[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF EMORY UNIVERSITY]

Relative Reactivities of the Common Ring Bromomethylcycloalkanes[1]

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Bromomethylcyclopentane, bromomethylcyclohexane, and bromomethylcycloheptane have each been prepared by treatment of the corresponding cycloalkylcarbinols with phosphorus tribromide and by the Hunsdiecker brominative decarboxylation of silver cycloalkylacetates. Infrared analysis of the products showed that the reaction of cyclopentylcarbinol with phosphorus tribromide gave a product containing about 20% of cyclohexyl bromide; cyclohexyl- and cycloheptylcarbinols gave no rearranged products. The Hunsdiecker reaction gave pure bromomethylcycloalkanes in moderate yields. Kinetic studies gave the following order of reactivities of the bromides toward thiophenoxide ion: bromomethylcycloheptane > bromomethylcylohexane > isobutyl bromide > bromoethylcyclopentane. An explanation is offered for this order of reactivities.

Many studies have been made dealing with the relative reactivities of functional derivatives of the common ring systems; in most of these studies the reactions involved were such that reaction occurred at a carbon atom which was a part of the ring system.[3] The influence of the common ring systems on reactions occurring at an adjacent carbon atom has been determined only in the case of certain carbonyl reactions.[4] No studies are reported in the literature dealing with the influence of ring size on displacement reactions at an adjacent saturated carbon atom.

The present investigation was undertaken to determine the influence of the three common rings on the rate of an S_N2 displacement reaction at an adjacent saturated carbon atom. To this end, the common ring bromomethylcycloalkanes have been synthesized and subjected to a typical S_N2 displacement reaction, *viz.*, reaction with sodium thiophenoxide. Thiophenoxide was chosen as the displacing agent because of its demonstrated exceptionally high nucleophilicity.[5] The reactions under kinetic conditions gave good second order rate constants. To demonstrate that the reactions studied kinetically are actually displacements, each of the reactions was carried out on preparative scale, and the resulting alkyl phenyl sulfides were isolated in high yields.

THE PREPARATION OF BROMOMETHYLCYCLOALKANES

It is well known that the bromomethyl derivatives of cyclopropane and cyclobutane cannot be prepared in a state of purity by reaction of the cycloalkylcarbinols with hydrogen bromide or phosphorus tribromide;[6] in both cases ring expansion occurs with formation of cyclobutyl and cyclopentyl bromides. A similar ring expansion is reported[7] to occur on treatment of cyclopentylcarbinol with aqueous hydrogen bromide at 100° leading to the formation of about equal amounts of bromomethylcyclopentane and cyclohexyl bromide. Other workers, however, have reported the preparation of bromomethylcyclopentane from the carbinol by treatment with hydrobromic acid[8] and phosphorus tribromide[9] with no mention of complication by ring expansion. Although Freundler reported[10] that bromomethylcyclohexane cannot be obtained in a pure state from the reaction of cyclohexylcarbinol with phosphorus tribromide, Hiers and Adams[11] have carried out this preparation with no reported difficulty from rearrangement, and others[12] have repeated the synthesis with comparable results. Bromomethylcycloheptane is reported only once in the literature;[8] it was prepared from the corresponding carbinol by the action of fuming hydrobromic acid at 100°. In summary, ring expansions definitely occur on reaction of the small ring cycloalkylcarbinols with hydrogen bro-

(1) This paper is taken from a thesis presented by Arthur H. Neal to the Graduate Faculty of Emory University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, December 1954.

(2) National Science Foundation Fellow, 1954.

(3) See Brown, Fletcher and Johannesen, *J. Am. Chem. Soc.*, **73**, 212 (1951); Van Straten, Nicholls, and Winkler, *Can. J. Chem.*, **29**, 372 (1951); Roberts and Chambers, *J. Am. Chem. Soc.*, **73**, 5034 (1951).

(4) See Menschutkin, *J. Chem. Soc.*, **89**, 1532 (1906); Zelinsky and Izgaryschew, *J. Russ. Phys.-Chem. Soc.*, **40**, 1379 (1908); Bhide and Sudburough, *J. Ind. Inst. Sci.*, **8**, 89 (1925); Vogel, *J. Chem. Soc.*, 1487 (1929); Lochte and Brown, *J. Am. Chem. Soc.*, **72**, 4297 (1950); Friess and Pinson, *J. Am. Chem. Soc.*, **74**, 1302 (1952).

(5) Quayle and Royals, *J. Am. Chem. Soc.*, **64**, 226 (1942); Bunnett and Davis, *J. Am. Chem. Soc.*, **76**, 3011 (1954).

(6) Demjanow, *Ber.*, **40**, 4959 (1907); Demjanow and Demjanow, *J. Russ. Phys.-Chem. Soc.*, **46**, 42 (1914); *Chem. Zentr.*, **85**, 1998 (1914); Smith and McKenzie, Jr., *J. Org. Chem.*, **15**, 74 (1950); Roberts and Mazur, *J. Am. Chem. Soc.*, **73**, 2509 (1951); Kuivila and Masterton, *J. Am. Chem. Soc.*, **74**, 4953 (1952).

(7) Nametkin and Morozova, *J. Russ. Phys.-Chem. Soc.*, **47**, 1607 (1915); *Chem. Abst.*, **10**, 3060 (1916).

(8) von Braun, Kuhn, and Siddiqui, *Ber.*, **59**, 1081 (1926).

(9) Noller and Adams, *J. Am. Chem. Soc.*, **48**, 1080 (1926).

(10) Freundler, *Compt. rend.*, **142**, 343 (1906).

(11) Hiers and Adams, *J. Am. Chem. Soc.*, **48**, 2385 (1926).

(12) Perlman, Davidson, and Bogert, *J. Org. Chem.*, **1**, 288 (1937) Lee, Ziering, Berger, and Heineman, *Chem. Abst.*, **41**, 6253 (1947); Solomon and Thomas, *J. Am. Chem. Soc.*, **72**, 2028 (1950).

mide or phosphorus tribromide, while the published literature leaves some question as to whether similar ring expansions occur with the common ring cycloalkylcarbinols.

In addition to the objective of obtaining pure samples of bromomethylcycloalkanes for our kinetic studies, it appeared desirable to determine whether ring expansion is characteristic of the reactions of common ring cycloalkylcarbinols with the commonly used reagent phosphorus tribromide. We have accordingly prepared each of the common ring cycloalkylcarbinols and subjected them to reaction with phosphorus tribromide. It was necessary also to prepare the bromomethylcycloalkanes by an independent method, free from rearrangements, in order to have authentic products for comparison with those derived from the carbinols. For this purpose, the Hunsdiecker brominative decarboxylation of the silver salts of carboxylic acids[13] was chosen. In only one case[14] has isomerization been reported during the Hunsdiecker reaction; in all other cases this reaction has been shown to be remarkably free from rearrangements and has been used to prepare such substances as neopentyl bromide[15] and cyclobutyl bromide[16] free from isomeric impurities.

