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The Grignard Reaction of 3-Halotropolone Methyl Ethers[1]

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The Grignard reaction of the methyl ethers (I and III) of 3-bromotropolone and those (II and IV) of 3-chlorotropolone with methylmagnesium iodide or phenylmagnesium bromide were investigated. When I or II was allowed to react with methylmagnesium iodide, 2-methoxyphenyldimethylcarbinol (V) and 2-methoxy-6-isopropylphenol (VI) were obtained. The reaction of I or II with phenylmagnesium bromide afforded 2-phenyl-7-halotropones (XIII or XVII), accompanied by 2-halobenzophenones (XV or XVIII) and the triphenylcarbinol derivative (XIV). The Grignard reaction of III or IV using phenylmagnesium bromide gave 2-phenyl-3-halotropones (XVI or XIX). The mechanistic pathway for the formation of these products was discussed.

The Grignard reaction of troponoid derivatives has attracted much attention as a useful tool for the synthesis of alkyl[2,3] and aryl derivatives.[4-10] In addition, peculiar interest is also attached to the mechanism of the Grignard reactions because they are one of the most complicated nucleophilic reactions of the troponoid system. For instance, unexpected abnormal substitution reactions[6,11-13] and rearrangement reactions leading to benzenoid derivatives,[7,10-13] as well as the expected normal substitutions, usually take place, depending on the variety of substituents presented on the tropone ring, the kind of Grignard reagents,[10,11] and the

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[1] Reaction of the Seven-membered Aromatic Compound with Organometallic Compound. VIII. Preceding paper: T. Mukai, H. Tsuruta and Y. Momotari, This Bulletin, **40**, 1967 (1967).

[2] T. Nozoe, T. Mukai and T. Tezuka, *ibid.*, **34**, 619 (1961).

[3] A. P. ter Borg, R. van Helden and A. F. Bickel, *Rec. Trav. Chim.*, **81**, 591 (1962).

[4] W. von E. Doering and C. F. Hisky, *J. Am. Chem. Soc.*, **74**, 5688 (1952).

[5] T. Nozoe, T. Mukai and I. Murata, *Proc. Japan Acad.*, **29**, 169 (1953).

[6] R. D. Haworth and P. B. Tinker, *J. Chem. Soc.*, **1955**, 911.

[7] T. Nozoe, T. Mukai, J. Minegishi and T. Fujisawa, *Sci. Repts. Tohoku Univ.*, **37**, 388 (1953).

[8] T. Nozoe, S. Seto, T. Ikemi, T. Sato and K. Watanabe, *ibid.*, **38**, 130 (1954).

[9] K. Kikuchi, *Nippon Kagaku Zassi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **77**, 1439 (1956).

[10] K. Kikuchi, *ibid.*, **81**, 505 (1960).

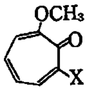
[11] K. Kikuchi, This Bulletin, **33**, 628 (1960).

[12] F. Osaki, M. S. Thesis, Tohoku Univ., 1963.

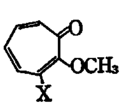
[13] T. Nozoe, T. Mukai and I. Murata, *Proc. Japan Acad.*, **28**, 142 (1952).

reaction conditions used.[14]

A few papers, however, have been reported on the Grignard reactions of the troponoid with two active functional groups, such as halogen or methoxyl groups.[13,14] To elucidate in more detail the Grignard reaction of such tropone derivatives, the reactions of 3-bromotropolone methyl ethers (I and III) and 3-chlorotropolone methyl ethers (II and IV) with methylmagnesium iodide and phenylmagnesium bromide were reinvestigated. In this series of experiments, an ethereal solution of the Grignard reagent was added to an ethereal solution of I—IV at room temperature in order to avoid the further reaction of tropone derivatives with an excess of the Grignard reagents present.

