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CYCLOPROPANES

XXXII. THE MECHANISM OF GRIGNARD FORMATION

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SUMMARY

Further evidence for the radical nature of the Grignard formation reaction is provided. Based on product analysis from the reaction of 1-halo-1-methyl-2,2-diphenylcyclopropane with magnesium metal in perdeuterated diethyl ether and tetrahydrofuran solvents, it is concluded that the radical intermediates formed largely disproportionate on the surface of the magnesium and not in solution. The stereochemical results, when optically active substrates are used, are consistent with a surface-radical mechanism. Neither the particle size nor the purity of the magnesium have any effect on the stereochemistry of the reaction.

INTRODUCTION

The radical nature of Grignard formation has been suggested by many workers[1-3]. That an ionic process was not involved was demonstrated by the work of both Kondyrew[4] and Brun[5] who showed that very little current was passed when magnesium "dissolves" in an ethereal solution of ethyl bromide. Based on a thermographic study of Grignard formation with a number of alkyl bromides in a variety of solvents Khyrak[6] concluded that his data was best accommodated by a free radical mechanism.

The formation of biphenyl in the reaction of magnesium with bromobenzene[7], the disproportionation and coupling observed[8] in the reaction β,β-dimethylphenethyl chloride with magnesium and the lack of stereospecificity in the reaction of geometrically isomeric vinyl halides[9] have all been interpreted to involve free radical intermediates as have our own previous studies on the optically active cyclopropyl halides[10,*].

The present study is concerned with further pursuing the question of the mechanism of the interaction of organic halides with magnesium in ether solvents by means of the optically active 1-methyl-2,2-diphenylcyclopropyl halide system, which provides a stereochemical tool for this purpose. In our earlier work[10], the Grignard reagents were carbonated in the conventional manner by pouring them into a slurry

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[*] Also see ref. 10c for an interesting example in which THF is captured. For other examples see ref. 11.

of Dry-Ice and ether. Since a large amount of 1-methyl-2,2-diphenylcyclopropane was formed by hydrolysis using this technique, it was impossible to determine the optical purity of any of this hydrocarbon arising during Grignard reagent formation. Because the optical purity of this hydrocarbon could provide an important clue to the mechanism of Grignard reagent formation, the earlier work[10] was repeated using a vacuum manifold system which enabled the formation and carbonation of the organometallics to be conducted under conditions which excluded moisture and air.

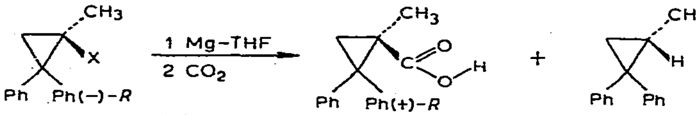
It had previously been shown that the hydrolysis of the Grignard solutions with D_2O gave both deuterated and undeuterated 1-methyl-2,2-diphenylcyclopropane. Since the amount of undeuterated hydrocarbon was dependent on the solvent, the reasonable proposal was made that it arises from solvent cleavage. In the present study the question of solvent cleavage in Grignard reagent formation was examined by means of perdeuterated solvents. Moreover, an examination of the side-products resulting from Grignard formation was also made in the hope that they would shed more light on the mechanism of the reaction. The effect of the magnesium particle size and purity on the course of the reaction was also investigated.

RESULTS

The effect of halogen

The results obtained previously[10] on the effect of halogen on the formation of Grignard reagents from optically active 1-methyl-2,2-diphenylcyclopropyl halides in THF revealed nothing with respect to the optical purity of the 1-methyl-2,2-diphenylcyclopropane formed in this reaction, since a considerable amount of this compound inevitably resulted from hydrolysis of the Grignard reagent during the carbonation step. The effect of halogen was therefore reinvestigated using the present technique. The results of this study are give in Table 1.

TABLE 1



THE EFFECT OF THE HALOGEN ON THE FORMATION OF THE GRIGNARD REAGENT FROM 1-METHYL-2,2-DIPHENYLCYCLOPROPYL HALIDE IN THF

Run	*Halide*	*Temp. (°C)*	*Time (min)*	*Acid*		*Hydrocarbon*	
				Yield (%)	*Optical[a,b] purity (%)*	*Yield (%)*	*Optical[b,c] purity (%)*
1	Cl	65	35	81	25.7	1.3	6.6 (Inv.)
2	Cl	65	185	89	25.4	1.0	5.3 (Inv.)
3	Br	65	35	70	18.5	6.0	6.2 (Ret.)
4	Br	65	180	79	16.2	4.8	4.2 (Ret.)
5	I	65	34	40	1.8	(4.4)[d]	0.8 (Ret.)
6	I	65	190	36	1.9	19.0	1.0 (Ret.)

[a] Based on $[\alpha]_{5461}$ 41.5°. [b] Corrected for optical purity of starting material. [c] Based on $[\alpha]_{5461}$ 150.65°. [d] Low yield due to a mechanical loss in work-up.

The data clearly reveal that the reaction proceeds with overall retention of configuration and that the optical purity and yield of the Grignard reagent (based on the acid formed) increases in the order $\mathrm{I} < \mathrm{Br} < \mathrm{Cl}$ as shown earlier[10]. Because of the technique employed, the present results show the trend in acid yields more clearly. In addition, it is seen that the 1-methyl-2,2-diphenylcyclopropane formed in the reaction has an optical purity which is decidedly lower than that of the acid from the same experiment. The hydrocarbons from the iodide and bromide show net retention of configuration and have optical purities which increase in the same order as that of the acids. The hydrocarbon from the chloride, although it has an optical purity which approximately equals that of the hydrocarbon from the bromide, is formed with a net *inversion of configuration.* Of greatest significance, however, is the fact that all of these hydrocarbons are very nearly racemic.

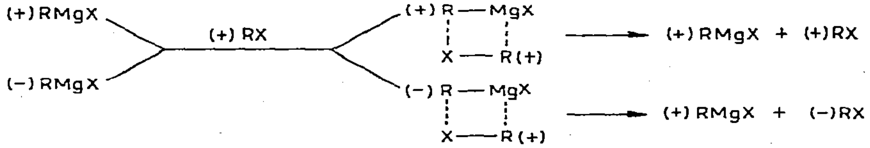
The optical purities of the acids and the hydrocarbons showed no significant change after prolonged refluxing of the Grignard reagent. The yields of acid from the bromide and chloride increase somewhat in the three hour runs, possibly due to greater consumption of starting material.

Halogen–metal interchange with Grignard reagents

It is necessary to deal with the possibility that the optical activity of the Grignard reagents might be due to a halogen–metal interchange reaction. That is, formation of the Grignard reagent could involve complete racemization, as has been observed with other optically active halides[12], but the racemic Grignard reagent could then interchange alkyl groups with unreacted optically active halide resulting in a net enrichment of one enantiomer as illustrated in Scheme 1.

SCHEME 1

ENANTIOMERIC ENRICHMENT BY HALOGEN–METAL INTERCHANGE



Halogen–metal interchange reactions involving Grignard reagents have, indeed, been reported[13].

Zakharkin and his coworkers[14] have made extensive studies of the exchange of Grignard reagents with ordinary alkyl and aryl halides. Highly solvating ethers such as tetrahydrofuran and dimethoxyethane favor the exchange. For a given alkyl or aryl group the ease of exchange was found to be $\mathrm{I} > \mathrm{Br} > \mathrm{Cl}$. On the basis of these studies, Zakharkin and his coworkers have concluded that the mechanism of the halogen–metal interchange reaction is the same for both organomagnesium and organolithium compounds. This would imply that the exchange proceeds with retention of configuration.

In the present investigation, the fact that the optical activities obtained increase in an order which is the reverse of what would be expected if exchange caused this activity strongly suggests that it is not taking place here. A direct test of exchange was, however, made in order to clarify this point.

Since the optical purity obtained when the Grignard reagent was made from the iodide was so low that for all intents and purposes it could be considered zero, optically active bromide was used in the test. The Grignard reagent was prepared from racemic 1-methyl-1-bromo-2,2-diphenylcyclopropane in a flask equipped with a neck containing a sintered glass disk which enabled it to be separated from unreacted magnesium. The tetrahydrofuran solution of the Grignard reagent was then transfered under argon to a flask containing the optically active bromide. After refluxing this mixture for three hours and then treating with carbon dioxide, the acid obtained was found to be completely racemic. Thus halogen–metal interchange could be ruled out as the source of the optical activity.

Formation of the Grignard reagent in ethers and perdeuterated ethers

Formation of the Grignard reagent from the optically active bromide in ethyl ether instead of THF does not greatly affect the optical purities of the products, but does affect their yields considerably. This is illustrated in Table 2.

TABLE 2

COMPARISON OF GRIGNARD REAGENT (RMgBr) FORMATION IN ETHER AND THF

Run	*Solvent*	*Temp. (°C)*	*Time (min)*	*Acid*		*Hydrocarbon*	
				Yield (%)	*Optical purity (%)*	*Yield (%)*	*Optical purity (%)*
1	Et_2O	35	29	26	20.4	22.9	3.7
2	THF	65	35	70	18.5	6.0	6.2

As was the case in THF, the optical purity of the 1-methyl-2,2-diphenylcyclopropane obtained as side product is much lower than that of the acid.