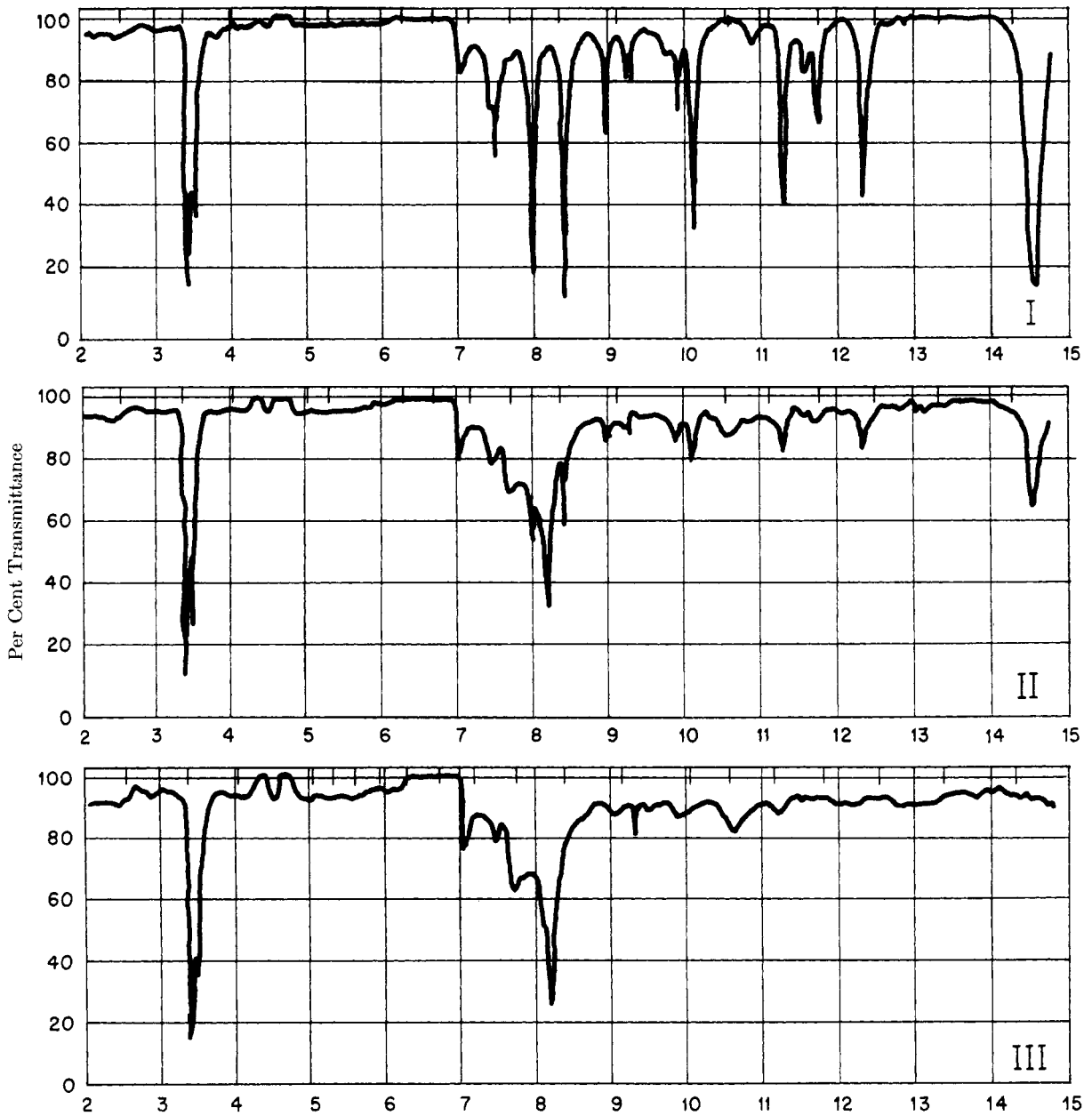
The synthetic sequences leading to bromomethylcyclopentane each used cyclopentyl bromide as starting material. Carbonation of the Grignard reagent of cyclopentyl bromide gave cyclopentyl carboxylic acid in 73% yield, and lithium aluminum hydride reduction of the acid gave cyclopentylcarbinol in 90% yield. Reaction of cyclopentylcarbinol with phosphorus tribromide gave bromomethylcyclopentane (impure, *vide infra*) in 65% yield. Cyclopentyl bromide was converted to cyclopentylacetic acid in 61% over-all yield by the malonic ester method. Formation of the silver salt and bromination according to the Hunsdiecker method gave bromomethylcyclopentane in 42% yield. The infrared spectra of the bromomethylcyclopentanes prepared by these two routes were quite different. The spectrum of the product derived from the carbinol showed twelve absorption maxima not found in the product obtained by the Hunsdiecker reaction. On comparison with the infrared spectrum of cyclohexyl bromide, the twelve extraneous bands were found to be characteristic of this substance. Assumption of Beer's law led to the estimation that the bromide obtained from cyclopentylcarbinol consisted of approximately 80% bromomethylcyclopentane and 20% cyclohexyl bromide. The bromomethylcyclopentane prepared by the Hunsdiecker method appears to be a pure substance; particularly convincing in this regard is the complete absence from its infrared spectrum of the strong 14.55 micron band characteristic of cyclohexyl bromide.

Bromomethylcyclohexane was prepared by two sequences also. Lithium aluminum hydride reduction of cyclohexanecarboxylic acid gave cyclohexylcarbinol in 95% yield, and treatment of the carbinol with phosphorus tribromide gave bromomethylcyclohexane in 47% yield. According to the second sequence, cyclohexyl bromide was converted by the malonic ester method to cyclohexylacetic acid (27%) and application of the Hunsdiecker reaction gave bromomethylcyclohexane in 58% yield. Samples of bromomethylcyclohexane prepared by the two methods showed identical infrared spectra. The sample prepared from the carbinol was also shown by the analytical method of Walling, Kharasch, and May[17] to contain no tertiary halogen; hence, the reaction proceeded without carbon skeletal rearrangement or hydrogen shift.

Cycloheptanone was the starting material for both synthetic sequences leading to bromomethylcycloheptane. Lithium aluminum hydride reduction of cycloheptanone gave cycloheptanol (89%) which on treatment with hydrobromic-sulfuric acids gave cycloheptyl bromide (92%). Since ring contraction leading to the formation of bromomethylcyclohexane and/or 1-bromo-1-methylcyclohexane might conceivably have occurred during the latter reaction, the product was shown to contain no tertiary halogen,[17] and its infrared spectrum was found not to show the characteristic absorption bands of bromomethylcyclohexane. Carbonation of the Grignard reagent from cycloheptyl bromide gave cycloheptylcarboxylic acid in 52% yield. Lithium aluminum hydride reduction of the acid gave cycloheptylcarbinol (74%) which on treatment with phosphorus tribromide gave bromomethylcycloheptane in 60% yield. According to the second synthetic procedure for bromomethylcycloheptane, cycloheptanone was condensed with ethyl cyanoacetate to give ethyl cycloheptylidenecyanoacetate (74%) which on catalytic hydrogenation over platinum oxide gave ethyl cycloheptylcyanoacetate (90%). Hydrolysis of the substituted cyanoacetic ester gave cycloheptylacetic acid (77%), and application of the Hunsdiecker reaction to this material gave bromomethylcycloheptane in 49% yield. The samples of bromomethylcycloheptane prepared by these two routes showed identical infrared spectra (Fig. 1), and the material prepared through the carbinol was shown[17] to contain no tertiary halogen.

It is clear from the present and previous[6,7] investigations that at least some rearrangement involving ring expansion occurs during the reactions of cyclopropyl-, cyclobutyl-, and cyclopentyl-

(13) Hunsdiecker and Hunsdiecker, *Ber.*, **75**, 291 (1942).
(14) Doering and Farber, *J. Am. Chem. Soc.*, **71**, 1514 (1949).
(15) Smith and Hull, *J. Am. Chem. Soc.*, **72**, 3309 (1950).
(16) Cason and Way, *J. Org. Chem.*, **14**, 31 (1949).
(17) Walling, Kharasch, and Mayo, *J. Am. Chem. Soc.*, **61**, 2693 (1939).



carbinol with phosphorus tribromide, while the corresponding reactions of cyclohexyl- and cycloheptyl-carbinol are free from rearrangements. The rearrangement reactions are adequately rationalized on the basis of a mechanism involving rearrangement of an intermediate carbonium ion in such manner as to place positive charge on the larger of two possible ring systems.[18] The absence of rearrangement on reaction of cyclohexyl- and cycloheptyl-carbinol with phosphorus tribromide suggests that these reactions proceed by way of an S_N2 type mechanism,[19] since if a carbonium ion intermediate were involved rearrangement would be expected. Indeed, ring expansions of six- and seven-membered rings are known for certain reactions proceeding by an S_N1 mechanism.[20]

DISCUSSION OF KINETIC RESULTS

Rates of reaction of bromomethylcyclopentane, bromomethylcyclohexane, bromomethylcycloheptane, and isobutyl bromide (an analogously branched aliphatic bromide) with sodium thiophenoxide in absolute ethanol were determined at 5° intervals in the temperature range 35–50°. To demonstrate that the reactions under study are straightforward substitutions, the same bromides used in the kinetic experiments were allowed to

(18) Royals, *Advanced Organic Chemistry*, Prentice-Hall, Inc., New York, N. Y., 1954, pp. 225 ff.

