

2-phenylpropan-1-ol: b.p. 108–109° (14 mm.),  $n_D^{25}$  1.5221; naphthylurethan, m.p. 100–101°.

**Hydrolysis of 3-bromo-2-phenyl-1-propene.**—A mixture of 154 g. (0.78 mole) of 3-bromo-2-phenyl-1-propene and 350 ml. of a 10% aqueous sodium hydroxide solution was refluxed eight hours with vigorous stirring. The reaction mixture was worked up in the usual manner to give 82 g. (0.61 mole) of 2-phenyl-2-propen-1-ol (79% yield); b.p. 106–107° (7 mm.),  $n_D^{25}$  1.5655; 3,5-dinitrobenzoate, m.p. 116°.

**3-Chloro-2-phenyl-1-propene.**—This compound was prepared by treating 2-phenyl-2-propen-1-ol with thionyl chloride in the presence of pyridine. Fifty-one grams of pyridine and 50 ml. of dry chloroform were placed in a 250-ml. erlenmeyer flask and cooled to 0–10°, and 71 g. (0.60 mole) of thionyl chloride was added over a period of ten minutes while the temperature was kept below 10°. This solution was then added over a period of two hours to a solution of 62 g. (0.46 mole) of 2-phenyl-2-propen-1-ol dissolved in 100 ml. of dry chloroform. The temperature was kept below 10°. When all of the thionyl chloride had been added, the mixture was refluxed for one hour. The reaction mixture was worked up in the usual manner and distilled to yield 35 g. (0.23 mole) of 3-chloro-2-phenyl-1-propene (50% yield): b.p. 87–88° (5 mm.),  $n_D^{25}$  1.5550,  $n_D^{25}$  1.5538,  $n_D^{25}$  1.5525,  $d_4^{20}$  1.0820,  $d_4^{25}$  1.0790; 3,5-dinitrobenzoate (from silver 3,5-dinitrobenzoate), m.p. 116–117°.

There was no depression of melting point when the 3,5-dinitrobenzoate was mixed with the 3,5-dinitrobenzoate from 2-phenyl-2-propen-1-ol.

*Anal.* Calcd. for C<sub>9</sub>H<sub>9</sub>Cl: Cl, 23.30. Found: Cl, 23.41, 23.37.

3-Chloro-2-phenyl-1-propene is a painful lachrymator and vesicant.

**Reaction with Potassium Iodide in Acetone at 20°.**—The usual procedure was followed.<sup>2</sup> With the modified second-order equation  $k = 2.303 \frac{1}{4} bt \log \frac{5-z}{5(1-z)}$ , a plot of  $\log \frac{5-z}{5(1-z)}$  vs. time gave a straight line between 16 and 61% reacted. Representative data are given in Table II.

**Reaction with Sodium Ethoxide in Ethanol at 50°.**—The procedure was the same as that previously described and the data were calculated using the rate expression for a second-order reaction. The sodium ethoxide solution was 0.04975 *M* and the 3-chloro-2-phenyl-1-propene was 0.05000 *M*. A plot of  $\log \frac{b(a-x)}{a(b-x)}$  vs. time gave a straight line between 29 and 77% reacted. Representative data are given in Table II.

TABLE II

RELATIVE REACTIVITY OF 3-CHLORO-2-PHENYL-1-PROPENE  
Potassium iodide in acetone at 20°

Time, hr.	0.75	2.00	3.00	3.50	4.50
Reacted, %	15.8	34.8	47.0	53.4	60.8
$k$ , hr. <sup>-1</sup> mole <sup>-1</sup> l.	1.17	1.12	1.12	1.17	1.12
	0.509	0.484	0.488	0.507	0.489
Av. $k$					1.14 ± 0.02

Relative reactivity<sup>a</sup>

2.27

Sodium ethoxide in ethanol at 50°

Time, hr.	6.25	11.5	14.0	41.0	52.0
Reacted, %	29.4	42.6	47.7	73.2	76.8
$k$ , hr. <sup>-1</sup> mole <sup>-1</sup> l.	1.34	1.30	1.32	1.34	1.29
Av. $k$					1.32 ± 0.02

Relative reactivity<sup>b</sup>

1.12

<sup>a</sup> Allyl chloride as 1.00 with  $k = 0.502$ . <sup>b</sup> Allyl chloride as 1.00 with  $k = 1.18$ .

**Infrared Spectra.**—The infrared spectra data were obtained through the courtesy of R. K. Kitson and the Chemical Division, Polychemicals Department, E. I. du Pont de Nemours and Company, Inc. The spectra were made in the liquid phases using a Perkin-Elmer Model 21 double-beam spectrophotometer. Sodium chloride optics were used with a cell thickness of 0.037 mm. The following are the principal wave lengths in microns (w = weak, vw = very weak, m = medium, s = strong, vs = very strong).

