

## CYCLOPROPANES

### XXXIII. REACTION OF LITHIUM METAL SURFACES WITH OPTICALLY ACTIVE 1-HALO-1-METHYL-2,2-DIPHENYLCYCLOPROPANE\*\*\*

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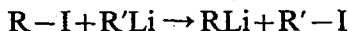
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#### SUMMARY

The reaction of lithium metal surfaces with optically active 1-halo-1-methyl-2,2-diphenylcyclopropane leads to the formation of the corresponding lithium derivative which is partially racemized. The amount of racemization observed is a function of the halide used ( $I > Br > Cl$ ), the sodium content of the lithium metal as well as its particle size.

#### INTRODUCTION

The reaction of lithium metal with alkyl halides, in which the halide is attached to a tetrahedrally hybridized ( $sp^3$ ) carbon atom, results in the formation of lithium reagents with loss of stereochemical integrity. Thus, both *exo*- and *endo*-norbornyl chloride\*\*\* give rise to an identical mixture of norbornyllithium. Similarly, menthyl and neomenthyl chloride produce the same mixture of epimeric lithium reagents<sup>3</sup>. If instead of forming the alkylolithium by treating the alkyl halide directly with lithium metal the halide [ $R = (-)$ -2-octyl] is treated with an alkylolithium ( $R' = 2$ -butyl) reagent then



the new lithium reagent formed is capable of maintaining its configuration to a modest degree<sup>4,\*\*\*\*</sup>. The degree of retention of configuration is both solvent- and temperature-dependent<sup>4,†</sup>. Both NMR<sup>6</sup> and theoretical calculations<sup>7</sup> indicate a polar covalent character for the carbon-lithium bonds in alkylolithiums. It is therefore

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\*\* For a preliminary communication of this work see ref. 1.

\*\*\* Applequist and Chmurney reported that by changing the temperature from refluxing pentane, 36° (yields of lithium reagent  $\approx 10\%$ ) to 20° (yields of lithium reagent 1-4%) the *exo/endo* ratio is changed toward greater stereospecificity. However, at 20° only the *exo*-norbornyl chloride, rather than both *exo* and *endo*, was used to determine the isomer ratio by carbonation of the lithium reagent, see ref. 2.

\*\*\*\* For a comparable result in which a dialkylmercury is used instead of an alkyl halide, see ref. 5.

† For a review of bonding in cyclopropanes, see ref. 10.

not entirely clear in the reaction of alkyl halides with lithium metal whether the loss of configuration occurs during or subsequent to alkyllithium formation.

In contrast, when the halogen is attached to a trigonally hybridized ( $sp^2$ ) carbon atom as in geometrically isomeric vinyl halides, the reaction with lithium metal surfaces proceeds to yield vinylolithium reagents with complete retention of geometric configuration<sup>8a-f</sup>. This holds equally true when vinyl bromides are treated with butyllithium to form vinylolithium by the halogen-lithium exchange reaction<sup>8d,9</sup>. The configurational stability of vinylolithium reagents is also solvent- and temperature-dependent<sup>8f,9</sup>.

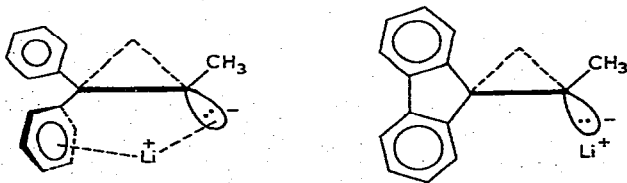
The situation with cyclopropyl halides is of interest since the hybridization of the cyclopropyl carbon atoms approximates to that of trigonally hybridized ( $sp^2$ ) carbon<sup>10</sup>. As in the case of vinyl bromides, reaction of geometrically isomeric<sup>11</sup> or optically active<sup>12</sup> cyclopropyl bromides with alkyllithium leads to the formation of the cyclopropyllithium reagent in which the configuration is completely retained. However, the configurational stability of the cyclopropyl-carbon-lithium bond is unaffected by time, temperature or solvent. In contrast to the trigonally hybridized vinylic systems the direct metallation of cyclopropyl halides with metallic lithium leads to the formation of the corresponding lithium derivative which is *partially racemized*<sup>13</sup>. Furthermore, the amount of racemization is dependent on the halogen (Cl, Br, I) used, the percentage of sodium in the lithium and the particle size of the lithium.

## RESULTS

### *The cyclopropyl system*

It has previously been shown<sup>12</sup> that formation of 1-methyl-2,2-diphenylcyclopropyllithium from the corresponding optically active bromide or iodide using the halogen-metal interchange reaction with *n*-butyllithium in ether occurs with 100% retention of configuration\*. It was found that the optical stability of the cyclopropyl carbon to lithium bond was unaffected by time, temperature or solvent.

An examination of a scale model of the 1-methyl-2,2-diphenylcyclopropyl system suggested the possibility that interaction of the lithium cation with the  $\pi$  cloud in the face of aromatic ring adjacent to it might be the cause of the configurational stability of 1-methyl-2,2-diphenylcyclopropyllithium. Such an interaction has recently been suggested in explanation of the NMR spectrum of fluorenyllithium<sup>15</sup>. In a test of this hypothesis it was found that 1-methyl-2,2-biphenylenecyclopropyllithium which differs from the diphenyl compound in that the possibility for such an interaction is eliminated, can be obtained with an optical purity of at least 93%. (The details of this



\* For assignment of relative and absolute configurations see ref. 14.

experiment and the synthesis of the necessary optically active compounds are given in the Experimental section.) This indicates that the interaction alluded to is of little or no importance as a cause of the configurational stability of 1-methyl-2,2-diphenylcyclopropyllithium and is consistent with some earlier findings<sup>11</sup>.

#### The effect of halogen

The formation of the cyclopropyllithium reagent directly from the metal results in a considerable degree of racemization, just as in the case of the direct formation of the analogous Grignard reagent<sup>14b,16</sup>. In Table 1 are the results of a study in which the lithium reagents were formed from the cyclopropyl halides using a 25 micron dispersion containing 1% sodium, and then carbonated. 1-Methyl-2,2-diphenylcyclopropane is formed as a byproduct in this reaction.

In all cases both the acid and the hydrocarbon are formed with overall retention of configuration<sup>14,★</sup>.

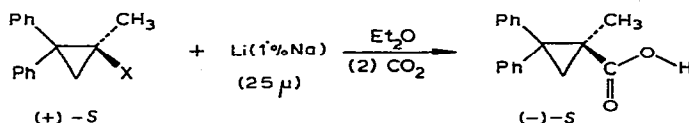


TABLE 1

FORMATION OF LITHIUM REAGENTS FROM 1-METHYL-2,2-DIPHENYLCYCLOPROPYL HALIDES AND LITHIUM (1% Na), 25  $\mu$  IN ETHER

Run	Halide	Temp. <sup>a</sup> (°C)	Time (min)	Acid		Hydrocarbon	
				Yield (%)	Optical <sup>b,c</sup> purity (%)	Yield (%)	Optical <sup>c,d</sup> purity (%)
1	Cl	25	40	72.5	68.6	1.7	62.2
2	Cl	25	60	76.5	65.5	2.6	61.7
3	Br	26	32	59.7	44.8	0.34	52.1 <sup>e</sup>
4	Br	26	42	70.0	41.0	2.8	63.9
5	I	25	33	42.4	36.2	10.8	73.0
6	I	25	41	59.8	35.6	2.4	70.2
7	I <sup>f</sup>	24	42	71.6	36.9	3.0	70.9

<sup>a</sup> Average temperature. <sup>b</sup> Based on  $[\alpha]_{5461} 41.5^\circ$ . <sup>c</sup> Corrected for optical purity of starting material. <sup>d</sup> Based on  $[\alpha]_{5461} 150.65^\circ$ . <sup>e</sup> Obtained by measuring rotation of 0.0023 g of material. <sup>f</sup> LiCl added.

