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Conjugate Additions of Grignard Reagents to alpha,beta-Unsaturated Esters

V. Additions of *n*-Butylmagnesium Bromide to *sec*-Butyl Esters of Maleic, Fumaric, Citraconic, and Mesaconic Acids

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n-Butylmagnesium bromide reacts with *sec*-butyl maleate, fumarate, citraconate and mesaconate by addition to the carbon-carbon double bond (1,4-addition) as well as by addition to one of the carbonyl groups (1,2-addition). 1,4-Additions lead to substituted succinic esters, while 1,2-additions followed by 1,4-additions result in saturated lactones. With maleic and fumaric esters the yields of simple 1,4-addition product (*n*-butylsuccinic ester) are rather low, but the yield from the maleic ester is greatly improved by cuprous chloride catalysis. The yields from citraconic and mesaconic esters are quite satisfactory with respect to the amounts of 1,4 addition product formed, but the products are mixtures of the two isomeric methyl-*n*-butylsuccinic esters. From mesaconic ester the major product is the α,α'-disubstituted ester, whereas the product from citraconic ester is mainly the α,α-disubstitute. In the presence of cuprous chloride citraconic and mesaconic esters are to a large extent reduced (to pyrotartaric ester). The effect of inverse addition of the Grignard reagent has been studied with certain esters. The mechanisms of the reactions are considered.

This paper is concerned with the behaviour of the *sec*-butyl esters of maleic, fumaric, citraconic and mesaconic acids in reactions with Grignard reagents under certain conditions which have previously been found favourable for conjugate addition in the reactions of esters of mono-carboxylic α,β-unsaturated acids such as *sec*-butyl crotonate[1]:

$$CH_3CH{=}CH{-}COO\text{-}sec\text{-}C_4H_9 \xrightarrow{n\text{-}C_4H_9MgBr} CH_3\underset{\displaystyle n\text{-}C_4H_9}{\underset{|}{C}}H{-}CH_2COO\text{-}sec\text{-}C_4H_9$$

Reactions between maleic and fumaric esters and metalloörganic compounds have occasionally been described in the literature [2-6] and maleic anhydride has also been included in these studies [4-6]. In most cases methyl or ethyl esters have been employed, and the reactions have generally taken place as 1,2-additions (to the carbonyl group), although 1,4-additions (to the carbon-carbon double bond) have often been reported as well. The products obtained have thus been either unsaturated or saturated diketones or tertiary alcohols (*cf.* Ref.[7]). Usually, no yields are given.

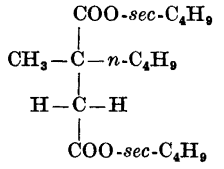
Marvel *et al.*[6], however, have obtained about 30 % yield of diethyl *iso*propylsuccinate from equivalent amounts of either diethyl maleate or fumarate and *iso*propylmagnesium bromide, when the Grignard reagent was added to the ester (no special mention was made of addition time or temperature). Furthermore, the same authors report that the 1,4-addition of *iso*propylcadmium reagent to diethyl maleate also gives a 30 % yield of diethyl *iso*propylsuccinate; in this case the ester was added to the reagent at 0° during 3 1/2 h. This latter result is remarkable, since usually cadmium reagents are believed to react by nucleophilic substitutions rather than as additions, and are consequently quite unreactive towards double bonds [8].

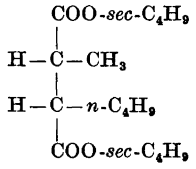
Also a zinc reagent has apparently been used in reactions of this type, since Michael [9] report the formation in 20—25 % yield of diethyl ethylsuccinate and diethyl α-methyl-α'-ethylsuccinate by the prolonged action of ethyl iodide and zinc upon diethyl fumarate and citraconate, respectively. No details are mentioned.