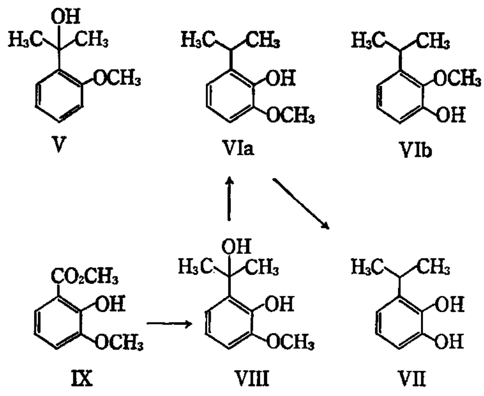


I X=Br
II X=Cl



III X=Br
IV X=Cl

The reaction of I with 2.5 equivalents of methylmagnesium iodide afforded an oil in a 80% yield; this oil was found by vapor phase chromatographic analysis to be composed of four compounds in a ratio of 1 : 10 : 10 : 1. The oil was, by the use of column chromatography, separated into two main components (V and VI), both of which had the same formula, $C_{10}H_{14}O_2$. Compound (V), with a shorter retention time in the vapor phase chromatography, showed the presence of a hydroxyl group (3571 cm^{-1}) in its IR spectrum, but it was not phenolic. The NMR spectrum of V exhibited signals ascribed to two methyl groups (singlet at τ 8.51, 6H) and a methoxyl group (singlet at τ 6.14, 3H) besides a phenyl group (multiplet at τ 2.97, 4H). These data suggest that V is *o*-methoxyphenyl dimethyl carbinol. The final decision of the structure of V was made by a comparison of its infrared spectrum and vapor phase chromatographic retention time with those of an authentic sample.[15] The ultraviolet spectrum of compound VI exhibited an absorption maximum at 277 mμ, suggesting that VI is a rearranged benzenoid derivative. Compound VI indicated the presence of a hydroxyl group (3524 and 1220 cm^{-1}) and adjacent three hydrogens of substituted benzene (779 and 821 cm^{-1}) in the infrared spectrum. Its NMR spectrum showed signals due to an isopropyl group (doublet at τ 8.79 and multiplet at τ 6.77, J=7 cps, 7H), a methoxyl group (singlet at τ 6.14, 3H), a hydroxyl group (singlet at τ 4.48, 1H), and aromatic protons (ABC-type pattern centered at τ 3.33). The demethylation of VI by treating it with hydrobromic acid in acetic acid afforded an oily product (VII), $C_9H_{12}O_2$, which was soluble in a dilute sodium hydroxide solution and which showed green coloration with ferric chloride, indicating the presence of the phenolic hydroxyl group. The NMR spectrum of VII was almost the same as that of VI, except for the lack of a singlet ascribed to the methoxyl group. On the basis of the above data, two structures VIa and VIb may be proposed for the rearranged product VI, and the structure VII, for the demethylated product. However, compound VI was sparingly soluble in a dilute sodium hydroxide solution and showed no coloration with ferric chloride. These facts suggest that the phenolic hydroxyl group of VI is hindered severely, leading to VIa being preferred to VIb. The structural proof of VI was carried out by the synthesis of VI using proven manner.



The reaction of methyl 3-methoxysalicilate (IX)[16] with methylmagnesium iodide afforded colorless crystals (VIII), $C_{10}H_{14}O_2$, which showed infrared and NMR spectra consistent with the structure of the expected 2-hydroxyisopropyl-6-methoxyphenol (see Experiment Section). Catalytic hydrogenation of VIII in the presence of a trace of acid resulted in the consumption of one equivalent of hydrogen and produced an oil, which was found to be completely identical with VI by a comparison of their infrared spectra. Thus compound VI was proved to be 6-isopropyl-2-methoxyphenol (VIa).

The Grignard reaction of 2-chloro-7-methoxytropone (II) with methylmagnesium iodide afforded an oil in a good yield; this oil was composed of seven products in a ratio of 20 : 2 : 2 : 2 : 1 : 1 : 1. The major product was found to be VI, and one of the minor products (ratio 2) was found to be V, by a comparison of their retention times in vapor phase chromatography with those of authentic

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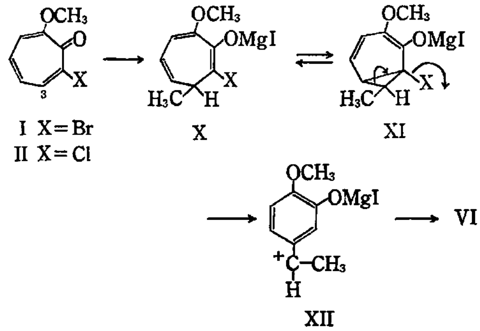
[14] For example, when 3,7-dibromotropolone methyl ether was treated with *o*-tolylmagnesium bromide at room temperature, triphenyl carbinol derivatives were obtained, but 2-tolyl-3,7-dibromotropone was obtained as the main product at −30°C.