Examination of the runs involving bromide and iodide, reveal that unlike halogen-metal interchange, considerable racemization is involved in the formation of the cyclopropyllithium directly from the metal as reflected in the optical purities of the acids. This is also what was observed in the direct formation of the Grignard reagent<sup>14b,16</sup>. Another point of similarity with Grignard formation is that here the

\* For further evidence that carbonation of organometallics results in retention of configuration see ref. 4, 8a and 17.

optical purity of the acid also increases in the order  $I < Br < Cl$ .

The optical purities of the hydrocarbons do not fit the pattern. In the case of Grignard formation the hydrocarbons are all considerably more racemic than the acid from the same experiment<sup>16</sup>. Here, however, the optical purity of the 1-methyl-2,2-diphenylcyclopropane is, in the case of the iodide and bromide, considerably higher than that of the corresponding acid, while in the case of the chloride it is slightly lower.

In order to check if the lithium halide generated by the metallation in some way affected the optical results, an experiment with the iodide was run in the presence of 1.3 molar equivalents of lithium chloride. If the lithium chloride had some effect on the optical purity of the products obtained from the chloride, then perhaps its presence in an iodide experiment would cause an increase in the optical purities of the products. Complexes of organolithium compounds with lithium halides have been reported by several workers<sup>18</sup>. Waack and Doran<sup>18b</sup> have found that LiI, LiBr and LiCl are about equally effective in complexing with phenyllithium, but there is some indication that complexing ability increases in the order  $LiI < LiBr < LiCl$ . It has also been demonstrated that Li-Li exchange occurs between the organolithium reagent and the lithium halide. In the present case, as is seen by comparison of runs 5, 6 and 7 in Table 1, added LiCl does not affect the stereochemical results even if lithium-lithium exchange occurs.

TABLE 2

EFFECT OF SODIUM CONTENT ON STEREOCHEMISTRY OF METALLATION OF 1-METHYL-1-IODO-2,2-DIPHENYLCYCLOPROPANE WITH LITHIUM OF 25  $\mu$  PARTICLE SIZE IN ETHER

Run	Sodium content (%)	Temp. <sup>a</sup> (°C)	Time (min)	Acid		Hydrocarbon	
				Yield (%)	Optical <sup>b,c</sup> purity (%)	Yield (%)	Optical <sup>d</sup> purity (%)
1	0.002	26	42	68.8	12.6	2.8	54.4
2	0.020	26	43	65.6	15.4	4.0	58.0
3	1.0	25	41	59.8	35.6	2.4	70.2
4	100.0	25	38	0		34.9	63.4

<sup>a</sup> Average temperature. <sup>b</sup> Based on  $[\alpha]_{5461}$  41.5°. <sup>c</sup> Corrected for optical purity of starting iodide. <sup>d</sup> Based on  $[\alpha]_{5461}$  of 150.65°.

#### The effect of sodium content

The results of an examination of the effect of the sodium content of the lithium on the stereochemistry of metallation are given in Table 2. The lithium dispersions used in this study were all of 25  $\mu$  particle size. In the experiment with pure sodium a dispersion of 12–15  $\mu$  particle size was used. Since only the iodide reacts readily with all of the lithium preparations, it was used in this study. Overall retention of configuration is observed for both acid and hydrocarbon in all cases.

With regard to the optical purities of the acids, it can be seen that there is very little difference between the two obtained from low sodium content metals (runs 1 and 2). On the other hand, comparison of these two with the acid obtained using 1% sodium (run 3) shows they are only 1/3–1/2 as active.

The hydrocarbons exhibit the same phenomenon observed earlier (see Table 1) in that they all have considerably higher optical purities than the corresponding acids. It is noteworthy that the decrease of sodium content decreased their optical purities by a much smaller factor than is the case with the acids.

When pure sodium was used (run 4) no acid could be obtained. Since sodium reagents are known to cleave ethers rapidly<sup>19</sup> it is reasonable to assume that most of the hydrocarbon is the result of that process and to compare its optical purity with those of the acids obtained in the lithium reactions. It is thus seen that sodium, which by itself causes high retention, acts to increase the retention when it is present in the lithium in a relatively small quantity.

#### *Effect of particle size*

Having established that sodium content considerably affects the steric outcome of the metallation reaction, the effect of particle size at constant sodium content was investigated next.

As is evident from inspection of Table 3 the large particle size results in about a 50% reduction of the optical purity of both the acid and the hydrocarbon. Although not as high as usually found, the optical purity of the hydrocarbon is still significantly higher than that of the acid.

TABLE 3

THE EFFECT OF PARTICLE SIZE ON STEREOCHEMISTRY OF METALLATION OF 1-METHYL-1-iodo-2,2-DIPHENYLCYCLOPROPANE WITH LITHIUM CONTAINING 1% SODIUM IN ETHER

Run	Particle size	Surface area (cm <sup>2</sup> ) <sup>a</sup>	Temp. <sup>b</sup> (°C)	Time (min)	Acid		Hydrocarbon	
					Yield (%)	Opt. purity <sup>f,d</sup> (%)	Yield (%)	Opt. purity <sup>d,e</sup> (%)
1	25	2782	25	41	59.8	35.6	2.4	70.2
2	150	464	25	35	75.2	19.2	0.6	35.3

<sup>a</sup> Calculated for 0.62 g of metal. <sup>b</sup> Average temperature. <sup>c</sup> Based on  $[\alpha]_{5461} 41.5^\circ$ . <sup>d</sup> Corrected for optical purity of starting material. <sup>e</sup> Based on  $[\alpha]_{5461} 150.65^\circ$ .

#### *Exchange of the lithium reagents with unreacted halide*

The possibility that the activities observed in these experiments result from halogen-metal interchange of racemic lithium reagents with unreacted active halide must be considered.

That it is possible for the cyclopropyllithium reagent to exchange with unreacted iodide was indicated by an experiment in which one half equivalent of lithium (25  $\mu$ , 1% Na) was stirred in ether with optically active iodide for 71 min. It was noticed that very little of the metal was used up during this time, and carbonation gave only 12.6% of acid based on lithium. This acid, however, had an optical purity of 57%. The small amount of partially active lithium reagent in the presence of a great excess of active iodide underwent exchange thereby increasing the activity of the lithium reagent.

Other observations, however, indicate that halogen-metal interchange cannot be an important source of the optical activity under the usual conditions used for

metallation. Racemic lithium reagent when stirred in ether for 19 min with optically active 1-methyl-1-iodo-2,2-diphenylcyclopropane gave on carbonation acid with an optical purity of 7.1%. A similar experiment in which the lithium reagent was stirred with optically active bromide for 32 min gave acid of 2.8% optical purity. It should be pointed out, that while the concentration of halide remains constant in these experiments thus favoring exchange, this is not the case in the metallation experiments, where there is a very large excess of lithium present and the concentration of halide is constantly decreased due to formation of the lithium reagent. To the extent that exchange does take place in the two previous examples, it appears to be favored by the iodide as might be expected. Since the ease of halogen-metal interchange decreases in the order  $I > Br > Cl$ , were this process important under the conditions of metallation the same order of optical purities should result. As the order actually found is the reverse,  $Cl > Br > I$  (see Table 1) halogen-metal interchange cannot be an important source of optical activity under the conditions of metallation.

