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REACTION OF ORGANOMAGNESIUM COMPOUNDS WITH DERIVATIVES OF CYCLOHEXENE-1-CARBOXYLIC ACID

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Abstract—Phenylmagnesium bromide adds to the nitrile (IIa) in the 1,2-manner and to the ester (IIb) first in the 1,2 and subsequently in the 1,4-manner. The acid (IIc) and the amide (IIf) undergo both 1,2; and 1,4-additions. The unsubstituted amide (IId) gives predominantly 1,2-addition. The ketone (IVg) unlike ketones with one alkyl group undergoes 1,4-addition. The reaction of other Grignard reagents as well as phenyllithium with the same conjugated derivatives was also studied. Factors that determine 1,2 and 1,4-addition are discussed.

THE reaction of Grignard reagents with α,β-unsaturated compounds has been known to consist not only of addition to the functional group, but is also accompanied by 1,4-addition and condensation reactions.[1]

Renewed interest in the course of Grignard reactions stems from the work on the structure of Grignard compounds. The dimeric structure,[2] $R_2Mg{\cdot}MgBr_2$, containing complexed solvent[3] was assumed owing to the absence of exchange[2] of labelled magnesium between magnesium bromide and ethylmagnesium bromide[4] and other evidence. This structure explained the results of kinetic measurements and accounted for the fact that only half of the Grignard reagent reacted with nitriles.[5] The same effect was found in the reaction of diethylmagnesium with di-isopropyl ketone.[6] Kinetic evidence also[5,7–9] pointed to a two-stage reaction of Grignard reagents or dialkylmagnesium compounds, R_2Mg, with ketones or nitriles. RMg·OR′, its dimer or complex with $MgBr_2$, were assumed to be intermediate compounds.[7,8,10] The differences observed between dialkylmagnesium derivatives and Grignard reagents

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[1] M. S. Kharasch and O. Reinmuth, *Grignard Reactions of Nonmetallic Substances* p. 196. Prentice-Hall, New York (1954).

[2] R. E. Dessy, G. S. Handler, J. H. Wotiz and C. A. Hollingworth, *J. Amer. Chem. Soc.* **79**, 3476 (1957).
R. E. Dessy and R. M. Jones, *J. Org. Chem.* **24**, 1685 (1959).
R. E. Dessy, *J. Org. Chem.* **25**, 2260 (1960).

[3] A. Kirmann and R. Hamelin, *C. R. Acad. Sci., Paris* **251**, 2990 (1960); R. Hamelin, *Bull. Soc. Chem.* 684, 915, 926 (1961).

[4] This name will be reserved for the Grignard reagent prepared from the alkyl halide and magnesium, without taking into consideration the real structure of the compound. When the structure is referred to, the structural formula RMgX will be given.

[5] S. J. Storfer and E. I. Becker, *J. Org. Chem.* **27**, 1868 (1962).

[6] A. Kirmann, M. Vallino and J. F. Fauvarque, *C. R. Acad. Sci., Paris* **254**, 2995 (1962).

[7] J. Miller, G. Gregorious and H. S. Mosher, *J. Amer. Chem. Soc.* **83**, 3966, 5051 (1961).

[8] D. O. Gowan and H. S. Mosher, *J. Org. Chem.* **27**, 1 (1962).

[9] M. Anteunis, *J. Org. Chem.* **26**, 4214 (1961); **27**, 596 (1962).

[10] H. O. House and D. D. Traficante, *J. Org. Chem.* **28**, 355 (1963).

such as lower reactivity of the latter with ketones,[9,11] different ratios of addition-enolization and addition-reduction reactions with ketones,[7,8,10,12] (these ratios depending also on the halogen in the Grignard reagent[7,13]) were explained by catalysis of addition by $MgBr_2$,[9,12] by a cyclic transition state in which the magnesium halide takes part[7,8] or by removal of the alkoxide ion by magnesium halide.[10]

The ratios of 1,2 to 1,4-addition to α,β-unsaturated ketones or esters also vary when Grignard reagents are replaced by dialkylmagnesium,[6,14] but only a slight effect was found in other cases.[15] It was also noticed that the halogen atom has an effect on the extent of 1,4-addition to unsaturated esters.[16]

More recent work has thrown doubt on the dimeric nature of Grignard reagents, but IR spectra have shown[17] that allylmagnesium halide can exist in the monomeric or dimeric form, depending on the halogen of the starting allyl halide and ebullioscopic determinations of molecular weights have shown that ethylmagnesium bromide and chloride are monomeric in tetrahydrofuran solution.[18] Phenylmagnesium bromide has the structure $C_6H_5MgBr{\cdot}2Et_2O$ in the solid state and in ether solution is different from diphenylmagnesium.[19] Asymmetric reduction experiments have shown[20] no difference between Grignard reagents and dialkylmagnesium compounds.

Although alkyl–alkyl, or aryl–aryl, unlike the alkyl–halogen[2] exchange is very fast in diphenyl[19] and dialkyl[21,22]–magnesium and a Schlenk equilibrium may take place in solution, the doubt concerning the structure of individual Grignard reagents and of the reacting species remains great and the attempt to interpret the course of Grignard reactions, and of 1,4-addition in particular, in terms of the structure of the reagent can lead to uncertain results.

The factors governing the extent of 1,2 and 1,4-addition could be studied by using one type of Grignard reagent and varying the functional group conjugated with the C=C double bond. Although many of these reactions have been studied by different authors, no conclusions can be reached since the conditions of the reactions varied and doubts have been expressed concerning the quantitative reproducibility of the addition reactions.[23] Further, different batches of magnesium containing various impurities e.g. copper may influence the course of the reaction. As it is impossible to interpret the results in the literature, it was decided that the use of a single unsaturated group linked to various functional groups would eliminate factors depending on these groups.

Cyclohexenyl was chosen as the unsaturated group in order to maintain an

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[11] N. M. Bikales and E. I. Becker, *Chem. & Ind.* 1831 (1961).

[12] C. G. Swain and H. B. Boyles, *J. Amer. Chem. Soc.* 73, 870 (1951).

[13] H. J. Shine, *J. Chem. Soc.* 8 (1951).

[14] J. Munch-Peterson and S. Jacobsen, *C. R. Acad. Sci. Paris* **255**, 1355 (1962); *Acta Chem. Scand.* **17**, 825 (1963).

[15] H. O. House, D. D. Traficante and R. A. Evans, *J. Org. Chem.* **28**, 348 (1963).

[16] J. Munch-Peterson and V. K. Andersen, *Acta Chem. Scand.* **15**, 293 (1961).

[17] Ch. Prévost, *Bull. Soc. Chem.* 679 (1959).

[18] E. C. Ashby and W. E. Becker, *J. Amer. Chem. Soc.* **85**, 118 (1963).

[19] G. D. Stucky and R. E. Rundle, *J. Amer. Chem. Soc.* **85**, 1002 (1963).

[20] D. O. Gowan and H. S. Mosher, *J. Org. Chem.* **28**, 204 (1963).

[21] C. R. McCoy and A. L. Alfred, *J. Amer. Chem. Soc.* **84**, 912 (1962).

[22] R. E. Dessy, F. Kaplan, C. R. Coe and R. M. Salinger, *J. Amer. Chem. Soc.* **85**, 1191 (1963).