(19) See, for example, Gerrard, Nechvatal, and M. Wilson, *J. Chem. Soc.*, 2088 (1950).

(20) Wallach, *Ann.*, **353**, 327 (1907); Ruzicka and Brugger, *Helv. Chim. Acta*, **9**, 399 (1926).

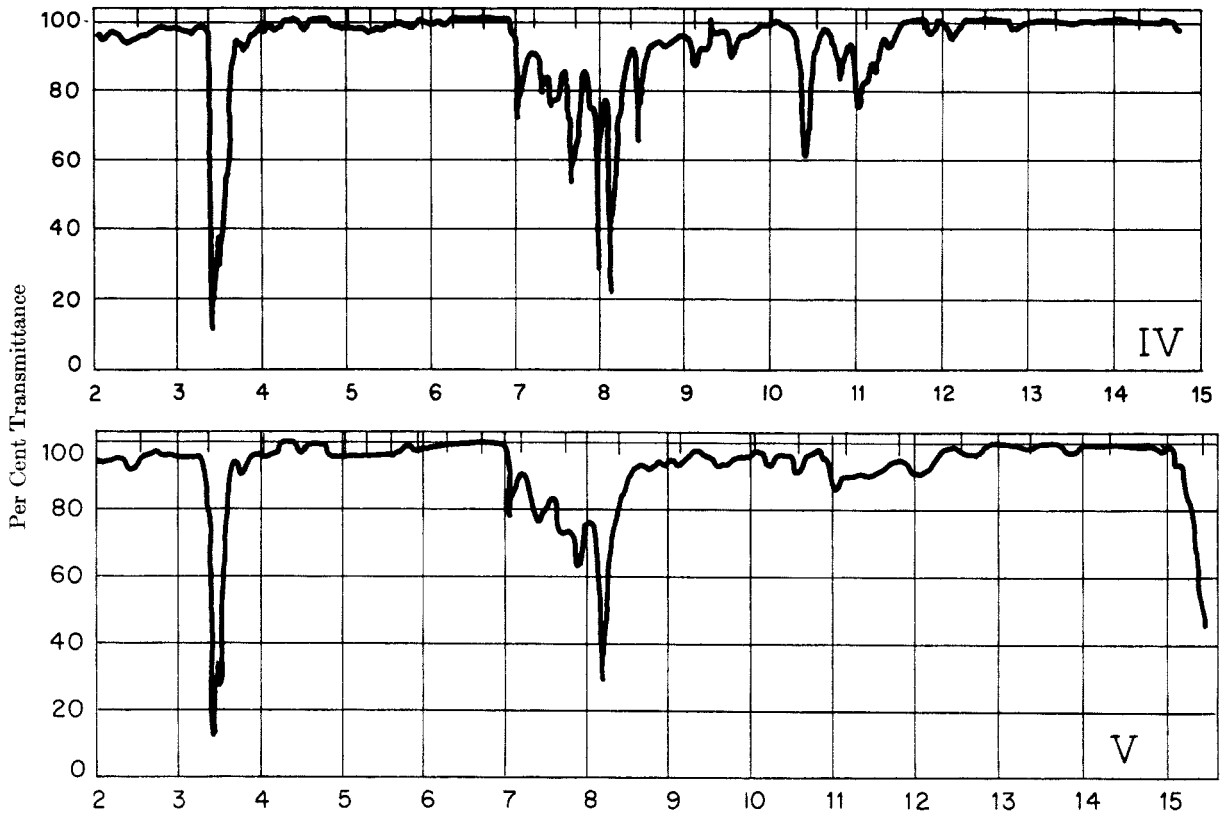


FIG. 1. INFRARED ABSORPTION SPECTRA OF: I, cyclohexyl bromide; II, product from cyclopentylcarbinol and PBr_3; III, bromomethylcyclopentane; IV, bromomethylcyclohexane; V, bromomethylcycloheptane.

react with sodium thiophenoxide on a sufficiently large scale that the products could be isolated. The conditions, except for concentration, were identical with those prevailing in the rate experiments. In each case, alkyl phenyl sulfides were isolated in high yield; the results of these experiments are summarized in Table I. Second-order rate constants were calculated using the standard equation. Good second-order constants were obtained in each case; typical rate data for variation of rate constants with temperature are illustrated by Fig. 2 for the reaction of bromomethylcyclohexane. Complete experimental data for the kinetic runs are given in the Experimental Section. In Table III are given the relative reaction rates for the four bromides studied. Due to the relatively small differences in reactivity of the bromides and the very similar temperature coefficients, the calculated thermodynamic activation constants are of doubtful significance and have not been given. Certainly, the relative rates give the best criterion for determining the effect of ring size on these reactions.

As is illustrated by the data of Table III, the relative reactivities of the halides studied toward S_N2 displacement are in the order bromomethylcycloheptane > bromomethylcyclohexane > isopropyl bromide > bromomethylcyclopentane; *i.e.*, in the common ring series of bromomethylcycloalkanes, S_N2 reactivity at a methylene unit adjacent to the ring steadily increases with increase in ring size. There is ample reason to believe that polar effects play a minor, if not negligible, role in determining this order of relative reactivities. As Friess and Pinson[4] have pointed out, the polar effects of the common ring cycloalkyl groups and of the isopropyl group are about the same, their conclusion being supported by infrared studies

TABLE I

SYNTHESIS OF ALKYL PHENYL SULFIDES, R—CH_2—S—C_6H_5

R—	B.p., °C.	mm.	n_D^{25}	Yield, %	Sulfur Calc'd	Sulfur Found
Isopropyl[a]	103–104.5	11	1.5410	86	19.28	19.70
Cyclopentyl[b]	131.5–132.5	5	1.5638	85	16.67	16.95
Cyclohexyl[b]	151–152	7	1.5592	94	15.54	15.42[c]
Cycloheptyl[b]	158–162	5–6	1.5628	87	14.55	14.68[c]

[a] V. N. Ipatieff, H. Pines, and B. S. Friedman, *J. Am. Chem. Soc.*, 60, 2731 (1938) report b.p. 107–108°/13 mm., n_D^{25} 1.5430. [b] New compound. [c] Analyses by Galbraith Microanalytical Laboratories, Knoxville Tennessee.