#### *Effect of lithium metal on the lithium reagent*

The possibility that lithium metal causes racemization by metal-metal interchange or in some other way was examined. Optically pure lithium reagent prepared by halogen-metal interchange with *n*-butyllithium was added to a large excess of the lithium metal with which the greatest amount of racemization was observed (25  $\mu$ , 0.002% Na) and the resultant slurry stirred for 15 min and then carbonated. As the acid obtained was optically pure, racemization is not caused by the action of lithium metal on lithium reagent. This experiment does not exclude lithium metal-alkyl-lithium exchange, it only says that even if exchange is occurring it does not affect the stereochemistry.

#### DISCUSSION

Although formation of 1-methyl-2,2-diphenylcyclopropyllithium from *n*-butyllithium and optically active 1-methyl-2,2-diphenylcyclopropyl bromide or iodide occurs with complete retention of configuration the present results show that there is a considerable amount of racemization when metallic lithium is used. Furthermore, as is the case with the formation of the analogous Grignard reagent the optical purity of the lithium reagent is dependent on the halide used and increases in the order  $I < Br < Cl$ . As discussed earlier, halogen-metal interchange of racemic lithium compound with unreacted optically active halide makes little or no contribution to the observed activity under the conditions of the reaction. It was also demonstrated that lithium metal does not racemize the lithium reagent.

The racemization observed in forming the lithium reagent finds a parallel in the formation of the analogous Grignard reagent<sup>14b,16</sup>. A scheme (Fig. 1) similar to that advanced for the mechanism of Grignard reagent formation can also explain the results obtained with lithium metal.

Once again it is seen that the steric results may be explained by initial transfer of one electron to the carbon-halogen bond resulting in either the formation on the metal surface of a radical anion or what is in essence a loose radical pair. The radical anion either collapses to form lithium reagent with retention of configuration or undergoes disruption of the carbon-halogen bond forming the loose radical pair by pathway

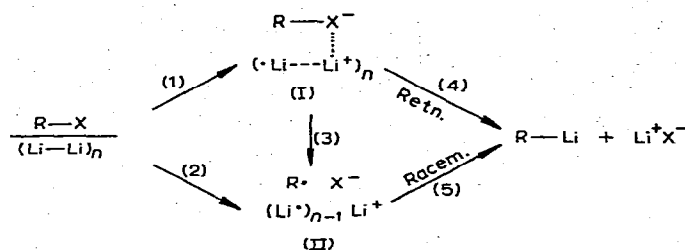


Fig. 1. A mechanistic scheme for the formation of lithium reagents.

(3). Combination of the loose radical pair results in the formation of racemic lithium reagent. The explanation of the halogen effect is the same in this case as it is for the Grignard reaction. As the halogen is changed from iodide to bromide to chloride the bond energy increases and collapse of the intermediate radical ion to the lithium reagent becomes more rapid resulting in a decrease of the proportion of loose radical pair formed. In this way the amount of retention of the lithium reagent increases in the order  $I < Br < Cl$ .

The overall increase in retention with lithium compared to magnesium can be explained on the basis of the lower ionization potential of lithium (124.3 kcal/mole compared to 176.2 kcal/mole for the first ionization potential of magnesium) which would facilitate electron transfer and thus tend to make the reaction more concerted.

Sommer and Mason<sup>20</sup> have proposed that a concerted mechanism is responsible for the formation of optically active silyllithium derivative with high retention of configuration (88%) when an optically active disilane is cleaved by lithium. These results can also be explained by the scheme in Fig. 1. The results of Grovenstein and Cheng<sup>21</sup> also fit into our reaction scheme. These workers showed that the reaction of lithium metal with 1-chloro-2-methyl-2-phenylpropane (neophyl chloride) gives rise to the formation of 2-methyl-2-phenylpropyllithium containing some 1,1-dimethyl-2-phenylethyllithium. The rearrangement product is the result of phenyl migration in the neophyl radical formed as a loose radical pair [Fig. 1; (II)].

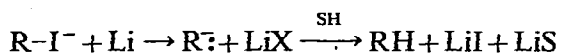
Unlike the present cyclopropyl system, the formation of alkenyllithium reagents appear to proceed with *complete retention* of configuration regardless of whether they are formed by halogen-metal interchange or by direct metallation<sup>8c</sup>. A completely concerted mechanism has also been invoked to explain the complete retention of configuration when alkenyllithiums are formed by direct metallation<sup>8</sup>. The scheme in Fig. 1 can also explain these results if it is assumed that none of the loose radical pair is formed in these cases. The possibility that any vinylic radical<sup>22</sup> or cyclopropyl radical<sup>23</sup> formed retains its configuration may be ruled out on the basis of recent work which has shown that these radicals are incapable of maintaining their configuration in solution. A mechanism like that proposed in Fig. 2 can also explain the retention of vinylolithiums.



Fig. 2. Stereospecific formation of vinylolithium by an addition-elimination mechanism.

In this case, two lithium atoms would undergo *cis* addition to the double bond followed by *trans* elimination of lithium halide giving the unsaturated lithium reagent with complete retention of configuration. The addition of lithium and other alkali metals to appropriately substituted double bonds is known. For instance, Wright and his coworkers<sup>24</sup> have studied the addition of alkali metals to *cis*- and *trans*-stilbene and other olefins. The addition of sodium, potassium and lithium to *cis*- or *trans*-stilbene in various solvents always led on carbonation to *meso*-diphenylsuccinic acid with varying amounts of the *d,l* isomer, depending on the solvent used<sup>23c</sup>. The dilithium or disodium adduct of *trans*-stilbene in dimethoxyethane gives a 3/1 mixture of *meso*-diphenylbutane when treated with dimethylsulfate. These examples show that under the proper conditions, with a properly substituted double-bond, lithium and other alkali metals can add to form stable adducts. In the case of vinylic halides it is suggested that an adduct of transitory existence is formed at the metal surface, which may react by a pathway unavailable in the case of hydrocarbons but which predominates when it is available. Recently, Wittig and Klumpp<sup>25</sup> have shown that the reaction of norbornadiene with lithium to give norbornene and nortricyclene can be explained by initial formation of the *exo*-1,2-dilithium adduct.

Although the trends for Grignard formation and lithium reagent formation as reflected in the optical activities of the acids are similar, the situation is not so clear cut with respect to the optical activities of the hydrocarbons (Table 1). The hydrocarbons from the Grignard reactions are all almost racemic<sup>16</sup>, while those from lithium reagent formation have an activity about equal to or greater than that of the acid. The fact that the optical purities of the hydrocarbons from the iodide and bromide are higher than that of the acid means that solvent cleavage by the lithium reagent cannot be their major source. Were this the case, their optical purities would then be equal to those of the corresponding acids. Some process leading to an intermediate with high retention of configuration which is then rapidly diverted to hydrocarbon before it can either racemize or form lithium reagent could account for the unexpectedly high optical purities of the hydrocarbons. Such a process might be the transfer of a second electron to the ion radical [(I) in Fig. 1] in such a way that the carbanion formed cleaves solvent before combining with a lithium cation:



Such a process might be expected to be most prevalent with the iodide, since it has the lowest bond strength and can most readily accommodate the additional electrons. The lower ionization potential of lithium compared to magnesium would also be consistent with the occurrence of such a process here, but not with magnesium.

A possible explanation for the increase in retention of the acid with increasing sodium content (see Table 2) is that the electron transfer is facilitated by the impurity metal, possibly by reducing the ionization potential. In this way, the intermediate ion-radical [(I) in Fig. 1] is more readily formed and rapidly diverted to lithium reagent and the opportunity for racemization via the loose radical pair [(II) in Fig. 1] is reduced. The increased optical activity obtained when 100% sodium was used (see Table 2, run 4) is consistent with this picture.

The effect of sodium in increasing yields or promoting metallations which did



not go at all\*\* is consistent with a reaction scheme such as that in Fig. 1 which involves a stepwise transfer of electrons to the halide.