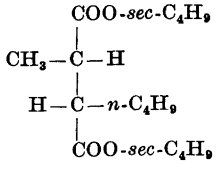
Much better results have been reported [10] with tetraethyl ethylenetetracarboxylate to which methyl-, ethyl- and phenylmagnesium bromides have been added (in yields of 79, 56 and 71 %, respectively) without taking any special precautions (cooling or prolonged addition time).

In the present investigation, elucidation of the following three questions has been attempted: 1. Does conjugate addition to the double bond take place and in what yield? 2. Could any difference in this respect be found between geometrically isomeric esters (such as maleic and fumaric esters)? 3. Which would be the orientation (if any) of addition to unsymmetrically substituted esters (such as citraconic and mesaconic esters)? The possible catalytic effect of cuprous chloride on the course of the reactions has also been investigated.

From maleic and fumaric esters only one simple 1,4-addition product is possible: *d,l-n*-butylsuccinic ester; but from citraconic and mesaconic esters, in fact, three different racemic methyl-*n*-butylsuccinic esters are conceivable: *d,l-α*-methyl-*α*-*n*-butylsuccinic, *d,l-erythro-* and *d,l-threo-α*-methyl-*α'*-*n*-butylsuccinic esters:





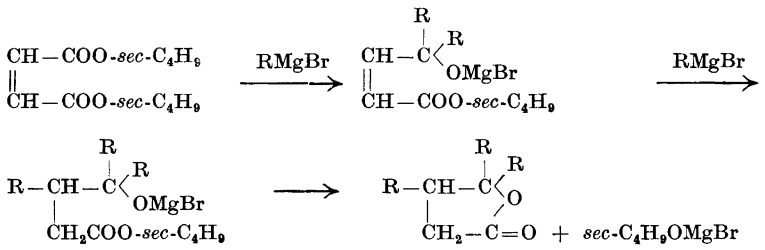


Since the addition process can hardly be visualized as being stereospecific (*cf.* below), the possibility that only one of the two different stereo-isomers (or a mixture of unequal amounts thereof) is formed has not been considered *.

The results of the addition reactions with *n*-butylmagnesium bromide are given in Table 1.

Non-catalyzed additions. When the general procedure [1] is followed, the maleic and fumaric esters give rather unsatisfactory yields (30—40 %) of the conjugate addition product (*n*-butylsuccinic ester), considerable amounts (17 %) of 1,2-addition product (lactone, see below) being formed. From the citraconic and mesaconic esters, on the other hand, quite satisfactory yields (66 and 55 %, resp.) of addition products are obtained, with only little lactone being produced. In one run with mesaconic ester a small quantity of reduction product (se below) was isolated.

The high-boiling by-products (II, IV and VII) are believed to be lactones, which are formed by initial 1,2-addition to one ester group, followed by 1,4-addition and ring-closure, according to the following scheme (*e.g.* with maleic ester):



The lactone structure of II, IV and VII has been confirmed by analyses and infra-red spectroscopy. The formation of small amounts of lactones has also been observed by earlier workers [2,5].

The reduction process is discussed below.

Cuprous chloride catalyzed reactions. Since cuprous chloride has been previously found to catalyze 1,4-addition in competition with 1,2-addition [7,12] and reduction [13], this catalytic procedure was also tried in the present work, but the results were not entirely consistent with the earlier findings.

In the case of the maleic ester the yield of the conjugate addition product was indeed considerably increased (to 67 %); very little lactone was now produced. The reaction with the fumaric ester was little affected by the presence of cuprous chloride; the amount of 1,4-addition product was somewhat increased at the expense of the lactone.

In the case of the citraconic and mesaconic esters, however, the yield of the 1,4-addition product was strongly decreased (to 30 and 20 %, resp.) by the presence of cuprous chloride, and the reduction of the double bond (leading to

* It is quite likely, however, that one of the stereo-isomeric α,α'-disubstituted acids has been isolated in a comparatively pure form (by the recrystallizations during the identification work, see experimental part), since the melting point of our α,α'-compound is rather sharp and considerably higher (136°) than that reported in the literature [11]: 85—105°. No attempt has been made to determine the configuration.

