertiary alcohol and the secondary hydrogen in the secondary alcohol which are involved in the chain transfer. Hence some conclusions can be drawn concerning the reactivity of the corresponding radicals in abstracting hydrogen atom. In general, the oxygen-headed free radical can be expected to be the most reactive in this respect. However, since it would only be ten to one hundred times as reactive as a carbon-headed radical, this suggests that the initiator radical could not be expected to play a major role in the branching reaction.

In the polymerization of olefinic compounds branched chains can be formed whenever a growing chain undergoes a chain transfer reaction with either a monomer or a polymer molecule. Monomer chain transfer, however, leads only to the formation of a terminal double bond in the polymer chain, and it is this double bond which can ostensibly be incorporated into another polymer chain, leading to a branched chain. Hence a monomer transfer step does not by itself lead to a branched chain but only opens the possibility of such a branched chain. Chain transfer constants for several monomers have been determined,[2-4] and these may help in estimating the possible frequency of branched chains.

It is, therefore, safe to assume that the formation of branched chains occurs predominantly through chain transfer between radicals and polymer chains, generally by abstraction of hydrogen (or other atoms) from the polymer. One of the questions which often arises concerning polymeric chain transfer is whether the attacking radical is more likely to be an initiator fragment or the chain radical itself. In view of the great predominance in concentration of the latter over the former, one

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(1) Presented in part at the 126th Meeting, American Chemical Society, Division of Polymer Chemistry, New York, September, 1954. This work was carried out under the sponsorship of the Aeronautical Research Laboratory, Wright Air Development Center, under Contract No. AF 33(616)-337.

(2) J. L. O'Brien and F. Gornick, This Journal, **77**, 4757 (1955).

(3) F. R. Mayo, R. A. Gregg and M. S. Matheson, *ibid.*, **73**, 1691 (1951).

(4) B. Baysal and A. V. Tobolsky, *J. Polymer Sci.*, **8**, 529 (1952).

might come to the conclusion that the initiator fragment has too short a lifetime to participate to any extent in chain transfer. In that case, the branching reaction in any polymerization should not be affected by the type of initiator used. However, if the chain transfer activity of the initiator fragment is very much greater than that of the chain radical, it is possible that certain initiators may affect the extent of branching. As a starting point, it would be of interest to obtain a measure of the chain transfer activity of different types of radicals. These might include the three principal types, *i.e.*, oxygen-, carbon- and sulfur-headed radicals, which might be expected to show considerable differences. If sufficiently accurate methods of evaluating the extent of branching were available, then a study of the polymers initiated by these different types of radicals could be very informative. However, in the absence of such methods, some other approach is required.

The approach used in this work was to study the lability of a given hydrogen atom in four compounds, *viz.*, 2-methyl-2-propanethiol, 2-methyl-2-propanol, 2-methylpropionitrile and 2-propanol. This was done by determining the chain transfer efficiency of these compounds in the bulk polymerization of styrene. If it is known which hydrogen atom in these compounds is participating in the chain transfer reaction with the styryl radicals, then some conclusions could be drawn concerning the reverse reaction, *i.e.*, the activity of the corresponding free radicals in abstracting hydrogen atoms. Although this would by no means afford a rigorous measure of the relative activity of the radicals in abstracting hydrogen from a given compound, it could be expected to distinguish at least between different orders of magnitude in such reactivities. Hence, if the appropriate hydrogen atoms are involved, then the dehydrogenation activity of the four radicals, $(CH_3)_3CS^\cdot$, $(CH_3)_3CO^\cdot$, $(CH_3)_2(CN)C^\cdot$ and $(CH_3)_2CHO^\cdot$ could be estimated. In those cases where some doubt can exist concerning the particular hydrogen atom participating in chain transfer, use was made of the isotope effect by preparing appropriate deuterated compounds.

Although some qualitative measure of the reactivity of the given hydrogen atom in these compounds may be available, very few quantitative data have been obtained. Such data may throw some light on the effect of different initiators on the branching reaction during polymerization.