The marked decrease in acid yield along with the corresponding increase in hydrocarbon yield observed when this Grignard reagent is formed in ether instead of THF found a reasonable explanation[10] based on increased solvent cleavage in ether by the radical intermediate. The question of solvent cleavage was, however, reexamined in a definitive manner.

In order to determine the extent of solvent cleavage unequivocally the Grignard reagent was formed from optically active 1-methyl-2,2-diphenylcyclopropyl bromide in THF-d_8 and ethyl ether-d_{10} and then carbonated. The results of these experiments are given in Table 3.

If the results are considered only from the point of view of the processes which produce 1-methyl-2,2-diphenylcyclopropane, it is seen that solvent cleavage[10] is far more important in THF than in ether. That is, in THF, solvent cleavage is an important source of that hydrocarbon which is formed, while in ether it is unimportant compared to other sources of the hydrocarbon.

The yields and optical purities of the acids in the THF-d_8 experiments seem particularly significant. Only in the case of the chloride (see Table 1) has a yield in this range been attained. Taking averages, it is seen that the yield of Grignard (as reflected in the acid yields) from the bromide is 15% higher in THF-d_8 than it is in ordinary

TABLE 3

FORMATION AND CARBONATION OF THE GRIGNARD REAGENT FROM (+)-1-METHYL-1-BROMO-2,2-DIPHENYLCYCLOPROPANE IN DEUTERATED ETHERS

Run	*Solvent*	$[\alpha]_{5461}$ *bromide*	*Temp.* (°C)	*Acid*		*Hydrocarbon*		
				Yield (%)	*Opt.*[a] *purity* (%)	*Overall yield RH+RD* (%)	*RD in H.C.* (%)	*Opt.*[b] *purity* (%)
1	THF-d_8	+131.21	65	88	13.0	1.0	29.2±0.3	10.3
2	THF-d_8	+131.21	65	93	13.2	1.4	28.1±0.2	7.7
3	Et$_2$O-d_{10}	+131.21	35	25	18.2	20.2	6.7±0.2	4.6

[a] Based on $[\alpha]_{5461}$ 41.5°. [b] Based on $[\alpha]_{5461}$ 150.65°.

THF. Furthermore, along with the increased yields of acids in THF-d_8 there is also a decrease in their optical purities. In contrast to this, the yields of 1-methyl-2,2-diphenylcyclopropane in THF-d_8 are significantly lower in THF-d_8 than they are in ordinary THF while the optical purities are somewhat higher.

Unlike the THF experiments, comparison of the results obtained in ether-d_{10} (Table 3, run 3) with those obtained in ordinary ether (Table 2, run 1) reveal no significant differences in the yields and optical purities of the acids and hydrocarbons.

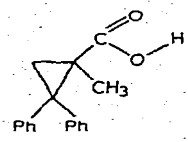
A possible explanation for the difference in yields and optical purities in THF-d_8 compared to THF may be a deuterium isotope effect. If in ordinary THF, solvent cleavage by a racemic intermediate accounts for a good deal of the 1-methyl-2,2-diphenylcyclopropane formed, a kinetic isotope effect in THF-d_8 might result in this racemic intermediate being diverted to racemic Grignard reagent, increasing the yield of acid and decreasing its optical purity. At the same time, the fraction of this hydrocarbon formed by a path which involves retention of optical activity is not diluted by racemic hydrocarbon which ordinarily would result from solvent cleavage. Thus, in the THF-d_8 experiment the hydrocarbon yield goes down while its optical purity goes up.

The lack of change found in the ether-d_{10} experiment with regard to the optical purities and yields of the products compared to the ordinary ether experiment is consistent with the unimportance of solvent cleavage in this solvent. Since there is little chance for a kinetic isotope effect, the results are the same in ether-d_{10} as in ether.

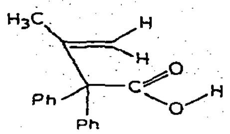
Product analysis

The Grignard reagent from 5.0 g of racemic bromide was formed in ether and carbonated using the same technique employed in the previous experiments. Identification of the minor products was then undertaken.

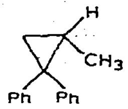
The NMR spectrum of the acid fraction indicated that besides 1-methyl-2,2-diphenylcyclopropanecarboxylic acid (I) a small amount of impurity was present. Fractional crystallization of the acid resulted finally in a fraction which contained the cyclopropyl acid and the impurity in approximately equal amounts. The methyl esters, formed by treatment of the mixtures with diazomethane were easily separated by gas–liquid chromatography. Collection of the impurity fraction and examination with



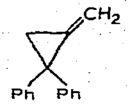
(I)



(II)



(III)



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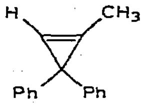
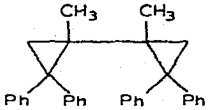
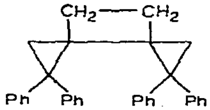


(V)



(VI)



(VII)

NMR revealed that it had all of the peaks of the impurity in the acid mixture with the addition of a peak for the ester methyl group at 3.69 ppm. The NMR showed a phenyl singlet at 7.23 ppm, vinylic absorptions at 5.15 and 4.70 ppm, the ester methoxyl singlet at 3.69 ppm, and allylic methyl at 1.75 ppm. These peaks were in the ratio of 10/1/1/3/3. The acid impurity was identified as 2,2-diphenyl-3-methyl-3-butenoic acid (II). The same acid resulted when 2-methyl-3,3-diphenylallyl bromide was converted to the Grignard reagent and carbonated[15]. This acid was formed from the cyclopropyl bromide in 1.0% yield while 1-methyl-2,2-diphenylcyclopropanecarboxylic acid was formed in 34% yield.

Examination of the oil obtained by molecular distillation of the neutral fraction showed that it was almost entirely composed of 1-methyl-2,2-diphenylcyclopropane, 2,2-diphenylmethylenecyclopropane and 1-methyl-3,3-diphenylcyclopropene (V). The NMR spectrum shows all of the peaks associated with the first of these compounds plus those exhibited by authentic 2,2-diphenylmethylenecyclopropane (IV): two sharp vinyl multiplets centered at 5.36 and 5.56 ppm, and the sharp triplet corresponding to the cyclopropyl methylene centered at 1.75 ppm. In addition, the infrared spectrum of the mixture shows the vinylic methylene absorptions of this compound at 895 cm^{-1}. All of these absorptions were easily detected in the mixture.

Besides the absorptions for the first two compounds, the NMR spectrum showed a doublet at 2.1 ppm separated by 1 Hz. Closs and Closs[16] have reported that the allylic methyl group of 1,3,3-trimethylcyclopropene (V) gives a doublet at 1.9 ppm separated by 1.1 Hz. Since attempts to separate 1-methyl-3,3-diphenylcyclopropene from the other components of the mixture were unsuccessful, another approach was used to establish its presence in the mixture. Schroder[17] has shown that 1,3,3,-trimethylcyclopropene is completely isomerized to the exocyclic methylene derivative when it is refluxed in a tertiary alcohol containing the corresponding potassium alcoholate. The same method was tried on the present mixture.

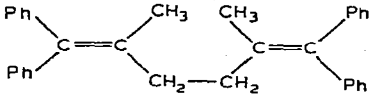
Using NMR spectroscopy the mole percentages of the three compounds in the hydrocarbon fraction were found to be: 1-methyl-2,2-diphenylcyclopropane (III) 65.6%, suspected 1-methyl-3,3-diphenylcyclopropene (V) 9.0%, and 2,2-diphenylmethylenecyclopropane (IV) 25.4%. If the mixture contained 1-methyl-3,3-diphenylcyclopropene, complete isomerization to the exomethylene derivative would be expected to increase the amount of 2,2-diphenylmethylenecyclopropane to 34.4%. Treatment of the mixture with potassium tert-butoxide in tert-butanol resulted in the complete disappearance of the peak at 2.1 ppm attributed to the allylic methyl of the cyclopropene and an increase in the amount of 2,2-diphenylmethylenecyclopropane to 33.8%.

The residue remaining after the molecular distillation of the above hydrocarbons consisted of thick oil. By means of slow crystallization from ether a white crystalline solid was obtained. This material was also one of the components of the main band obtained by preparative thin-layer chromatography of the oil.

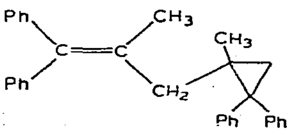
All of the data obtained for this substance, m.p. 183–184°, are consistent with dimeric structure (VI). It had an NMR spectrum exhibiting phenyl absorption from 6.59 to 7.48 ppm, a singlet at 1.24 ppm, and a quartet corresponding to an AB system between 0.42 and 0.92 ppm. The ratio of the intensities of these absorptions was 20/6/4 respectively. The quartet, representing four protons is in a region where cyclopropyl protons are generally found. The coupling constant of 6 Hz is in the range of 5.6 Hz consistently observed for 1,1-disubstituted 2,2-diphenylcyclopropanes. The substance gave a correct elemental analysis and the mass spectrum showed a molecular weight of 414. The fragmentation pattern showed both phenyls are on the same carbon atom and was entirely consistent with the dimeric structure*. The yield of (VI) was 1–1.5%. In a separate experiment** (VI) was isolated from a reaction starting with optically active bromide in order to ascertain whether the dimer would be optically active. The dimer isolated was racemic.