[15] A. Béhal and M. Tiffeneau, *Bull. Soc. Chim. Paris*, [4], **1908**, 315; *Chem. Zentr.*, **1908**, Ib 1625.

[16] I. A. Pearl, *J. Org. Chem.*, **12**, 85 (1947).

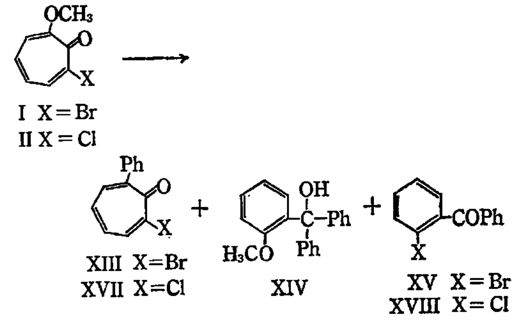
samples. The remaining products could not be elucidated because they were only minor products.

Thus, it may be concluded that the reaction of I and II with methylmagnesium iodide took place in almost the same manner, giving mainly V and VI, although the yields of the products were different. There are precedent examples similar to the formation of the rearranged product V in the Grignard reaction of other troponoids.[7-13] Thus, V apparently results from a nucleophilic attack by methylmagnesium iodide on the carbonyl carbon of the tropone ring, followed by ring contraction with the elimination of the halogen atom and by the further reaction of another molecule of methylmagnesium iodide. On the other hand, the formation of VI is an interesting example of the rearrangement of the troponoid occurring by means of the attack of the nucleophilic reagents,[17] and it can conveniently be interpreted by the following scheme. Methylmagnesium iodide may attack the C_3-position of I or II in the 1,4-addition manner, giving a cycloheptatriene-type intermediate (X) or its valence isomer (XI), which then undergos ring contraction with the elimination of the halogen atom, as shown by the arrow, to give a benzylium-type intermediate (XII). Another molecule of the reagent then attacks the intermediate (XII), leading to the formation of VI. Otherwise, VI may result from the concerted reaction of the intermediate (X or XI) with methylmagnesium iodide.



The Grignard reaction of another type of methyl ether (III and IV) of 3-halotropolone was investigated using methylmagnesium iodide. In the cases of both III and IV, the products were oils which were unstable and which turned into resineous tars upon standing in air. Although purification was attempted after complete hydrogenation, the reduced product showed the presence of nearly the same amounts of the nine components in the vapor-phase chromatography. This complex result made us abandon any further investigation of the reactions of III and IV.

To find what differences arise when the Grignard reagent is changed, the reactions of compounds I—IV with phenylmagnesium bromide were investigated. A preliminary report[13] has already pointed out that, upon reaction with phenylmagnesium bromide, I afforded mainly triphenylmethyl derivatives, while III gave crystals, mp 115—115.5°C, which were assumed to be bromophenyltropone. The reaction of 2-bromo-7-methoxytropone (I) with 2.2 equivalents of phenylmagnesium bromide afforded three kinds of products: 2-bromo-7-phenyltropone (XIII),[18] mp 80°C, *o*-methoxyphenyldiphenylcarbinol (XIV),[20] mp 126°C, and *o*-bromobenzophenone (XV),[19] an oil, in 20, 10 and 10% yields, respectively. The structures of these products were elucidated by mixed melting point determinations or by comparisons of the infrared spectra with those of authentic samples. The formation of XIV has already been reported,[13] but XIII and XV were isolated first in this experiment. Compound XIII is a product arising from the normal replacement of the methoxyl group at the C_7 position by the phenyl group, while XV is a rearranged product resulting from the attack of the phenyl group on the carbonyl carbon atom of I, followed by ring contraction, with the elimination of the methoxyl group. However, no other tropone derivatives, such as phenyltropolone or its methyl ether,[13] resulting from the substitution by the phenyl group could be isolated.