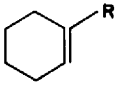
[23] J. Munch-Peterson, *J. Org. Chem.* **22**, 170 (1957); *Acta Chem. Scand.* **12**, 967 (1958).

approximately fixed conformation of this group during the reaction. The functional groups studied were carboxyl and its derivatives, carbomethoxy, carboxamide, mono and dimethylamide, nitrile and also benzoyl and acetyl.

RESULTS

Commercial magnesium of one batch was first used, but later it was found that in reactions with phenylmagnesium bromide (I) the results are changed only a little by the use of a different magnesium or even by addition of cuprous chloride.

The reaction of I with one equivalent of 1-cyanocyclohexene (IIa) in ether and subsequent treatment of the reaction mixture with hydrochloric acid gave a precipitate insoluble in water and in ether which analyses well enough for the hydrochloride of the imine (III) from which the α,β-unsaturated imine could be obtained by action of sodium hydroxide. Sulfuric or hydrobromic acids dissolve the unsaturated imine.



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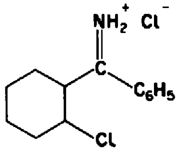

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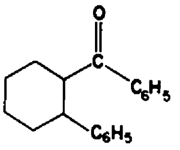

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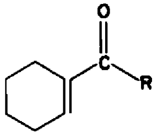

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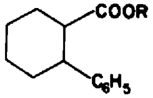

VI

a; R = CN
b; = $COOCH_3$
c; = COOH
d; = $CONH_2$

e; R = $CONHCH_3$
f; = $CON(CH_3)_2$
g; = C_6H_5
h; = $C_{10}H_7$
i; = $CH_2C_6H_5$
j; = CH_3
k; = H

Since this imine is hydrolysed only slowly it can be separated from ether-soluble products or starting material and gives pure 1-cyclohexenyl phenyl ketone (IVg) slowly at room temperature and faster when refluxed. The yield of IVg was raised by the use of excess over 2 equivalents of I, as noticed earlier in the reaction with nitriles.[5] [Addition of cuprous chloride to the Grignard reagent (I) lowers the yield of IVg, but only traces (not more than 5%) of V were found.] The same result was obtained when diphenylmagnesium was used instead of I.

The reaction of methyl cyclohexene-1-carboxylate (IIb) with I gave 1-benzoyl-2-phenylcyclohexane (V) containing predominantly the *cis*-isomer. The highest yield of V was obtained when an excess of I was used. A portion of IIb was recovered when only one mole of I was used and no 1-cyclohexenyl phenyl ketone (IVg) could be isolated. Only traces of VIj could be detected by saponification of the reaction mixture.

1-Cyclohexenyl phenyl ketone (IVg) yielded only 1-benzoyl-2-phenylcyclohexane (V) in the reaction with I. The result is the same as on addition of cuprous chloride,[24] the product being predominantly *cis*.[24] The same product was obtained with diphenylmagnesium. Excess of I or diphenylmagnesium did not change the composition of the product, neither did the use of equimolecular amounts of I and acetone (to give the hypothetical compound $C_6H_5Mg{\cdot}OC(CH_3)_2C_6H_5$ before the addition of IVg.

Methyl-*trans*-2-phenylcyclohexanecarboxylate (VIj) reacted slowly with excess of I. Sixty per cent of the starting material was recovered after refluxing four hours in ether. *Trans* and *cis*-2-phenylcyclohexanecarboxylic acid (VIk) reacted even more slowly. Ten per cent only of VIk reacted with I after refluxing 13 hours in ether.

Cyclohexene-1-carboxylic acid (IIc) gave optimal yields with at least three moles of I and after refluxing 17 hours in ether. The products consisted of V (45%) predominantly *cis* and 2-phenylcyclohexanecarboxylic acid (VIk; 32%), also mostly the *cis*-isomer. The ketone (V) was formed even after short reaction times. No 1-cyclohexenyl phenyl ketone (IVg) could be isolated from the product of reaction. The presence of an enolate product which stops further addition of I to the carbonyl was detected by treatment of the reaction mixture with acetyl chloride, which gave as a neutral product the enol ester (VII) characterised by its spectrum, analysis and saponification to *trans*-1-benzoyl-2-phenylcyclohexane (V).

Cyclohexene-1-carboxamide (IId) reacts slowly with I. Refluxing with 3 moles of I in ether solution for four hours yielded 15% of the unsaturated ketone (IVg) and after 20 hours using 9 moles of I gave 70% of IVg.

The substituted amides are even more resistant to the action of I than IId. Mixtures of IVg, V and the substituted amide of VIk were obtained, and after longer reaction periods V and the substituted amide of VI were the products of the reaction. Thus IIf gave after refluxing 20 hours in ether–benzene, 35% of V and 25% of the dimethylamide of VI. The amide was not isolated pure. Its content in the reaction mixture was evaluated by nitrogen analysis and then by reduction to the tertiary amine (VIII) which has the *cis*-configuration, since it yields a methiodide different from that obtained by treatment with methyl iodide of the product of reduction of the dimethylamide of *trans*-VIk by lithium aluminium hydride. The latter compound is evidently *trans*-VIII. Use of tetrahydrofuran as solvent accelerates the reaction, but also causes destruction of the products by secondary reactions, since the yields dropped after longer refluxing periods. The N-methyl amide (IIe) reacted with I more slowly than IIf, but no clear-cut results could be obtained. It seems that the initially formed products react further with I at a rate comparable to that of IIe.

The influence of the change in the Grignard reagent on the course of the reaction with some of the derivatives of IIc were also studied, although less thoroughly than in the case of phenylmagnesium bromide (I). 1-Cyanocyclohexene (IIa) gave with α-naphthylmagnesium bromide the corresponding imine and this, on hydrolysis, the conjugated ketone (IVh). This ketone was cyclized to benzhexahydrofluorenone (IX).

Benzylmagnesium chloride gave with IIa the corresponding imine which hydrolysed more rapidly than the imines obtained before to benzyl cyclohexenyl ketone (IVi).

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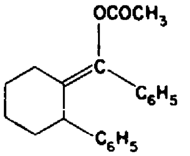
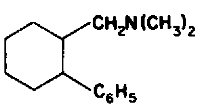
[24] H. E. Zimmerman, *J. Org. Chem.* 20, 549 (1955).

The same Grignard reagent gave with the unsaturated acid (IIc) the allylic carbinol (X) the product of two 1,2-additions and a very small amount of a mixture of *cis* and *trans*-XI products of 1,4-addition.

Cyclohexylmagnesium bromide gave with IIc mostly the product of 1,2; 1,4-addition (XII) and only a very slight amount of the acid corresponding to a 1,4-addition.

A 1,2-addition was also observed in the reaction of 1-cyanocyclohexene (IIa) with methylmagnesium bromide, where 1-cyclohexenyl methylketone (IVj) was the only product, except a small amount of a product of dimerization of IIa. The ketone (IVj) reacted with methylmagnesium bromide to yield the carbinol (XIII) as found before.[25] In presence of cuprous chloride the product of 1,4-addition (XIV) was obtained and a small amount of XIII. Phenylmagnesium bromide (I) reacted with IVj by 1,2-addition and subsequent dehydration to yield the corresponding diene and a small amount of the product of 1,4-addition. Addition of cuprous chloride to I before reaction with IVj raised only slightly the amount of the product of 1,4-addition (the total amount of the product of 1,4-addition and of the carbinol was 20% as determined by elementary analysis).