Along with the closed dimer discussed above a few milligrams of a white solid, m.p. 156–157°, were isolated from the first fraction of the preparative thin-layer chromatogram. Although this material gave an elemental analysis which corresponded to an isomer of (VI) the mass spectrum revealed that it was a hydrocarbon of molecular weight 412, slightly contaminated with (VI) (molecular weight 414). The mass spectrum further showed that two phenyls were on the same carbon, that a fragment corresponding to C_2H_4 is cleaved from the molecule and that it splits in half to a fragment of mass 206.

The NMR of this material showed phenyl absorptions at 6.71 to 7.60 ppm, a quartet corresponding to an AB system from 0.55 to 1.54 ppm, and a singlet centered at about 1.15 ppm. Although the compound was slightly impure the relative intensities of the quartet and singlet were about 1/1. The position of the quartet is consistent with the cyclopropane structure as is the 5 Hz coupling constant and is in line with a 1,1-disubstituted-2,2-diphenylcyclopropane structure. We have tentatively assigned structure (VII) to this compound. A vigorous attempt was made to detect the presence of other possible dimeric substances such as (VIII) and (IX). The former is a decomposition product of the 1-methyl-2,2-diphenylcyclopropyl radical in solution[18]. All attempts failed to reveal the presence of these dimers.



(VIII)



(IX)

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* We are indebted to Mr. R. Golke for obtaining and interpreting the mass spectra reported here. It should be pointed out that (VI) is probably a mixture of *erythro* and *threo*.

** We are indebted to Dr. J. Ollman for performing this experiment.

TABLE 4

THE EFFECT OF PARTICLE SIZE ON THE FORMATION OF THE GRIGNARD REAGENT FROM OPTICALLY ACTIVE BROMIDE IN THF

Magnesium	*Acid*		*Hydrocarbon*	
	Yield (%)	*Opt. purity* (%)	*Yield* (%)	*Opt. purity* (%)
Turnings	62	16.0	7.8	6.1
Turnings[a]	45	15.0		
Powder[b]	75	17.4	5.4	5.2

[a] Magnesium of 99.9995% purity[8]. [b] Average of runs 3 and 4, Table 1.

Particle size and purity of magnesium

In order to ascertain what if any effect particle size has on the stereochemistry of Grignard formation, the Grignard reagent was formed from optically active bromide and magnesium turnings in THF. In Table 4 the results of this experiment are compared with those obtained with the magnesium powder normally used in this study. These results show that the stereochemistry of Grignard reagent formation is apparently unaffected by particle size.

The magnesium used in all our work was ordinary magnesium which contained many impurities[10]. To ascertain the effect of these impurities on the stereochemistry of the reaction a sample of magnesium which was 99.9995% pure was used*. Carbonation of the Grignard reagent yielded acid (I) of 15% optical purity which indicates that purity of the magnesium has little if any effect.

DISCUSSION

The results obtained in the study of Grignard reagent formation provide strong evidence for the involvement of surface bound intermediates and the generation of radicals.

Examination of the optical purity of the 1-methyl-2,2-diphenylcyclopropane generated in the formation of the Grignard reagent (Table 1, Table 2, run 1) shows that in all experiments it is very nearly racemic. This result is consistent with what could be expected if a cyclopropyl radical were the major source of this hydrocarbon.

The results of the experiments in perdeuterated ethers show that of the processes involved in the generation of the Grignard reagent, solvent cleavage is only of minor importance. It may be argued that moisture is the source of the hydrogen found in these experiments and the fraction of hydrocarbon resulting from solvent cleavage is greater than these experiments indicate. This, however, does not seem likely on the basis of the technique used and the reproducibility of the results.

In both ethyl ether and perdeuterated ethyl ether there is a great deal of hydrocarbon formation, yet deuterium incorporation indicates little solvent cleavage. In order to account for such a large yield of hydrocarbon with such a low amount of

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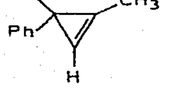
* We are indebted to Prof. E. C. Ashby for this sample.

deuterium incorporation, an appreciable amount of water would have had to be present in the ether-d_{10} experiment. Under these circumstances[10] the optical purity of the hydrocarbon would approach that of the acid since the Grignard reagent would be an important source of the former and the only source of the latter. The optical purities of the hydrocarbons in the ether and ether-d_{10} experiments are, however, about the same and lower than that of the acid by about a factor of four.

The fact that the amount of hydrogen incorporation was essentially constant in both THF-d_8 experiments (Table 3, runs 1 and 2) even though in one experiment (run 2) the amount of starting material was doubled seems to be a reasonable basis for excluding moisture as the source of hydrogen. It does not seem likely that just the right proportion of water to give the same result would appear in both experiments. The reproducibility of the deuterium incorporation data is consistent with a set of reactions, of relative rates such that a constant fraction of deuterium incorporation is always obtained.

The source of the hydrogen in the THF-d_8 experiments, although apparently not due to water is not entirely evident. If water is ruled out as its source, the only one remaining is the starting material and the products derived from it. The disproportionation of two cyclopropyl radicals to form hydrocarbon and olefin would account for the hydrogenated material. In ordinary THF this process no doubt does occur since a small amount of 2,2-diphenylmethylenecyclopropane can be detected in the neutral fraction from this reaction. However, only a minute trace of this material relative to the amount of 1-methyl-2,2-diphenylcyclopropane present could be detected in the neutral material obtained in the THF-d_8 experiments by means of NMR and gas–liquid chromatography. Although the destruction of the olefin by some side process is conceivable, it may be that the hydrogen observed comes from attack of the intermediate radical or the Grignard reagents on high molecular weight side products. Such processess will be examined in detail in the discussion of hydrocarbon formation in ether. It should be pointed out that if it is assumed that the deuterated hydrocarbon is completely racemic, the optical purity of the hydrogenated material, based on an average of the two experiments, is 12.6%. This could suggest that this material is derived from the Grignard reagent. As discussed earlier, a comparison of the yields and stereochemistry of Grignard reagent formation in THF and THF-d_8 suggest that there may be less solvent cleavage in THF-d_8 due to a kinetic isotope effect.

The ethyl ether-d_{10} experiment, (Table 3, run 3) besides revealing very little solvent cleavage gives the same results as observed in ordinary ether (Table 2, run 1). Since a considerable amount of hydrocarbon is formed despite the virtual absence of solvent cleavage and since, as discussed earlier, the intervention of moisture seems unlikely, the source of hydrogenation of material must be the starting halide or compounds derived from it. NMR reveals the hydrocarbons formed in the ether-d_{10} experiment were in the following proportions to each other:

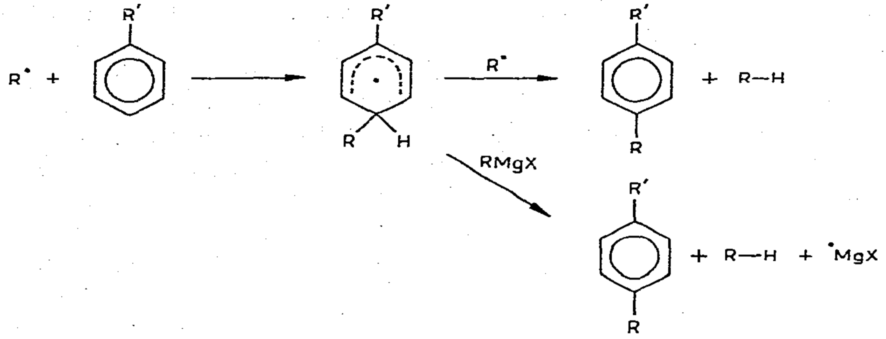


1 / 5.34 / 9.84

the last figure representing the total of deuterated and non-deuterated hydrocarbon.

The fraction of the total saturated hydrocarbon formed which is due to disproportionation is then 6.34/9.84 or 0.644. Since 0.067 of the saturated hydrocarbon is deuterated it comes from solvent cleavage. The remaining 0.289 of the hydrocarbon comes from some process or processes which cause hydrogen incorporation. If it is assumed that solvent cleavage and disproportionation give completely racemic 1-methyl-2,2-diphenylcyclopropane then the optical purity of the remaining hydrocarbon is 4.6/0.289 or 15.9%. This optical purity suggests that a good deal of the hydrocarbon unaccounted for by disproportionation and solvent cleavage may have come from the Grignard reagent.