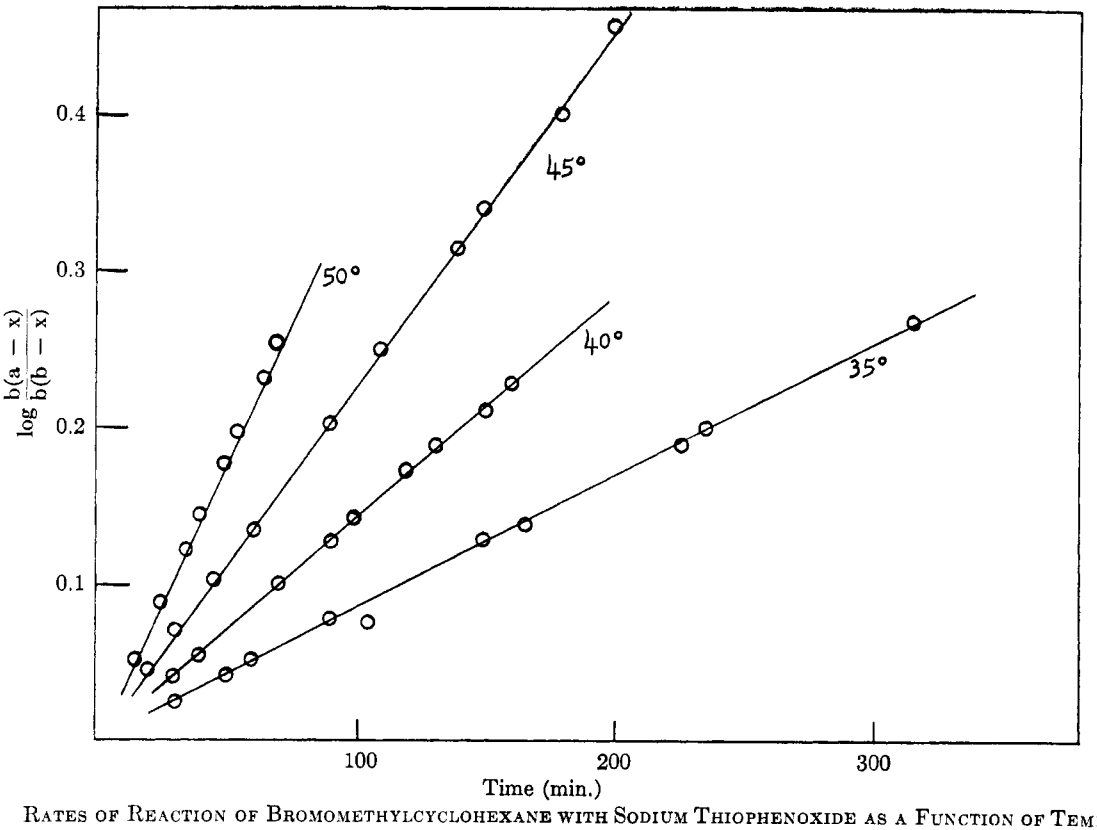


FIG. 2. RATES OF REACTION OF BROMOMETHYLCYCLOHEXANE WITH SODIUM THIOPHENOXIDE AS A FUNCTION OF TEMPERATURE.

TABLE II

RATE DATA FOR REACTION OF BROMOMETHYLCYCLOHEXANE WITH SODIUM THIOPHENOXIDE AT 45°

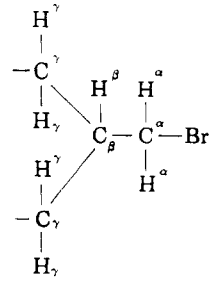
Time	Ml. of 0.01941 *N* base for titration	$\log \frac{b(a-x)}{a(b-x)}$	$k \times 10^3$ (l. sec^{-1} $mole^{-1}$)	
30	23.13	0.0676	5.77	
60	27.95	0.133	5.68	
110	32.14	0.250	5.82	
150	33.85	0.340	5.82	
200	35.20	0.457	5.85	
			5.78	Average

TABLE III

RELATIVE RATES FOR THE REACTIONS OF ALKYL BROMIDES, R—CH_2Br WITH SODIUM THIOPHENOXIDE

R—	35°	40°	45°	50°
Cyclopentyl	1.00	1.00	1.00	1.00
Isopropyl	1.05	1.11	1.08	1.07
Cyclohexyl	1.46	1.55	1.53	1.49
Cycloheptyl	2.95	2.94	2.83	2.78

of carbonyl absorption in the series of methyl cycloalkyl ketones. This conclusion has also been supported for the cyclopentyl and cyclohexyl groups by work of Roberts and Chambers.[21] It is reasonable to conclude, therefore, that the differences in reactivity do not arise from differences in the energy of the carbon-bromine bonds or differences in charge density at this bond. Steric effects must be responsible for the observed reactivities. The over-all steric influence of a substituent group in an S_N2 displacement, however, may be considered as consisting of two factors. One steric factor[22] is the ease of approach of the nucleophilic reagent to the carbon end of the carbon-bromine bond. Another effect[23] is the ease with which the three non-reacting groups attached to the reacting bond may become coplanar with the central carbon atom in the transition state. An examination of scale models of the bromides studied in this series offers some explanation for the reactivities observed. In the discussion which follows, reference to parts of the bromide molecules will be made in accordance with the diagram below.



(21) Roberts and Chambers, *J. Am. Chem. Soc.*, **73**, 5030 (1951).

(22) Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell Univ. Press, Ithaca, N. Y., 1953, Chap. VII.

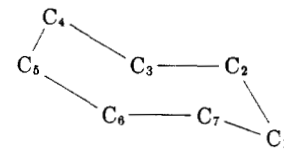
(23) Hughes, *Quart. Revs.*, **5**, 245 (1951).

Thus, the *alpha* carbon and hydrogens are those of the bromomethyl group, the *beta* carbon carries the bromomethyl group and the *beta* hydrogen, etc.

In the molecule of bromomethylcyclopentane, only one orientation of the bromomethyl group is possible because of the rigid, essentially planar structure of the cyclopentane ring. The C_α-Br bond is projected generally outward from the cyclopentane ring with consequent considerable shielding of the back side of the *alpha* carbon. Furthermore, the bromomethyl group is not free to rotate about the C_α-C_β bond so that no more favorable conformation could be achieved without considerable deformation of the ring structure and consequent high energy requirement. In addition, it appears that serious interference of the *alpha* and *gamma* hydrogens should occur in the transition state. From consideration of these factors in comparison with the other models in the series, it is apparent why bromomethylcyclopentane is the least reactive.

The preferred form of the bromomethylcyclohexane molecule would certainly appear to be the chair form of the ring with the bromomethyl group in an equatorial position. In this conformation, the back side of the *alpha* carbon is slightly shielded by the *gamma* hydrogens. Hindrance to rearward attack does not seem to be greatly reduced by rotation about the C_α-C_β bond unless the rotation is so extreme as to now cause interference of the bromine atom with *gamma* hydrogens. Steric hindrance to the reaction due to the *alpha* hydrogens becoming coplanar with the *beta* carbon in the transition state would appear to be slight. Although Orloff[24] has aptly pointed out the fallacy of assuming any one conformation of a cyclohexane derivative to be the most stable or the most reactive one, consideration of these steric factors indicates clearly that bromomethylcyclohexane should be more reactive toward S_N2 displacement than the corresponding cyclopentane compound.

Although conformational analysis of cycloheptane derivatives has not achieved the state of development characteristic of the cyclohexane series, there is evidence that the cycloheptane ring is a more flexible system than is the cyclohexane ring. Thus, whereas only *cis*-cyclohexane-1,2-diol gives a boric acid complex and forms an acetonide, both *cis*- and *trans*-cycloheptane-1,2-diol show these reactions.[25] This would seem to indicate that the energy barrier to interconversion of various cycloheptane conformations is low. Examination of Stuart-Briegleb models indicates that in any of the various conformations of the cycloheptane ring certain hydrogen atoms are oriented upward or downward from the general plane of the carbon ring in positions corresponding to that designated as "polar' or "axial"[24] in the case of cyclohexane. Certain other hydrogen atoms project generally outward in the plane of the ring and correspond to "equatorial" hydrogens. One such (perhaps idealized) conformation is diagrammed below:



In this conformation, carbon atoms 2, 3, 6, and 7 occupy a plane, while carbon 1 is below this plane and carbons 4 and 5 are above. This conformation provides a staggered conformation of adjacent hydrogens about the ring except that the hydrogens of carbons 4 and 5 are opposed. A slight shift of either carbons 4 or 5 upward from this idealized conformation would improve the staggering of adjacent hydrogens without introducing serious interference of non-adjacent hydrogen atoms. This conformation shows four hydrogens above and three below the general plane of the ring in a polar position, while the other seven hydrogens (one on each carbon) occupy equatorial positions. With a bromomethyl substituent at any one of the seven equatorial positions, there is reasonable freedom of rotation about the C_α-C_β bond. Comparing this model for bromomethylcycloheptane with the one referred to above for bromomethylcyclohexane, it appears that there is (a) less hindrance to backside attack, and (b) less interference between bromine and *gamma* hydrogen, thus permitting easier attainment of the coplanar configuration necessary in the transition state. Consideration of these factors, together with the greater general flexibility of the cycloheptane ring, would seem to rationalize the increased reactivity of bromomethylcycloheptane.