VII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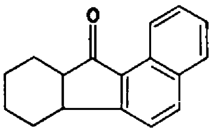
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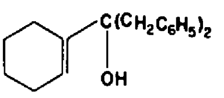
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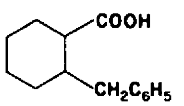
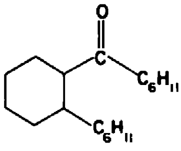

XI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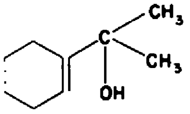
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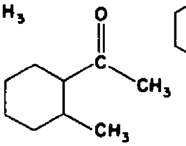
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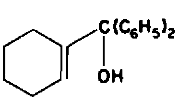
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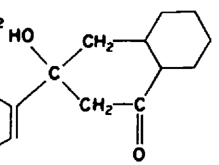
XVI

The modes of addition of organolithium compounds were also examined, particularly with the unsaturated compounds that give 1,4-addition with Grignard reagents. Phenyllithium gave with an equimolecular amount of cyclohexene-1-carboxylic acid (IIc) the ketone IVg. When excess of phenyllithium was used the carbinol (XV) resulting from two successive 1,2-additions was obtained even after very short reaction periods. The same carbinol was obtained from phenyllithium and the ketone IVg. The ketone (IVg) was also obtained in the reaction of phenyllithium with either amide IId or IIf.

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[25] D. Nightingale, E. C. Millberger and A. Tomisek, *J. Org. Chem.* 13, 357 (1948).

The unsaturated acid (IIc) yielded with methyllithium a product of dimerization of the ketone (IVj) to which the structure XVI was assigned on the basis of analysis, IR (3500 cm^{-1}(s), 1700 cm^{-1}(s)) and UV absorption.

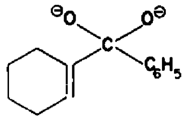
DISCUSSION

The most striking result in this study is the almost exclusive 1,2-addition of the Grignard reagents to 1-cyanocyclohexene (IIa). The reaction with IIa stops after addition of one molecule of the Grignard reagent, since an addition of a second molecule to the initially formed product (the magnesium salt of the unsaturated imine) would place two or nearly two negative charges on the nitrogen. The 1,2-addition to IIa is in agreement with the known facts and the generalization, that steric effects govern the extent of 1,4-addition. Thus, α,β-unsaturated aldehydes undergo 1,2-addition, whereas the extent of 1,4-addition to α,β-unsaturated ketones gets larger with the increasing size of the groups linked to the carbonyl.[26] The linearity of the nitrile group and its small size favour 1,2-addition.

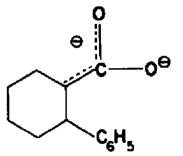
The exact meaning of "steric effects" in these cases is not clear. Is it a "steric hindrance" which influences the frequency factor of the reaction rate or a potential energy factor? It seems that the second factor determines mainly the course of these additions. The "steric hindrance" for all 1,4-additions remains approximately constant, but is not the case for 1,2-additions. The activation energy for 1,2 and 1,4-additions is different in all cases and depends mostly on the electronic influence of the activating substituent on the double bond. It can be assumed that these fast nucleophilic attacks will be the easier on the 2-position of the conjugated system, if other factors do not interfere, since this carbon is the most positively charged in the system.

Methyl cyclohexene-1-carboxylate (IIb) also undergoes first a 1,2-attack, then elimination of an ethoxide ion to give the ketone (IVg) and a subsequent 1,4-addition with formation of V. All these reactions subsequent to the first 1,2-addition are faster than the first and no intermediate can be isolated. The inverse sequence i.e. first a 1,4 and then a 1,2-addition is excluded, since methyl 2-phenylcyclohexane carboxylate (VIj) reacts slowly with I and it can be safely assumed that its enolate with the negative charge will undergo the nucleophilic attack even more slowly.

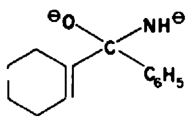
The large extent of 1,4-addition to cyclohexene-1-carboxylic acid (IIc) may be considered to be determined only by the repulsion between the negative charge on the carboxylate formed in the first step of the reaction of IIc with I and the negatively charged attacking carbon of the Grignard reagent. This interaction and also the formation in the 1,2-addition of the intermediate XVII, having two negative charges on the oxygens linked to the same carbon will raise the activation energy for this reaction relatively more than for the 1,4-addition, where XVIII is formed, in which



XVII



XVIII



XIX

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[26] For a discussion see E. E. Royals, *Advanced Organic Chemistry* p. 698, Prentice-Hall (1954); and G. F. Wright in Newman's, *Steric Effects in Organic Chemistry* p. 406, J. Wiley, New York (1956).

the two negative charges are spread over three atoms. This is probably an important factor, but is certainly not unique, as cyclohexene-1-carboxamide (IId) also forms, in the first step of the reaction with I, an anion by proton abstraction, and nevertheless undergoes 1,2-addition to give XIX, which is hydrolysed to IVg. The amide (IIf) on the other hand, which does not form an intermediate with a negative charge on the functional group, undergoes 1,4-addition to an extent comparable to that of IIc.

It is striking that the compounds that undergo 1,4-addition are both relatively unreactive and with large groups on the functional carbon. The amides and also the salts of carboxylic acids are among the least reactive carbonyl compounds. If Hammond's postulate[27] is accepted, then the transition state, for the least reactive species, will be similar to the product; and that of the most reactive compound similar to the starting substance. In the case of amides and salts the transition state for 1,2-addition will make the functional carbon nearly tetrahedral, and when large groups are present on this carbon, large compression energy barriers will prevent this addition. Since the potential energy barrier for a 1,4-addition will not increase largely by formation of a tetrahedral carbon on the cyclohexene ring, the extent of 1,4-addition will be raised. The ester grouping is not smaller than the carboxylate, but since the reaction of I with IIb is much faster than with IIc, the functional carbon in the transition state for 1,2-addition will be more nearly trigonal, the compression energy is small and 1,2-addition is observed. When the group linked to the carbonyl is very large, like phenyl, e.g. in IVg, then even a slight deformation of the trigonal carbon towards smaller valency angles will cause large interactions and 1,4-addition. The activating effect of the benzoyl group on the 4-position of the conjugated system by its electron withdrawing power and the retention of the conjugation of the carbonyl group with the phenyl when 1,4-addition takes place also contribute to this mode of addition taking precedence. In cyclohexenyl ketones linked to smaller groups like alkyls exclusive 1,2-addition occurs[25] in the reaction with alkylmagnesium halides. It seems however that an electronic effect causes a somewhat larger extent of 1,4-addition of phenylmagnesium bromide to cyclohexene-1 alkyl ketones (about 15%) than to methyl cyclohexene-1-carboxylate IIb, although the last substance is the less reactive. This effect may be due to a greater stabilization of a negative charge α to a ketone carbonyl, than α to an ester group. When both the carbonyl group and the double bond are located in the cyclohexane ring only the carbonyl was found to be attacked by methylmagnesium bromide in absence of cuprous chloride.[28]

The connection between reactivity of the functional group and the extent of 1,2-addition can be also compared with the extent of this mode of addition with different organometallic compounds. It was found that the amount of 1,4-addition increases with decreasing reactivity of the organometallic compound.[29] The explanation advanced is that decreased reactivity of the organometallic compound increases the extent of deformation of the valency angles of the trigonal carbon towards tetrahedral in 1,2-additions, increasing thus the potential energy for this mode of reaction and favouring 1,4-addition. Benzylmagnesium chloride and cyclohexylmagnesium bromide both give less 1,4-addition with IIc than phenylmagnesium bromide (I).