Studies on the formation of Grignard reagents in aromatic solvents[19] suggest that the following processes could be occurring on the magnesium surface:



Such processes could also occur in the present case, by attack of radicals on the aromatic rings of the starting halide, on those of any of the products of disproportionation and possibly also on those of Grignard reagents, with subsequent removal of hydrogen from the addition product by a cyclopropyl radical. The results obtained when the Grignard was formed in ether seem consistent with the intervention of such processes since they would explain the presence of hydrocarbon not accounted for by solvent cleavage and disproportionation as well as the many substances found in small amounts after removal of the light hydrocarbons. The concentration of intermediates containing labile hydrogen on the surface of the magnesium may be great enough so that radicals generated in the formation of the Grignard reagent encounter them before they have become completely racemic. These intermediates can also react with Grignard reagents to produce hydrocarbon and magnesium(I) halide. Hydrocarbon formed in this manner should have the optical purity of the Grignard reagent.

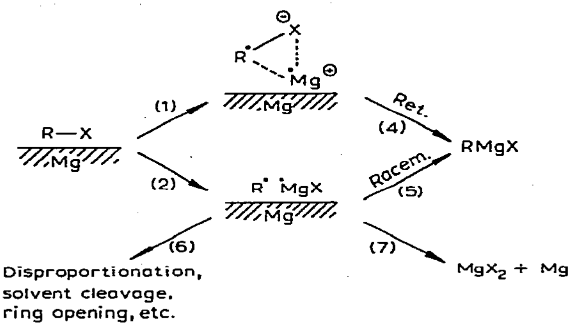
It has been pointed out that the isolation of dimeric products from the Grignard reaction is a strong indication that radicals are involved in this reaction[1,2]. In the present case, the formation of the closed dimer (VI), not only points to the involvement of radical intermediates, but taken with the lack of solvent cleavage is a strong indication of the surface bound nature of these intermediates. It has been shown[18] that when the 1-methyl-2,2-diphenylcyclopropyl radical is generated in solution it either cleaves solvent forming the cyclopropane, or isomerizes to the allyl radical. Here it was found that there is very little solvent cleavage and only a small amount of product attributable to the allyl radical was detected. It seems unlikely that dimerization of the bulky, tertiary, 1-methyl-2,2-diphenylcyclopropyl radical to the above closed dimer would be a particularly favorable process[18]. Since in addition to solvent cleavage and disproportionation, this radical can also isomerize to the highly stabilized allyl derivative, it is very unlikely that the closed dimer is formed in solution.

The fact that the open acid (II) is formed is an indication that some of the cyclopropyl radical either isomerizes in solution or on the surface of the magnesium to form an allylic Grignard reagent, which although predominantly a primary Grignard reagent[20] is carbonated to yield the tertiary acid[21] (II).

A mechanistic scheme which fits the present results is shown in Scheme 2.

SCHEME 2

A MECHANISTIC SCHEME FOR GRIGNARD REAGENT FORMATION



The processes pictured in Scheme 2 are assumed to take place on the surface of the magnesium. Interaction of the cyclopropyl halide and magnesium by pathway (1) gives a radical anion in close association with a univalent magnesium cation. It has been proposed[22] that such unstable radical anions are formed in the first step of the electro-reduction of alkyl halides. In the present case the tight anion radical cation radical pair collapses by pathway (4) to Grignard reagent with complete retention of configuration. Alternatively collapse may proceed by pathway (3) to a loose radical pair, which may also be formed directly from magnesium by pathway (2). Bodewitz, Blomberg and Bickelhaupt have recently provided evidence consistent with the incursion of such a radical pair in an elegant CIDNP experiment[23]. In the loose radical pair racemization takes place. Combination of the cyclopropyl radical with the magnesium halide radical produces racemic Grignard reagent. The organic radical may, however, escape capture by magnesious halide and undergo disproportionation, ring opening and dimerization. It may also attack the benzene rings of adsorbed species and to a small extent the solvent.

This mechanism is in accord with the effect of halide on the stereochemistry and amount of Grignard reagent formation. The energy of the carbon–halogen bond increases in the order $I < Br < Cl$ as do the optical purities and yields of the Grignard reagents. This is consistent with the amount of loose radical pair formed being determined by the strength of the carbon–halogen bond[3,10].

However, as the halogen is changed from iodide to bromide to chloride, not only does the bond strength increase, but more energy is required to add an additional electron to the carbon–halogen bond. As a result, the lifetime of the intermediate radical ion decreases in this order and the reaction becomes more concerted with the consequence that there is less loose radical pair formed and thus less racemization and loss of material to side processes.

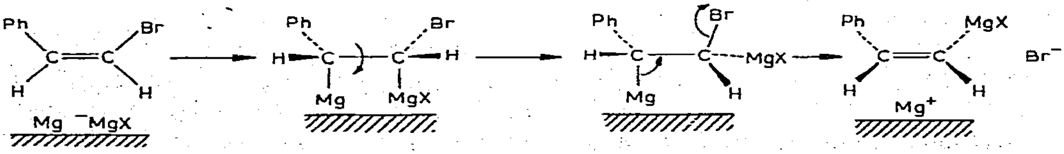
The net inversion of configuration of the hydrocarbon observed when the Grignard reagent was formed from the chloride in THF (Table 1, runs 1 and 2) may be due to the strength of the carbon–chloride bond. If this bond were not completely broken when the cyclopropyl radical attacked a hydrogen source some inversion of configuration would result since the chlorine atom would tend to block reaction at the "front" of the molecule.

We must now turn our attention to an explanation of the differences found when the Grignard was formed from the bromide in tetrahydrofuran and ether. It will be recalled that the yield of Grignard reagent is drastically reduced in ether while the yield of side products increases. At the same time there is no difference in the stereochemistry of the reaction (see Table 2). The experiments in deuterated solvents rule out increased solvent cleavage in ether as the explanation (see Table 3). An explanation of these results will be found in the differing abilities of the two solvents to stabilize the intermediates involved. From the literature on aromatic radical anions, it appears that ethyl ether is one of the poorer solvents for the formation of such species from alkali metals while tetrahydrofuran is effective in promoting their formation[24]. Tetrahydrofuran has also been found to give a blue solution with Na–K while ethyl ether does not[25]. Possibly due to its greater solvating ability THF stabilizes the intermediate radical anion and any magnesium(I) halide formed to a much greater extent than does ether. Because stabilization of the radical anion is not so great in ether, more loose radical pair is formed in this solvent. Since magnesium(I) halide is also less stabilized more of it is destroyed by pathway (7). Thus, much of the radical instead of forming racemic Grignard reagent is diverted to side products in ether. It can be seen that in this way although less Grignard reagent is formed there need not be any change in the stereochemistry of the reaction since the relative amounts of material which result in Grignard reagent from pathways (4) and (5) can remain constant.

The results of Yoshino, Manabe and Kikuchi[9a] which are in many respects similar to those cited above seem also to be explicable on the same basis. They obtained better yields of Grignard reagent from the β-bromostyrenes and fewer side products in THF compared with in ether. No deuterium incorporation was found when their Grignard reagent was formed in THF-d_8 while in the present case the yield of deuterated material was quite low. A major point of difference, however, is the great effect solvent had on the stereochemistry of styryl Grignard formation, while in the present case there was no effect. A possible explanation of this might be that an additional stereospecific pathway is available in the styryl case which is favored by THF but not by ether. Such a mechanism might be attack on the double bond by magnesious halide as illustrated in Scheme 3.

SCHEME 3

STEREOSPECIFIC FORMATION OF STYRYL GRIGNARD BY ADDITION–ELIMINATION



A similar mechanism may be written with the participation of two magnesium(I) halide molecules. The *cis* addition at the metal surface, followed by a *trans* elimination results in complete retention of configuration of the starting halide. If, as suggested earlier, the stability of magnesium(I) halide is less in ether than in THF, the contribution of this pathway would be decreased in ether causing the observed decrease in retention[9a].

Finally it should be pointed out that despite the surface nature of the reaction neither the physical state of the magnesium (powder or turnings) nor its state of purity has any effect on the stereochemistry of the reaction.

EXPERIMENTAL

Rotations at the 5.461 mercury line were measured on a Bendix–Ericson Model 987 ETL/NPL polarimeter equipped with a Texas Instrument Model FWS recorder. The instrument was zeroed on solvent, the cell was dried by blowing dry air through it and then was filled with solution. The observed rotations were then read directly from the recorder chart. The instrument was calibrated with a standard sucrose solution. After adjusting the instrument with the standard sucrose solution calibrations were made relative to a magnetic standard supplied by Bendix–Ericson. Rotations were taken on chloroform solutions unless otherwise indicated.

An F&M Model 500 programmed temperature gas chromatograph with a thermistor detector was used for analysis and separation. Unless otherwise indicated a 2′ × 1/4″ copper column, packed with 20% SF-96 on Chromosorb-P was used in separations. Infrared spectra were obtained with a Perkin–Elmer Model 137 infrared spectrophotometer. The NMR spectra were obtained using a Varian A-60 nuclear magnetic resonance spectrometer. Tetramethylsilane was used on an internal standard. Deuterium percentages in sample of 1-methyl-2,2-diphenylcyclopropane were obtained by measuring the peak heights of 9 to 15 NMR spectra of the methyl triplet[3,10]. A Varian Model recorder attached to the Model A-60 NMR spectrometer aided in obtaining the numerous spectra needed.