The decreased optical purity with increased particle size (Table 3) can be connected with the effect of sodium if it is assumed that the sodium is most effective when it is at or near the metal surface. It can thus be seen that with everything else remaining constant, an increase in particle size and its concomitant reduction in total surface area simply reduces the total amount of sodium available at the surface and this results in a reduction of the optical purity in line with the effect of sodium content at constant particle size.

#### 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 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' x 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 A60 nuclear magnetic resonance spectrometer. Tetramethylsilane was used as an internal standard.

All compounds of the 1-methyl-2,2-diphenylcyclopropane system were prepared as previously described<sup>14</sup>.

#### *General procedure*

Preparation of 1-lithio-1-methyl-2,2-diphenylcyclopropanes was performed 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<sub>2</sub> 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 bulk 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

\* The effect of sodium in facilitating metallation with lithium has been described previously, usually in passing, see ref. 26.

\*\* For comprehensive studies on effect of sodium content in lithium see ref. 27.

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<sub>2</sub> was run into the system. A large excess of CO<sub>2</sub> 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 atmosphere pressure with CO<sub>2</sub> and the CO<sub>2</sub> 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<sub>2</sub> were thoroughly stirred with the magnetic stirrer.

Where finely divided lithium was used it was necessary to filter the reaction mixture away from the metal under an argon atmosphere. (CAUTION! Filtration of this mixture in air will result in fires.) Therefore, after all the CO<sub>2</sub> had evaporated, argon was again run into the system. By means of a hose attached to an outlet on the system argon was led into the reaction flask through the 14/20 joint. The reaction flask could then be removed from the manifold while still under a positive pressure of argon. A stopper was inserted in the greaseless joint and a spout with a sintered glass disk was placed in the 19/38 joint of the reaction flask. The reaction mixture was then forced through the sintered glass disk into a receiving flask. By washing the residual metal with several portions of anhydrous ether all of the reaction mixture could be separated from the metal. It should be noted that the anhydrous lithium salt of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid is soluble in anhydrous ether. It was found that separation of the reaction mixture from the metal could be speeded up by modifying the spout described above so that a vacuum could be applied to it.

Once the lithium was freed of reaction mixture it was necessary to destroy it. The reaction flask was quickly removed to a hood. By using anhydrous ether, the lithium metal was quickly rinsed into a 2 or 3 l beaker. Isopropyl alcohol was then added to destroy the lithium.

#### *Reactions with lithium*

*Reaction of (-)-1-methyl-1-iodo-2,2-diphenylcyclopropane with 25 micron particle size lithium metal containing 1% sodium in ether.* The lithium metal employed in this reaction was in the form of a dispersion in paraffin which contained 30 weight per cent of metal and had an average particle size of 25 microns. Under an atmosphere of argon 3.33 g of this dispersion (containing 1.0 g of metal) were placed in the reaction

flask previously described. Anhydrous ether was added, and the mixture was stirred with a magnetic stirrer for several minutes in order to dissolve the wax away from the metal. The solution was then filtered through the spout containing the sintered glass disk, referred to earlier. This entire operation was repeated several times in order to completely free the metal of wax. By allowing argon to flow through the reaction flask for several minutes most of the residual ether was evaporated and any metal stuck in the neck of the flask could be tapped into the bulb. The reaction flask was transferred to the manifold and under an argon flow the spout was replaced with the L-shaped tube previously described, containing 0.8077 g (0.00242 mol) of (–)-1-methyl-1-iodo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{22} - 195.94 \pm 0.58^\circ$ ). The contents of the flask were now finally dried by reducing the pressure to less than 0.005 mmHg.

As described previously the ether had been dried over lithium aluminum hydride. After degassing the ether four times 10 ml were allowed to distill into the reaction flask. The reaction flask was then brought to room temperature and 1 atmosphere with argon. "Dry-Ice" was placed in the condenser and the slurry of lithium powder stirred by means of a magnetic stirrer. All of the iodide except for some traces adhering to the addition tube was added within 2 min. The initial temperature was 22° but rose to 28° after the iodide was added. As the reaction proceeded the temperature dropped to 22°. After several minutes a yellow color appeared. The reaction flask was quenched with liquid nitrogen 33 min after the addition of the iodide was begun. The reaction mixture was carbonated by condensing CO<sub>2</sub> into a storage bulb and then subliming the CO<sub>2</sub> into the reaction flask. After the CO<sub>2</sub> had evaporated the reaction mixture was filtered from the metal. The residue was washed several times with ether, the washings filtered from the metal and added to the original filtrate.

The ethereal solution was acidified by extracting with dilute aqueous hydrochloric acid. The ethereal solution was then extracted 3 times with dilute aqueous sodium hydroxide, the basic extracts were combined and extracted 3 times with ether to remove any residual neutral material. Acidification of the basic washings gave the solid acid which was filtered, washed with water and dried. The acid obtained weighed 0.2575 g (42.4 %) and had m.p. 172.5–180.5° and  $[\alpha]_{5461}^{23} + 14.51 \pm 0.03^\circ$  (*c* 1.458). The infrared spectrum was that of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid<sup>14</sup>.

The ether was evaporated from the neutral fraction giving 0.2285 g of crude dry neutral material. A portion of this (0.1087 g) was chromatographed on "Alcoa" alumina using hexane as the eluant. By means of gas-liquid chromatography of a 2' × 1/4" SF-96 column (20% by weight on Chromosorb P) it was shown that the first few fractions (each about 10 ml) contained 1-methyl-2,2-diphenylcyclopropane contaminated with a small amount of 1-methyl-1-iodo-2,2-diphenylcyclopropane. These were combined, concentrated and rechromatographed on alumina using hexane as the eluant. By this procedure was obtained 0.028 g of material with NMR spectrum and VPC retention time identical to that of 1-methyl-2,2-diphenylcyclopropane<sup>14</sup>. The rotation of this material in CHCl<sub>3</sub> gave  $[\alpha]_{5461}^{23} + 106.98 \pm 78^\circ$  (*c* 1.290). The total yield based on all of the neutral material obtained was 10.8%.

The previous experiment was repeated utilizing 2.1 g of the same lithium dispersion (containing 0.62 g of metal) and 0.8121 g (0.00244 mol) of (–)-1-methyl-1-iodo-2,2-diphenylcyclopropane ( $[\alpha]_D^{26.5} - 163.81^\circ$ ;  $[\alpha]_{5461}^{24} - 198.84 \pm 0.97^\circ$ ). The ether used was distilled from lithium aluminum hydride into a graduated tube containing lead/sodium alloy. After degassing the ether 4–5 times 6 ml were allowed to

condense in the reaction flask. The procedure described previously was followed in conducting the reaction. All but a trace of the iodide was added within 3 min. The initial temperature was 21° but rose slowly to 29° during the course of the reaction.

A yellow color was detected 26 min after the start of the iodide addition. The reaction was allowed to continue for 15 min more and was then quenched with liquid air. The reaction mixture was carbonated and worked up as previously described. Acidification of the basic extracts gave the solid acid which was filtered, washed with water and dried to give 0.3663 g (59.8%) of material with m.p. 172–180°,  $[\alpha]_{5461}^{26} + 14.46 \pm 0.03^\circ$  (*c* 1.490). The infrared spectrum was that of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The ethereal extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated. The oil obtained was distilled in a molecular still with the pot temperature +35° and pressure 0.001–0.005 mmHg to yield 0.0400 g of material. From this material 0.01195 g (2.4%) of pure 1-methyl-2,2-diphenylcyclopropane were obtained by gas-liquid chromatography with  $[\alpha]_{5461}^{25} + 103.43 \pm 0.33^\circ$  (*c* 0.596).