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[27] G. S. Hammond, *J. Amer. Chem. Soc.* **77**, 334 (1955).

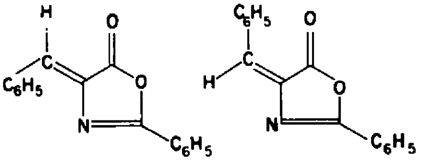
[28] M. S. Kharash and P. O. Tawney, *J. Amer. Chem. Soc.* **63**, 2308 (1941).

[29] H. Gilman and R. H. Kirby, *J. Amer. Chem. Soc.* **63**, 2046 (1941); G. Wittig, F. J. Meyer and G. Lange, *Liebigs Ann*, **571**, 167 (1951).

This may be connected with the larger reactivity of the first Grignard reagents relative to I.

The results obtained with organolithium compounds confirm that 1,2-addition is more favoured for these compounds than for Grignard reagents. It should however not be assumed that the preponderant 1,2-addition is an intrinsic characteristic of organo-alkali compounds. There are cases known when the contrary is true. Indenones undergo 1,2-addition with Grignard reagents and 1,4-addition with organolithium compounds.[30] This observation can also be understood on the basis of the relative energy content of the ground and transition states. In the indenones, particularly when complexed with the organometallic compound, there is an interaction between the oxygen and the hydrogen on the 7-position. This perhaps moves the oxygen out of the plane of the molecule, raises the energy of the ground state and lowers the activation energy for 1,2-addition by the Grignard reagent. For the organolithium compound the potential energy effects are of lesser importance and the course of the reaction is influenced more by the electronic effects. The partly positive charge on the carbonyl carbon is dispersed by cross conjugation with the phenyl ring and the double bond and the positive charge on the 3-carbon (4-position of the conjugated system) is increased by the action of the inductive effect of the carbonyl through the phenyl ring in addition to the mesomeric electron withdrawal. These effects raise the extent of 1,4-addition.

Another example of the role played by potential energy interaction can be illustrated on the basis of the results of Filler[31] for the addition of phenylmagnesium bromide (I) to the azlactones (XX and XXI). Whereas XX yields the product of 1,2-addition, XXI gives 1,4-addition. This is contrary to what would be expected, if simple "steric hindrance" was assumed to determine the course of the reaction. These results can however be explained if it is realized that the ground state energy of XX but not of XXI is raised by steric interactions between the phenyl and the carbonyl. The activation energy for the 1,2-addition to XX is thus lowered. In XXI, on the other hand, there is an interaction between the *ortho*-hydrogens of the phenyl and azlactone rings, which moves the phenyl out of the plane of the azlactone ring and 1,4-addition is favoured.



XXI XX

It is clear from the above considerations that the extent of 1,2- and 1,4-additions are governed mainly by their relative activation energies and are not necessarily determined by display of cyclic mechanisms,[32] that would be favourable to 1,4-addition in the case of Grignard reagents and to 1,2-additions for organolithium compounds. A similar conclusion was reached recently by House *et al.*[33] An alternative explanation

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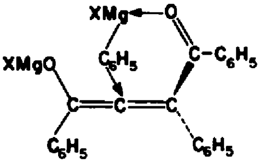
[30] We are indebted to Prof. E. D. Bergmann for this information.

[31] R. Filler, K. B. Rap and Y. S. Rao, *J. Org. Chem.* **28**, 711 (1963).

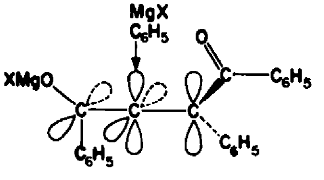
[32] R. E. Lutz and W. G. Revely, *J. Amer. Chem. Soc.* **63**, 3178, 3180 (1941).

[33] H. O. House, D. D. Traficante and R. A. Evans, *J. Org. Chem.* **28**, 348 (1963).

to the cyclic mechanism[34] (XXII) for the second step of addition of phenylmagnesium bromide (I) to dibenzoylacetylene is possible. The intermediate (XXIII) formed in the first step of reaction is of the allenic type and the π orbital which is attacked by I is located in the plane of the phenyl ring. The approach of I in this plane to the required orbital will be easier from the side of the OMgX grouping than of the phenyl ring. This steric interference explains the stereoselective formation of the adduct without assumption of a cyclic mechanism. A similar mechanism was advanced[35] to explain the formation of *cis*-cinnamic acid derivatives during decarboxylation of the unsaturated diacids in quinoline solution. A non-cyclic mechanism for conjugate addition of I is also supported by the work of Fuson,[36] who has found that 1,6 instead of 1,4-addition takes place when it is sterically more favourable.

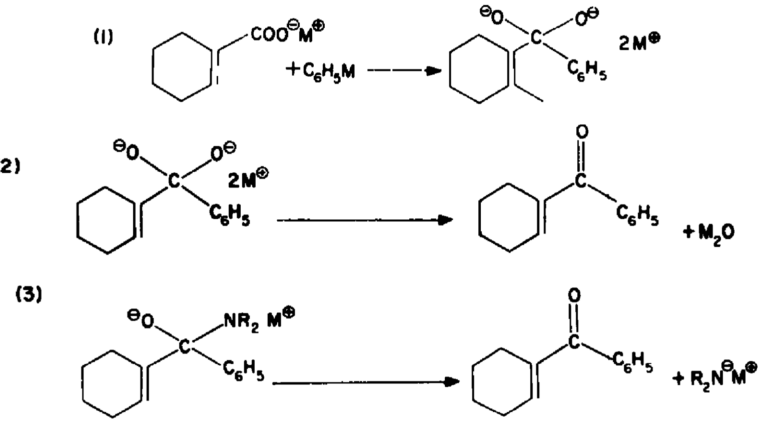


XXII



XXIII

The absence of 1-cyclohexenyl phenyl ketone (IVg) in the reaction of cyclohexene-1-carboxylic acid (IIc) with I shows that the rate of reaction (1) is slower than intramolecular elimination of MgO (2), the subsequent reaction with IVg being the fastest. In the reaction of IIc with phenyllithium the ketone (IVg) can be isolated, since (1) in this case is much faster than (2). This is the basis of the method[37] for preparation of ketones from carboxylic acid salts. Reaction (2) is also relatively fast: when acid IIc is heated 15 minutes with excess of phenyllithium the product consists mostly of XV.



It seems that the corresponding intramolecular elimination (3) in the reaction of I

[34] R. E. Lutz, C. L. Dickerson, W. J. Welstead and R. G. Bass, *J. Org. Chem.* **28**, 711 (1963).

[35] J. Klein and A. Y. Meyer, in press.

[36] R. C. Fuson and G. W. Griffith, *J. Amer. Chem. Soc.* **79**, 1941 (1957).

[37] J. F. Arens and D. A. Van Dorp, *Nature, Lond.* **157**, 190 (1946); D. A. Van Dorp and J. F. Arens, *Rec. Trav. Chim.* **65**, 338 (1946).

with amides is much slower than (2) since IVg can be obtained from the reaction of I with cyclohexene-1-carboxamide (IId) after long reaction periods by hydrolysing the product in the acidified aqueous solution obtained in the decomposition of the reaction mixture. It appears that the amide is preferable as starting material in the reaction with I, when IVa is the desired product.