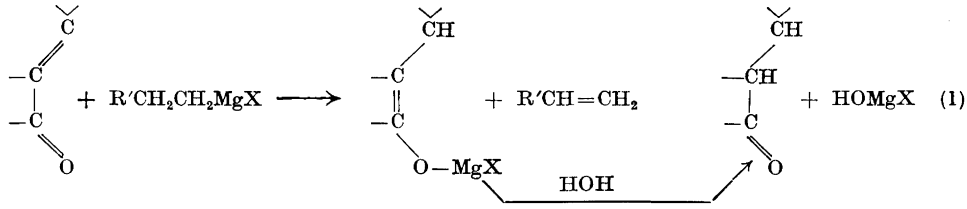
Table 1. Additions of *n*-butylmagnesium bromide to *sec*-butyl esters of maleic (mal), fumaric (fum), citraconic (cit) and mesaconic (mes) acids.

Ester	Catalyst	Products		b. p., °C/mm	n_D^{20}	yield %	remarks
mal	none	I[a]	(1,4-add.)	106—107/0.6	1.4353	39	
		II[b]	(lactone)	143/1	1.4600	17	
mal	CuCl	I	(1,4-add.)			57	ice-salt cooling; ester added during 1.5 h.
		II	(lactone)			6	
mal	CuCl	I	(1,4-add.)			67	
		II	(lactone)			very little	
fum	none	I[c]	(1,4-add.)	113/1	1.4341	19	
		II[d]	(lactone)	131/0.7	1.4600	10	
fum	CuCl	I	(1,4-add.)			32	ester added during 3 h.
		II	(lactone)			17	
fum	CuCl	I	(1,4-add.)			38	
		II	(lactone)			13	
cit	none	III[e,f]	(1,4-add.)	125/2	1.4390	62—70	
		IV[g,h]	(lactone)	110—120/1	1.4665	4	
cit	CuCl	V[i,f]	(reduct.)	87— 92/0.9	1.4283	31—22	
		III	(1,4-add.)	108—110/0.6	1.4372	38—46	
		V[j,f]	(reduct.)	81/0.6	1.4275	9—0	
mes	none	VI[k]	(1,4-add.)	109/1	1.4355	42—55	
		VII[h]	(lactone)	129/0.7	1.4597	4—0	
		V	(reduct.)	87/0.9	1.4261	40	
mes	CuCl	VI	(1,4-add.)	108/0.7	1.4354	21	

I: Di-*sec*-butyl *n*-butylsuccinate[a]. II: β,γ,γ-Tri-*n*-butyl-γ-butyrolactone[b]. III: Di-*sec*-butyl methyl-*n*-butylsuccinate, 90 % α,α-, 10 % α,α'-isomer[e,f]. IV: Believed to be $\beta(\alpha)$-methyl-β,γ,γ-tri-*n*-butyl-γ-butyrolactone[g,h]. V: Di-sec-butyl methylsuccinate (pyrotartrate)[i,f]. VI: Di-*sec*-butyl methyl-*n*-butylsuccinate, 30 % α,α-, 70 % α,α'-isomer[k,f]. VII. Believed to be $\alpha(\beta)$-methyl-β,γ,γ-tri-*n*-butyl-γ-butyrolactone[h].