Experimental Procedures

Materials.—Dow **styrene** was distilled under nitrogen through a 200-mm. Vigreux column to give a product which boiled at 46° (20 mm. Hg). This styrene was then stored under nitrogen in a refrigerator. The nitrogen used throughout was Airco high purity. Eastman Kodak Co. **2-methyl-2-propanethiol** was distilled and the fraction with b.p. 66° was used. Eastman **2-methyl-2-propanol** was purified by recrystallization. **2-Methylpropionitrile** was prepared by the dehydration of isobutyramide. A mixture of 2.3 moles of the finely powdered amide and 2.4 moles of phosphorus pentoxide was heated. The nitrile began to come over almost at once. Vacuum was applied intermittently to reduce the time of the reaction. The crude nitrile was collected in a flask which was cooled by ice-water. The nitrile was then redistilled over 10 g. of phosphorus pentoxide, the fraction boiling at 101–102° was again redistilled over phosphorus pentoxide and the fraction boiling at 101.5° (n^{25}_D 1.3712) was taken. Eastman **2-propanol** was distilled and the fraction with b.p. 81.5° (n^{20}_D 1.3777) was used. The benzene used for viscosities was J. T. Baker reagent grade.

Preparation of Deuterated Compounds.—For these preparations, use was made of both deuterium oxide and deuterium gas, as supplied by the Stuart Oxygen Co., San Francisco, Calif. In all cases, analogous compounds were also prepared using ordinary water and hydrogen.

(a) **2-Deuteroxy-2-methylpropane.**—This was prepared from aluminum *t*-butoxide (Matheson Co.) by refluxing with a stoichiometric amount of deuterium oxide for 2 hr., with stirring, then distilling to dryness. The distillate was redistilled over a small quantity of additional oxide. The procedure was repeated using ordinary water. Physical constants are shown in Table I.

TABLE I

PHYSICAL CONSTANTS OF $(CH_3)_3COD$

	Found		Lit. value
	$(CH_3)_3COD$	$(CH_3)_3COH$	$(CH_3)_3COH$
B.p., °C. (760 mm.)	84.2	82.5	82.8
F.p., °C.	27.0	25.0	25.5
n^{20}_D	1.3879	1.3877	1.3878

(b) **Deuteroxypropane.**—This was prepared from aluminum isopropoxide (Matheson Co.) in the same way as described above. Physical constants are shown in Table II.

TABLE II

PHYSICAL CONSTANTS OF $(CH_3)_2CHOD$

	Found		Lit. value
	$(CH_3)_2$-CHOD	$(CH_3)_2$-CHOH	$(CH_3)_2$-CHOH
B.p., °C. (760 mm.)	83.2	82.8	82.3
n^{20}_D	1.3778	1.3774	1.3776

(c) **2-Deuteroxy-2-deuteropropane.**—This compound was prepared by the low pressure deuteration of acetone with deuterium gas over platinum.[5] Preliminary experiments with ordinary hydrogen at 2 atmospheres, in presence of a 10% platinum-on-charcoal catalyst, gave a 93% yield of isopropyl alcohol after 12 hr. The catalyst was then separated by filtration, under nitrogen, after which the alcohol was distilled under nitrogen, at reduced pressure, below 40°, with ferrous salts present in the still-pot, to destroy any peroxides.

Polymerizations.—The polymerizations were carried out in one-ounce amber bottles with screw caps. The caps contained butyl gaskets which had been extracted with ethanol-toluene azeotrope. The required amount of styrene and the transfer agent were added to each bottle and the bottles were flushed with nitrogen. They were then placed in an oil-bath maintained at the required temperature ±0.2°. The bottles were then removed at 4 ± 0.5% conversion and coagulated in 200 cc. of anhydrous methanol. The polymer was filtered, redissolved in 100 cc. of benzene and reprecipitated in 500 ml. of methanol. The polymer was then filtered and dried in an oven at 105° for 4 hr.