*Reaction of (–)-1-methyl-1-iodo-2,2-diphenylcyclopropane with 25 micron particle size lithium metal (containing 1% sodium) in ether in the presence of added lithium chloride.* With the exception of added LiCl this experiment was carried out as previously described and utilized 0.8362 g (0.0025 mol) of 1-methyl-1-iodo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{24} - 198.84 \pm 0.97^\circ$ ), 2.1 g of the dispersion (0.62 g of metal) and 6.5 ml of ether distilled from lithium aluminum hydride into lead/sodium alloy. After freeing the lithium metal from the paraffin in the usual manner and drying it in a stream of argon, 0.1397 g (0.0033 mol) of LiCl which had been dried at 131° and 0.005 mmHg for several hours was rapidly added to the reaction flask. The reaction was then carried out as previously described. All but a small amount of iodide was added in 3 min. The initial temperature was 20° but rose to 27.5° and dropped to 26° during the course of the reaction. A faint yellow color appeared 26 min after the start of the iodide addition. The reaction was allowed to proceed 16 min more and then was quenched with liquid nitrogen. The lithium reagent was then carbonated as described earlier. The reaction mixture was freed from the metal and worked up in the usual manner. Acidification of the basic extracts gave the solid acid, which was filtered, washed with water and dried to give 0.4503 g (71.6%), m.p. 171–180° and  $[\alpha]_{5461}^{25} + 15.00 \pm 0.03^\circ$  (*c* 1.567). The infrared spectrum checked with that of authentic acid.

The ethereal extracts were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated. The oil obtained was distilled in a molecular still at pot temperature of 40° and at 0.005 mmHg yielding 0.0428 g of distillate. By means of gas-liquid chromatography 1-methyl-2,2-diphenylcyclopropane was obtained  $[\alpha]_{5461}^{25} + 104.56 \pm 0.34^\circ$  (*c* 0.582). The yield of this hydrocarbon was 3.0%.

*Reaction of (–)-1-methyl-1-iodo-2,2-diphenylcyclopropane with 25 μ particle size lithium metal containing 0.002% sodium in ether.* The lithium metal employed in this reaction was in the form of a dispersion in mineral oil which contained 30 weight per cent of metal. Under an atmosphere of argon 2.1 g of the dispersion (0.62 g of the metal) were added to the reaction flask. The lithium was freed of the mineral oil using the same technique employed with the paraffin dispersion and dried in a stream of argon. The L-shaped tube containing 0.8205 g (0.00246 mol) of 1-methyl-1-iodo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{24} - 198.84 \pm 0.97^\circ$ ) was then placed in the flask. The reaction was run in 6 ml of ether which had been distilled from lithium aluminum hydride into

lead/sodium alloy. The procedures outlined earlier were followed. All but a trace of the iodide was added in 2 min. The initial temperature was 19° but rose to 24° upon addition of the iodide, and to 27° during the course of the reaction. A yellow color was detected 24 min after the start of the iodide addition. The reaction was allowed to proceed 18 more minutes and was then quenched with liquid nitrogen. The reaction mixture was carbonated and then freed from the metal in the usual manner.

The basic extracts obtained by the usual procedure gave the solid acid upon acidification. This was filtered, washed with water and dried to yield 0.4258 g (68.8%) with m.p. 178–182° and  $[\alpha]_{5461}^{24.5} - 5.15 \pm 0.03^\circ$  (*c* 1.452). The infrared spectrum was that of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

After drying the ethereal extracts over molecular sieves (4A) and filtering the solution, the solvent then was distilled off. The residual oil was then distilled in a molecular still with pot temperature of 35° and pressure 0.01–0.005 mmHg to give 0.0262 g of material. By means of gas-liquid chromatography 1-methyl-2,2-diphenylcyclopropane with  $[\alpha]_{5461}^{26} + 80.22 \pm 0.37^\circ$  (*c* 0.542) was separated from the distillate. The yield of this hydrocarbon was 2.8%.

*Reaction of (-)-1-methyl-1-iodo-2,2-diphenylcyclopropane with 25 micron particle size lithium metal containing 0.020% sodium in ether.* The lithium metal employed in this reaction was in the form of a dispersion in paraffin which contained 30 weight per cent of metal. The reaction was run in the usual way, employing 0.7882 g (0.00236 mol) of 1-methyl-1-iodo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{24} - 198.84 \pm 0.97^\circ$ ), 0.62 g of lithium (from 2.1 g of dispersion) and 6.2 ml of ether which was dried over lithium aluminum hydride and distilled into lead/sodium alloy. All of the iodide was added in 1 min. The temperature at the start of the reaction was 21° but rose to 26° soon after the addition of the iodide and then dropped to 25° for the remainder of the reaction. A yellow color was detected 26 min after the start of the iodide addition. The reaction was allowed to proceed 17 min more and was then quenched with liquid nitrogen. The carbonation step was carried out in the usual manner. The reaction mixture was then freed from the metal and worked up as before. From the basic extracts were obtained 0.3889 g (65.5%) of acid with m.p. 180–183° and  $[\alpha]_{5461}^{24} + 6.26 \pm 0.03^\circ$  (*c* 1.542). The infrared spectrum was that of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The ethereal layer was filtered from the Na<sub>2</sub>SO<sub>4</sub> it had been dried over, and concentrated. The oil obtained was distilled in a molecular still with pot temperature 33–40° and pressure 0.01–0.02 mmHg to give 0.0505 g of distillate. By means of gas-liquid chromatography 1-methyl-2,2-diphenylcyclopropane with  $[\alpha]_{5461}^{23} + 85.83 \pm 0.31^\circ$  (*c* 0.6350) was separated from the distillate. The yield of this hydrocarbon was 4.0%.

*Reaction of (+)-1-methyl-1-iodo-2,2-diphenylcyclopropane with 150 micron particle size lithium metal containing 1% sodium in ether.* The lithium metal employed in this reaction was in the form of a dispersion in mineral oil containing 30 weight per cent of metal. Following the usual procedure, the reaction was carried out utilizing 0.7862 g (0.00236 mol) (+)-1-methyl-1-iodo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{30} + 200.78 \pm 0.65^\circ$ ), 0.62 g of lithium (in 2.1 g of dispersion) and 6.2 ml of ether which had been distilled from LiAlH<sub>4</sub> into lead/sodium alloy. At the start of the reaction the temperature was 2.15°, but rose to 27.5° soon after the addition of the iodide and gradually dropped to 24° as the reaction progressed. All of the iodide was added in 2

min. A yellow color appeared 15 min after the start of the iodide addition. After allowing the reaction to proceed 20 min longer, it was quenched with liquid nitrogen and then treated with carbon dioxide. The reaction mixture was freed from metal and worked up in the usual manner. Acidification of the basic extracts gave the solid acid which was filtered, washed with water and dried to give 0.448 g (75.2%). The solid had m.p. 177–183° and  $[\alpha]_{5461}^{22} - 7.89 \pm 0.03^\circ$  (*c* 1.539). The infrared spectrum was that of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The ethereal extracts were dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated. The oil obtained was distilled in a molecular still at pot temperature 37–40° and pressure 0.004–0.006 mmHg to give 0.0210 g of distillate. From this by means of gas-liquid chromatography were obtained 0.00312 g of 1-methyl-2,2-diphenylcyclopropane with  $[\alpha]_{5461}^{23} - 52.56 \pm 1.93^\circ$  (*c* 0.156). The yield of the hydrocarbon was 0.64%.