[a] Calc. for $C_{16}H_{30}O_4$ (286.40): C 67.09; H 10.56. Found: C 67.85; H 10.84. [b] Calc. for $C_{16}H_{30}O_2$ (254.41): C 75.53; H 11.89. Found: C 75.05; H 11.69. [c] Calc. for $C_{16}H_{30}O_4$ (286.40): C 67.09; H 10.56. Found: C 67.55; H 10.40; infra-red spectroscopy showed identity between I_{mal} and I_{fum}. [d] Calc. for $C_{16}H_{30}O_2$ (254.41): C 75.53; H 11.89. Found: C 75.35; H 11.43; infrared spectroscopy showed identity between II_{mal} and II_{fum}. [e] Calc. for $C_{17}H_{32}O_4$ (300.43): C 67.96; H 10.74. Found: C 69.00; H 11.02; the product contaminated with IV. By saponification of III and distillation methyl-*n*-butylsuccinic anhydride was obtained. Calc. for $C_9H_{14}O_3$ (170.20): C 63.51; H 8.29. Found: C 63.95; H 8.12. [f] Infra-red spectra showed great similarity between I, III, V, and VI. [g] This product was obtained in only one run and only as a by-product from the saponification of III. [h] Infra-red spectrum showed great similarity to II; the product was not further investigated. [i] Infra-red spectra showed identity between V_{cit} and V_{mes}. [j] Calc. for $C_{13}H_{24}O_4$ (244.32): C 63.90; H 9.90. Found: C 64.65; H 9.98. [k] Calc. for $C_{17}H_{32}O_4$ (300.43): C 67.96; H 10.74. Found: C 68.10; H 10.88.

methylsuccinic (pyrotartaric) ester) now became correspondingly dominating. This reaction could be written:



(1)

The mechanism of the reduction process is considered below (eqn. 5). The observation that cuprous chloride promotes reduction in competition with 1,4-addition of the Grignard reagent was surprising in view of the above-mentioned findings by Brändström and Forsblad [13], who report a pronounced effect of this catalyst to favour addition over reduction in the reaction of Grignard reagents with alkylidenecyanoacetic esters. This apparent inconsistency is discussed below.

Table 2. Ratios of isomeric methyl-*n*-butylsuccinic esters formed from citraconic and mesaconic esters, determined by infra-red spectroscopy (IR) and by gas-liquid chromatography* (GLC).

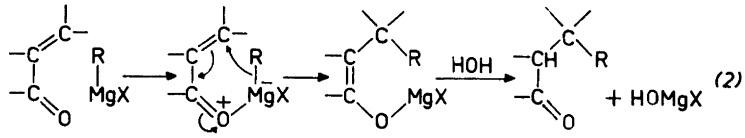
		Uncatalyzed		CuCl-catalyzed		CuCl-catalyzed inverse addition	
		IR	GLC	IR	GLC	IR	GLC
Citraconic	*α,α*	>80 %	90 %	>80 %	90 %	>80 %	90—95 %
	α,α'	<20 »	10 »	<20 »	10 »	<20 »	10— 5 »
Mesaconic	*α,α*	25 %	30 %	25 %	30 %		
	α,α'	75 »	70 »	75 »	70 »		

* Carried out and interpreted by A. Jart, Danish Fat Research Institut, Copenhagen.

*The formation of isomeric methyl-*n*-butylsuccinic esters from citraconic and mesaconic esters.* Regarding the question of the methyl-*n*-butylsuccinic esters obtained by the addition processes with citraconic (*cis*) and mesaconic (*trans*) esters, it was found that both isomers (*α*-methyl-*α*-*n*-butylsuccinic and *α*-methyl-*α'*-*n*-butylsuccinic esters) were formed, but in very different quantities in the two cases. More than 80 % of the *α,α*-isomer and less than 20 % of the *α,α'*-isomer was found in the product from the citraconic ester, while the product from the mesaconic ester contained the isomers in an approximately opposite ratio (Table 2). The ratios were determined by comparing the infra-red spectra of the crude mixtures of isomeric acids, obtained by saponification of the addition products, with the spectra of known mixtures of authentic acids. Although this procedure does not lead to exact values for the ratios, the difference in reactivity of the two geometrically isomeric esters with respect to orientation is quite clear. Somewhat more accurate values were obtained by gas chromatography, see experimental part.