Similarly, the reaction of 2-methoxy-3-bromotropone (III) with phenylmagnesium bromide afforded 2-phenyl-3-bromotropone (XVI),[21] mp 108°C, and XV in 30 and 5% yields. However, the previously reported product, with a mp of 115—115.5°C, could not be obtained.[13] The product XVI is, of course, a normal substitution product resulting from the replacement of the methoxyl group at the C_2-position by the phenyl group.

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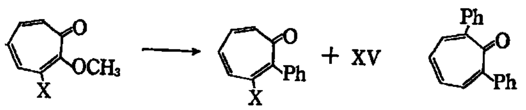
[17] E. J. Forbes, D. C. Warrell and W. J. Fry, *J. Chem. Soc., (C)*, **1967**, 1693.

[18] T. Nozoe, T. Mukai and J. Minegishi, *Proc. Japan Acad.*, **28**, 287 (1952); W. von E. Doering and J. R. Mayer, *J. Am. Chem. Soc.*, **75**, 2387 (1953); T. Mukai, *Sci. Repts. Tohoku Univ., I*, **38**, 280 (1954).

[19] E. Bergmann, *J. Org. Chem.*, **4**, 1 (1939).

[20] A. Baeyer, *Ann.*, **354**, 168 (1900).

[21] T. Toyooka, M. S. Thesis of Tohoku Univ., 1957.



III X=Br XVI X=Br XX
IV X=Cl XIX X=Cl

The Grignard reaction of 2-chloro-7-methoxytropone (II) and phenylmagnesium bromide took place in almost the same manner as the reaction of the bromo derivative (I), giving 2-chloro-7-phenyltropone (XVII),22) mp 74°C, 2,7-diphenyltropone (XX),23) mp 125°C, and *o*-chlorobenzophenone (XVIII), an oil, in 8, 1.5 and 20% yields, respectively. The formation of XX can be explained by the reaction of XVII with another reagent. The Grignard reaction of 2-methoxy-3-chlorotropone (IV) with phenylmagnesium bromide also afforded 2-phenyl-3-chlorotropone (XIX),21) mp 132°C, in 60% yield.

From the results obtained in this experiment, the following noticeable facts can be deduced. First, the reaction of methylmagnesium iodide failed to form tropone derivatives, but it did result in the formation of two benzenoid derivatives (V and VI), each with no halogen substituents. This rearrangement indicates that the reagent attacked mainly the carbonyl carbon atom and C_3-position. This may be ascribed to the fact that methylmagnesium iodide reacts as a stronger nucleophile than phenylmagnesium bromide. Second, phenylmagnesium bromide attacked the methoxyl group of the tropone ring, thus leading to the normal substitution products, phenylhalotropones. In addition, this reagent also attacked the carbonyl carbon atom to give rearranged products. It is of interest that the severely-hindered methoxyl group could be replaced by the phenyl group in a considerable yield in the cases of III and IV. Haworth and Tinker6) have observed abnormal substitution in the reaction of 2-methoxy-6-methyltropone with phenyl magnesium bromide, in which case 2-phenyl-3-methyltropone was formed. It should be noted that no such abnormal substitution took place in the Grignard reactions of III and IV.

Unfortunately, it is impossible to explain reasonably all of the results described above. At any rate, they give some knowledge regarding the nucleophilic reactions of the troponoid systems.

Experimental

Reaction of 2-Bromo-7-Methoxytropone (I) with Methylmagnesium Iodide. Formation of V and VI. A solution of methylmagnesium iodide (7.0 mm) dissolved in ether (16 m*l*) was added, drop by drop over a 15 min period, to a solution of I (600 mg; 2.8 mm) in benzene (5 m*l*) and ether (40 m*l*). After 30 min of stirring, the reaction mixture was decomposed with 2 N sulfuric acid; the organic layer separated here was washed with 1 N potassium hydroxide solution and with water, and was dried over sodium sulfate. The evaporation of the organic layer afforded an yellow oil (455 mg). The vpc analysis (20% silicone grease at 160°C) showed it to contain four components in a relative intensity of 1 : 10 : 10 : 1 in order of retention time. When the oil was subjected to chromatographic separation using a column of neutralized alumina (Brockman II-III, 15 g), one of the main products (V) was eluted by petroleum ether - benzene (from 10 : 1 to 2 : 1). ν_{max}^{neat} 3571, 3460, 1235, 1183, 1029, 755 cm^{-1}. V was proved to be *o*-methoxyphenyldimethylcarbinol by a comparison of its infrared spectrum with that of an authentic sample.15) Subsequent elution with petroleum ether - benzene (1 : 1) provided VI as a colorless oil; bp 122°C/25 mmHg. λ_{max}^{MeOH} mμ (log ε); 277(3.53). ν_{max}^{neat} 3571, 2967, 1284, 1272, 1220, 1063, 1048, 821, 779, 734 cm^{-1}.