*Reaction of (-)-1-methyl-1-bromo-2,2-diphenylcyclopropane with 25 micron particle size lithium metal containing 1% sodium in ether.* To 1.0 g of lithium powder (from 3.33 g of dispersion) in 10 ml of ether, which had been dried with  $\text{LiAlH}_4$  before transfer to the reaction flask were added 0.9228 g (0.003322 mol) of 1-methyl-1-bromo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{23.5} - 129.47 \pm 0.57^\circ$ ;  $[\alpha]_{\text{D}}^{25.5} - 111.6 \pm 0.9^\circ$ ). The bromide was added in 5 min. The starting temperature was 22° but rose to 30° on addition of the bromide, falling gradually to 21° as the reaction progressed. About 10 min after the start of the bromide addition a yellow color appeared. The reaction was allowed to proceed for 22 min more and was then quenched with liquid nitrogen. The reaction mixture was treated with carbon dioxide and then filtered from the lithium. The usual work up gave a basic extract from which on acidification the solid acid was obtained. The dried acid weighed 0.4847 g (59.7%), had m.p. 172.5–180°, and  $[\alpha]_{5461}^{22} + 18.33 \pm 0.17^\circ$  (*c* 1.500) and an infrared spectrum which fitted that of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The solvent was evaporated from the ethereal extracts in an air stream. The residue was then distilled in a molecular still with pot temperature 38–40° and pressure 0.005 mmHg. The distillate was a small amount of yellow oil. From this oil was obtained by means of gas-liquid chromatography 0.00230 g of 1-methyl-2,2-diphenylcyclopropane with  $[\alpha]_{5461}^{24} + 77.39 \pm 2.61^\circ$  (*c* 0.230). The yield of hydrocarbon was 0.34%.

The previous experiment was repeated using 1.1140 g (0.00388 mol) 1-methyl-1-bromo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{25} + 131.21 \pm 0.66^\circ$ ), 1.0 g of lithium (from 3.33 g of dispersion) and 10 ml of ether which was dried by distilling it from  $\text{LiAlH}_4$  into lead/sodium alloy. The temperature was 21° at the start of bromide addition, rose slowly to 30° and then slowly dropped to 26°. All of the bromide was added in less than one minute. After 24 min a faint yellow color was detected. The reaction was allowed to continue for 18 more minutes and was then quenched with liquid nitrogen. The reaction mixture was treated with carbon dioxide in the usual way. After the carbonation step the reaction mixture was freed from metal and worked up.

The solid acid precipitated from the basic extracts upon acidification. It was filtered, washed and dried to give 0.6825 g (70%) with  $[\alpha]_{5461}^{25} - 16.96 \pm 0.16^\circ$  (*c* 1.592), and m.p. 173–179°. The infrared spectrum was that of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

The ethereal extract was dried over  $\text{Na}_2\text{SO}_4$ . It was then filtered and concentrated to give an oil which was distilled in a molecular still at pot temperature 39–40°

and pressure 0.002–0.005 mmHg. The amount of distillate obtained was 0.0766 g. A portion of the distillate was fractionated by gas-liquid chromatography. The infrared spectrum of the 1-methyl-2,2-diphenylcyclopropane obtained in this way showed some anomalous peaks. Further investigation showed that the contaminant could be separated from the desired hydrocarbon on a 2' × 1/4" "Ucon polar" column. The 1-methyl-2,2-diphenylcyclopropane which was obtained from this second fractionation had  $[\alpha]_{5461}^{24} - 96.22 \pm 0.69^\circ$  (*c* 0.2912). The yield of 1-methyl-2,2-diphenylcyclopropane was 2.8%.

*Reaction of (+)-1-methyl-1-chloro-2,2-diphenylcyclopropane with 25 micron particle size lithium metal containing 1% sodium in ether.* To a slurry of 1.0 g of lithium powder (from 3.33 g of dispersion) in 10 ml of ether which had been dried over  $\text{LiAlH}_4$  were added 0.9533 g (0.00392 mol) of 1-methyl-1-chloro-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{25} + 75.16 \pm 0.23^\circ$ ). All of the chloride was added in 3 min. At the start of the addition the temperature was 21°, rising gradually to 28° after the addition and then dropping gradually to 25°. A yellow color was detected 25 min after the start of the chloride addition. The reaction was allowed to proceed another fifteen minutes before quenching with liquid nitrogen. The reaction mixture was then treated with carbon dioxide. After the  $\text{CO}_2$  had evaporated, the reaction mixture was filtered from the metal under argon.

The usual work up gave an aqueous basic fraction and an ethereal extract. Acidification of the basic extract gave the solid acid, which was filtered, washed with water and dried. The dried acid weighed 0.7155 g (72.5%), had m.p. 174–184 and  $[\alpha]_{5461}^{21} - 28.49 \pm 0.16^\circ$  (*c* 1.562). The infrared spectrum was that of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

By means of gas-liquid chromatography 1-methyl-2,2-diphenylcyclopropane having  $[\alpha]_{5461}^{24} - 93.57 \pm 0.29^\circ$  (*c* 0.700) was separated from the neutral fraction. The yield of hydrocarbon was 1.7%.

The previous experiment was repeated using 0.8034 g (0.00332 mol) 1-methyl-1-chloro-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{24} + 73.74 \pm 0.64^\circ$ ) 0.8 g of lithium powder (from 2.66 g of dispersion) and 8 ml of ether which had been dried by distilling it from  $\text{LiAlH}_4$  into lead/sodium alloy. All of the chloride was added to the stirred slurry of lithium powder in ether in 3 min. The temperature at the start of the chloride addition was 21° rising gradually to 28° as the reaction progressed. After stirring for 43 min a yellow color was detected. The reaction was allowed to proceed another 17 min and was then quenched with liquid nitrogen. The reaction mixture was then treated with carbon dioxide. After evaporation of the carbon dioxide the reaction mixture was freed from the lithium in the usual manner.

From the work up of the reaction mixture, a basic extract was obtained which on acidification gave the solid acid. The dried acid weighed 0.6394 g (76.5%), had  $[\alpha]_{5461}^{23} - 26.60 \pm 0.17^\circ$  (*c* 1.484), m.p. 173.5–181° and an infrared spectrum which matched that of authentic acid.

The ethereal fraction was dried over  $\text{Na}_2\text{SO}_4$ . It was then filtered and concentrated, giving an oil. The oil was distilled in a molecular still with pot temperature 36–40° and pressure 0.002–0.006 mmHg. By means of gas-liquid chromatography 1-methyl-2,2-diphenylcyclopropane having  $[\alpha]_{5461}^{23} - 91.03 \pm 0.32^\circ$  (*c* 0.6240) was separated from the distillate. The yield of this hydrocarbon was 2.6%.

*Reaction of (+)-1-methyl-1-iodo-2,2-diphenylcyclopropane with 12–15 micron*

*particle size sodium in ether.* The sodium used in this experiment was in the form of a dispersion in mineral oil, containing 35% metal by weight. The technique used to free the metal from mineral oil was similar to the procedure employed with lithium dispersions. The reaction itself was carried out in the same way the reactions with lithium were.

To a slurry of 1.54 g of sodium powder (from 4.4 g of dispersion) in 4.7 ml of ether which had been dried by distilling from  $\text{LiAlH}_4$  into lead/sodium alloy were added 0.6161 g (0.00185 mol) of 1-methyl-1-iodo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{30} + 200.78 \pm 0.65^\circ$ ). All of the iodide was added in less than 1 min. At the start of the iodide addition the temperature was  $20^\circ$ , but it rose gradually to  $29^\circ$  and then dropped to  $27^\circ$  as the reaction progressed. A yellow color appeared 25 min after the start of the iodide addition. The reaction was allowed to continue 13 min more and was then quenched with liquid air. The reaction mixture was treated with carbon dioxide and then freed from metal in the usual manner.

Work up gave basic extracts which upon acidification produced no precipitate whatsoever.