The position of isobutyl bromide in the reactivity series (about equal to that of bromomethylcyclopentane) is somewhat unexpected. Examination of the scale model of isobutyl bromide, however, shows that when the bromomethyl group is so oriented that the *alpha* carbon is most accessible from the rear, the bromine atom seriously interferes with freedom of rotation of the two methyl groups. Formation of the transition state, then, would involve a decrease in entropy leading to lower reaction rate. This effect could account for the fact that isobutyl bromide is of about the same reactivity as bromomethylcyclopentane, despite the fact that it would appear to be less hindered in the classical sense.

The order of reactivities observed in the present work for common ring derivatives does not agree with that observed for other reactions previously studied. It is readily apparent, however, why no such parallel should exist. In the previous studies of reactions at a carbon atom adjacent to a ring

(24) Orloff, *Chem. Revs.*, **54**, 347 (1954).

(25) Hermans and Maan, *Rec. trav. chim.*, **57**, 643 (1938); see also, Boeseken, *Rec. trav. chim.*, **58**, 856 (1939).

system, the reactions involved attack at a carbonyl carbon. In these cases, the carbon atom attacked originally had a coordination number of three, with the three non-reacting groups already coplanar with the central carbon atom. The stereochemical factors involved would thus be quite different from those involved in S_N2 displacement at a saturated carbon atom.

EXPERIMENTAL[26]

Preparation of cyclopentanecarboxylic acid. The Grignard reagent prepared from 100 g. (0.67 mole) of cyclopentyl bromide was poured onto crushed Dry Ice in the usual manner. Work up of the reaction mixture gave 48 g. (64%) of cyclopentanecarboxylic acid, b.p. 79–80° (5 mm.), n_D^{20} 1.4533. In a repetition of this preparation, the yield was raised to 73%.

Preparation of cyclopentylcarbinol. In a dry box, 32 g. (0.84 mole) of lithium aluminum hydride was transferred to a reaction flask containing 300 ml. of dry ether. The mixture was stirred at the reflux for one hour and allowed to stand overnight. Excess hydride was destroyed by the cautious addition of 85 ml. of water with stirring. The reaction complex was decomposed by pouring onto a mixture of 1.5 kg. of crushed ice and 100 ml. of concentrated sulfuric acid and stirring until all solid matter was dissolved. The layers were separated, and the aqueous layer was twice extracted with 100-ml. portions of ether. The combined ether solutions were dried over potassium carbonate, and the ether was removed by flash distillation. Distillation of the residue at atmospheric pressure gave 68.4 g. (68.4%) of cyclopentylcarbinol, b.p. 159–167° (mostly 160–162°), n_D^{20} 1.4554. A later repetition of this experiment gave a 90% yield.

Preparation of bromomethylcyclopentane from cyclopentylcarbinol. Cyclopentylcarbinol (40 g., 0.40 mole) was treated with phosphorus tribromide according to the procedure of Bartleson, Burk, and Lankelma.[27] Their work-up procedure. was modified somewhat. The reaction mixture after standing 20 days at room temperature was cooled in the refrigerator and was transferred to a separatory-funnel. The lower layer was removed, and the organic layer was extracted once with 10 ml. of cold 85% phosphoric acid and twice with 10-ml. portions of ice-water. After drying over calcium chloride, the product was distilled through a 6-in. Vigreux column to give 42.2 g. (65%) of bromomethylcyclopentane, b.p. 53–54.5° (14 mm.), n_D^{22} 1.4866–1.4869. [Reported[8] b.p. 58–60° (15 mm.)]. Analysis of the product for tertiary bromide by the method of Walling, Kharasch, and Mayo[17] showed 0.5%, which is hardly more than the experimental error of the method. This bromide darkened considerably on standing for two weeks.

Preparation of cyclopentylacetic acid. A solution of 23 g. (1 mole) of sodium in 300 ml. of drum methanol was added to a solution of 149 g. (1 mole) of cyclopentyl bromide in 165 g. (1 mole) of diethyl malonate at such a rate that the reaction mixture was slightly alkaline to phenolphthalein at all times.[28] The mixture was stirred vigorously and heated to about 100° throughout the addition, which required 30 hours, and for one hour thereafter. After standing overnight, about 300 ml. of methanol was removed by distillation, and 300 ml. of water was added with stirring to dissolve sodium bromide. The organic layer then was separated, combined with three 50-ml. ether extracts of the aqueous layer, and dried over sodium sulfate. Removal of the ether and distillation of the residue through a Claisen head gave 168 g. of crude diethyl cyclopentylmalonate, b.p. 55–106° (mostly 90–106°) (2 mm.), n_D^{22} 1.4268–1.4464.

The crude alkylated malonic ester was added dropwise with stirring to 300 ml. of hot, 50% aqueous potassium hydroxide. After addition was complete, the mixture was heated to reflux with continued stirring for three hours. Water, 200 ml., then was added, and alcohol and water were co-distilled until the vapor temperature reached 100°. The remaining mixture was cooled, and a chilled solution of 175 ml. of concentrated sulfuric acid in 400 ml. of water was added slowly. A white solid separated immediately, and foaming began. The mixture was heated at the reflux with stirring for three hours, during which time the solid dissolved. After standing for two days, a layer of white needle crystals completely covered the surface of the liquid. After 12 additional hours of refluxing, an oil separated, but a small amount of solid again appeared at the layer interface. An additional 100-ml. portion of concentrated sulfuric acid was added, and the mixture was refluxed for 24 hours at 110°. On cooling, only an oil appeared. This was separated and combined with three 100-ml. extracts of the aqueous phase. The combined organic mixture was dried over sodium sulfate, and the ether was removed by distillation. The pot temperature was allowed to rise to 225° and was held at this temperature for one hour. The pot was then cooled, and the pressure was reduced to effect distillation. More decarboxylation occurred when the pot temperature reached 140° at 21 mm. After eight hours, the head temperature rose slowly, and distillation occurred irregularly between 120° and 135° (21 mm.). The yield of cyclopentylacetic acid was 78.6 g. (61%), n_D^{25} 1.4505. The amide, crystallized once from water, showed m.p. 144–145°. (Reported[29] m.p. of amide, 143–145°.)

Preparation of bromomethylcyclopentane from silver cyclopentylacetate. The silver salt was prepared from 78 g. (0.61 mole) of cyclopentylacetic acid by the procedure of Cason and Way.[16] After drying overnight in an oven at 110° and for 24 hours in a vacuum desiccator, the weight of the salt was 139 g. (97%). A 1-l., 3-necked, ground-joint flask was fitted with a stirrer, pressure-equalizing funnel, and distilling head connected to a short condenser. In the flask was placed 71 g. (0.30 mole) of dry silver cyclopentylacetate and 400 ml. of carbon tetrachloride, previously dried over phosphorus pentoxide. Approximately 50 ml. of the carbon tetrachloride then was distilled with stirring. The distilling head was replaced by a reflux condenser protected by a drying tube, and the reaction mixture was cooled to 0°. A solution of 48 g. (0.30 mole) of bromine in 25 ml. of dry carbon tetrachloride was added dropwise while the temperature of the reaction mixture was kept below 10°. The addition required about 40 minutes, and decarboxylation began when about two-thirds of the bromine had been added. When addition was complete, the solution was allowed to warm to room temperature and then was heated to reflux for one hour, after which time no evolution of carbon dioxide could be detected. The mixture was cooled to room temperature, and the solvent layer was decanted through a Buchner funnel. The residue was stirred with 150 ml. of carbon tetrachloride, and the mixture was filtered on the Buchner funnel with pressure. The combined carbon tetrachloride filtrates were extracted once with 2 *N* sodium hydroxide and dried briefly over calcium chloride. The solvent was removed by distillation at atmospheric pressure until the pot temperature reached 112°. Distillation of the residue under diminished pressure gave 21.2 g. (43%) of bromomethylcyclopentane, b.p. 66.5–70° (26 mm.), n_D^{27} 1.4843.