Viscosity and Molecular Weight Determination.—The viscosity of each polymer solution was determined in a Ubbelohde dilution viscometer having an outflow time of about 100 sec. for benzene and a negligible kinetic energy correction. The solutions were made up by dissolving 0.4 g. of polymer in 100 cc. of benzene. Two 20-cc. samples were removed and dried in an oven for 2 hr. at 100° to determine the concentration of the solution. Another 20-cc. sample was removed and used for the first viscosity determination. Two subsequent dilutions were then made for viscosity determinations. A plot of η_{sp}/c *vs.* c and ln η_r/c *vs.* c gave the intrinsic viscosity when extrapolated to zero concentration.

From the intrinsic viscosity values, the number-average molecular weights were calculated by means of the equation

$$M_n = 167{,}000\ [\eta]^{1.37} \qquad (1)$$

The above equation was suggested by Mayo, *et al.*,[3] from a comparison of viscosity and osmotic pressure data.

Results

The transfer constants for each of the four compounds used in the polymerization of styrene

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(5) L. Freedman and J. Turkevich, THIS JOURNAL, **74**, 1066 (1952).

were obtained in the usual manner[6] from the relation

$$\frac{1}{\bar{P}} = \frac{1}{\bar{P}_0} + C\frac{S}{M} \qquad (2)$$

where

$\bar{P}$ = number-average degree of polymerization of the polymer obtained in presence of the solvent

$\bar{P}_0$ = number-average degree of polymerization of the polymer obtained in absence of solvent

S/M = molar ratio of solvent to monomer

C = transfer constant, *i.e.* k_{tr}/k_p where k_{tr} is the rate constant for the transfer reaction and k_p is the propagation rate constant

Since the above equation reflects an instantaneous relation, the polymerizations were restricted to very low conversions in order to avoid the complications of concentration changes. Values for the degree of polymerization were calculated from the intrinsic viscosity data using equation 1, and $1/\bar{P}$ plotted against S/M, the slope of the resulting line yielding the value of the transfer constant in accordance with equation 2. A typical plot for the 2-methyl-2-propanol is shown in Fig. 1. It can be seen that the plot is linear, as expected. Furthermore, in order to be certain that the effect on the degree of polymerization was purely due to chain-transfer and not to retardation or acceleration caused by possible impurities, a careful check was kept on the polymerization rate.

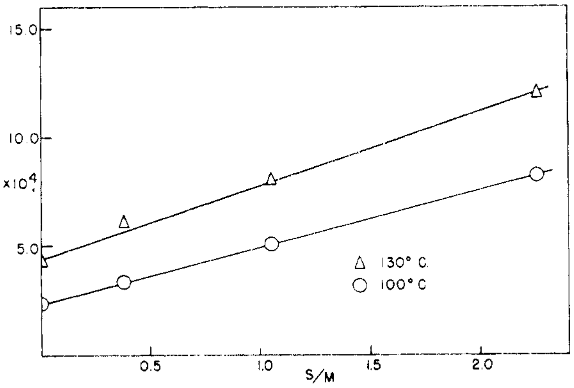

Fig. 1.—Chain transfer of styrene with 2-methyl-2-propanol.

The results for the four compounds studied are shown in Tables III to VI inclusive. It can be seen that, in general, the compounds studied behaved as chain-transfer agents, and did not affect the polymerization rate. The latter generally decreased as expected from the dilution effect, in accordance with the known second-order dependency of the rate on styrene concentration.

Table III

Transfer Constants of 2-Methyl-2-propanethiol

$S/M \times 10^4$	Rate %/hr.	[η]	$1/\bar{P} \times 10^3$	C
		60°		
0.78	0.1	1.58	0.33	
1.57	.1	1.13	0.53	3.1
3.13	.1	0.70	1.03	
6.25	.1	0.42	2.04	
		100°		
0	2.2	2.02	0.24	
1.16	2.2	1.25	.44	1.8
2.32	2.2	0.94	.68	
4.63	2.2	0.67	1.06	

Table IV

Transfer Constants of 2-Methylpropionitrile

S/M	Rate %/hr.	[η]	$1/\bar{P} \times 10^4$	$C \times 10^4$
		100°		
0	2.2	2.02	2.41	
0.38	1.4	1.54	3.45	
1.05	1.0	1.19	4.91	2.7
2.26	0.2	0.81	8.31	
		130°		
0	15.6	1.30	4.39	
0.38	10.6	1.11	6.14	
1.05	7.6	0.83	8.11	3.5
2.26	5.0	0.62	12.12	