All compounds of the 1-methyl-2,2-diphenylcyclopropane system were prepared as previously described[3,10]. The magnesium powder used in the formation of Grignard reagents was identical to that used previously unless stated otherwise. In order to insure its dryness the magnesium was heated with a bunsen flame while the reaction flask was kept at 0.005 mmHg or less and open to the liquid nitrogen trap.

General procedure

Preparation of 1-metallo-1-methyl-2,2-diphenylcyclopropanes was done on a vacuum manifold system. Reactions were done in a 100 ml flask especially constructed for use on the manifold. The flask was fitted with a closed "Dry-Ice" condenser fused directly to it, a neck ending in a Kimax greaseless vacuum joint by which the flask was attached to the vacuum system, a 19/38 female joint, and a 14/20 female joint. A closed L-shaped tube with a 19/38 male joint placed in the appropriate neck of the flask held the solid halides. By rotating this tube the solid could be dumped into the reaction mixture with the aid of a little tapping. The 14/20 joint held either a 14/20 stopper or a thermometer in a 14/20 joint. Directly attached to the manifold were an argon cylinder (Matheson, 99.998% purity) and a CO_2 cylinder (Matheson, 99.99% purity). A mercury barometer served as an escape valve for the gases.

Before the start of any reaction, the reaction flask with the metal and magnetic stirring bar in the bulb and the halide to be used in the L-shaped tube was placed on the manifold and pumped out at 0.005 mmHg or less in order to remove any residual moisture. Solvents were distilled from lithium aluminum hydride into a graduated tube with a 19/38 female joint and containing lead–sodium alloy. This was quickly transferred to the manifold and degassed by the freeze-thaw technique. The required amount of solvent was then allowed to distill into the reaction flask, where it was condensed with liquid nitrogen. The entire system was then brought to atmospheric pressure with argon. After allowing the reaction flask to warm to room temperature, and increasing the flow of argon, the 14/20 stopper was removed from the reaction flask, and rapidly replaced with a thermometer equipped with a 14/20 joint. (The thermometer had been stored in a tube over "Drierite" before use.) The argon flow was then decreased and the reaction carried out. (Specific details for each reaction are given below.)

At the end of the reaction, the argon flow was again increased, the thermometer removed and replaced with a 14/20 stopper. The reaction flask was then isolated from the system and cooled with liquid nitrogen. The entire system was evacuated as was the reaction flask once its contents had frozen solid. After making sure that the stopcock to the barometer and all the stopcocks in the carbon dioxide line were open, CO_2 was run into the system. A large excess of CO_2 was either condensed directly into the reaction flask or else it was first condensed in a storage bulb and then sublimed into the reaction flask. The system was then brought back to atmospheric pressure with CO_2 and the CO_2 in the reaction flask was vented through the barometer as it evaporated. In order to ensure complete carbonation the reaction mixture and the solid CO_2 were thoroughly stirred with the magnetic stirrer.

Reaction of (−)-*1-methyl-1-bromo-2,2-diphenylcyclopropane with magnesium in refluxing tetrahydrofuran for* 30 *minutes*

To a stirred slurry of 0.22 g of magnesium powder in 5 ml of tetrahydrofuran which had been dried by distilling it from $LiAlH_4$ were added 0.9972 g (0.00348 mole) of 1-methyl-1-bromo-2,2-diphenylcyclopropane ($[\alpha]^{23.5}_{5461}$ $-129.47 \pm 0.57°$). At the start of the bromide addition the temperature was 60°. After a few minutes it climbed to 66° where it stayed for the remainder of the reaction. As the reaction proceeded the solution became green. Stirring was stopped after about 30 min, the reaction mixture cooled to room temperature, and then frozen with liquid nitrogen 35 min after the start of bromide addition. The reaction mixture was then treated with carbon dioxide. Upon evaporation of the CO_2, the solution was filtered through a sintered glass funnel in order to separate it from the remaining metal. The residue was washed 3–4 times with THF, adding the washings to the original filtrate. After this process the only residue remaining was magnesium. The THF was evaporated and replaced with a mixture of ether and dilute HCl.

The work-up procedure outlined earlier was now followed eventually giving an ethereal fraction and an aqueous basic extract. The basic extract was acidified precipitating the solid acid which was filtered, washed and dried. The acid obtained weighed 0.6105 g (70%), had $[\alpha]^{23}_{5461}$ $+7.62 \pm 0.03°$ (*c* 1.657), m.p. 171–181° and an infrared spectrum which matched that of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The oil obtained on evaporating the solvent from the ethereal extracts was dissolved in benzene and dried over sodium sulfate. The solution was filtered from the drying agent and the benzene evaporated, giving an oil. From this oil by means of gas–liquid chromatography 1-methyl-2,2-diphenylcyclopropane was obtained which had ($[\alpha]^{23}_{5461}$ +9.13±0.20° (*c* 0.985)). The NMR and infrared spectra matched those of authentic material. The yield of hydrocarbon was 6.0%.

Reaction of (−)-1-*methyl*-1-*bromo*-2,2-*diphenylcyclopropane with magnesium in refluxing tetrahydrofuran for* 180 *minutes*

To a stirred slurry of 0.22 g of magnesium powder in 5 ml of tetrahydrofuran which had been dried by distilling it from lithium aluminum hydride into lead–sodium alloy were added 0.9053 g (0.00316 mole) of 1-methyl-1-bromo-2,2-diphenylcyclopropane ($[\alpha]^{23.5}_{5461}$ −128.55±0.71°). The addition of bromide took about 5 min and the reaction initiated about 3 min after the addition started. The temperature rose to 67° during the initiation and was maintained at reflux for the remainder of the reaction. After 180 min the reaction mixture was frozen with liquid nitrogen and then treated with carbon dioxide in the usual manner. The carbonated reaction mixture was separated from the residual magnesium as described earlier. The THF was evaporated, ether was added to the residue and the reaction mixture was then worked up in the usual way.

Acidification of the basic extracts gave 0.6280 g (79%) of the solid acid which after filtering, washing with water and drying had $[\alpha]^{25}_{5461}$ +6.60±0.03° (*c* 1.402), m.p. 173–181°, and the infrared spectrum of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The ethereal extract was dried over anhydrous sodium sulfate, filtered and concentrated. The residue was dissolved in methanol and filtered. After evaporation of the solvent, the residue was fractionated by gas–liquid chromatography as described earlier. The 1-methyl-2,2-diphenylcyclopropane was obtained in a 4.8% yield and had $[\alpha]^{25}_{5461}$ +6.22±0.81° (*c* 0.370).

Reaction of (+)-1-*methyl*-1-*chloro*-2,2-*diphenylcyclopropane with magnesium in refluxing tetrahydrofuran for* 30 *minutes*

To a stirred slurry of 0.22 g magnesium in 5.5 ml of tetrahydrofuran (dried as previously described) were added 1.1108 g (0.0046 mole) of 1-methyl-1-chloro-2,2-diphenylcyclopropane ($[\alpha]^{25}_{5461}$ +75.16±0.23°). Addition of the chloride was begun when the temperature of the solvent reached 60°. All but a few milligrams of the chloride was added in 3 min. Initiation occurred about 10 min after the start of the addition. At this point the temperature rose to 67° and the reaction mixture turned brown-green in color. Reflux was maintained for about 25 min more. The reaction mixture was then frozen with liquid nitrogen and treated with carbon dioxide in the usual manner. The resulting solution was freed from metal as previously described. After the THF was distilled off and replaced with ether, the usual work-up gave a basic extract and an ethereal extract. The acid obtained after acidification of the basic extracts, filtering, washing and drying weighed 0.8480 g (80.8% based on the amount of chloride which reacted) had $[\alpha]^{22.5}_{5461}$ −10.68±0.03° (*c* 1.470), m.p. 171.5–181.5°, and the infrared spectrum of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

Concentration of the ethereal extracts gave an oil which distilled from 42–51°

at 0.005 mmHg. By means of GLC 1-methyl-2,2-diphenylcyclopropane was separated from the distillate. The hydrocarbon had $[\alpha]^{24}_{5461}$ +13.01±0.19° (*c* 1.037). In order to ensure that there was no chloride present, the hydrocarbon was repurified by GLC. After this process the hydrocarbon had $[\alpha]^{24}_{5461}$ +9.97±0.54° (*c* 0.5515). The yield of repurified hydrocarbon was 1.3%.

Reaction of (+)-1-*methyl*-1-*chloro*-2,2-*diphenylcyclopropane with magnesium in refluxing tetrahydrofuran for* 180 *minutes*

To a stirred slurry of 0.33 g of magnesium powder in 7.5 ml of tetrahydrofuran (dried as previously described) were added 1.5299 g (0.00627 mole) of 1-methyl-1-chloro-2,2-diphenylcyclopropane ($[\alpha]^{25}_{5461}$ +75.16±0.23°). Addition of the chloride took about 30 sec and was begun when the solvent temperature reached 60°. About 8 min after the chloride addition the solution was light green in color. After 185 min the reaction mixture was frozen with liquid nitrogen and then treated with carbon dioxide. Using the procedure indicated earlier an aqueous basic fraction and an ethereal fraction were obtained. The solid dry acid obtained from the basic fraction weighed 1.4061 g (89%), had $[\alpha]^{25}_{5461}$ −10.54±0.07° (*c* 1.480), m.p. 172–181.5° and the infrared spectrum of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The ether layer was concentrated and the resulting oil was distilled in a molecular still with pot temperature 30–46° and pressure about 0.005 mmHg. The distillate was purified by GLC giving 1-methyl-2,2-diphenylcyclopropane with $[\alpha]^{24}_{5461}$ +8.03±0.47° (*c* 0.6350). GLC of this material on the same column showed no contaminants were present. Yield of the hydrocarbon was 1.0%.