A comparison of the results obtained with these in the literature for conjugate addition to open chain compounds, shows that less 1,4-addition was observed. The reaction of Grignard reagents, among them I, with open-chain unsaturated carboxylic acids[38] gave yields of higher than 40%. Unsaturated esters give sizeable amounts of 1,4-addition[1] particularly when secondary O-alkyl groups[16,23,39] were present. It seems that 1,4-additions are more difficult in the cyclohexenyl system. This can be explained by axial interaction of the entering phenyl group with the hydrogens in positions *meta* to the attacked carbon. This is plausible since the study of the steric course of conjugate addition of Grignard reagents to cyclohexenones was found to be axial.[40]

EXPERIMENTAL

The IR spectra of liquid products were taken as such and in KBr pellets for solids. The UV spectra were measured in ethanol.

Grignard magnesium was used (Matheson, Coleman and Bell). Later, Mg turnings (Baker & Adamson) were also used for the preparation of phenylmagnesium bromide.

1-*Cyanocyclohexene* (IIa) was prepared by the reaction of cyclohexanone with hydrogen cyanide[41] and subsequent dehydration with thionyl chloride.[42]

Cyclohexene-1-*carboxylic acid* (IIc) was prepared by alkaline saponification of the nitrile.[43]

Cyclohexene-1-*carbonyl chloride*. Thionyl chloride (120 ml) was added to 40 g of IIc, the solution left overnight at room temp and next day refluxed 1 hr. The thionyl chloride was distilled (water bath) and 50 ml toluene added yielding 38 g of the acid chloride b.p. 110° (25 mm).

Cyclohexene-1-*carboxamide* (IId). The chloride of IIc (17 g) was added dropwise to 150 ml 30% NH_4OH cooled in an ice-bath. The precipitate m.p. 126–128[44] was collected after 3 hr and washed with water.

N-*methyl-cyclohexene*-1-*carboxamide* (IIe). The acid chloride (17 g) was added dropwise to 150 ml 25% methylamine aq. cooled in an ice-bath. The solution was kept for 2 hr at room temp, water was then added and the amide extracted with benzene. Distillation gave then 13 g of IIe b.p 170°–175° (25 mm), which solidified, m.p. 60°. (Found: C, 68·73; H, 9·33; N, 9·75, Calc. for C_8H_{13} NO; C, 69·06; H, 9·35; N, 10·07%). V_{max} 1640, 3320 cm^{-1}.

N,N-*Dimethyl-cyclohexene*-1-carboxamide (IIf). The acid chloride (25 g) was added dropwise to 250 ml of 25% dimethylamine aq. cooled in an ice bath. The solution was diluted with water after 2 hr and extracted with benzene. The benzene solution (150 ml) was washed with water and then refluxed for 2 hr with 7g *p*-toluenesulfonic acid in a Dean-Stark apparatus. The solution was cooled, washed with water and distilled, yielding 20 g of a liquid, b.p. 140–145° (25 mm). V_{max} 1645 cm^{-1} (Found: C, 70·1; H, 9·84; N, 8·80; Calc. for $C_9H_{15}NO$: C, 70·59; H, 9·8; N, 9·15%).

Methyl cyclohexene-1-*carboxylate* (IIb). The acid chloride of IIc (15 g) was added dropwise to

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[38] J. H. Wotiz, J. S. Matthews and H. Greenfield, *J. Amer. Chem. Soc.* **75**, 6342 (1953).

[39] J. Munch-Peterson and V. K. Andersen, *Acta Chem. Scand.*, **15**, 271 (1961). J. Munch-Petersen, C. Bretting, P. M. Jorgensen, S. Refn and V. K. Andersen, *ibid.* **15**, 277 (1961). V. K. Andersen and J. Munch-Petersen, *ibid.* **16**, 947 (1962)

[40] H. O. House and H. W. Thompson, *J. Org. Chem.* **28**, 360 (1963); A. J. Birch and R. Robinson, *J. Chem. Soc.* 501 (1943); R. F. Church, R. E. Ireland and D. R. Shridhar, *J. Org. Chem.* **27**, 707, (1962).

[41] D. Billimoria and N. F. MacLagan, *J. Chem. Soc.* 3067 (1951).

[42] L. Ruzicka and W. Brugger, *Helv. Chim. Acta.* **9**, 402 (1926).

[43] E. J. Boorman and R. P. Linstead, *J. Chem. Soc.* 258 (1935).

[44] M. Mousseron, *Bull. Soc. Chim. Fr.* 604 (1946).

100 ml methanol cooled in ice. Next day water was added and the ester extracted with benzene. Distillation gave 12·8 g IIb, b.p. 95° (20 mm). V_{max} 1715; 1650 cm^{-1}.

trans-2-*Phenylcyclohexane carboxylic acid* was prepared by the Diels-Alder reaction between cinnamic acid and butadiene and subsequent hydrogenation.[45]

Methyl-trans-2-*phenylcyclohexanecarboxylate* (VIb). The acid (20 g) and 100 ml thionyl chloride were mixed and left overnight at room temp, then refluxed for 1 hr. The thionyl chloride was distilled on the water bath, toluene (100ml) added and the mixture then distilled *in vacuo*. The solid residue was treated with 100 ml methanol and left 12 hr. Benzene and water were then added, the organic layer separated and washed with water. Distillation gave 22 g of the ester, b.p. 110°–115° (0·8 mm). V_{max} 1725 cm^{-1}. Found: C, 76·82; H, 8·31; Calc. for $C_{14}H_{18}O_2$: C, 77·07; H, 8·26%).

N,N-*Dimethyl*-trans-2-*phenylcyclohexane carboxamide*. The acid chloride was prepared as above from 5 g acid and 25 ml thionyl chloride. It was dissolved in 20 ml dry tetrahydrofuran and added dropwise to 50 ml cooled 25% dimethylamine aq. The mixture was left overnight at room temp. Water was then added and the product extracted with benzene. Distillation yielded 5 g amide, b.p. 138° (0·3 mm). The amide solidified, m.p. 60°, after crystallization from ligroin, m.p. 76–77°. $\bar{V}_{max}$ 1645 cm^{-1}. (Found: C, 78·21; H, 9·36; N, 5·95; Calc. for $C_{15}H_{21}NO$: C, 77·92; H, 9·09; N, 6·06%).

N,N-*Dimethyl*-(2-trans-*phenylcyclohexyl*) *methylamine* (VIII). A solution of 3·5 g amide in 50 ml anhydrous ether was added dropwise to a stirred suspension of 1·5 g $LiAlH_4$ in 50 ml ether. The mixture was refluxed 2 hr then left overnight. Ethanol (15 ml) was added dropwise with cooling, then 50 ml 30% NaOH aq. The organic layer was separated, washed (dil NaOH, and then with 10% HCl aq.).

The acid solution was made alkaline (30% NaOH aq.) and then extracted with ether. Distillation yielded 3 g of the tertiary amine *trans*-VIII, b.p. 115–117° (1 mm). V_{max} (cm^{-1}) 2850, 2780, 2700, 1625 (w). (Found: C, 83·21; H, 10·45; N, 6·43; Calc. for $C_{15}H_{23}N$: C, 82·95; H, 10·6; N, 6·45%).

This amine gave with excess methyl iodide in ethanol and subsequent distillation of the solvent an oil which solidified on trituration with ethyl acetate. m.p. 198–200°. (Found: 53·76; H, 7·24; Calc. for $C_{16}H_{26}IN$: C, 53·48; H, 7·24%;).

