

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

Epoxyethers. XIV.^{1,2} The Reaction with Grignard Reagents without Rearrangement

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Epoxyethers which contain two alkyl groups on the epoxide carbon atom were shown to react with Grignard reagents without rearrangement. From epoxyether I the methoxy alcohols III, IV, and V were prepared in about 75% yield using phenyl-, α -naphthyl-, and *p*-tolylmagnesium bromide, respectively. The structures of III and V were proven by independent synthesis. Epoxyether II gave the methoxyalcohol VI, the structure of which was shown by degradation. The methoxyalcohols were characterized by pinacol rearrangements.

One of the reactions studied early in the investigation of the chemistry of epoxyethers was the reaction with Grignard reagents.³ The two examples of epoxyethers used at that time were prepared from *alpha*-bromopropiophenone and desyl chloride. Each of these epoxyethers reacted with phenylmagnesium bromide to give two isomeric products. One product resulted from the attack of the Grignard reagent upon the ketal carbon of the epoxide and the other product resulted from rearrangement of the epoxyether to an *alpha*-methoxyketone followed by reaction with the Grignard reagent. The rearrangement could be eliminated by the use of diphenylmagnesium instead of the Grignard reagent. Subsequent investigation of the rearrangement of epoxyethers⁴ showed that rearrangements involving migration of an alkyl group were significantly more difficult than those involving migration of an aryl group or a hydrogen. Those results led to the prediction⁴ that dialkyl epoxyethers such as I or II might react with the Grignard reagent without the complication of rearrangement and provide a useful route to the methoxyalcohols

of the type shown by formula III-VI. The present investigation has confirmed that prediction.

The epoxyether I reacted smoothly with three different aromatic Grignard reagents to give about 75% yield of products. The product from phenylmagnesium bromide was a low-melting solid III, the structure of which was proven by independent synthesis. The methoxyketone VII had previously been prepared in this laboratory⁵ and when allowed to react with methylmagnesium bromide gave III in 51% yield.

The product from the reaction of I with *p*-tolylmagnesium bromide was also synthesized independently by the same approach. The methoxyketone VIII was prepared in 57% yield from the parent ketone by bromination followed by solvolysis of the bromoketone with methyl alcohol. The methoxyketone VIII, when treated with methylmagnesium bromide, gave 54% of IV identical in all respects with the product from the epoxyether.

A second example of a dialkyl epoxyether (II) also reacted readily with phenylmagnesium bromide to give 80% of a crystalline methoxyalcohol (VI). Evidence for the structure VI was the isolation of 54% of cyclohexanone from a cleavage reaction with strong base. Since the epoxyether II is known to rearrange to an *alpha*-methoxy cycloheptanone in the presence of magnesium bromide,⁴ rearrange-

(1) The previous paper in this epoxyether series involved the determination of stereochemistry, *J. Org. Chem.*, **23**, 336 (1958).

(2) This work was supported in part by the Office of Ordnance Research, U. S. Army.

(3) C. L. Stevens, M. L. Weiner, and C. T. Lenk, *J. Am. Chem. Soc.*, **76**, 2698 (1954).

(4) C. L. Stevens and S. J. Dykstra, *J. Am. Chem. Soc.*, **76**, 4402 (1954).

(5) C. L. Stevens and C. T. Lenk, *J. Org. Chem.*, **19**, 538 (1954).

ment prior to addition of the Grignard reagent would be expected to result in a cycloheptanol derivative. The isolation of cyclohexanone from the basic degradation eliminates the cycloheptanol structure for VI.

In each of the Grignard reactions reported here the nucleophilic reagent has cleanly attacked the ketal carbon, which is in accord with the direction of opening of the oxide ring in the other acid catalyzed reactions of epoxyethers. A comparison of the synthetic approach to the methoxyalcohols *via* the epoxyethers with the approach followed in the independent synthesis indicates the former is the method of choice.