Table V

Transfer Constants of 2-Propanol

S/M	Rate %/hr.	[η]	$1/\bar{P} \times 10^4$	$C \times 10^4$
		2-Propanol (redistilled)		
		100°		
0	2.3	2.02	2.41	
0.43	2.0	1.65	3.17	1.7
1.73	1.8	1.12	5.34	
		130°		
0	15.6	1.30	4.39	
0.43	12.2	1.09	5.57	2.7
1.16	8.6	0.92	7.0	
1.73	7.4	0.78	8.76	
		2-Propanol (from oxide)		
		100°		
0.43	1.95	1.76	2.87	1.6
1.73	1.66	1.22	4.76	
		2-Propanol (from acetone)		
		100°		
0.43	1.9	1.80	2.79	1.7
1.15	1.6	1.29	4.39	
		2-Deuteroxypropane (from oxide)		
		100°		
0.43	2.0	1.66	3.11	
1.14	1.7	1.32	4.27	1.6
1.71	1.4	1.14	5.20	
		2-Deuteroxy-2-deuteropropane (from acetone)		
		100°		
0.43	2.0	1.86	2.65	0.78
1.73	1.5	1.42	3.68	

The values obtained for the transfer constant of the thiol agree quite well with those obtained by Mayo, *et al.*[7] As expected, the other three compounds showed a very low value for the transfer constant, when compared with that of the thiol. At the temperatures studied, the transfer activity of these compounds decreased in the following order: 2-methylpropionitrile, 2-propanol, 2-methyl-2-propanol.

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(6) F. R. Mayo, This Journal, **65**, 2324 (1943).

(7) R. A. Gregg, D. M. Alderman and F. R. Mayo, *ibid.*, **70**, 3740 (1948).

TABLE VI

TRANSFER CONSTANTS OF 2-METHYL-2-PROPANOL

S/M	Rate %/hr.	$[\eta]$	$1/P \times 10^4$	$C \times 10^5$
		2-Methyl-2-propanol (recryst.)		
		100°		
0	2.2	2.02	2.41	
0.35	2.0	1.92	2.55	5.5
0.93	1.4	1.78	2.83	
2.11	...	1.52	3.51	
		130°		
0	15.6	1.30	4.39	
0.35	10.5	1.16	5.08	
0.93	7.2	1.13	5.27	10
1.15	...	1.07	5.64	
1.41	...	1.06	5.75	
2.11	2.5	1.05	5.83	
		2-Methyl-2-propanol (from oxide)		
		100°		
0	2.2	2.02	2.41	
0.35	1.6	1.92	2.56	5
0.93	1.1	1.74	2.92	
1.41	0.6	1.69	3.08	
		130°		
0	15.6	1.30	4.39	
0.35	12.0	1.25	4.60	8
0.93	8.4	1.18	5.10	
1.41	6.0	1.09	5.50	
		2-Deuteroxy-2-methylpropane		
		100°		
0	2.2	2.02	2.41	
0.24	...	1.99	2.51	
0.35	1.6	1.99	2.50	2.9
0.72	...	1.87	2.59	
0.92	1.2	1.85	2.68	
		130°		
0	15.6	1.30	4.39	
0.24	11.0	1.27	4.51	
0.46	9.3	1.23	4.78	7.8
0.75	8.6	1.18	4.94	
1.13	7.0	1.13	5.27	
1.13	7.0	1.07	5.68	

For the sake of convenience, the transfer constants of the four compounds, together with the calculated differences in activation energy between the transfer and propagation reactions ($E_{tr} - E_p$), are shown in Table VII. These results become more significant if they are used to calculate the actual rate constant of the transfer reaction (k_{tr}) from the known value of the propagation rate constant (k_p) for styrene. Using the value given by Matheson, *et al.*,[8] *i.e.*, $k_p = 2.2 \times 10^7 \exp(7800/RT)$, it is possible to calculate the absolute values for the transfer reaction rate constant, which are shown in Table VIII.