Reaction of phenylmagnesium bromide (I) *with* IIa. A solution, of 10g IIa in 30 ml anhydrous ether was added dropwise to a magnetically stirred Grignard solution, prepared from 2·4 g Mg, 17 g bromobenzene and 50 ml anhydrous ether. The reaction mixture was refluxed 5 hr cooled and treated with (a) HCl or (b) H_2SO_4.

(a) The reaction mixture was cooled by an ice-bath and 100 ml 10% HCl aq. added dropwise. The mixture was then refluxed 90 min, cooled and the precipitate (4 g) of the imine hydrochloride m.p. 203° collected. V_{max} 3320(s), 3000–2400(br), 1645(s) cm^{-1}. Found: C, 57·3; H, 7·16; Cl, 25·0; N, 5·0; Calc. for $C_{13}H_{17}Cl_2N$: C, 60·46; H, 6·6; Cl, 27·5; N, 5·43%). The ether layer was separated, washed with water and distilled, giving, after a forerun containing some of the starting materials and biphenyl, 1·8 g of a liquid b.p. 135° (2·5 mm). $\bar{V}_{max}$ 1645, 1615 cm^{-1}.

The aqueous solution was boiled 15 hr and extracted with benzene. Distillation of the benzene layer gave 4·1 g IV g[46] b.p. 120°–125° (0·5 mm). $\bar{V}_{max}$ 1645, 1615 cm^{-1}. (Found: C, 83·5; H, 7·5, Calc. for $C_{13}H_{14}O$: C, 83·8; H, 7·5%).This product gave a red dinitrophenylhydrazone m.p. 163°. (butyl acetate). Found: N, 15·1; Calc. for $C_{19}H_{18}N_4O_4$: N, 15·3%).

The product, b.p. 135° (2·5 mm) gave with dinitrophenylhydrazine solution first a yellow precipitate m.p. 127° (ethanol). (Found: N, 15·1) and from the filtrate a red dinitrophenylhydrazone m.p. 163°.

The imine hydrochloride (5 g) was dissolved in 150 ml ethanol and a solution of 5 g KOH in 5 ml water was added. The ethanol was distilled, water was added to the residue and the imine extracted with benzene. Distillation gave 1·5 g of an oil, b.p. 132° (1 mm). (Found: C, 83·83; H, 8·07; N, 7·1; Calc. for $C_{13}H_{15}N$: C, 84·3; H, 8·1; N, 7·6%). V_{max} 3350, 3060, 1640, cm^{-1}.

(b) The reaction mixture was poured slowly on a mixture of 200–300 g ice and excess of 50% H_2SO_4. If necessary more ice was added to keep the solution cold. The layers were separated and the aqueous solution left for a week at room temp or boiled for 15 hr. Extraction with benzene and distillation gave 7 g IVg, b.p. 135° (2 mm) which solidified, m.p. 25°.

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[45] J. Klein and G. Levin, *J. Amer. Chem. Soc.* **80**, 1707 (1958).

[46] R. E. Christ and R. C. Fuson. *J. Amer. Chem. Soc.* **59**, 893 (1937).

A yield of 11·7 g IVg was obtained from the H_2SO_4 aq. layer, when 10 g of IIa were reacted with a Grignard solution prepared from 5·3 g Mg, 38 g bromobenzene and 100 ml ether.

Reaction of IIa *with diphenylmagnesium.* A solution of 100 ml of dry dioxan in 100 ml anhydrous ether was added dropwise with stirring to a Grignard solution obtained by reacting 26 g Mg and 155 g bromobenzene in 300 ml ether. The reaction mixture was stirred 2 hr and left overnight. The supernatant liquid was decanted, then centrifuged and the solution transferred under nitrogen to a container. The diphenylmagnesium content (1·5 Molar) was estimated by titration of an aliquot portion with HCl.

To 50 ml of this diphenylmagnesium solution, 3·5 g IIa dissolved in 20 ml ether were added. After refluxing and workup by method b, 4·5 g IV g were obtained.

Reaction of IIb *with phenylmagnesium bromide.* A solution of 6 g IIb in 30 ml anhydrous ether was added dropwise during 30 min to a stirred Grignard solution prepared from 4·8 g Mg and 36 g bromobenzene in 100 ml ether. The mixture was refluxed 4 hr, then cooled and poured on a mixture of ice and 50% H_2SO_4 aq. Benzene was added, the organic layer separated and washed with water. Evaporation of the solvent left a solid residue, which gave on crystallization from ethanol 6·3 g almost pure *cis*-V[24], m.p. 110–112°. $\bar{V}_{max}$ 1685, 772, 752 cm^{-1}.

Distillation of the filtrate gave 2 g of a mixture of *cis*- and *trans*-V, b.p. 170°–180° (2 mm), containing a small amount of VIj as shown by a shoulder at 1725 cm^{-1}.

The reaction between equimolecular amounts of IIb (6 g) and phenylmagnesium bromide lowered the yield of V to 2·8 g and gave 1·5 g starting ester.

Reaction of IVg *with phenylmagnesium bromide.* A solution of 6·2 g IVg in 30 ml anhydrous ether was added during 30 min to a Grignard reagent from 2·4 g Mg and 17 g bromobenzene in 50 ml ether. The solution was refluxed 4 hr, cooled and poured on ice and 50% H_2SO_4 aq. Benzene was added, the organic layer separated and washed with water. Evaporation of the solvent left a solid residue, which gave on crystallization from ethanol 8 g *cis*-V m.p. 112–114°. Distillation of the filtrate yielded 1·1 g of a mixture of *cis*- and *trans*-V, b.p. 170–175° (1 mm).

Reaction of IVg *with diphenylmagnesium.* A solution of 4·7 g IVg in 20 ml anhydrous ether was added during 15 min to 50 ml of a 1·5 molar solution of diphenylmagnesium. The solution was refluxed 4 hr, cooled and worked up as above, yielding 5·1 g *cis*-V m.p. 112–114° and 1·8 g of a mixture of *cis* and *trans*-V b.p. at 170–175° (1 mm).

Reaction of IVg *with phenylmagnesium bromide-acetone.* A Grignard solution was prepared from 4·8 g Mg, 34 g bromobenzene and 80 ml ether. Acetone (5·8 g) dissolved in 20 ml ether was added dropwise during 30 min. The reaction mixture was stirred 30 min more and then 5 g IVg dissolved 30 ml ether were added. Refluxing for 4 hr was followed by the usual work-up, yielding 3·9 g *cis*-V m.p. 110–111° and 2·1 g of a mixture of *cis*- and *trans*-V, b.p. 170–175° (1 mm).

Reaction of VIj *with phenylmagnesium bromide.* A solution of 7·2 g *trans*-VIj in 30 ml anhydrous ether was added to a Grignard solution prepared from 1·6 g Mg and 11·5 g bromobenzene in 50 ml ether. The solution was refluxed 5 hr and then worked up as above. Distillation gave 4·7 g starting ester b.p. 140–150° (20 mm) and 3·6 g viscous oil, b.p. 180–185° (0·6 mm), which showed IR bands at 3450 and 1680 cm^{-1} the intensity of the latter band indicating no more than 30% of V in the product.

Reaction of IIc *with phenylmagnesium bromide.* A solution of 7·5 g IIc in 30 ml anhydrous ether was added dropwise to a Grignard reagent prepared from 4·8 g Mg and 34 g bromobenzene in 100 ml ether. The reaction mixture was refluxed 20 hr, then left 15 hr at room temp, and finally poured on ice and 50% H_2SO_4 aq. The aqueous layer was extracted twice with benzene. The organic layer was washed (10% Na_2CO_3 aq., then with water) and the solvent distilled. The residue gave on crystallization from ethanol 6·5 g *cis*-V m.p. 110–112°. The filtrate yielded on distillation 1·9 oil b.p. 160–165° (0·8 mm), which consisted mostly of *cis* and *trans*-V (IR).