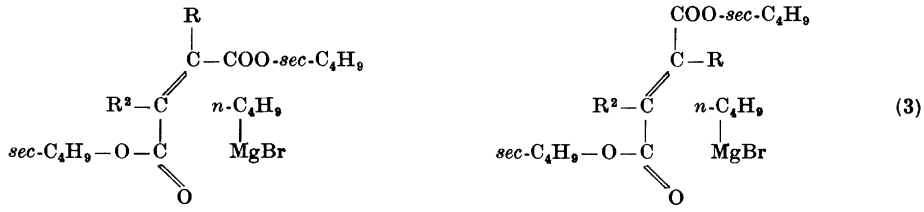
DISCUSSION

For the conjugate addition of Grignard reagents to α,β-unsaturated systems the following cyclic mechanism has been proposed [14]:



(2)

In the case of the esters under consideration, the first step in the above scheme should be represented as follows:



(3)

a. R = R^2 = H: Maleic
b. R = H, R^2 = CH_3: Citraconic
c. R = CH_3, R^2 = H: »
d. R = R^2 = H: Fumaric
e. R = H, R^2 = CH_3: Mesaconic
f. R = CH_3, R^2 = H: »

From this mechanism no stereospecificity could be expected and, in cases where α-methyl-α'-*n*-butylsuccinic esters (3*b* and *e*, above) are formed, the reaction products should be mixtures of nearly equal parts of *erythro*- and *threo*-isomers.

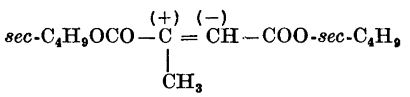
In the reactions with maleic and fumaric esters (3*a* and *d*), two factors should be important for the yield; the reactivity of the double bond and the steric conditions for the cyclic mechanism. Obviously, the configuration of the fumaric ester is more favourable in the latter respect than that of the maleic ester. However, the double bond of the maleic ester is probably much more reactive than that of the fumaric ester, since maleic esters are under considerable steric strain because of the two ester groups in the *cis*-position, which prevent co-planarity between the two carbonyl groups and the ethylenic bond. This strain would be particularly high in the case of the *sec*-butyl esters, and this factor, apparently, is the more important one.

In the reactions with citraconic and mesaconic esters (3*b* or *c* and *e* or *f*) the same two factors, mentioned above for maleic and fumaric esters, should be operative, again resulting in a higher yield of addition product from the *cis*-isomer (citraconic ester) than from the *trans*-isomer (mesaconic ester).

One further point should be mentioned, which may be significant. Whereas the yield of addition product from fumaric ester was considerably less than from maleic ester, the total yield of addition *and* reduction products from mesaconic ester was only little less than the corresponding yield from citraconic ester. This was true of both the uncatalyzed and the catalyzed reactions.

These findings are in agreement with the view that the strain caused by the groups in the *cis*-position is an enhancing factor in the addition reaction since mesaconic ester may be expected to be under considerably more strain than fumaric ester, although less than citraconic and maleic esters.

Considering the above mechanism, an understanding may also be reached, as to why the two — structurally different — isomers predominate in the ester-mixtures produced by the two additions to citraconic and mesaconic esters. Here, again, two factors may be important: the polarization of the double bond and the steric conditions for the cyclic mechanism. In the case of citraconic ester (*cis*) the two ester groups are equal in stereo-chemical respect. The polarization of the double bond:



then, is apparently a more important directing factor than the overcrowding at the methyl-substituted carbon atom (situation 3*c*, above). Thus the α,α-disubstituted succinic ester is the main product. In the case of mesaconic ester (*trans*), the steric conditions for situation 3*e* (above) is much more favourable than situation 3*f*. The polarization factor then becomes of minor importance with the α,α'-compound now being produced in the larger quantity.

Effects of cuprous chloride catalysis. While the orientation of the addition to citraconic and mesaconic esters is rather unaffected by the presence of cuprous chloride during the addition process (*cf.* Table 2), the reduction of these esters (to pyrotartaric ester), which in the uncatalyzed reaction is only of minor importance in comparison to the 1,4-addition, becomes a dominating side-reaction when cuprous chloride is present.