TABLE VII

TRANSFER CONSTANTS IN STYRENE POLYMERIZATION

Compound	Transfer constant (C) 60°	100°	130°	$E_{tr} - E_p$, kcal.
2-Methyl-2-propanethiol	3.1	1.8	...	−3.4
2-Methylpropionitrile	...	2.7×10^{-4}	3.5×10^{-4}	2.6
2-Propanol	...	1.7×10^{-4}	2.7×10^{-4}	4.7
2-Methyl-2-propanol	...	5.5×10^{-5}	1.0×10^{-4}	6.0

TABLE VIII

ABSOLUTE VALUES FOR TRANSFER RATE CONSTANTS

Compound	Transfer rate constant (k_{tr} in l./mole/sec.) 60°	100°	130°	E_{tr}, kcal.	A, l./mole/sec. $\times 10^{-6}$
2-Methyl-2-propanethiol	496	1000	...	4.4	1.0
2-Methylpropionitrile	...	0.16	0.44	10.4	2.0
2-Propanol	...	.087	.34	12.5	2.32
2-Methyl-2-propanol	...	.03	.13	13.8	4.2

The most noticeable feature about the values listed in Table VIII is the fact that the differences in the reactivities appear to be due almost entirely to the differences in the activation energies, the steric factor being remarkably constant for all four compounds. This is not altogether surprising since these are all tertiary type compounds and are therefore similar from a structural viewpoint, so that the difference in reactivity could be expected to arise mainly from differences in activation energy for rupture of a particular bond. These activation energy values can be discussed more intelligently if some conclusions can be made concerning the particular bonds which are involved in the chain transfer reaction.

In the case of the thiol and nitrile, there should be no doubt as to which hydrogen atom is involved in the chain transfer process. It is known that it is the sulfur–hydrogen bond in a thiol which is ruptured by the attacking free radical, while the tertiary hydrogen in the nitrile is obviously most likely to be attacked in a radical chain transfer process. However, in the case of the two alcohols, no such unambiguous conclusions can be made as to the particular hydrogen atoms involved in the chain transfer. The secondary hydrogen in the 2-propanol might be considered as most likely for such an attack, but the choice in the case of the 2-methyl-2-propanol is more difficult, since it could be either the carbon–hydrogen or the oxygen–hydrogen bond which is involved. In a discussion of the free radical mechanism of oxidation of alcohols, Bartlett[9] favors primary rupture of a carbon–hydrogen bond. On the other hand, Steacie[10] shows several mechanisms in which there is chain transfer between a free atom and the hydroxyl hydrogen of an alcohol. In view of this ambiguity, it is interesting to note the isotope effect on the chain transfer activity of these two alcohols.

The transfer constants of the deuterated analogs of the two alcohols are shown together with those of the alcohols in Tables V and VI. For control purposes, there are included also data on the two alcohols prepared by the identical procedures used in the preparation of the deuterated compounds. It is obvious at once that the replacement of the

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[8] M. S. Matheson, E. E. Auer, E. B. Bevilacqua and E. J. Hart, THIS JOURNAL, **73**, 1700 (1951).

[9] P. D. Bartlett and K. Nozaki, *ibid.*, **69**, 2299 (1947).

[10] E. W. R. Steacie, "Atomic and Free Radical Reactions," first edition, Reinhold Publishing Corp., New York, N. Y., 1946, pp. 360–361.

hydroxyl hydrogen in the 2-methyl-2-propanol by deuterium decreases the transfer constant by almost 50% at 100°, although no isotope effect was noted at 130°. The small apparent decrease in the transfer constant at the higher temperature is apparently not due to any isotope effect but to the slight acceleration in polymerization rate caused by the alcohol when prepared through the aluminum alkoxide.

In the case of the 2-propanol, however, it is also quite clear that replacement of the hydroxyl hydrogen by deuterium shows no rate effect but that replacement of the secondary hydrogen shows a definite effect. Hence it can be concluded that the chain transfer reaction involves the carbon–hydrogen bond in the secondary alcohol and the oxygen–hydrogen bond in the tertiary alcohol. The fact that the isotope effect involves only a factor of 2 instead of the usual 4 or more may suggest that other groups, *e.g.*, methyl hydrogen are also participating in chain transfer. However, there is enough indication that the above bonds are primarily involved in this reaction and that chain transfer with the methyl hydrogens would certainly not be a lower energy reaction.