The methoxyalcohols III, IV, and VI were further characterized by an acid catalyzed pinacol-type rearrangement. The methoxyalcohol III was converted by concentrated sulfuric acid into the methyl ketone IX in 60% yield. With IV the same transformation was best done with concentrated hydrochloric acid in dioxane solution. The product of methyl migration X was formed in 58% yield. The methyl ketone IX is a known compound and the infrared and ultraviolet spectra of IX and X support the assigned structure. The carbonyl absorption bands in the infrared occur at 5.83 and 5.84 microns, respectively, indicating unconjugated carbonyl groups and the ultraviolet curves have no maxima near 240 m μ .

A similar rearrangement of the cyclohexyl methoxyalcohol VI would be expected to yield a cycloheptanone derivative. Instead, the methyl

ether group was cleaved, the aromatic group migrated, and the product was the known phenyl ketone XI. The carbonyl absorption band in the infrared occurred at 5.95 microns and the ultraviolet spectrum had λ_{\max} 240; ϵ 8,650.

EXPERIMENTAL

Reaction of epoxyethers I and II with the Grignard reagents. The following directions apply for each reaction. An ether solution of the Grignard reagent was prepared from 5.84 g. (0.24 g.-atom) of magnesium and 37.7 g. (0.24 mole) of bromobenzene and cooled to 0°. At this temperature 10 g. (0.06 mole) of epoxyether⁶ (1,2-epoxy-2-methyl-1-methoxy-1-phenylpropane, I) was added slowly. After addition was complete, the reaction was brought to the reflux temperature for five minutes and then poured onto a mixture of 50 g. of ice and 200 ml. of water containing 25 g. of dissolved ammonium chloride. The organic layer was separated, dried, and the ether evaporated. The residue was distilled to give 11.2 g. (72%) of 1,1-diphenyl-1-methoxy-2-methyl-2-propanol (III), b.p. 134–135° (4 mm.); n_D^{25} 1.5631; m.p. 51–52°.

Anal. Calcd. for C₁₇H₂₀O₂: C, 79.65; H, 7.87. Found: C, 79.79; H, 8.23.

From 5 g. (0.03 mole) of epoxyether I and 0.056 mole of α -naphthylmagnesium bromide was obtained 6.8 g. (79%) of 1-(α -naphthyl)-1-phenyl-1-methoxy-2-methyl-1-propanol (IV), b.p. 173–174° (0.4 mm.). The product was a glass at room temperature.

Anal. Calcd. for C₂₁H₂₂O₂: C, 82.32; H, 7.23. Found: C, 82.14; H, 7.23.

With *p*-tolylmagnesium bromide and the epoxyether I (5 g., 0.03 mole) the product was 73% of 1-phenyl-1-(*p*-tolyl)-1-methoxy-2-methyl-2-propanol (V), b.p. 125–130° (0.2 mm.); n_D^{25} 1.5623.

Anal. Calcd. for C₁₈H₂₂O₂: C, 80.0; H, 8.15. Found: C, 79.85; H, 8.11.

The reaction of 0.15 mole of phenylmagnesium bromide with 0.01 mole of epoxyether II (2-methoxy-2-phenyl-1-oxaspiro[2.5]octane)⁷ gave 80% yield of 1-(α -methoxybenzhydryl)cyclohexanol (VI), m.p. 137–139°.

Anal. Calcd. for C₂₀H₂₄O₂: C, 81.00; H, 8.10. Found: C, 81.18; H, 8.17.