The ethereal extracts were dried over  $\text{Na}_2\text{SO}_4$ . They were then filtered and concentrated giving an oil. The oil was distilled in a molecular still with pot temperature  $39\text{--}42^\circ$  and pressure 0.01–0.005 mmHg. By means of gas-liquid chromatography 1-methyl-2,2-diphenylcyclopropane with  $[\alpha]_{5461}^{24} - 94.50 \pm 0.67^\circ$  ( $c$  1.503) was separated from the distillate. The yield of hydrocarbon was 34.9%.

*Optical stability of 1-methyl-2,2-diphenylcyclopropyllithium in the presence of lithium metal.* Optically pure 1-methyl-2,2-diphenylpropyllithium was prepared from 1.1659 (0.0041 mol) 1-methyl-1-bromo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{25} + 130.07 \pm 0.66^\circ$ ) and 25 ml of an approximately 1.7 mol solution n-butyllithium in ether. The reaction was carried out under argon in an ordinary 100 ml 3 neck flask equipped with magnetic stirring bar, dropping funnel, thermometer and gas inlet. The bromide was dissolved in 10 ml of  $\text{LiAlH}_4$  dried ether. Butyllithium was added dropwise over a 7 min period; the solution then was stirred for an additional 8 min. The temperature was maintained at  $23\text{--}25^\circ$  throughout the entire reaction.

At the end of 15 min the reaction mixture was transferred under argon, to the usual reaction flask on the manifold. In this flask were 4.0 g of 25 micron lithium powder with sodium content 0.002% (from 13.43 g of dispersion) which had been previously freed from mineral oil in the usual manner, pumped dry and stored under argon. The mixture was then stirred for 15 min at  $26\text{--}27^\circ$ . After standing another 4 min, the mixture was frozen with liquid nitrogen and then treated with carbon dioxide. After separating the reaction mixture from the lithium it was worked up in the usual way. Acidification of the basic extracts gave the solid acid, which was washed with water and dried. The acid weighed 0.5463 g (53.5%), had  $[\alpha]_{5461}^{31} - 41.40 \pm 0.16^\circ$  ( $c$  1.528), m.p.  $182\text{--}187^\circ$  and an infrared spectrum which corresponded to that of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid.

*Reaction of (+)-1-methyl-1-iodo-2,2-diphenylcyclopropane with 0.5 equivalent of lithium in ether.* To 0.017 g (0.00244 g atom) of Li (containing 1% Na and of 25 micron particle size; from 0.0568 g dispersion) stirred in 6.0 ml of ether (dried by distilling from  $\text{LiAlH}_4$  into lead/sodium alloy) were added 0.7886 g (0.00236 mol) of 1-methyl-1-iodo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{30} + 200.78 \pm 0.65^\circ$ ), over a 3 min period. The temperature of the reaction mixture was  $22^\circ$  at the start of the addition



but rose gradually to 28°.

There was no noticeable disappearance of lithium as stirring continued. After 71 min, the reaction mixture was frozen with liquid nitrogen and treated with carbon dioxide. After evaporation of the CO<sub>2</sub>, the usual work up gave a basic aqueous fraction, which produced the solid acid on acidification with HCl. After filtration, washing and drying it weighed 0.0389 g (12.6% based on lithium), had  $[\alpha]_{5461}^{30} - 23.45 \pm 0.13^\circ$  (*c* 1.598) and m.p. 172.5–175°.

*Test of exchange of (±)-1-methyl-2,2-diphenylcyclopropyllithium with (+)-1-methyl-1-bromo-2,2-diphenylcyclopropane.* Racemic lithium reagent was prepared from 0.2391 g (0.000716 mol) of (±)-1-methyl-1-iodo-2,2-diphenylcyclopropane, and 0.72 g of 25 micron lithium powder containing 0.002% Na in 5.0 ml of ether which had been dried by distilling from LiAlH<sub>4</sub> into molecular sieves. The preparation was carried out in a 50 ml 3 necked flask with a stopcock in the bottom. The flask was equipped with a gas inlet, a screw shaped mechanical stirrer and a thermometer. By means of a mercury pressure release set-up, a positive pressure of argon was maintained in the flask. The reaction mixture was stirred 35 min at room temperature and then allowed to settle. After about 15 min the lithium reagent was transferred under argon through the stopcock in the bottom of the flask to the reaction flask used in conjunction with the manifold (described earlier) in which 0.5806 g (0.002 mol) of 1-methyl-1-bromo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{25} + 130.07 \pm 0.66^\circ$ ) were stored under argon. A small amount of lithium metal got through during this transfer. After completion of the transfer, the reaction mixture was stirred 32 min at 24–25°. The reaction mixture was then quenched with liquid nitrogen and carbonated in the usual manner. After evaporation of the CO<sub>2</sub> work up of the reaction mixture gave 0.0817 g (45%) of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid with  $[\alpha]_{5461}^{24} - 1.16 \pm 0.025^\circ$  (*c* 1.599).

*Test of exchange of (±)-1-methyl-2,2-diphenylcyclopropyllithium with (+)-1-methyl-1-iodo-2,2-diphenylcyclopropane.* Racemic 1-methyl-2,2-diphenylcyclopropyllithium was prepared by reaction of 0.7430 g (0.0022 mol) of (+)-1-methyl-1-iodo-2,2-diphenylcyclopropane with 0.93 g of 150 micron particle size lithium powder containing 1% sodium in 8.0 ml of ethyl ether. The ether had been dried by distilling from LiAlH<sub>4</sub> into molecular sieves just prior to use. The preparation was carried out in a 50 ml 3 necked flask with a stopcock in the bottom. The flask was equipped with a gas inlet, a mechanical stirrer and a thermometer. A mercury pressure release set-up was used to keep the flask under a positive pressure of argon. The reaction mixture was stirred at room temperature for 32 min and was then transferred under argon to the usual flask on the vacuum manifold which contained 0.4627 g (0.0014 mol) of 1-methyl-1-iodo-2,2-diphenylcyclopropane ( $[\alpha]_{5461}^{30} + 200.78 \pm 0.65^\circ$ ) under argon. During the transfer a small amount of metallic lithium came through. This reaction mixture was now stirred 19 min at 27°. At the end of this time it was frozen with liquid nitrogen and treated with carbon dioxide.

The usual work up gave a basic extract from which after acidification and drying 0.2434 g (43.5% based on racemic iodide) of 1-methyl-2,2-diphenylcyclopropanecarboxylic acid were obtained with  $[\alpha]_{5461}^{28} - 2.90 \pm 0.03^\circ$  (*c* 1.450) and m.p. 182–183.5°.

### *The 1-methyl-2,2-biphenylenecyclopropyl system*

**1-Bromo-2,2-biphenylenecyclopropanecarboxylic acid.** A solution of approximately 1 mole of 9-diazo fluorene in ether prepared by the oxidation of fluorenone hydrazone according to the method of Nenitzescy and Solominca<sup>28</sup> was slowly added while stirring and heating to approximately 2 moles of methyl 2-bromoacrylate<sup>29</sup>. The methyl 1-bromo-2,2-biphenylenecyclopropylcarboxylate formed in this way weighed 286.3 g (approximately 87%) and had m.p. 136–138°.

This ester was saponified by refluxing for 46 h in 3.6 l of methanol and 950 ml dioxane containing 48.7 g (0.87 mol) KOH and 300 ml water. The solvent was now removed and water was added to the residue. Much of this material, which did not dissolve and proved to be unreacted ester, was removed by extraction with ether. Acidification of the aqueous layer gave 163 g of the crude acid (59% based on all of the starting ester). Recrystallization of this material from tert-butanol/isopropanol gave white needles which melted at 161° with decomposition.