Anal. Calc'd for $C_6H_{11}Br$: Br, 49.01. Found: Br, 49.7.

(26) Boiling and melting points reported are uncorrected. Melting points were determined on a calibrated Fisher-Johns melting point block. All elemental analyses, except those noted already in Table I, were performed by Dr. G. Weiler and Dr. F. B. Strauss, Oxford, England.

(27) Bartleson, Burk, and Lankelma, *J. Am. Chem. Soc.*, **68**, 2513 (1946).

(28) Phillips, *Ind. Chemist*, **21**, 678 (1945).

(29) Wallach and Fleischer, *Ann.*, **353**, 304 (1907).

It is quite possible that distillation of the large amount of solvent through a simple distilling head led to some loss of product.

Preparation of cyclohexylcarbinol. Commercial cyclohexanecarboxylic acid (m.p. 29.5–30.5°) was reduced by means of lithium aluminum hydride by the procedure described above for cyclopentanecarboxylic acid. Four runs using 0.1, 0.2, and 0.5 mole were made. In each case, a 25% excess of lithium aluminum hydride was used. The dried ether solutions from each successive run were flash distilled from the same distilling pot, and the combined residues were distilled to give 108 g. (95%) of cyclohexylcarbinol, b.p. 88–91° (20 mm.), n_D^{20} 1.4637–1.4646.

Preparation of bromomethylcyclohexane from cyclohexylcarbinol. Following the procedure of Hiers and Adams,[11] 58 g. (0.51 mole) of cyclohexylcarbinol was treated with phosphorus tribromide. There was obtained 42.2 g. (47%) of bromomethylcyclohexane, b.p. 78–83° (26 mm.), n_D^{25} 1.4906.

Preparation of cyclohexylacetic acid. Diethyl malonate was alkylated with commercial cyclohexyl bromide essentially according to the procedure of *Organic Syntheses*.[30] The alkylation reaction was quite slow, requiring 36 hours for completion (2 mole scale). Considerable unchanged malonic ester and cyclohexyl bromide were recovered in the work-up; the crude alkylated ester, b.p. 115–135°, was obtained in 39% yield (189 g.).

The crude diethyl cyclohexylmalonate was added dropwise with stirring to a hot solution of 200 g. of potassium hydroxide in 200 ml. of water, and the mixture was heated to reflux for three hours. An additional 100 ml. of water then was added, and alcohol was distilled from the mixture until a head temperature of 90° was reached. The solution was cooled and extracted with 75 ml. of ether to remove unreacted ester. Four hundred ml. of 50% sulfuric acid was added, and the solution was refluxed overnight. The oil which formed was extracted with ether. The combined ether extracts were dried over sodium sulfate, and the ether was removed by distillation at atmospheric pressure. On continued heating, the pot temperature rose to 225° where further decarboxylation apparently took place. Distillation of the residue gave 75.6 g. (68%) of cyclohexylacetic acid, b.p. 108–110° (3 mm.). The amide, crystallized once from water, showed m.p. 165–166°. (Reported[31] b.p. 112° (3 mm.); m.p. of amide, 168°.)

Preparation of bromomethylcyclohexane from silver cyclohexylacetate. Cyclohexylacetic acid (75 g., 0.53 mole), was converted to the silver salt by the method of Cason and Way.[25] The yield of oven-dry salt was 130 g. (99%). The silver salt was decarboxylated by the procedure previously described for silver cyclopentylacetate. The product was distilled through a Todd column packed with glass helices to give 54.3 g. (58%) of bromomethylcyclohexane, b.p. 78.5° (19 mm.) to 80.5° (21 mm.), n_D^{28} 1.4877.

Anal. Calc'd for $C_7H_{13}Br$: Br, 45.13. Found: Br, 45.7.

Preparation of cycloheptanone. Cycloheptanone was prepared by the method of Blicke, Doorenbos, and Cox.[32] The yields obtained from the first step [preparation of 1-(nitromethyl)cyclohexanol] were quite variable. Eight runs of 1 or 2 moles each were made with yields varying from 40% to 61%. The electrolytic reduction was carried out in cells similar to those described.[32] Sheet lead 1/8 in. in thickness was cut to shape for the electrodes. A Sargent-Slomin electroanalyzer was used as the source of direct current. Reaction mixtures from the reduction were used directly for diazotization. Following diazotization, the cycloheptanone was obtained by distillation from a simple Claisen still under reduced pressure. The combined cycloheptanone from all of the individual runs was distilled through a Todd column packed with glass helices to give material b.p. 177–182° (746 mm.), n_D^{20} 1.4593–1.4633, m.p. of *2,4-dinitrophenylhydrazone*, 146–147°. (Reported[32] m.p. of 2,4-dinitrophenylhydrazone, 146–147°.)

Preparation of cycloheptanol. Lithium aluminum hydride (18 g., 0.48 mole) (transferred in a dry box) was stirred for one hour with 400 ml. of dry ether at the reflux. A solution of 168 g. (1.5 mole) of cycloheptanone in 350 ml. of ether then was added over a period of three hours. The mixture was heated to reflux for an additional three hours and allowed to stand overnight. The excess hydride was destroyed by the addition of 300 ml. of moist ether. Addition of about 35 ml. of water caused inorganic salts to flocculate and settle. The ether solution was decanted, and the solid was slurried with an additional 200 ml. of ether. The combined ether solutions then were dried over sodium sulfate, and the ether was removed by flash distillation. Distillation of the residue under reduced pressure gave 131.4 g. of cycloheptanol, b.p. 80.5° (11 mm.) to 79.5° (9 mm.), n_D^{20} 1.4750–1.4762. (Reported[33] n_D^{20} 1.4760.) By dissolving the inorganic salts from the reduction mixture in 10% hydrochloric acid, extracting with ether and distilling, an additional 19.6 g. of cycloheptanol was obtained. The combined yield was 151 g. (89%).

Preparation of cycloheptyl bromide. Following the procedure of Grummitt,[34] 112 g. (0.98 mole) of cycloheptanol was treated with a hydrobromic acid-sulfuric acid solution prepared from 260 g. of ice and 240 g. (0.67 mole) of bromine. Distillation gave 159.2 g. (92%) of cycloheptyl bromide, b.p. 74–84°, mostly 79–80° (12 mm.), n_D^{24} 1.5025. (Reported[35], b.p. 75° (12 mm.), n_D^{23} 1.4996.

Preparation of cycloheptylcarboxylic acid. A 300-ml., 3-necked Grignard flask with a stopcock at the bottom was fitted with a stirrer, dropping-funnel, and reflux condenser protected by drying tubes. In the flask was placed 6.1 g. (0.25 mole) of magnesium turnings and 50 ml. of dry ether. A solution of 44 g. (0.25 mole) of cycloheptyl bromide in 150 ml. of dry ether then was added over a period of one hour. The reaction started readily, and moderate cooling was necessary. Following complete addition of the bromide, the mixture was stirred overnight. At the end of this time about 1/4 of the original magnesium remained unreacted.