The alkaline layer was acidified with HCl and extracted twice with benzene. Distillation of the benzene solution yielded 4 g VIk as a viscous oil b.p. 150 (0·8 mm) V_{max} 3500–2500 (br), 1700 cm^{-1}. Chromatographic separation of the isomers on a column of silica by elution with benzene–pet ether (1:1) gave the *cis*-acid (80%) m.p. 72°–75° [47] which gave a benzylthiuronium salt m.p. 160°–162° [47], and elution with benzene—the *trans*-isomer m.p. 106–108° [47].

Addition of aniline to the reaction mixture at the end of the reaction and before the decomposition of the Grignard reagent by water, yielded the *trans*-ketone (V) and the *trans*-acid (VIk).

When acetyl chloride (15 g) was added to the reaction mixture after 20 hr reflux and the mixture

[47] C. D. Gutsche, *J. Amer. Chem. Soc.* 70, 4150 (1948).

left at room temp for 12 hr, VII was obtained in the neutral fraction as a viscous oil (5 g) 170° (2 mm) $\bar{V}_{max}$ 1760 cm^{-1}. (Found: C, 82·5; H, 7·29; Calc. for $C_{21}H_{22}O_2$: C, 82·35; H, 7·19%).

1 g of VII was dissolved in 30 ml ethanol and 5 ml 30% NaOH aq. added. The solution was boiled for 90 min, cooled, water added and the precipitate (0·8 g) m.p. 115–117° collected. Crystallization from ethanol yielded *trans*-V m.p. 122–123.[24] $\bar{V}_{max}$. 1685, 784, 762 cm^{-1}.

Reaction of IId *with phenylmagnesium bromide.* A solution of 4·1 g IId in 50 ml dry tetrahydrofuran was added to a Grignard solution prepared from 9·6 g Mg, 67 g bromobenzene in 150 ml ether. The reaction mixture was refluxed 6 hr, left overnight at room temp and then poured onto ice and 50% H_2SO_4, benzene was added and the layers separated. The aqueous layer was boiled, 15 hr, then extracted with benzene. Distillation of the benzene layer yielded 2·5 g IVg.

A similar experiment was carried out by addition of 4g IId dissolved in 50 ml benzene to a Grignard solution obtained from 7·2 g Mg and 51 g bromobenzene in 100 ml ether. This reaction mixture was refluxed 20 hr. A similar work-up as above yielded 4·5 g IVg, containing a small amount of V as shown by a shoulder at 1685 cm^{-1}.

Reaction of IIf *with phenylmagnesium bromide.* 13 g of IIf dissolved in 30 ml dry tetrahydrofuran were added to a Grignard reagent prepared from 4·8 g Mg, 34 g bromobenzene and 100 ml tetrahydrofuran. The solution was refluxed 5 hr, then cooled and poured on ice and 50% H_2SO_4. The aqueous layer was extracted with benzene and the organic layer washed (10% $NaCO_3$ aq. and water). Distillation gave 15·5 g oil, b.p. 155°–160° (2 mm) and 1·5 g V b.p. 195° (4 mm). The last fraction gave on crystallization from ethanol a product m.p. 108–110°.

14 g of the first fraction boiling at 155°–160° (2 mm) were dissolved in 50 ml anhydrous ether and added dropwise to a suspension of 2 g $LiAlH_4$ in 100 ml ether. The reaction mixture was refluxed 8 hr. Next day, 20 ml ethanol were added dropwise with cooling, then 100 ml 30% NaOH aq. Benzene was added and the layers separated. The organic layer was washed (dil. NaOH aq., then with 10% HCl aq.). The acid solution was made alkaline (30% NaOH) and extracted with ether. Distillation of the ether layer gave 4·7 g tertiary amine *cis*-VIII as an oil, b.p. 112°–114° (2 mm). $\bar{V}_{max}$ 2850, 2780, 2700, 1625 (w) cm^{-1}. (Found: C, 83·24; H, 10·9; N, 6·50; Calc. for $C_{15}H_{23}N$: C, 82·95; H, 10·6; N, 6·45%).

The tertiary amine *cis*-VIII gave with excess methyl iodide in ethanol and subsequent evaporation of the solvent an oily methiodide. Trituration with ethyl acetate yielded a white product m.p. 155°–157°. This m.p. was lowered to 148°–150° by an admixture of the methiodide of the *trans*-tertiary amine. (Found: C, 53·71; H, 7·20; Calc. for $C_{16}H_{26}IN$: C, 53·48; H, 7·24%).

*α-Naphthylcyclohexene-*1*-yl ketone* (IVh). 10·7 IIa dissolved in 30 ml anhydrous ether were added during 30 min to a Grignard solution prepared from 5·3 g Mg and 45 g α-bromonaphthalene in 150 ml ether. The reaction mixture was refluxed 4 hr, cooled and poured on ice and 50% H_2SO_4aq. The aqueous solution was separated, washed with ether then refluxed 15 hr, cooled and extracted with benzene. Distillation of the benzene solution gave 13·7 g IVh as a viscous oil, b.p. 195° (0·8 mm). $\bar{V}_{max}$ 1660 cm^{-1}. (Found: C, 86·3; H, 6·5; Calc. for $C_{17}H_{16}O$: C, 86·5; H, 6·7%).

The ketone (IVh) gave an oily dinitrophenylhydrazone which solidified on trituration with ethyl acetate. Crystallization from ethyl acetate–ethanol gave a red product m.p. 170–172°.

Cyclization of IVh. 7 g IVh and 70 g polyphosphoric acid were stirred 4 hr on a boiling water bath. The reaction mixture was then cooled and ice added. The precipitate was collected, washed with water and crystallized from ethanol, yielding 6·6 g IX m.p. 75°–77°. Recrystallization from ethanol raised the m.p. to 79°–80°. $\bar{V}_{max}$ 1695 cm^{-1}. (Found: C, 86·8; H, 6·3; Calc. for $C_{17}H_{16}O$: C, 86·5; H, 6·7%).

*Benzylcyclohexen-*1*-yl ketone* (IVi). A solution of 10·3 IIa in 30 ml anhydrous ether was added during 30 min to a benzylmagnesium chloride solution prepared from 5·3 g Mg and 27 g benzyl chloride in 100 ml ether. The solution was refluxed 4 hr, cooled, poured on ice and 50% H_2SO_4 aq. The ether layer was washed with water and distilled, yielding 6 g viscous oil, b.p. 190–195° (0·5 mm). Trituration of this oil with benzene–petrol ether yielded 1 g solid m.p. 190–197°. Crystallization from benzene gave a product m.p. 198–199°. $\bar{V}_{max}$ 3950, 2270 (m), 1625 (w) cm^{-1}. (Found: C, 82·68; H, 8·45; N, 8·58; Calc. for $C_{21}H_{26}N_2$: C, 82·35; H, 8·49; N, 9·15%).

The aqueous solution was boiled 15 hr, then cooled and extracted with benzene. Distillation of the benzene layer yielded 7·2 g IVi,[48] b.p. 140°–150° (2·5 mm). $\bar{V}_{max}$ 1680 cm^{-1}, which gave a

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[48] C. D. Gutsche and W. S. Johnson, *J. Amer. Chem. Soc.* **68**, 2239 (1946).

dinitrophenylhydrazone m.p. 166–7°[48]. (Found: C, 84·4; H, 7·8; Calc. for $C_{14}H_{16}O$: C, 84·0; H, 8·0%).