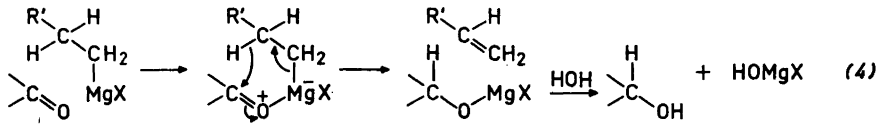
A general statement, that this catalyst appears to enhance the electrophilic reactivity of the carbon-carbon double bond, does not provide any explanation for this experimental fact. Tentatively, one might suggest that an understanding may be sought in the concept of a regular complex formation between cuprous chloride and the carbon-carbon double bond. A great deal of evidence for such complexes can be found in the literature [15], and they also have acquired some technical interest [16]. Andrews and his co-workers [17] have studied the partition of cuprous chloride between water and an organic solvent containing alkenes, unsaturated alcohols (such as allylalcohol) and a number of α,β-unsaturated acids (including those, the *sec*-butyl esters of which have been studied in the present series). Cuprous chloride appears usually to form 1:1 complexes with the unsaturated compounds; the bonding is presumed to occur between the cuprous ion and a carbon atom, an electron pair being furnished by the carbon-carbon double bond. It appears reasonable that, by this coordination, the reactivity of the double bond towards nucleophilic reagents should be augmented. There seems to be no general agreement as to the complexing properties of *cis*, *trans* isomers *, but the negligible effect of cuprous

* Basolo and Pearson (Ref.[15], p. 352 -353) state that *cis*-olefins form more stable complexes than do *trans*-olefins.

chloride on the reaction with fumaric ester indicate that the *trans* compound in this case is the poorer complexing agent, corresponding to the generally lower reactivity mentioned above.

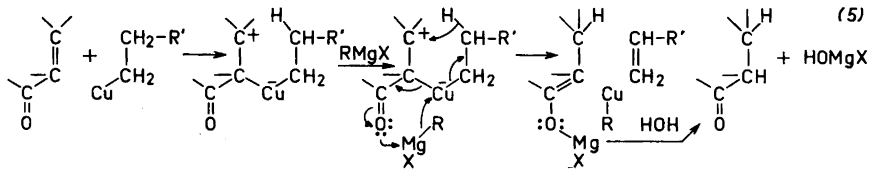
By the coordination also the overcrowding at the double-bonded carbon atoms should be increased. This might favour sterically less demanding reactions, in this case the reduction.

While the cyclic mechanism mentioned above for the 1,4-addition should still be valid in the case of cuprous chloride catalysis, this is not possible for the corresponding mechanism, which has been suggested [18] for the reduction of carbonyl compounds by means of Grignard reagents:



Reduction of the *carbon-carbon* double bond of an α,β-unsaturated carbonyl compound could not take place according to such a mechanism involving a *six*-membered ring and the coordination of the Grignard magnesium with *oxygen*. Provisionally, the following cyclic concerted mechanism is put forward (R = $R'CH_2CH_2$, *cf.* the over-all reaction (eqn. 1)):

$$RMgX + CuCl \rightleftharpoons RCu + MgXCl$$



This mechanism involves an exchange reaction between cuprous chloride and the Grignard reagent leading to the formation of a copper-alkyl compound [19], which is then supposed to coordinate with carbon instead of with oxygen. These synchronous shifts also account for the fact that the effect of cuprous chloride is a catalytic one, with the copper-alkyl being continuously regenerated. Nothing could be stated about the orientation of the attack of the cuprous chloride at the double bond, since the polarization effect and the steric effect have an opposite influence, and in this case the nature of the reaction product does not, of course, give any information.

Effects of using inverse addition procedure. As mentioned in the foregoing, the reduction-promoting action of cuprous chloride appeared to be in contrast to the effect found by Brändström and Forsblad [13]. However, these authors emphasize the importance of inverse addition (that is the addition of the Grignard reagent *to* the ester containing the cuprous chloride). With the three

Table 3. Yields of 1,4-addition and reduction products from reactions of *n*-butylmagnesium bromide with α,β-unsaturated esters under different conditions.