**3-Bromo-2-phenyl-1-propene (β-Phenylallyl Bromide).**—3.25 s, 5.11 w, 5.30 w, 5.55 m, 5.85 m, 6.20 s, 6.33 m, 6.67 s, 6.92 s, 7.19 m, 7.63 m, 8.20 s, 9.30–9.37 m, 9.56 w, 9.72 m, 10.25 m, 10.99 s, 11.90 w, 12.54 m, 12.88 s, 13.2 s, 13.3 vs, 13.9 s, 14.4 s.

**2-Phenyl-2-propen-1-ol (β-Phenylallyl Alcohol).**—2.95 vs, 3.26 s, 3.47 s, 5.10 w, 5.29 w, 5.50 w, 6.10 s, 6.22 m, 6.32 m, 6.67 s, 6.91 s, 7.1 s, 7.66 m, 8.15 m, 8.99 s, 9.31 m, 9.56 vs, 9.75 vs, 11.08 vs, 12.8 vs., 14.20 vs.

**3-Chloro-2-phenyl-1-propene (β-Phenylallyl Chloride).**—3.25 m, 3.51 w, 3.65 w, 5.08 w, 5.28 w, 5.49 w, 6.10 m, 6.20 m, 6.31 m, 6.66 s, 6.86 s, 7.13 m, 7.64 m, 7.91 s, 8.59 w, 9.03 w, 9.32 w, 9.70 m, 10.56 m, 11.01 s, 12.87 vs, 13.31 s, 14.35 vs.

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## Separation of Alkylated Ketones

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A method for the separation of the mixture of tetraalkylated ketones obtained in the Haller-Bauer alkylation was developed. Using this procedure, 2,2-dimethylcyclohexanone was synthesized in an over-all yield of 59% and 2-methyl-decalone in an over-all yield of 77%.

The Haller-Bauer method of alkylating ketones,<sup>3</sup> using sodamide and alkyl halides, has been widely used but very often leads to a mixture of products that is very difficult to separate. Thus, Haller<sup>4</sup> methylated 2-methylcyclohexanone (I) to produce a mixture of 85% of 2,2-dimethylcyclohexanone (II) and 15% of 2,6-dimethylcyclohexanone (III), determined by conversion to their benzylidene derivatives. Separation of II and III by distillation was difficult and the pure ketones were obtained in

very low yield by fractional crystallization of their semicarbazones and subsequent hydrolysis. Johnson and Posvic<sup>5</sup> were able to synthesize II in an over-all yield of 32% in four steps, using their very elegant isopropoxymethylene blocking group to direct the methyl group into the 2-position of the cyclic ketone. Using this enol ether method, Horning, Horning and Platt<sup>6</sup> alkylated 2,3-dimethylcyclohexanone to obtain 2,2,3-trimethylcyclohexanone in a 32% yield.

Although the method of Johnson and Posvic<sup>5</sup>

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(3) A. Haller, *Bull. soc. chim.*, [4] **31**, 1073 (1922).

(4) A. Haller, *ibid.*, [4] **39**, 1724 (1926); [4] **41**, 367 (1927).

(5) W. S. Johnson and H. Posvic, *This Journal*, **69**, 1361 (1947).

(6) E. C. Horning, M. G. Horning and E. J. Platt, *ibid.*, **71**, 1771 (1949).

ensures that only the tetraalkylated ketone with three of four alkyl groups on one side of the carbonyl will be obtained, the procedure is long and tedious. It seemed reasonable, therefore, that in those cases where a substantial amount of the desired unsymmetrical ketone could be produced by direct alkylation, a chemical separation of the mixture of products would be preferable. If a convenient chemical separation of II and III was found, a short, direct synthesis of pure II would be possible.

Elliot and Linstead<sup>7</sup> applied a chemical separation to obtain pure II from the mixture of alkylated ketones, using condensation with ethyl oxalate, decarbonylation, hydrolysis, and decarboxylation. However, their procedure, which was inferior to that of Johnson and Posvic, required over 3 days to carry out and produced II in less than 25% yield from the alkylated mixture. A much improved separation was developed by treating the mixture of the two ketones II and III with ethyl formate and sodium methoxide to produce a mixture of the formylated ketone, 2,2-dimethyl-6-hydroxymethylencyclohexanone (IV) and unreacted III. Only IV has a highly active hydrogen, so that when the reaction mixture is poured into ice-water, the sodium salt of IV is soluble in the water while III plus any unreacted II can be extracted with benzene. Steam distillation of the aqueous solution of IV produced II in an over-all yield of 59%, based on the original ketone I. It should be noted, however, that even if only 46% of 2,2-dimethylcyclohexanone (II) were produced in the alkylation instead of 85%, a final yield of II equal to that obtained in the four-step procedure of Johnson and Posvic would be possible.

If a tetraalkylated ketone with a hydrogen on both sides of the carbonyl group is desired, the method of Johnson and Posvic is not applicable. In those cases where a substantial proportion of the desired ketone is obtained by direct alkylation, the chemical separation is very successful. Thus, Cook and Lawrence<sup>8</sup> methylated decalone-1 (V) to obtain a mixture of predominately 2-methyldecalone-1 (VI) plus some 9-methyldecalone-1 (VII). In their synthesis, VI was not isolated in the pure state but was identified by fractional crystallization of its oxime in an unreported yield.