The Grignard flask was attached to one neck of a 1-l., 3-necked flask equipped with a stirrer and condenser with drying tube. In this flask was placed a slurry of 300 ml. of dry ether and 500 g. of powdered Dry Ice. The Grignard solution was added to the Dry Ice slurry according to the procedure suggested by Hussey.[36] After complete addition of the Grignard solution, another 500 g. of Dry Ice was added, and stirring was continued for three hours during which time the Dry Ice evaporated. The Grignard complex then was hydrolyzed by the dropwise addition of 100 ml. of 6 *N* hydrochloric acid with vigorous stirring. The ether layer was separated, and the aqueous layer was twice extracted with 100-ml. portions of ether. The combined ether solutions were washed with water and dried over sodium sulfate. After removal of the ether by flash distillation, the residue was distilled to give 18.6 g. (53%) of cycloheptanecarboxylic acid, b.p. 133–135° (9 mm.), n_D^{27} 1.4730. [Reported[37] b.p. 130–131° (8 mm.), n_D^{20} 1.4753.] About 2 g. of a colorless liquid with a hydrocarbon odor was collected in the cold trap during the distillation. In a second preparation of cycloheptanecarboxylic acid by this procedure using 0.60 mole of cycloheptyl bromide, the yield

(30) Gilman and Blatt, editors, *Org. Syntheses*, Coll. Vol. 1, 2nd ed., 250 (1941).

(31) Ipatieff and Rasuvajeff, *Ber.*, **59**, 306 (1926); Adams and Marshall, *J. Am. Chem. Soc.*, **50**, 1970 (1928); Gutt, *Ber.*, **40**, 2067 (1907).

(32) Blicke, Doorenbos, and Cox, *J. Am. Chem. Soc.*, **74**, 2924 (1952).

(33) Pines, Edeleanu, and Ipatieff, *J. Am. Chem. Soc.*, **67**, 2193 (1945).

(34) Grummitt, *Org. Syntheses*, **19**, 88 (1939).

(35) Zilinski, *Ber.*, **35**, 2691 (1902).

(36) Hussey, *J. Am. Chem. Soc.*, **73**, 1364 (1951).

(37) Reppe, Schlichting, Klager, and Toepel, *Ann.*, **560**, 1 (1948).

was only 43%, and 20 g. of this hydrocarbon was collected in the cold trap.

Preparation of cycloheptylcarbinol. Cycloheptylcarboxylic acid (54 g., 0.38 mole), was reduced with 14 g. (0.37 mole) of lithium aluminum hydride by the procedure described above for reduction of cyclopentylcarboxylic acid. The product, 36 g. (74%) showed b.p. 77–87°, mostly 79–82°, (4 mm.), n_D^{28} 1.4748. [Reported[8, 38] b.p. 204° (49 mm.), 80–90° (15 mm.); n_D^{20} 1.4685].

Preparation of bromomethylcycloheptane from cycloheptylcarbinol. Cycloheptylcarbinol (35 g., 0.27 mole), was treated with phosphorus tribromide by the procedure of Bartleson, Burk, and Lankelma.[27] After the reaction mixture had stood for ten days, the layers were separated, and the bromide layer was poured onto solid sodium bicarbonate. The crude bromide was removed by filtration and dried over calcium chloride. Distillation through a Claisen head gave 31.3 g. (60%) of bromomethylcycloheptane, b.p. 81–94° (10 mm.), n_D^{28} 1.4967. [Reported[8] b.p. 80–82° (15 mm.)]. This bromide darkened considerably on standing. It was washed successively with cold, conc'd sulfuric acid, with 5% sodium bicarbonate, and with water. It was dried over calcium chloride and distilled through a six-in. Vigreaux column to give material b.p. 77–82° (6 mm.), n_D^{28} 1.4967.

Anal. Calc'd for $C_8H_{13}Br$: Br, 41.82. Found, Br, 41.4, 41.5.

Analysis for the presence of tertiary bromide[17] showed about 1 mole-%.

Preparation of ethyl cycloheptylidenecyanoacetate. Cycloheptanone (136 g., 1.21 mole), was condensed with ethyl cyanoacetate by the method of Cope, Hofmann, Wyckoff, and Hardenbergh.[39] Distillation gave 184 g. (74%) of ethyl cycloheptylidenecyanoacetate, b.p. 135–150°, mostly 145–146° (3 mm.), n_D^{28} 1.4974–1.4982. [Reported[40] b.p. 162–163° (14 mm.), n_D^{19} 1.5003].

Preparation of ethyl cycloheptylcyanoacetate. Platinum oxide catalyst was prepared by the procedure of *Organic Syntheses.*[41] Ethyl cycloheptylidenecyanoacetate, 41.4 g. (0.2 mole), 100 ml. of absolute ethanol, and 0.2 g. of platinum oxide were charged into a Parr low-pressure hydrogenation apparatus. With hydrogen initially at 45 p.s.i., 3.5 hours of shaking were required for absorption of the theoretical quantity of hydrogen. The catalyst was removed by filtration, and the ethanol was distilled off at atmospheric pressure. Distillation of the residue gave 37.4 g. (90%) of ethyl cycloheptylcyanoacetate, b.p. 134–139° (3 mm.), n_D^{28} 1.4650. [Reported[40] b.p. 152–154° (12 mm.), n_D^{19} 1.4664].

Preparation of cycloheptylacetic acid. Ethyl cycloheptylcyanoacetate (149 g., 0.72 mole), was added dropwise with stirring to a hot solution of 175 g. of potassium hydroxide in 150 ml. of water at such a rate as to maintain reflux. After addition was complete, stirring at the reflux was continued for one hour. Stirring became quite difficult due to separation of a large mass of white solid. An additional 100 ml. of water was added, and stirring at the reflux was continued for 40 hours during which time the solid material slowly dissolved. At the end of this time, the evolution of ammonia was barely perceptible. The solution was cooled and acidified to *p*H 2 by the dropwise addition of cold 10% sulfuric acid. The white solid which formed was filtered off. The solubility characteristics of this solid suggested that it was a mixture of the substituted malonic acid and its monoamide. The solid was refluxed an additional 36 hours with 400 ml. of 50% aqueous potassium hydroxide. The solution was cooled and extracted with 100 ml. of ether to remove any unreacted ester. The alkaline solution was acidified slowly with a cold solution of 250 ml. of conc'd sulfuric in 350 ml. of water. The acid solution was stirred at the reflux for 15 hours during which time a large oil layer separated. The oil was separated, and the aqueous layer was thrice extracted with 100-ml. portions of ether. The combined organic material was dried over sodium sulfate. The ether was removed by distillation, and the residue was dried by adding 100 ml. of benzene and distilling off. On heating the residue to 220°, additional decarboxylation seemed to occur, and the temperature was held at this point for one hour. Distillation under reduced pressure then gave 85.4 g. (77%) of cycloheptylacetic acid, b.p. 118–122° (2 mm.), n_D^{30} 1.4676. The amide, twice crystallized from ethyl acetate, showed m.p. 146–147°. (Reported[42] m.p. of amide, 146–148°.)

Preparation of bromomethylcycloheptane from cycloheptylacetic acid. Cycloheptylacetic acid (79.7 g., 0.51 mole), was converted to the silver salt by the method of Cason and Way.[16] The yield of oven-dried salt was quantitative. Reaction of the silver salt with bromine was carried out as previously described for silver cyclopentylacetate. Following work-up in the previously described manner, the carbon tetrachloride solvent was removed by distillation through a 12-in. Vigreaux column. The solution was added to the pot at such a rate that the pot temperature was maintained below 85° and the head temperature below 77°. When most of the solvent had been removed, the distilling pot was transferred to a Todd column packed with glass helices. Removal of the remaining solvent and distillation of the residue under reduced pressure gave 37.5 g. (38.5%) of bromomethylcycloheptane, b.p. 78–79.5° (5 mm.), n_D^{28} 1.4949–1.4987. During distillation of the last portions of this material the pot temperature rose to 165°, and the head temperature dropped slightly. The last portions of distillate also had a slight yellow color, and a dark, viscous pot residue (20.8 g.) was obtained. It appears that some decomposition, perhaps dehydrohalogenation, of the bromomethylcycloheptane occurred. The bromide was washed successively with cold, conc'd sulfuric acid, with sodium bicarbonate solution, and with water, dried over calcium chloride, and redistilled through a six-in. Vigreux column to give material b.p. 84–84.5° (7 mm.), n_D^{27} 1.4966–1.4980.