Ester	Product	Normal addition no cat.	Normal addition CuCl	Inverse addition no cat.	Inverse addition CuCl
Ethyl *iso*propylidene-cyanoacetate	1,4-add.[a]	51 %	50 %	45 %	77 %
	reduct.[b]	17 »	18 »	14 »	5 »
Ethyl *iso*propylidene-malonate	1,4-add.[c]	60 %	42 %	61 %	89 %
	reduct.[d]	22 »	40 »	20 »	3 »
sec-Butyl citraconate[e]	1,4-add.	66 %	38—46 %		20 %
	reduct.	0 »	31—22 »		0 »

[a] Ethyl 2-cyano-3,3-dimethylheptanoate (ethyl 1,1-dimethylpentyl-cyano-acetate), b.p. 128°/13 mm, n_D^{20} 1,4412. Calc. for $C_{12}H_{21}O_2N$ (211.30): C 68.21; H 10.02. Found: C 68.05; H 9.80. [b] Ethyl *iso*propylcyanoacetate, b.p. 92—93°/13 mm, n_D^{20} 1.4238. This product did not give the correct analyses; it is probably contaminated with ethyl cyanoacetate, which may arise by a reversal of the condensation of this ester with acetone (the formation of ethyl *iso*propylidene-cyanoacetate). [c] 1,1-Dicarbethoxy-2,2-dimethylhexane (ethyl 1,1-dimethylpentyl-malonate), b.p. 132—133°/13 mm, n_D^{25} 1.4360. Calc. for $C_{14}H_{26}O_4$ (258.35): C 65.08; H 10.14. Found: C 65.50; H 9.98. [d] Ethyl *iso*propylmalonate, b.p. 96—98°/13 mm, n_D^{25} 1.4223. Calc. for $C_{10}H_{18}O_4$ (202.24): C 59.38; H 8.97. Found: C 59.60; H 8.77. [e] See Table 1.

esters of Table 3 we have, therefore, investigated the influence of changing conditions in this respect.

Our results with *iso*propylidenecyanoacetic ester are, in fact, in complete accordance with those of Brändström and Forsblad: cuprous chloride has no effect upon the addition/reduction ratio in the normal addition, but when inverse addition is used, the reduction is largely suppressed and the addition favoured.

With citraconic ester, on the other hand, the normal, uncatalyzed addition procedure appear to be the method which gives the best yields of 1,4-addition. The presence of cuprous chloride strongly favours the reduction when normal addition procedure is used (*cf.* also Table 1), and the catalyzed, inverse addition method, although preventing reduction, gives very low yield of 1,4-addition product, a non-destillable residue being the main reaction product.

Finally, with *iso*propylidenemalonic ester cuprous chloride promotes reduction in the normal addition procedure, but prevents reduction in the inverse procedure, whereas the yields in the uncatalyzed reactions are independent of the addition method.

The results with *iso*propylidenecyanoacetic and citraconic esters with respect to the competition between 1,4-addition and reduction are obscured by the rather low yields of the products in question. The results with *iso*-propylidenemalonic ester, on the other hand, may perhaps be taken as typical, since here, apparently, other reactions take place only to a small extent.

These results are not inconsistent with the above suggested mechanisms. The increased reduction in the normal addition procedure is already considered (eqn.5). In the inverse addition, on the other hand, the cuprous chloride is mixed with the ester, and the Grignard reagent is then slowly added. The catalyst could thus be expected to coordinate with the double bond of the ester, and, by the subsequent slow addition of the Grignard reagent, the ordinary cyclic mechanism (eqn. 2) could be operative, only with an activated double bond.

EXPERIMENTAL

Microanalyses are by Mr. Preben Hansen, Microanalytical Division, The Chemical Laboratory, The University of Copenhagen. Fractional distillations were through a simple 45 cm × 8 mm Podbielniak-type column with a tantalum wire spiral, a heated jacket and a partial reflux head. All products were checked by infra-red spectroscopy using a Beckman IR 2 single-beam spectrophotometer with sodium chloride optics. The spectra of the solid compounds (*i. e.* the methylbutylsuccinic acids) were recorded using the potassium bromide technique, whereas those of the liquids were measured in solutions in carbon tetrachloride.