Found: C, 72.22; H, 8.54%. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49%.

The aqueous alkaline extract was acidified with 6 N hydrochloric acid and extracted with ether. The evaporation of the ether layer gave a viscous yellow oil (94 mg), which in turn afforded 10 mg of VI when submitted to column chromatography using silicagel as the absorbent and benzene as the eluting solvent. The yield and the ratio of the products were practically unchanged when the amount of methylmagnesium iodide was changed from 2 to 4 equivalents.

Hydrolysis of VI. Preparation of VII. A mixture of VI (250 mg), acetic acid (2 m*l*), and 47% hydrobromic acid (2 m*l*) was refluxed for 1 hr at 140°C under a stream of nitrogen. The reaction mixture was then diluted with a large amount of water and extracted with ether. The ether layer was washed with 2 N sodium carbonate and with water, and dried over sodium sulfate. The subsequent evaporation of the ether furnished a brown oil (200 mg), which was passed through a column of silica gel (using petroleum ether-ether (10 : 2) as the eluent) and distilled to give a colorless, hygroscopic oil (VII), bp 119—121°C/26 mmHg. Compound VII was soluble in a 2 N sodium hydroxide solution, and it gave deep green complex with ferric chloride in ethanol. λ_{max}^{MeOH} mμ(log ε), 278(3.58); ν_{max}^{neat} 3497(broad), 2976, 2882, around 1250, 821, 782, 734 cm^{-1}; NMR in CCl_4 (60 Mc): τ 8.80 (doublet, J=7.0 cps, 6H), 6.88 (septet, J=7.0 cps, 1H), *ca.* 4.5 (very broad peak, 2H. Shift to a lower field in CF_3COOH), 3.38 (9 peaks, 3H).

Found: C, 68.83; H, 7.92%. Calcd for $C_9H_{12}O_2 \cdot 1/4\ H_2O$; C, 68.98; H, 8.04%.

Preparation of VIII. A solution of *o*-vanilline methyl ether (IX) (1.82 g; 10 mm) dissolved in ether (70 m*l*) was added, drop by drop, to a solution of methylmagnesium iodide (50 mm) in ether (70 m*l*) at room temperature. After the reaction mixture had then been refluxed for 30 min, it was decomposed with 20% ammonium chloride and acetic acid (4 m*l*). The organic layer separated here was washed with saturated sodium bicarbonate and with water, and dried over sodium sulfate. The evaporation of the solvent afforded crystals which were recrystallized from methanol or benzene to afford crystals (1.30 g) with a mp of 122—125°C as the first crop and then crystals containing the starting ester (410 mg), mp 54—56°C (*vide infra*).

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22) T. Mukai, This Bulletin, **32**, 272 (1959).
23) T. Mukai, *ibid.*, **31**, 852 (1958).

Several recrystallizations of the crystals from methanol gave colorless prisms (VIII), mp 124—125°C. Compound VIII gave greenish-yellow complex with ferric chloride in ethanol. λ_{max}^{MeOH} mμ (log ε), 219 (3.82), 280 (3.40); ν_{max}^{KBr} 3559, 3195(b), 2985, 1290, 1266, 1222, 1056, 952, 892, 788, 746 cm^{-1}; NMR in $CDCl_3$ (60 Mc) τ 8.39 (singlet, 6H), 6.18 (singlet, 3H), 6.13 (singlet, 1H), 3.23 (singlet, 3H), 2.34 (singlet, 1H). Two peaks, those at τ 6.13 and 2.34, disappeared upon the addition of deuterium oxide.