This acid was resolved by forming the salt with 1 molar equivalent of cinchonine in ethyl acetate and then recrystallizing it several times from ethyl acetate/ethanol. The acid resolved in this way gave  $[\alpha]_D^{29} 141.5 \pm 1.7^\circ$  (*c* 1.490, acetone). (Found: C, 60.97; H, 3.72; Br, 25.44.  $C_{16}H_{11}BrO_2$  calcd.: C, 60.97; H, 3.52; Br, 25.36%.)

The optically active methyl ester was produced from the  $\alpha$ -bromoacid  $[\alpha]_D^{29} 141.5 \pm 1.7^\circ$  by dissolving it in THF and treating with an ethereal solution of diazomethane. This material, recrystallized from ether/benzene had m.p. 140–140.5°. Its infrared spectrum was identical to that of the racemic ester and it had  $[\alpha]_D^{24} 112.2 \pm 1^\circ$  (*c* 2.438, acetone). (Found: C, 62.25; H, 3.93; Br, 24.50.  $C_{17}H_{13}BrO_2$  calcd.: C, 62.02; H, 3.98; Br, 24.28%.)

**1-Bromo-1-methyl-2,2-biphenylenecyclopropane.** Optically active 1-bromo-biphenylenecyclopropylcarbinol was prepared by aluminum hydride reduction<sup>30</sup> of the above optically active ester. To a solution of 1.5 g of  $LiAlH_4$  in 55 ml of anhydrous ether were added 1.6 g of solid  $AlCl_3$  while stirring and cooling in an ice bath. After allowing this solution to come to room temperature a solution of approximately 0.032 mol of optically active methyl-1-bromo-2,2-biphenylenecyclopropylcarboxylate in benzene/ether was added with stirring. Stirring was continued for 3.5 h after the addition was complete. The reaction mixture was then hydrolyzed by the dropwise addition of saturated  $NH_4Cl$  solution. After filtering the reaction mixture and washing the solid residue several times with benzene, the organic layer was extracted with water. Evaporation of the solvent gave 8.7 g (90%) of a light yellow solid m.p. 117–119°, which was converted to the mesylate without further purification.

To a cooled solution of 8.2 g of the above carbinol in 60 ml of dry pyridine were added 4.6 g (3.1 ml) of methanesulfonyl chloride. After storing this mixture in a refrigerator for several hours, it was poured into a mixture of ice and water. The solid material which precipitated was filtered, washed thoroughly with water, dried and used in the following reduction without further purification.

To 2.5 g of  $LiAlH_4$  in 100 ml of anhydrous ether were added, with cooling and stirring, a slurry of 10.1 g (0.026 mol) of the above mesylate in about 200 ml of dry benzene and 50 ml of dry toluene. Stirring was continued for 20 h after the addition was complete. The reaction mixture was hydrolyzed by pouring it into a large beaker cooled in an ice bath and then adding a saturated aqueous  $NH_4Cl$  solution. The liquid material was filtered from the solid precipitate and the residue was washed several

times with ether. The organic layer was separated from the aqueous layer and then extracted several times with water. Concentration of the organic layer gave an orange oil which was chromatographed on an alumina column. Elution with petroleum ether (30–60°) gave 4.6 g (62%) of crystalline 1-bromo-1-methyl-2,2-biphenylenecyclopropane. This material recrystallized from methanol had m.p. 93.5–94°, and  $[\alpha]_D^{23}$   $27.5 \pm 1.3^\circ$  (*c* 1.855, acetone). (Found: C, 67.54; H, 4.84; Br, 27.90.  $C_{16}H_{13}Br$  calcd.: C, 67.38; H, 4.59; Br, 28.02%.)

*Methyl 1-methyl-2,2-biphenylenecyclopropylcarboxylate.* To 384 ml (3.6 mol) of refluxing methyl methacrylate were added an ethereal solution containing approximately 0.6 moles of 9-diazofluorene<sup>28</sup>. After the addition was complete about 300 ml of benzene was added and the mixture was refluxed overnight. The solvent and excess methyl methacrylate were then stripped off, and the remaining material was dissolved in methanol filtered away from the insoluble residue.

The analytical sample of the ester was recrystallized from 95% ethanol and had m.p. 95°. (Found: C, 82.03; H, 6.18.  $C_{18}H_{16}O_2$  calcd.: C, 81.79; H, 6.10%.)

*1-Methyl-2,2-biphenylenecyclopropanecarboxylic acid.* To the above methanolic solution of the ester were added 40 g (0.7 mol) KOH in 250 ml  $H_2O$ . The solution was refluxed overnight and then concentrated. Water was added to the residue and this solution was then extracted several times with ether. Acidification of the aqueous solution gave a white solid which was filtered and dried.

Concentration of the ethereal extracts gave about 108 g (0.43 mol) of unreacted ester. This was resaponified using 1250 ml of ethanol, 48.2 g (0.86 mol) KOH and 500 ml  $H_2O$ . After refluxing overnight the reaction mixture was worked up as described above. The acid obtained here was added to that obtained in the first saponification. After recrystallization from acetone/water 121 g (about 80%) of acid m.p. 220–221° were obtained. (Found: C, 81.56; H, 5.68.  $C_{17}H_{14}O_2$  calcd.: C, 81.58; H, 5.64%.)

This acid was resolved using one half equivalent of quinine in acetone. After several recrystallizations of the quinine salt from acetone the acid was obtained with  $[\alpha]_D^{29} -213.6 \pm 1.4^\circ$  (*c* 1.740, acetone). The other enantiomer was obtained by recovering the partially resolved acid from the mother liquor of the quinine resolution and forming the salt with one equivalent of cinchonine in ethanol. The acid obtained in this way had  $[\alpha]_D^{21} 214 \pm 3^\circ$  (*c* 0.910, acetone).

*Carbonation of the product from the reaction of n-butyllithium with (+)-1-methyl-1-bromo-2,2-biphenylenecyclopropane in ether.* The following reaction was carried out in a conventional 3 necked flask equipped with a mechanical stirrer, pressure equalized dropping funnel, a condenser fitted with a drying tube and a gas inlet. It was done under an atmosphere of argon.

To a stirred solution of 0.5 g (0.002 mol) of 1-methyl-1-bromo-2,2-biphenylenecyclopropane ( $[\alpha]_D^{23} 27.5 \pm 1.3^\circ$ ) in 25 ml of anhydrous ether were added over 5 min 18 ml of approximately 1.5 mol ethereal n-butyllithium. As the n-butyllithium was added the solution turned bright orange. The temperature of the reaction mixture was 20–22°. Stirring was continued another 5 min. The reaction mixture was then poured into a mixture of crushed "Dry-Ice" and anhydrous ether.

After evaporation of the "Dry-Ice" the reaction mixture was acidified with dilute HCl and extracted with ether. The ethereal extracts were then extracted with dilute NaOH. Acidification of the basic extract precipitated the solid acid. An estimated 0.050 g (approximately 10%) of the acid was obtained. Its infrared spectrum

in KBr was identical with that of resolved 1-methyl-2,2-biphenylenecyclopropanecarboxylic acid in the same medium and it had  $[\alpha]_D^{23} - 199 \pm 4^\circ$  (c 0.630, acetone). Similar transformations have been shown to take place with overall retention of configuration in the 1-methyl-2,2-diphenylcyclopropane series<sup>14,17</sup> and it was assumed that such is the case here. This assumption means that 1-bromo-2,2-biphenylylcyclopropanecarboxylic acid and 1-methyl-2,2-biphenylenecyclopropanecarboxylic acid of the same sign of rotation have the same configuration. Such a configurational relationship has been established for the corresponding 2,2-diphenylcyclopropanecarboxylic acids<sup>14</sup>.

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