Anal. Calc'd for $C_8H_{15}Br$: Br, 41.82. Found: Br, 42.2, 42.4.

Preparation of alkyl phenyl sulfides: General procedure. The alkyl bromide (10–20 g., 0.07–0.15 mole) was placed in a 250-ml. Erlenmeyer flask. A solution of sodium thiophenoxide then was prepared as follows. A quantity of thiophenol 2% in excess of the moles of bromide taken was dissolved in that volume of 1.185 *N* stock solution of sodium in absolute ethanol equivalent to the thiophenol used. This sodium thiophenoxide solution then was added to the bromide, and the stoppered reaction flask was placed in a constant temperature bath at 50°. Precipitation of sodium bromide began almost immediately. After standing overnight in the bath, the reaction mixture was poured into an equal volume of water. The oil which formed was extracted with four 100-ml. portions of ether. The combined ether extracts were washed once with 50 ml. of 2 *N* sodium hydroxide solution and twice with 100-ml. portions of water. The ether solution was dried over magnesium sulfate, and the solvent was removed by flash distillation. The products were obtained by distillation of the residues through a six-in. Vigreux column under reduced pressure. The products were colorless, mobile liquids with mild odors. Data on the individual sulfides are summarized in Table I.

Kinetic studies. Reactions were run in an American Instrument Company constant-temperature bath which maintained the required temperature to ±0.04°. Reactions were timed with an electric stopclock manufactured by Standard Electric Time Corp. Bath temperatures were read from a $^1/_{10}$-degree thermometer previously calibrated

(38) Rozanov, *J. Russ. Phys.-Chem. Soc.*, **61**, 2313 (1929); *Chem. Abst.*, **24**, 3766 (1930).

(39) Cope, Hofmann, Wyckoff, and Hardenbergh, *J. Am. Chem. Soc.*, **63**, 3452 (1941).

(40) Vogel, *J. Chem. Soc.*, 2010 (1928).

(41) Gilman and Blatt, editors, *Org. Syntheses*, Coll. Vol. 1, 2nd ed., 463 (1941).

(42) Wallach, *Ann.*, **353**, 301 (1907).

TABLE IV

SUMMARY OF EXPERIMENTAL SECOND-ORDER RATE CONSTANTS

Bromide	35°	40°	45°	50°
Bromomethylcyclopentane	1.50 ± 0.04	2.35 ± 0.04	3.73 ± 0.05	6.00 ± 0.05
	1.52 ± 0.06	2.34 ± 0.05	3.77 ± 0.05	6.02 ± 0.05
Isobutyl bromide	1.57 ± 0.04	2.59 ± 0.06	4.08 ± 0.06	6.47 ± 0.04
	1.60 ± 0.07	2.60 ± 0.05	4.05 ± 0.07	6.46 ± 0.02
Bromomethylcyclohexane	2.17 ± 0.01	3.61 ± 0.02	5.70 ± 0.03	8.90 ± 0.16
	2.22 ± 0.00	3.62 ± 0.02	5.78 ± 0.05	9.07 ± 0.15
Bromomethylcycloheptane	4.45 ± 0.04	6.85 ± 0.02	10.6 ± 0.1	16.6 ± 0.2
	4.48 ± 0.02	6.92 ± 0.05	10.7 ± 0.1	16.8 ± 0.1

against a National Bureau of Standards calibrated thermometer. Standard volumetric apparatus was used.

The bromomethylcycloalkanes used in the kinetic studies were those obtained by brominative decarboxylation of silver cycloalkylacetates previously described. These materials were redistilled through a Todd fractionating column, and middle cuts of constant b.p. and refractive index were taken for use in the kinetic experiments. The isobutyl bromide was a commercial product (Matheson) which was refluxed for five hours with an equal volume of water, dried over calcium chloride, and distilled through a three-ft. Todd column packed with glass helices. A middle cut, b.p. 89.8° (737 mm.), n_D^{25} 1.4333, was taken for use. Commercial thiophenol (Matheson) was used without further purification; iodimetric analysis[43] indicated it to be 99.6% pure. The absolute ethanol used as solvent was prepared from commercial absolute ethanol by the procedure of Lund and Bjerrum.[44]

The general procedure for kinetic runs was as follows. A quantity of the alkyl bromide sufficient to prepare 200 ml. of exactly 0.1 *M* solution was accurately weighed and quantitatively transferred to a 200-ml. volumetric flask. The flask was placed in the constant-temperature bath, and after the contents had reached bath temperature, the solution was diluted to volume with absolute ethanol, also at bath temperature. A solution of 0.13 *M* sodium thiophenoxide was made up as follows. A stock solution of sodium in absolute ethanol was filtered through a Gooch funnel and standardized against weighed samples of potassium acid phthalate. The volume of this solution necessary to prepare 200 ml. of 0.13 *M* solution was calculated, and the required volume was measured into a 200-ml. volumetric flask. A quantity of thiophenol 1% in excess of the equivalents of sodium ethoxide taken then was weighed and quantitatively transferred to the flask. This solution then was diluted to volume at bath temperature as described above for the bromide solution.

A 50-ml. aliquot of the sodium thiophenoxide solution at bath temperature was pipetted into a 100-ml. volumetric flask already at bath temperature. To start the reaction, a 50-ml. aliquot of the bromide solution, at bath temperature, was pipetted into the sodium thiophenoxide solution, and the flask was quickly shaken to mix the reactant solutions. The stopcock was started when half of the bromide solution had been added to the reaction flask. At suitable time intervals, 10-ml. aliquots of the reaction mixture were withdrawn and discharged into 10 ml. of 0.1 *N* hydrochloric acid solution. The excess acid then was back-titrated with standard 0.02 *N* sodium hydroxide solution using lacmoid indicator. On addition of the 10-ml. aliquot of reaction mixture to the aqueous hydrochloric acid, a cloudy suspension was usually formed. This had the effect of "spreading" the lacmoid color change, but very reproducible endpoints were achieved by preparing a color standard and titrating to this same color in every case.

Concentrations of standard solutions were chosen so that about 16–40 ml. were used over the time intervals representing 20 to 70% reaction. In a few cases, however, reactions were followed to 95% completion with satisfactory results. Duplicate runs were made for each compound at each temperature. Four to six samples were taken in each run.

Second-order rate constants were calculated for each run using the standard equation:

$$k = \frac{2.303}{t(a - b)} \log \frac{b(a - x)}{a(b - x)}$$

where t = time in seconds, a = initial conc'n of sodium thiophenoxide, b = initial conc'n of alkyl bromide, a − x = conc'n of unreacted thiophenoxide at time t, b − x = conc'n of unreacted alkyl bromide at time t. Individual values of k obtained from each titration then were averaged to obtain k for the run. Over the entire series of rate determinations, in only one run was the average deviation of the individual rate constants from the average rate constant as high as 4%. In most cases the deviations from the mean were less then 2%. Table IV gives a summary of all rate constants obtained with their mean deviations.

In a few runs, a downward trend in the value of the rate constant was noted during the course of the reaction. This effect was most noticeable in the case of isobutyl bromide. Since the effect was not noticed in all runs with isobutyl bromide and was noted in certain runs using other bromides, it cannot be attributed to impurities or to a peculiarity of the reaction. This behavior was probably due to volatility or incomplete transfer of the bromide making the value of b in the rate equation less then the value 0.05 used in the calculations.

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(43) Siggia, *Quantitative Organic Analysis via Functional Groups*, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 85.

(44) Lund and Bjerrum, *Ber.*, **64**, 210 (1931).