Found: C, 65.96; H, 7.93%. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74%.

Reduction of VIII. Preparation of VI. A solution of VIII (100 mg; 0.55 mm) dissolved in ethanol (10 *ml*) containing a drop of concentrated hydrochloric acid was hydrogenated in the presence of 5% Pd-C (100 mg). It absorbed 1 equivalent of hydrogen (12.5 *ml*; Calcd 12.3 *ml*) in 2 hr. The filtration of the catalyst, followed by the evaporation of the solvent, afforded a residue. After an ethereal solution of the residue had been washed with water and dried over magnesium sulfate, the ether was removed, thus affording a pale yellow oil (87 mg) whose infrared spectrum was completely identical with that of VI.

Reaction of 2-Chloro-7-Methoxytropone (II) with Methylmagnesium Iodide. To a solution of II (500 mg; 2.9 mm) dissolved in ether (25 *ml*) and benzene (5 *ml*), there was added methylmagnesium iodide (8.7 mm) in ether (25 *ml*) for 15 min. After the reaction mixture had then been stirred for 30 min, it was decomposed with 2 N sulfuric acid and extracted with ether. The combined ether extract was washed with water, dried over sodium sulfate, and evaporated to give a yellowish-brown oil (530 mg), which showed seven peaks in a vapor-phase chromatogram (20% silicone grease at 160°C). The relative ratio of the four main peaks was 1 : 1 : 1 : 10 in order of retention time. The largest peak corresponds to VI, and one of the other three peaks to V.

Reaction of 2-Bromo-7-Methoxytropone (I) with Phenylmagnesium Bromide. *(a)* A solution of phenylmagnesium bromide (7.5 mm) in dry ether (22 *ml*) was added, drop by drop at room temperature, to a solution of I (610 mg; 2.8 mm) dissolved in a mixture of ether (50 *ml*) and benzene (15 *ml*) for 15 min. After 1 hr of stirring, the white precipitate (Grignard complex) formed was filtered off in a nitrogen stream and decomposed by adding ethanol (12 *ml*) and a large amount of ether. The organic layer was washed with 2 N sulfuric acid, 2 N potassium hydroxide, and water and dried over sodium sulfate. The evaporation of the solvent afforded a yellow oil (230 mg), which was then dissolved in benzene and passed through a column of alumina (Brockman O-I, 6 g). The evaporation of an elute with benzene gave a yellow oil (15 mg) whose infrared spectrum was identical with that of authentic *o*-bromobenzophenone.[19] The evaporation of a subsequent elute with benzene afforded yellow crystals (90 mg), which were then recrystallized from ethanol to give 2-bromo-7-phenyltropone (XIII), mp 79—80°C. Identification was made by the mixed-melting-point method and by a comparison of the infrared spectrum with that of an authentic sample.[18] Subsequent elution with ether-ethanol (1 : 25) gave crystals (30 mg), mp 84—89°C, whose infrared spectrum (ν_{max}^{KBr} 3067, 2967, 1582, 1548, 1479, 1350, 1248, 1245, 1199, 1167, 1099, 969 cm^{-1}) did not show the C=C and C=O bands characteristic of tropone derivatives. The structure of the product was not elucidated. On the other hand, the filtrate separated from the Grignard complex was treated in the usual manner to afford a yellow oil (200 mg), which was passed through a column of alumina (Brockman O-I, 5 g). A yellow oil (60 mg) obtained from an elute with benzene was proved to be *o*-bromobenzophenone (XV) contaminated by a small amount of *o*-methoxyphenyldiphenylcarbinol (XIV) by an inspection of its infrared spectrum. Subsequent elution with benzene gave XIII (30 mg), mp 73—75°C. The aqueous potassium hydroxide extract was acidified with 2 N sulfuric acid and extracted with benzene. The evaporation of the benzene extract and the recrystallization of the residue obtained from cyclohexane afforded yellow crystals (100 mg), mp 108°C, which proved to be 3-bromotropolone, a hydrolyzed product of the starting material (I).