Reaction of IIc *with cyclohexylmagnesium bromide.* A Grignard solution was prepared from 4·8 g Mg, 37 g bromocyclohexane and 100 ml anhydrous ether; and 7·5 g IIc dissolved in 30 ml ether were added dropwise. The mixture was poured on ice and HCl aq. after being refluxed 20 hr. The ether layer was washed (10% Na_2CO_3 aq. and water). Distillation gave 4·6 g oil b.p. 160–165° (1 mm which solidified. Crystallization of this product from ethanol gave XII m.p. 84°–85. $\bar{\nu}_{max}$ 1700 cm^{-1}. (Found: C, 82·1; H, 11·3. Calc. for $C_{19}H_{32}O$: C, 82·6; H, 11·6%).

The alkaline solution gave on acidification, extraction with benzene and distillation 2·7 g IIc and 0·3 g acid b.p. 150°–155° (0·7 mm).

Reaction of IIc *with benzylmagnesium chloride.* To a Grignard solution prepared from 4·8 g Mg, 30 g benzyl chloride and 100 ml ether, a solution of 7·5 g IIc in 30 ml anhydrous ether was added dropwise. The reaction mixture was refluxed and treated as above. Distillation of the neutral layer gave 9·8 g oil, b.p. 160–165° (1 mm). $\bar{\nu}_{max}$ 3550, 1665 cm^{-1}. (Found: C, 86·5; H, 8·3; Calc. for $C_{21}H_{24}O$: C, 86·3; H, 8·2%).

From the acid fraction, 1·5 g of a mixture of *cis* and *trans*-XI b.p. 145°-150° (1 mm) were obtained, which gave a benzylthiuronium salt m.p. 140–145°.

*Cyclohexen-*1*-yl methyl ketone* (IVj). A solution of 32 g IIa in 100 ml anhydrous ether was added dropwise to a Grignard solution prepared by bubbling methyl bromide through a stirred and cooled mixture of 10 g Mg and 150 ml ether. The solution was refluxed 8 hr, then cooled and poured on ice and 50% H_2SO_4. Separation of the layers and distillation of the ether solution gave 2·2 g impure IVj b.p. 90°–95° (28 mm) and 1·8 g of a product, b.p. 150°–160° (0·5 mm) which gave on crystallization from ethanol a solid m.p. 138°–140°, showing no carbonyl absorption in the IR and containing 12·2% N.

The aqueous solution was left at room temp for 6 days and then extracted with benzene. Distillation yielded 22·5 g IVj, b.p. 95°–100° (25 mm)[49]. $\bar{\nu}_{max}$ 1685, 1655 cm^{-1}. (Found: C, 77·49; H, 9·41; Calc. for $C_8H_{12}O$: C, 77·42; H, 9·67%). The ketone (IVj) gave a red dinitrophenylhydrazone m.p. 202–203°.

Reaction of IVj *with methylmagnesium bromide–cuprous chloride.* A Grignard solution was prepared from 2·4 g Mg and methyl bromide in 50 ml ether. The solution was cooled (ice bath) and 0·3 g cuprous chloride added in 3 portions alternately with a solution of 4·2 g IVj in 25 ml ether. The solution was refluxed 2 hr and then treated as before. Distillation gave 2 g liquid, b.p. 85–90° (20 mm), $\bar{\nu}_{max}$ 3450, 1705, 1690 (sh) cm^{-1}. This oil gave a dinitrophenylhydrazone, m.p. after crystallization from ethanol, 124°–125°. (Found: C, 56·6; H, 6·2; Calc. for $C_{15}H_{20}N_4O_4$: C, 56·25; H, 6·25%).

Reaction of IVj *with phenylmagnesium bromide–cuprous chloride.* The reaction was carried out as above with phenylmagnesium bromide, yielding 5·9 g oil, b.p. 110–115° (1·5 mm) showing weak hydroxyl and carbonyl bands at 3400 and 1705 cm^{-1}. The analysis (Found: C, 89·6; H, 8·4%) shows a joint carbinol and ketone content of no more than 20%.

The reaction carried out in the absence of cuprous chloried gave a product with a slightly weaker carbonyl band.

*Methanol-*1*-cyclohexen-*1*-yldiphenyl* (XV). (a). *From* IVg. To a phenyllithium solution prepared from 3·5 g Li, 43 g bromobenzene and 100 ml anhydrous ether, a solution of 9·5 g IV g in 30 ml ether was added during 15 min. The solution was refluxed for 15 min, then poured onto ice. The ether layer was separated, washed with water and the ether evaporated. The residue was crystallized from ethanol and yielded 5·9 g XV m.p. 150°.[50] (Found: C, 86·0; H, 7·4; Calc. for $C_{19}H_{20}O$ C, 86·3%; H, 7·57). From the filtrate, 1·5 g of a product, b.p. 170–175° (0·4 mm) consisting mostly of XV was obtained. $\bar{\nu}_{max}$ 3450 cm^{-1}.

(b) *From* IIc: A solution of 7·5 g of IIc in 30 ml of anhydrous ether was added during 15 min to a phenyllithium solution prepared from 4·2 g Li, 51 g bromobenzene and 120 ml ether. The solution was refluxed 5 hr, cooled and poured onto ice. After a similar workup as above, 3 g XV m.p. 145–147° was obtained. Distillation of the filtrate gave 4 g IV g and 2 g, b.p. 170–175° (0·4 mm) consisting mostly of XV.

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[49] J. English Jr. and V. Lamberti, *J. Amer. Chem. Soc.* **74**, 1909 (1952).

[50] E. A. Braude and J. A. Coles, *J. Chem. Soc.* 2014 (1950).

Similar results were obtained, when the reaction mixture was refluxed for 30 min only.

When 7·5 g IIc were reacted with a phenyllithium solution prepared from 1·8 g Li and 22·5 g bromobenzene, 7 g IV g and 1 g XV were obtained.

Reaction of IIf *with phenyllithium.* A solution of 5·1 g IIf in 30 ml anhydrous ether was added during 30 min to a phenyllithium solution prepared from 0·6 g Li, 7·5 g bromobenzene and 40ml ether. The solution was refluxed 4 hr, cooled and poured onto ice. The ether layer was separated washed (10% HCl aq. and water). Distillation gave 4·5 g IVg b.p. 120–125° (0·4 mm).

Reaction of IIc *with methyllithium.* To a solution prepared from 2·8 g Li, 30 g methyl iodide and 100 ml ether and cooled in an ice-bath, a solution of 12·6 g IIc in 40 ml ether were added during 30 min The solution was left overnight at room temp. The usual work-up gave in the neutral fraction 1·5 g IVj. b.p. 95° (22 mm) and 2·4 g viscous oil, b.p. 170–175° (0·5 mm), which was crystallized from benzene–pet ether and gave 0·5 g solid m.p. 123°–125°. $\overline{V}_{max}$ 3500 cm^{-1}. λ_{max} 270 mμ (ε 200) 310 mμ (ε 80). (Found: C, 77·49; H, 9·41; Calc. for $C_{16}H_{26}O_2$: C, 77·42; H, 9·67%).

From the acid fraction 4·5 g IIc b.p. 110° (0·8 mm) were recovered.