Reaction of (−)-1-*methyl*-1-*iodo*-2,2-*diphenylcyclopropane with magnesium in refluxing tetrahydrofuran for* 30 *minutes*

To a stirred slurry of 0.22 g of magnesium in 4.0 ml of tetrahydrofuran were added 0.8179 g (0.00245 mole) of 1-methyl-1-iodo-2,2-diphenylcyclopropane ($[\alpha]^{24}_{5461}$ −202.56±0.64°). Addition of the iodide took about 2 min and was commenced when the solvent temperature reached 62°. The reaction initiated almost immediately. After 34 min the reaction mixture was frozen with liquid nitrogen and then treated with carbon dioxide. The resulting solution was filtered from the residual metal.

After distilling out the THF and replacing it with ether, the usual work-up gave an aqueous basic extract and an ethereal extract. From the basic extract the solid acid was obtained on acidification. The dried acid weighed 0.2451 g (39.8%), had $[\alpha]^{25}_{5461}$ +0.76±0.05° (*c* 1.479), m.p. 166–180° and the infrared spectrum of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The ethereal fraction was concentrated and the resulting oil distilled in a molecular still with pot temperature 33–45° and pressure 0.003–0.008 mmHg. By means of GLC 1-methyl-2,2-diphenylcyclopropane was separated from the distillate, having $[\alpha]^{25}_{5461}$ +1.23±0.26° (*c* 1.139). The yield of the hydrocarbon was 4.4%.

Reaction of (+)-1-*methyl*-1-*iodo*-2,2-*diphenylcyclopropane with magnesium in refluxing tetrahydrofuran for* 180 *minutes*

To a stirred slurry of 0.22 g of magnesium in 4.0 ml of tetrahydrofuran (dried as previously described) were added 0.7813 g (0.00234 mole) of 1-methyl-1-iodo-2,2-diphenylcyclopropane ($[\alpha]^{30}_{5461}$ +200.78±0.65°). Most of the iodide was added in

1 min, but some adhered to the neck of the flask and was washed in a few minutes after the addition was started. The iodide was added when the solvent began to reflux. Initiation occurred immediately. The reaction mixture was refluxed a total of 180 min then frozen with liquid nitrogen and treated with carbon dioxide.

After freeing the resulting solution from magnesium by filtering through a sintered flass funnel into a flask cooled in Dry-Ice, the THF was distilled and replaced with ether.

The usual work-up gave a basic aqueous fraction and an ethereal fraction. Acidification of the basic extracts gave the solid acid which was filtered, washed and dried. The dry acid weighed 0.2110 g (35.8%), had $[\alpha]_{5461}^{24}$ $-0.78\pm0.05°$ (*c* 1.507), m.p. 165–180°.

Reaction of (−)-1-*methyl*-1-*bromo*-2,2-*diphenylcyclopropane with magnesium in refluxing diethyl ether*

To a mixture of 0.21 g magnesium in 10 ml of diethyl ether (dried by distilling from lithium aluminum hydride) were added 1.0258 g (0.00358 mole) of 1-methyl-1-bromo-2,2-diphenylcyclopropane ($[\alpha]_{D}^{25.5}$ $-111.6\pm0.9°$). The stirred reaction mixture was brought to reflux and initiated shortly thereafter. After refluxing for 29 min, the reaction mixture was frozen with liquid nitrogen and treated with carbon dioxide. Work-up of the reaction mixture gave a basic aqueous extract and ethereal neutral extract. Acidification of the basic extract gave, after drying, 0.235 g (26%) of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid, m.p. 159–177°, $[\alpha]_{D}^{23}$ $+7.27\pm1.11°$ (*c* 2.253). The ethereal layer was dried over anhydrous sodium sulfate, filtered and concentrated. The remaining oil was distilled in a molecular still at 70° and 0.25–0.3 mmHg. The distillate was then fractionated by GLC. 1-Methyl-2,2-diphenylcyclopropane obtained by this method had $[\alpha]_{5461}^{23}$ $+5.54\pm0.59°$.

Reaction of (+)-1-*methyl*-1-*bromo*-2,2-*diphenylcyclopropane with magnesium in refluxing tetrahydrofuran*-d_8

To a stirred slurry of 0.22 g of magnesium powder in 5.7 ml of tetrahydrofuran-d_8 (obtained from Volk; dried over 4A molecular sieves) were added 1.0560 g (0.00368 mole) of 1-methyl-1-bromo-2,2-diphenylcyclopropane ($[\alpha]_{5461}^{24}$ $+131.21\pm0.66°$). The bromide addition was begun when the solvent temperature reached 60°. Most of the bromide was added in 4 min; the remainder was washed in by the refluxing solvent after several minutes. The solution was refluxed for 50 min before initiation occurred. Reflux was continued another 29 min, after which the reaction mixture was frozen with liquid air and treated with carbon dioxide in the usual manner. Upon completion of this step, the reaction mixture was again frozen with liquid air, the manifold and reaction flask were evacuated and the tetrahydrofuran-d_8 was allowed to distill into a tube cooled with liquid air. After bringing the reaction flask back to atmospheric pressure with argon, dried THF was added and the work-up described earlier was followed.

From the basic fraction was obtained 0.8127 g (87.6%) of dry acid which had $[\alpha]_{5461}^{24}$ $-5.40\pm0.03°$ (*c* 1.566), m.p. 180–183.5° and the infrared spectrum of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The neutral fraction was dried over sodium sulfate, filtered and concentrated. The resulting oil was distilled in a molecular still with oil bath temperature 40.0°, and pressure 0.005 mmHg. Only a small amount of distillate was obtained. Using the NMR peak height analysis described earlier the percentage of 1-methyl-2,2-diphenylcyclopropane containing deuterium at the 1-position was found to be 29.2±0.3. By means of GLC 1-methyl-2,2-diphenylcyclopropane was separated from the distillate with $[\alpha]^{25}_{5461}$ $-15.50\pm0.83°$ (*c* 0.362). The yield of hydrocarbon was 0.95%.

The previous experiment was repeated using a slurry of 0.44 g of magnesium powder in approximately 10 ml of THF-d_8 (Volk; dried over 4A molecular sieves) to which 1.9982 g (0.00695 mole) of 1-methyl-1-bromo-2,2-diphenylcyclopropane ($[\alpha]^{24}_{5461}$ $+131.21\pm0.66°$) were added. Addition of the bromide was begun when the solvent temperature reached 50°. All of the bromide was added in a few seconds. Initiation occurred in 3 min. The solution was refluxed a total of 29 min. It was then frozen with liquid nitrogen and treated with carbon dioxide. After the CO_2 had evaporated, the THF-d_8 was recovered by the procedure; the procedure and work-up described earlier were then followed.

Acidification of the basic extract gave the solid acid which after filtration, washing and drying weighed 1.6311 g (93.2%) had $[\alpha]^{29}_{5461}$ $-5.47\pm0.03°$ (*c* 1.530 g), m.p. 177–182°, and the infrared spectrum of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The ethereal extract was dried over sodium sulfate, filtered and concentrated. The resultant oil was distilled in a molecular still with oil bath temperature 36–45° and pressure 0.005 mmHg. The distillate was examined by NMR spectroscopy and the 1-methyl-2,2-diphenylcyclopropane in it was found to contain 28.1±0.2% deuterium at the 1-position.

By means of GLC 1-methyl-2,2-diphenylcyclopropane was separed from the distillate. The hydrocarbon had $[\alpha]^{26}_{5461}$ $-11.57\pm0.20°$ (*c* 1.029) and was obtained in 1.4% yield.

Reaction of (+)-1-methyl-1-bromo-2,2-diphenylcyclopropane with magnesium in refluxing diethyl ether-d_{10}

To a stirred slurry of 0.21 g of magnesium powder in 7.0 ml of diethyl ether-d_{10} (obtained from Merck Sharpe and Dohme; dried over 4A molecular sieves) were added 1.4024 g (0.00488 mole) of 1-methyl-1-bromo-2,2-diphenylcyclopropane ($[\alpha]^{24}_{5461}$ $+131.21\pm0.66°$). The reaction mixture was brought to the boiling point and approximately 5 min thereafter the reaction initiated. The reaction mixture was refluxed for 34 min after initiation and then frozen with liquid nitrogen. After carbonating the reaction mixture in the usual manner and allowing the CO_2 to evaporate, the reaction mixture was again frozen with liquid nitrogen, the manifold and flask evacuated, and the ether-d_{10} allowed to distill into a tube cooled with liquid nitrogen. The reaction flask was then brought back to atmospheric pressure with argon, THF was added to the reaction mixture, and the solution was filtered away from the residual metal. After the usual work-up, basic aqueous fraction and a neutral ethereal fraction were obtained.