(b) A solution of phenylmagnesium bromide (9.0 mm) in ether (30 *ml*) was added, drop by drop over a 30 min period, to a solution of I (660 mg; 3.0 mm) dissolved in a mixture of ether (50 *ml*) and benzene (12 *ml*), and then it was worked up just as in (a). The solid complex was decomposed with 2 N sulfuric acid and extracted with benzene. The benzene layer was washed with 2 N potassium hydroxide and then with water, and dried over sodium sulfate. The evaporation of the benzene afforded a brown oil (280 mg), which was then passed through a column of alumina as in (a). Elution from petroleum ether-benzene (1 : 1) to benzene afforded a mixture of XIV and XV (40 mg). Compound XIII (50 mg), mp 74°C, was obtained from the elute with benzene, and a viscous yellow oil (40 mg), from the elute with ether-methanol (1 : 25). The filtrate separated from the complex also afforded a yellowish-brown oil (470 mg), which was separated by the use of column chromatography using alumina. The evaporation of the elute with petroleum ether-benzene (1 : 1) gave XV (45 mg) and colorless crystals (75 mg), mp 105—110°C. The recrystallization of the latter crystals from ethanol afforded colorless prisms, mp 125—126°C, which were proved to be *o*-methoxyphenyldiphenylcarbinol (XIV) by the mixed melting point method and by a comparison of the infrared spectrum with that of an authentic sample.[20] Compound mp XIII (55 mg), mp 65—70°C, was obtained from the elute with benzene, and a viscous oil (*ca.* 100 mg), from an elute with ether. The aqueous alkaline extract gave no 3-bromotropolone when it was treated as has been described in (a).

Reaction of 2-Methoxy-3-Bromotropone (III) with Phenylmagnesium Bromide. *(a)* A solution of phenylmagnesium bromide (5.0 mm) dissolved in ether (10 *ml*) was added, drop by drop over a 20 min period, to a solution of III (430 mg; 2.0 mm) in ether (30 *ml*). After the mixture had then been stirred for 1.5 hr, the deposited white Grignard complex was filtered out and the solution was decomposed with ethanol (5 *ml*) and extracted with ether. The ether layer was washed with 2 N sulfuric acid, 1 N potassium hydroxide, and water, and dried over sodium sulfate. The evaporation of the ether afforded a viscous reddish-yellow oil, which, upon standing, yielded yellow crystals (85 mg), mp 96—103°C. The residual part was dissolved in petroleum ether-benzene (1 : 1) and passed through a column of alumina (Brockman III, 13 g). Yellow crystals (75 mg), mp 93—100°C, were obtained by the evaporation of the elute with petroleum ether - benzene (1 : 1) and benzene. The crystals obtained here were combined and recrystallized from ethanol to afford 2-phenyl-3-bromotropone (XVI), mp 108°C. On the other hand, the ethereal filtrate separated from the complex was washed with 2 N sulfuric acid, 2 N potassium hydroxide, and water, and dried over sodium sulfate. The residual oil obtained by the evaporation of the ether was dissolved in petroleum ether - benzene (1 : 1) and passed through a column of alumina to give oily crystals (30 mg); these crystals did not show the bands characteristic of tropone derivatives in the infrared spectrum and could not be elucidated, because of their small amount. An aqueous potassium hydroxide solution was acidified with 2 N sulfuric acid and extracted with benzene; from the extract no clear compound could be obtained except for phenol.

(b) Reaction at −30°C. A solution of phenylmagnesium bromide (6.9 mm) dissolved in ether (20 m*l*) was added, at −30°C (dry ice-acetone) over a 15 min period, to a solution of III (500 mg; 2.3 mm) in ether (40 m*l*). The solution was then stirred at −30°C for an additional 30 min. After the complex formed had been filtered, the complex part and the filtrate were separately treated in the manner described in (a). The complex part gave a brown oil (390 mg), which was then dissolved in petroleum ether - benzene (2 : 1) and passed through a column containing alumina. The evaporation of an elute with benzene-ether (9 : 1) afforded pale yellow crystals (240 mg), mp 57—60°C, while an elute evaporated with ether gave a yellow oil (15 mg). The crystals were found by a mixed melting point determination to be recovered III. An aqueous potassium hydroxide extract was acidified with concentrated hydrochloric acid and extracted with ether. The ether was washed with water and dried over sodium sulfate. The evaporation of the solvent gave an oil with phenolic odor (165 mg); this oil was dissolved in benzene, and hydrogen bromide gas was passed into the solution. The deposited HBr-salt was neutralized with a saturated sodium bicarbonate solution and extracted with benzene. The evaporation of the benzene-extract afforded 3-bromotropolone (60 mg), mp 101—102°C. On the other hand, the filtrate separated from the complex afforded a yellow oil (102 mg); this oil was dissolved in petroleum ether - benzene (1 : 1) and passed through an alumina column. Evaporation of an elute with benzene gave XVI (32 mg), mp 104—106°C, while an elute with ether yielded a yellow oil (15 mg), which was found by an inspection of its infrared spectrum to be identical with the oily product isolated from the complex part.