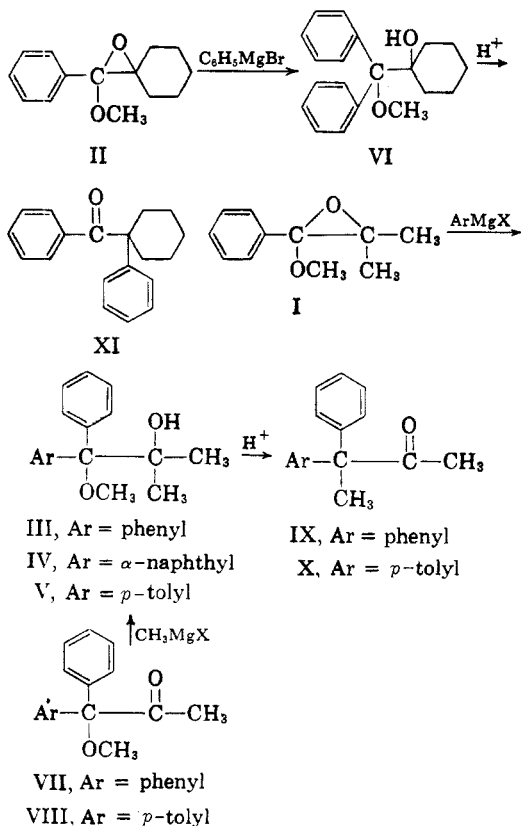
Methoxyalcohols III and V by independent synthesis. 1,1-Diphenyl-1-methoxy-2-propanone⁸ (1 g., 4.1 mmoles) was allowed to react with excess methylmagnesium iodide in ether solution at the reflux temperature for five minutes. From the reaction was obtained 0.41 g. (51%) of III, m.p. 51–53°. A mixture melting point with III from the epoxyether was not depressed.

The synthesis of V started with phenylacetone. The Organic Syntheses⁹ procedure for diphenylacetone was used except that toluene was substituted for benzene. From 37 g. (0.277 mole) of phenylacetone was obtained 32 g. (52%) of 1-phenyl-1-(*p*-tolyl)-2-propanone, b.p. 130–132° (0.8 mm.); n_D^{25} 1.5730.

From 1 g. of the ketone was obtained 0.55 g. of an oxide derivative, m.p. 134–136°.

Anal. Calcd. for C₁₆H₁₇NO: C, 80.27; H, 7.16. Found: C, 80.47; H, 7.35.

The ketone was brominated and the resulting bromoketone solvolyzed in methyl alcohol according to the procedure published for the preparation of III.⁸ From 7 g. of ketone was obtained 4.55 g. (57%) of 1-phenyl-1-(*p*-tolyl)-



(6) C. L. Stevens and T. H. Coffield, *J. Am. Chem. Soc.*, **80**, 1919 (1958).

(7) C. L. Stevens and E. Farkas, *J. Am. Chem. Soc.*, **74**, 618 (1952).

(8) E. M. Schultz and S. Mickey, *Org. Syntheses*, **29**, 38 (1949).

1-methoxy-2-propanone, b.p. 120–121° (0.15 mm.); n_D^{25} 1.5652.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.16. Found: C, 80.54; H, 7.23.

Excess methylmagnesium bromide reacted with 2.26 g. of the α -methoxyketone to give 1.3 g. (54%) of V, identical with the product from the epoxyether reaction as shown by the physical properties, b.p. 110–112° (0.08 mm.), n_D^{25} 1.5623 and the infrared spectra.

Cleavage of 1-(α -methoxybenzhydryl)-cyclohexanol (VI) with base. A solution of 3.2 g. of methoxyalcohol VI in 10 ml. of 40% sodium hydroxide and 10 ml. of 95% glycerin was heated to the reflux temperature and 10 ml. of distillate removed and discarded. The remainder was heated at the reflux temperature for 1 hr., after which a distinct odor of cyclohexanone was present. Ten ml. of water was added and a 10-ml. portion of distillate collected. After this procedure was repeated once, the 20 ml. of distillate were combined, saturated with sodium chloride, and extracted with ether. The ether was evaporated and the cyclohexanone content of the residue determined by the method of Iddles and Jackson.⁹ The yield of 2,4-dinitrophenylhydrazone of cyclohexanone was 54% and the identity was established by comparison with an authentic sample.