However, if the mixture of VI and VII was treated with ethyl formate and sodium ethoxide, a mixture of the formylated ketone VIII plus unreacted VI was produced. Since only VIII has a highly active hydrogen, addition of ice-water to the reaction mixture, followed by extraction with benzene, removed the unreacted VI. Subsequent distillation gave pure VI in a 77% over-all yield. The alternative method for the introduction of the 2-methyl group into decalone would have been the long, tedious procedure of introduction of a carbethoxy group, alkylation and then ketone cleavage of the alkylated  $\beta$ -keto ester. Because of the number of steps involved in this alternative procedure, the over-all yield would be low. Thus, even if less

than 50% of VI were produced in the direct alkylation, the final yield would be greater than by the indirect method.

In the synthesis of tetraalkylated ketones with only two  $\alpha$ -hydrogens, a convenient chemical separation of the mixture of isomeric ketones obtained by alkylation has been developed. The method is useful only in those cases where the desired ketone is produced in substantial amounts in the alkylated mixture. If direct alkylation does not produce a substantial percentage of the desired isomer, an indirect method, such as the introduction of a blocking group or an activating group, must be employed. However, direct alkylation, followed by this chemical separation, should be seriously considered in every case because of the great saving of time and material.

### Experimental<sup>9</sup>

**2,2-Dimethylcyclohexanone (II).**—To a solution of 22 g. (0.19 mole) of 2-methylcyclohexanone (I) in 125 ml. of anhydrous ether in a 500-ml., three-necked flask, fitted with a condenser, a stirrer and a dropping funnel, was added, in small portions, 7.6 g. (0.20 mole) of sodamide. After the initial vigorous reaction had subsided and the mixture had been heated under reflux to expel the ammonia, 28.4 g. (0.20 mole) of methyl iodide was added dropwise, with stirring, over a period of 30 minutes and the mixture was heated under reflux for 3 hours. The reaction mixture was poured into 500 ml. of ice-water and the organic layer was washed successively with 50-ml. portions of 1 *M* tartaric acid solution, 1 *M* sodium thiosulfate solution, 1 *M* sodium bicarbonate solution and water. The ether solution was dried over magnesium sulfate and the ether was removed by distillation to leave a residue of a mixture of 2,2-dimethylcyclohexanone (II) and 2,6-dimethylcyclohexanone (III). This crude mixture plus 27.5 g. (0.37 mole) of ethyl formate was added dropwise, with stirring, to an ice-cold suspension of 70 g. (1.30 moles) of alcohol-free sodium methoxide in 150 ml. of dry benzene. After the mixture, protected with nitrogen, had stood overnight at room temperature, it was poured into 200 ml. of ice-water. The benzene layer was extracted twice with cold dilute sodium hydroxide and the aqueous layers were combined with the original aqueous layer. After an extraction with ether, the combined aqueous solution was acidified with 10% hydrochloric acid, saturated with sodium chloride, and extracted with ether. The ether was removed by distillation, and the crude 2,2-dimethyl-6-hydroxymethylencyclohexanone was dissolved in 1500 ml. of 5% sodium hydroxide solution. After a slow distillation, the distillate was saturated with sodium chloride and extracted several times with ether. The ether extracts were dried over magnesium sulfate, the ether was removed by distillation, and the residue was distilled through a 6-inch, helix-packed column to yield 14.1 g. (59%) of 2,2-dimethylcyclohexanone (II), b.p. 168–170° (740 mm.) (2,4-dinitrophenylhydrazone, m.p. 125–126°).

**2-Methyldecalone-1 (VI).**—Using the above procedure, 10.0 g. (0.066 mole) of decalone was methylated with 2.75 g. (0.07 mole) of sodamide and 10.0 g. (0.07 mole) of methyl iodide. The crude methylated product was treated with 24 g. (0.40 mole) of ethyl formate and 7.5 g. of sodium methoxide in 320 ml. of dry benzene, as described above. (Working up the alkali-soluble fraction produced only 0.6 g. of crude material, indicating that very little 9-methyldecalone-1 was produced in the methylation.) The benzene solution of the alkali-insoluble portion was dried over magnesium sulfate, the benzene was removed by distillation, and the residue was distilled through a 6-inch, helix-packed column to yield 7.9 g. (77%) of 2-methyldecalone-1 (VI), b.p. 96–99° (4 mm.), 2,4-dinitrophenylhydrazone, m.p. 222–223° (reported<sup>8</sup> m.p. 223–224°).

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(9) All melting points are corrected.

(7) G. H. Elliot and R. P. Linstead, *J. Chem. Soc.*, 776 (1938).

(8) J. W. Cook and C. A. Lawrence, *ibid.*, 817 (1937).