Reaction of 2-Chloro-7-Methoxytropone (II) with Phenylmagnesium Bromide. A solution of phenylmagnesium bromide (8.7 mm) in ether (27 m*l*) was dropped into a solution of II (500 mg; 2.9 mm) dissolved in a mixture of benzene (5 m*l*) and ether (45 m*l*). After the mixture had been stirred for 1 hr, the precipitated complex was separated and treated in the manner described for the reaction of I with phenylmagnesium bromide. The complex part gave a brown oil (330 mg); this oil was dissolved in petroleum ether-benzene (2 : 1) and passed through a column of alumina (Brockman O-I, 12 g), The evaporation of an elute with petroleum ether - benzene (2 : 1) afforded a colorless oil (25 mg), whose infrared spectrum was very similar to that of *o*-bromobenzophenone and which afforded an oxime (mp 130°C) in a sealed tube.[24] The oil was identified as *o*-chlorobenzophenone (XVIII). Evaporation of a subsequent elute with benzene afforded a yellow oil (160 mg) which was separated using preparative thin-layer chromatography of silica gel developed by benzene; two kinds of crystals (mp 65—69°C, 50 mg; mp 121—121.5°C, 30 mg) were thus obtained. The compound with the lower melting point was recrystallized from cyclohexane to give a sample with a mp of 74—74.5°C; it was proved to be 2-chloro-7-phenyltropone (XVII) by a comparison of its infrared spectrum with that of an authentic sample[22] and by the mixed melting point method. The other crystal was found to be 2,7-diphenyltropone by a comparison of its infrared spectrum with that of an authentic sample.[23] On the other hand, the filtrate part gave a brown oil (430 mg) which was dissolved in petroleum ether - benzene (2 : 1) and separated using a column of alumina (Brockman O-I, 12 g). An elute with petroleum ether - benzene (2 : 1) was evaporated to give *o*-chlorobenzophenone (XVIII) (85 mg). Besides these products, more than ten products (each product in a quantity less than 10 mg) were obtained, but their structures could not be elucidated.

Reaction of 2-Methoxy-3-Chlorotropone (IV) with Phenylmagnesium Bromide. A solution of phenylmagnesium bromide (6.4 mm) in ether (30 m*l*) was added, drop by drop over a 10 min period, to a solution of IV (500 mg; 2.9 mm) dissolved in ether (50 m*l*). After the mixture had been stirred for 1 hr, the complex formed was filtered out and decomposed with 47% borontrifluoride etherate (4 m*l*), and the resulting solution was worked up in the usual manner. The evaporation of the ether gave crystals (400 mg) which were then recrystallized from cyclohexane to afford yellow prisms, mp 127—129°C (142 mg). The filtrate was dissolved in benzene and passed through a column of alumina (Brockman II-III, 12 g). An elute with benzene was evaporated to furnish yellow crystals (161 mg), mp 104—120°C. These crystals were combined and recrystallized from cyclohexane to afford a sample with a mp of 131—132°C; this was proved to be 2-phenyl-3-chlorotropone (XIX) by a comparison of the infrared spectra and by mixed melting point determination with an authentic sample.[21] The filtrate separated from the complex was treated like the above complex; this gave a brown oil (280 mg), which was dissolved in benzene and passed through a column of alumina (Brockman II-III, 12 g). Evaporation of an elute with benzene afforded XIX (82 mg), mp 120—122°C. The total yield of XIX was 385 mg.

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[24] J. Meisenheimer and H. Meis, *Ber.*, **57**, 295 (1924).