Acidification of the basic fraction, gave after drying, 0.3099 g (25.2%) of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid with $[\alpha]^{31}_{5461}$ $-7.55\pm0.03°$ (*c* 1.467) and m.p. 156–174.

The ethereal extract was dried over anhydrous sodium sulfate, filtered and concentrated. The residual oil was distilled in a molecular still at 39–40° and 0.003

mmHg. By means of GLC 1-methyl-2,2-diphenylcyclopropane was separated from the distillate. The hydrocarbon had $[\alpha]^{31}_{5461}$ $-6.95\pm0.03°$ (*c* 1.715). Using the NMR peak height analysis described earlier, deuterium incorporation at the 1-position was found to be $6.7\pm0.2\%$. The yield of hydrocarbon was 20.2%.

Reaction of (+)-1-*methyl*-1-*bromo*-2,2-*diphenylcyclopropane with magnesium turnings in refluxing tetrahydrofuran*

The procedure followed here was the same as that used in the corresponding experiments with magnesium powder. To 0.22 g of magnesium turnings in 5.0 ml of tetrahydrofuran which had been dried by distilling from $LiAlH_4$ into lead–sodium alloy were added 1.0324 g (0.0036 mole) of 1-methyl-1-bromo-2,2-diphenylcyclopropane ($[\alpha]^{23}_{5461}$ $+128.78\pm0.64°$). The addition of bromide took about 3 min and was started when the temperature of the THF was 45°. The reaction initiated about 10 min after the THF began to reflux. After maintaining the reaction mixture at reflux for another 31 min, it was frozen with liquid nitrogen and then treated with carbon dioxide in the usual manner. The carbonated reaction mixture was filtered through a sintered glass funnel, the residue washed with several portions of dry THF and the washings added to the filtrate.

The usual work-up gave a basic extract which upon acidification yielded 0.5643 g (62.2%) of dried acid. The acid had $[\alpha]^{22}_{5461}$ $-6.51\pm0.03°$ (*c* 1.527), m.p. 172.5–180, and the infrared and NMR spectra of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The ethereal extract was dried over anhydrous sodium sulfate, filtered and concentrated to give an oil which was distilled in a molecular still at 35–38° and 0.002–0.004 mmHg. By means of GLC 1-methyl-2,2-diphenylcyclopropane was separated from the distillate. The hydrocarbon had $[\alpha]^{22.5}_{5461}$ $-9.00\pm0.09°$ (*c* 2.220), and its yield was 7.9%.

Reaction of (+)-2,2-*diphenyl*-1-*methylcyclopropyl bromide with high purity magnesium in refluxing THF*

A solution of 0.997 g (0.00348 mole) of (+)-2,2-diphenyl-1-methylcyclopropyl bromide ($[\alpha]^{30}_{Hg}$ $+129.8°$) in 5 ml of dry tetrahydrofuran (THF) was mixed with 0.25 g (0.103 mole) of high purity magnesium turnings under a dry argon atmosphere. The mixture was heated at reflux for 30 min with constant stirring. No apparent reaction occurred. Ethylene bromide (ca. 0.1 ml) was added and heating continued. Ten minutes after addition of the ethylene bromide, the mixture began to foam. The heat source was removed and the mixture continued to reflux for ca. 10 min. The mixture was then heated at reflux for an additional 20 min. After being cooled to room temperature, the mixture was pale gray in color and somewhat cloudy. It was frozen by immersing the reaction vessel in liquid nitrogen. The argon atmosphere was replaced with one of Coleman grade carbon dioxide, which condensed in the cooled reaction vessel. After an estimated 10 g of carbon dioxide had condensed, the mixture was allowed to warm slowly to room temperature. As soon as possible, stirring was begun. After all the CO_2 had evaporated, the mixture was filtered. The solid material (excess magnesium) was washed several times with THF and these washings were combined with the original filtrate. The THF was then removed at reduced pressure and replaced with a mixture of ether and 3 *N* hydrochloric acid. The layers were separated and the ether layer was washed twice with water. Acidic products were extracted from the ether solution with 2 *N* sodium hydroxide solution. The basic extract was washed twice with ether. Upon acidifying the basic solution with concentrated HCl, a white solid formed. This was filtered, washed with water and dried in a vacuum desiccator giving 0.3943 g (0.00157 mole, 45 %) of 2,2-diphenyl-1-methylcyclopropane carboxylic acid: m.p. 178–184°, $[\alpha]_{\mathrm{Hg}}^{24}$ $-6.49°$ (*c* 1.55 in $CHCl_3$), 15 % optically pure.

Test of exchange of the Grignard reagent from (±)-1*-methyl-*1*-bromo-*2,2*-diphenylcyclopropane with* (+)-1*-methyl-*1*-bromo-*2,2*-diphenylcyclopropane in tetrahydrofuran refluxed for* 180 *minutes*

The Grignard reagent from (±)-1-methyl-1-bromo-2,2-diphenylcyclopropane was prepared by refluxing 0.5945 g (0.0021 mole) of the racemic bromide and 0.13 g of magnesium in 6.0 ml of anhydrous THF for 80 min under an argon atmosphere. Stirring was accomplished with a magnetic stirring bar. The reaction was carried out in a flask having a neck containing a sintered glass disk and ending in a standard ground glass joint. The Grignard reagent could thus be separated from unreacted magnesium.

After cooling to room temperature the Grignard reagent was transferred under argon to the reaction flask used in conjunction with the manifold (described earlier) in which 0.4992 g (0.00174 mole) of 1-methyl-1-bromo-2,2-diphenylcyclopropane ($[\alpha]_{5461}^{24}$ $+131.21 \pm 0.66°$) was stored under argon. The solution was then refluxed and stirred for 180 min under argon. At the end of this time it was frozen with liquid nitrogen and treated with carbon dioxide in the usual manner. After all the carbon dioxide had evaporated, the solution was transferred to another flask, the THF distilled out and replaced with ether. Acidification of the basic extracts gave the acid, which after filtration, washing and drying weighed 0.2473 g (47.4 %), had $[\alpha]_{5461}^{30}$ 0.00, m.p. 181.5–183, and the infrared spectrum of the expected acid.

Products from the reaction of (±)-1*-methyl-*1*-bromo-*2,2*-diphenylcyclopropane and magnesium in refluxing diethyl ether*

To a stirred slurry of 1.1 g of magnesium powder in 25 ml of dry ether were added 4.9485 g of racemic 1-methyl-1-bromo-2,2-diphenylcyclopropane. The reaction mixture was brought to reflux and soon initiated. After 50 min of refluxing the mixture was frozen with liquid air, and then carbonated in the usual manner. Following the usual work-up a basic aqueous fraction and a neutral ethereal fraction were obtained.

Acidification of the acid fraction gave a white solid which after drying weighed 1.5370 g with m.p. 162–179°. Examination of the NMR spectrum of this material revealed that it was 1-methyl-2,2-diphenylcyclopropanecarboxylic acid with a small amount of another substance. By means of fractional crystallization from methanol of a 0.5107 g sample of this acidic fraction the impurity was concentrated until by means of NMR it was estimated to be present in an amount approximately equal to that of the known acid. Besides peaks belonging to 1-methyl-2,2-diphenylcyclopropanecarboxylic acid, the NMR spectrum of this mixture showed a singlet at 1.8 ppm and two peaks, each somewhat split at 4.8 ppm and 5.2 ppm. In addition, protruding from the normally broad envelope of peaks between 7.0 and 7.6 ppm characteristic of the phenyls of the cyclopropyl acid was an intense singlet centered at about 7.3 ppm. The acids were converted to their methyl esters with diazomethane. By means of GLC on a 2′ × $\frac{1}{4}$″ copper column packed with 20% QF-1 on Chromsorb P, the two esters were cleanly separated; a pure sample of the unknown acid being obtained in this way. The NMR spectrum of this material showed a sharp singlet at 7.23 ppm, slightly split peaks at 5.15 ppm and 4.70 ppm, a singlet at 3.69 ppm and a slightly split singlet at 1.75 ppm, in the ratio of 10/1/1/3/3 respectively, in agreement with that expected from 2,2-diphenyl-2-methyl-2-butenoic acid (II) methyl ester. The authentic acid synthesized by carbonation of the Grignard reagent from 2-methyl-3,3-diphenylallyl bromide[15] had an NMR spectrum identical to that of the above acid. The yields of the acids obtained were 34% for the cyclopropyl acid and 1% for the open acid.

The neutral ethereal extract was dried over anhydrous sodium sulfate, filtered and concentrated. The resulting oil was then distilled in a molecular still at 0.005 mmHg and 38–40°. The NMR spectrum of this oil showed that it was a mixture of three components. The known absorptions for 1-methyl-2,2-diphenylcyclopropane (III) as well as those for 2,2-diphenylmethylenecyclopropane (IV) were present. Besides these absorptions, there was a doublet at 2.1 ppm, with separation of about 1 Hz. The allylic methyl group of 1,3,3-trimethylcyclopropene absorbs at 1.90 ppm and is split by long range coupling of the vinylic H by 1.1 Hz[16].