Pinacol rearrangement of the methoxyalcohols III, IV, and VI. One-half gram of III was dissolved in 5 ml. of concentrated sulfuric acid, allowed to stand at room temperature for 2 hr., and then poured onto cracked ice. The resulting mixture was extracted with ether and the ether solution washed and dried. After the solvent was removed the residue crystallized. Recrystallization from petroleum ether gave 0.26 g. (60%) of the known 1,1-diphenyl-1-methyl-2-propanone,¹⁰ m.p. 40–42°. The semicarbazone¹¹ melted at 175–177°.

(9) H. A. Iddles and C. E. Jackson, *Ind. Eng. Chem., Anal. Ed.*, **6**, 454 (1934).

(10) K. Sisido and H. Nozaki, *J. Am. Chem. Soc.*, **70**, 777 (1948).

(11) W. Parry, *J. Chem. Soc.*, **99**, 1169 (1911).

For the pinacol rearrangement of IV, a solution of 0.4 g. of the methoxyalcohol in 5 ml. of dioxane and 5 ml. of concentrated hydrochloric acid was allowed to remain at room temperature overnight. The product was isolated as from the sulfuric acid procedure and recrystallized from petroleum, m.p. 98–100°. The yield was 0.21 g. (58%).

Anal. Calcd. for $C_{20}H_{18}O$: C, 87.55; H, 6.61. Found: C, 87.59; H, 6.87.

The methoxyalcohol VI gave 36% of 1-phenylcyclohexyl phenyl ketone,¹² m.p. 73–75° using the sulfuric acid procedure. Because the yield was low, an infrared spectrum was taken of an aliquot of the total crude product to determine whether a ketone was present with an unconjugated carbonyl group. Only the absorption band corresponding to the conjugated carbonyl (6.0 microns) appeared in the spectrum.

The hydrochloric acid-dioxane procedure gave 66% of the same ketone, m.p. 65–70°, but in this case an aliquot of the total crude ketone gave an infrared spectrum which contained a very small unconjugated carbonyl band at 5.85 microns.

The fused zinc chloride-acetic anhydride procedure of Lyle and Lyle¹² gave 100% of crude product, m.p. 58–66° with no evidence for the isomeric ketone.

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[CONTRIBUTION FROM THE RESEARCH STATION, THE BRITISH PETROLEUM COMPANY LIMITED]

Preparation and Physical Properties of Sulfur Compounds Related to Petroleum. VIII. *trans*-2-Thiabicyclo[3.3.0]octane

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trans-2-Thiabicyclo[3.3.0]octane has been synthesized; its physical properties are recorded, and it has been characterized by the preparation of derivatives.

In previous papers in this series, the preparation and properties of eight of the nine possible thiabicyclo-octanes containing fused five- and six-membered rings, have been described.^{1–3} The preparation and properties of the remaining isomer, *trans*-2-thiabicyclo[3.3.0]octane (V), referred to in a

note⁴ on the *cis-trans* isomerization of cyclic sulfones, are detailed below.

In view of the attention recently paid to systems which contain two *trans*-1,2-fused five-membered rings, *trans*-2-thiabicyclo[3.3.0]octane is of special interest; little has been reported of these systems and only a few are known.⁵ Until recently, stereochemical considerations indicated that in such a system the *trans*-configuration would involve considerable strain within the molecule. The work of

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(2) S. F. Birch, R. A. Dean, N. J. Hunter, and E. V. Whitehead, *J. Org. Chem.*, **22**, 1590 (1957).

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(4) S. F. Birch, R. A. Dean, and E. V. Whitehead, *Chem. & Ind. (London)*, 409 (1956).

(5) H. Booth, F. E. King, J. Parrick, and R. L. St. D. Whitehead, *Chem. & Ind. (London)*, 466 (1956).