The absolute values for the chain transfer rate constants listed in Table VIII can also be satisfactorily explained in the light of this information. Thus the activation energy for the rupture of the respective bonds would be expected to increase from the weakest sulfur–hydrogen bond of the thiol to the strongest oxygen–hydrogen bond of the tertiary alcohol. Furthermore the active hydrogen in the nitrile molecule would be activated to a greater extent than that of the secondary alcohol, since the nitrile group is much more polar than the hydroxyl. The relative uniformity in and low value of the frequency factor is also quite reasonable, since, in all of these compounds, the reactive hydrogen atom is shielded by three large substituent groups, *i.e.*, either three methyl groups or two methyl groups and a nitrile or hydroxyl group.

In view of the great differences found in the case of formation of these radicals, some semi-quantitative conclusions can be drawn about the relative activity in hydrogen abstraction of the four radicals corresponding to the four compounds studied. Thus the thiol radical can be safely assumed to have by far the lowest activity in abstracting hydrogen atoms, while the *t*-butoxy radical would be expected to be the most reactive. The isobutyronitrile and the hydroxy-isopropyl radicals can both be considered as carbon-headed free radicals and should be not too different in their reactivity toward hydrogen abstraction. Hence it might be concluded that an oxy radical, such as may be obtained from peroxides, may be only 5 or 10 times more active in hydrogen abstraction than a carbon-headed radical, such as forms the head of a growing radical chain. In view of the much greater predominance of growing chain radicals over initiator radicals during polymerization, it would, therefore, seem highly doubtful that the type of initiator used could seriously affect the degree of branching in the polymer chain.

AKRON 4, OHIO

[CONTRIBUTION FROM ABBOTT LABORATORIES]

Halogen Substituted Aryl Alkamine Ethers

BY M. VERNSTEN, H. B. WRIGHT AND M. B. MOORE

RECEIVED JUNE 18, 1956

A variety of halogenated phenols and naphthols has been used in the preparation of cyclic-aminoalkyl ethers for a study of their fungistatic activity.

The interest in this Laboratory in anesthetic aminoalkyl ethers[1] led to their testing for other types of biological activity. Nearly all proved to be fungistatic, and the members with halogen substituents exhibited greatly enhanced activity against fungi.

The aryl alkamine ethers here reported (Tables I–VI) were prepared for a study of the effects of position and kind of halogen, of more than one such substituent and of other substituents. Except for a few used for comparison, the amines of the aminoalkyl groups were cyclic.

Variations in .the cyclic amine usually exert much less effect upon the fungistatic activity than upon the animal toxicity. For this reason, the minimally toxic 4-morpholinyl derivatives are to be preferred. With respect to the aryl portion of the molecule, the fungistatic tests indicate superiority of the *p*-biphenylyl structure over other isomers. One halogen either on the same ring as the ether group or on the other ring of the biphenyl seems to confer maximum activity, no advantage being shown by two or three halogens. There appears to be little difference between chlorine and bromine derivatives. A second benzene ring (which may be condensed with the first) or a fairly large alkyl group is necessary for good antifungal activity.

Experimental[2]

The ethers were prepared by one of three methods.

I. (**Compounds 36–47**).—An aryloxyalkyl halide was refluxed with a large excess (up to ten equivalents) of the appropriate cyclic amine for about two hours. Distillation of most of the excess amine was followed by solution of the residue in chloroform, and water extraction of the remaining excess amine from the chloroform solution. The residual oil obtained by distillation of the chloroform was dissolved in dry ether, decolorized with carbon, filtered and the solid hydrochloride precipitated and recrystallized from 2-propanol.

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(1) (a) H. B. Wright and M. B. Moore, THIS JOURNAL, **73**, 2281 (1951); (b) **73**, 5525 (1951); (c) **75**, 1770 (1953); (d) **76**, 4396 (1954).

(2) All melting points are corrected.