Using NMR spectroscopy, the relative amounts of 1-methyl-2,2-diphenylcyclopropane (III), 1-methyl-2,2-diphenylcyclopropene (V), and 2,2-diphenylmethylenecyclopropane (IV) in the mixture were determined by measuring the areas of the respective methyl peaks and methylene peaks with a planimeter (applying a correction factor of $\frac{3}{2}$ in the latter case because the area is proportional to only 2 protons). The results of 5 area determinations on 3 different spectra were averaged. The percentages of each component in the mixture were 1-methyl-2,2-diphenylcyclopropane (III), 65.5; 1-methyl-3,3-diphenylcyclopropene (V), 9.0; 2,2-diphenylmethylenecyclopropane (IV), 25.4. The overall yields of these compounds were 23%, 3.2% and 9.1% respectively.

Although 1-methyl-2,2-diphenylcyclopropene could not be separated from the mixture, further proof of its presence was obtained by isomerizing it to 2,2-diphenylmethylenecyclopropane with potassium tert-butoxide in tert-butyl alcohol[17].

To a 50 ml flask, fitted with reflux condenser and drying tube, were added 20 ml of tert-butyl alcohol and 0.6 g of metallic potassium. The mixture was stirred with a magnetic stirrer until the potassium dissolved. A solution of 0.3069 g of mixture of three components described above, in 10 ml of tert-butyl alcohol was then added. After refluxing the reaction mixture approximately 24 h, it was worked up. Most of the tert-butyl alcohol was distilled out, and the remainder evaporated in an air stream. Water was added to the residue and the mixture was extracted with ether. After washing the ethereal extract several times with water, it was dried over anhydrous sodium sulfate, filtered and concentrated. The dark oil that remained was distilled in a molecular still at 38–40° and 0.003–0.005 mmHg. Examination of the distillate by NMR spectroscopy revealed that the peak at 2.1 ppm was completely absent. Using the NMR procedure described above the mixture was found to contain 33.8% 2,2-diphenylmethylenecyclopropane and 66.2% 1-methyl-2,2-diphenylcyclopropane. On the basis of complete isomerization the amount of 2,2-diphenylmethylenecyclopropane expected was 34.4%.

The residue remaining after the removal of the low molecular weight hydrocarbons was freed from stopcock grease by dissolving it in hot methanol, filtering and concentrating. The thick oil which remained was found to give a crystalline precipitate when dissolved in ether and allowed to stand at room temperature. More crystalline material precipitated when the corked flask was cooled in a refrigerator for about 24 h. After syringing the supernatant liquid away from the solid, it was washed with ether and then recrystallized from the same solvent. In this way 0.0331 g of this material was obtained. The NMR spectrum of this material had a broad envelope of phenyl absorptions from 6.59–7.48 ppm, a singlet at 1.24 ppm and a quartet from 0.42–0.92 ppm with a coupling constant of 6 Hz. These peaks were in the ratio of 20/6/4 respectively. The position, multiplicity and relative intensities of the peaks found in the NMR spectrum are entirely consistent with dimeric structure (VI).

The elemental analysis of this material, m.p. 183–184, was also in accord with this structure. (Found: C, 92.58; H, 7.36. $C_{32}H_{30}$ calcd.: C, 92.71; H, 7.29%.)

The mass spectrum[18] of this compound gave a molecular weight of 414, showed that the compound had exactly 32 carbon atoms and gave a fragmentation pattern completely consistent with the above dimeric structure. Fragments corresponding to phenyl, diphenylmethyl and tetraphenylbutadiene were among those found.

Isolation of dimer (VI) from a reaction starting with optically active bromide showed (VI) to be completely racemic.

The residual oil was also subjected to separation by preparative thin layer chromatography on silica using benzene as the eluant. The first band on the plate was removed and extracted with chloroform. Concentration of the extract gave an oil which contained a good deal of the light hydrocarbons which were found in the molecular distillate. This oil was distilled in a molecular still to remove the remainder of the light hydrocarbon fraction using the conditions mentioned earlier. The residue was crystallized with hexane. The first crop obtained was primarily an impure sample of the above closed dimer (VI). From the mother liquor after repeated fractional crystallization from hexane were obtained a few milligrams of a white solid, m.p. 156–157°. The NMR spectrum of this substance had phenyl absorption from 6.71–7.60 ppm, a quartet with absorption between 0.55 and 1.54 ppm and a singlet at 1.15 ppm. The quartet had a coupling constant of 5 Hz. The absorptions were in the ratio of 21/5.5/5.5 respectively. The elemental analysis of this material gave C 92.69%, H 7.39%.

The mass spectrum[18] of this material revealed that it was a substance of molecular weight 412 contaminated with the closed dimer (VI) of mol.wt. 414, discussed above. The substance of mol.wt. 412 gave fragments corresponding to phenyl, diphenylmethyl, C_2H_4 and split to a fragment of mass 206.

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REFERENCES

1 M. S. Kharasch and O. Reinmuth, *Grignard Reactions of Non-Metallic Substances*, Prentice-Hall, Inc., New York, 1954.

2 E. C. Ashby, *Quart. Rev.*, 21 (1967) 259.
3 H. M. Walborsky and A. E. Young, *J. Amer. Chem. Soc.*, 83 (1961) 2595; H. M. Walborsky, *Record. Chem. Progr.*, 23 (1962) 75; and references cited therein.
4 W. Kondyrew, *Ber. Deut. Chem. Ges. B*, 58 (1925) 459.
5 P. Brun, *J. Chim. Phys.*, 36 (1939) 147.
6 M. P. Khyrak, *Chem. Abstr.*, 61 (1964) 13165*a*.
7 M. Anteunis and J. Van Schoote, *Bull. Soc. Chim. Belg.*, 72 (1963) 787.
8 G. Rüchhardt and H. Trautwein, *Chem. Ber.*, 95 (1962) 1197.
9 (a) T. Yoshino, Y. Manabe and Y. Kikuchi, *J. Amer. Chem. Soc.*, 86 (1964) 4670; (b) G. J. Martin and M. L. Martin, *Bull. Soc. Chim. Fr.*, (1966) 1635; G. J. Martin and N. Naulet, *Bull. Soc. Chim. Fr.* (1970) 4001.
10 (a) H. M. Walborsky and A. E. Young, *J. Amer. Chem. Soc.*, 86 (1964) 3288; (b) H. M. Walborsky and A. E. Young, *Baskerville Chem. J.* (*C.C.N.Y.*), 14 (1965) 1; (c) H. H. Grootveld, C. Blomberg and F. Bickelhaupt, *Tetrahedron Lett.*, (1971) 1999.
11 F. R. Jensen and K. L. Nakamaye, *J. Amer. Chem. Soc.*, 88 (1966) 3437; G. M. Whitesides, M. Witanowski and J. D. Roberts, *J. Amer. Chem. Soc.*, 87 (1965) 2854; E. Pechold, D. G. Adams and G. Fraenkel, *J. Org. Chem.*, 36 (1971) 1368.
12 C. W. Porter, *J. Amer. Chem. Soc.*, 57 (1935) 1436.
13 R. D. Chambers, W. K. R. Musgrave and J. Savory, *Proc. Chem. Soc.*, (1961) 113; R. Pierce, A. F. Meiners and E. T. McBee, *J. Amer. Chem. Soc.*, 75 (1953) 2516; R. Sullivan, J. R. Lacher and J. D. Park, *J. Org. Chem.*, 29 (1964) 3644.
14 L. I. Zakharkin, O. Yu. Okhlobystin and K. A. Bilevitch, *Tetrahedron*, 21 (1965) 881; *J. Organometal. Chem.*, 2 (1964) 309.
15 J. P. Oliver, *M.S. thesis*, Florida State University, unpublished results, 1965.
16 G. L. Closs and L. E. Closs, *J. Amer. Chem. Soc.*, 83 (1961) 1003.
17 G. Schroder, *Chem. Ber.*, 96 (1963) 3178.
18 H. M. Walborsky and Jong-Chen Chen, *J. Amer. Chem. Soc.*, 92 (1970) 7573; 93 (1971) 671.
19 Ref. 2, pp. 64–65; I. P. Gregerov and M. Ya. Turkina, *J. Gen. Chem. USSR*, 33 (1963) 1849.
20 G. M. Whitesides, J. E. Norlander and J. D. Roberts, *J. Amer. Chem. Soc.*, 84 (1964) 2010.
21 W. G. Young *et al.*, *J. Org. Chem.*, 7 (1942) 233.
22 J. L. Webb, C. K. Mann and H. M. Walborsky, *J. Amer. Chem. Soc.*, 92 (1970) 2042; and references cited therein.
23 H. W. H. J. Bodewitz, C. Blomberg and F. Bickelhaupt, *Tetrahedron Lett.*, (1972) 281.
24 J. Smid, *Angew. Chem., Int. Ed. Engl.*, 11 (1972) 112; and references cited therein.
25 J. L. Down, J. Lewis, B. Moore and G. Wilkinson, *J. Chem. Soc.*, (1959) 3767.