Preparation of starting materials. sec-*Butyl* esters were prepared from commercial acids according to the general esterification procedure previously described [20]: *maleinate*, b.p. 85°/0.8 mm, n_D^{20} 1.4432, yield 85 %; *fumarate*, b. p. 80°/0.5 mm, n_D^{20} 1.4430, yield 32 % (65 % fumaric acid recovered); *citraconate*, b. p. 86–87°/0.5 mm, n_D^{20} 1.4457, yield 72 %; *mesaconate*, b. p. 89.5°/0.6 mm, n_D^{20} 1.4491, yield 93 %. The identity of the esters was checked by elementary analyses. Infra-red spectra of *sec*-butyl maleate and fumarate agreed with those published in the literature [21]. The spectra of citraconic and mesaconic esters differed from one another, which was taken as evidence that the stereochemical structures were retained during the esterification processes.

The spectra of these four esters, as well as of those products mentioned in the following, which are saturated *sec*-butyl esters * have all been found to show a strong absorption, split in three peaks, around 1 111 cm^{-1} (9.00 μ). This group of bands is, therefore, considered to be a characteristic absorption for *sec*-butyl esters of carboxylic acids.

Ethyl isopropylidenecyanoacetate, b. p. 113°/17 mm, n_D^{25} 1.4653, was prepared according to Wideqvist [22], *diethyl isopropylidenemalonate*, b. p. 108–110°/13 mm, n_D^{20} 1.4484, according to Cope and Hancock [23].

Additions of n-*butylmagnesium bromide to* sec-*butyl esters of maleic, fumaric, citraconic and mesaconic acids.* The uncatalyzed reactions were carried out as described previously [1]; during 1.5–2 h, 0.1 mole of ester, dissolved in 100 ml of ether, was added to a Grignard solution, prepared from 6.3 g (0.26 g-atom) of magnesium turnings, 42.5 g (0.31 mole) of *n*-butyl bromide and 120 ml of ether, and cooled in ice-water during the addition.

In the cuprous chloride catalyzed reactions [20,7,12] the same amounts of the reagents were used, but 0.3 g of cuprous chloride was added in one portion after the Grignard solution had been cooled in ice-water for 15 min. The ester was dissolved in 200 ml of ether and added over a 2–3 h period. In one case with maleic ester cooling in ice-salt was applied during the addition of cuprous chloride and the ester, but the yield was no better than that obtained when only ice-water was used.

In the inverse addition reactions the Grignard solution was transferred to a siphoning vessel. From this it was added, by means of nitrogen pressure, dropwise to the ester cooled in ice-water during 1.5–2 h under vigourous stirring. When the inverse addition reaction was cuprous chloride catalyzed, the catalyst was added to the ester before adding the Grignard solution.

The inverse reactions with *iso*propylidenecyanoacetic ester were somewhat disturbed by the almost instantaneous formation of a viscous, sticky precipitate when the addition of the Grignard reagent was started. The addition of another 100 ml of ether and the

* And also of all other *sec*-butyl esters recorded during the work of this series.

interruption of the cooling seemed to improve dissolution of the precipitate and the effeciency of the stirring.

Identification of products. The products were isolated by fractional distillations and investigated by microanalyses and infra-red spectroscopy (*cf.* Table 1).

The spectra of the addition products, esters I, III and VI, are very similar and can hardly be distinguished significantly. The spectrum of the reduction product V shows a strong resemblance to those of the three addition products. These four spectra all show a carbonyl band at 1 725 cm^{-1} and the group of absorption bands at 1 111 cm^{-1}, which is considered to be characteristic for *sec*-butyl esters (se above), but no absorption was found for C=C or OH. These data, as well as the low refractive indices constitute strong evidence that the products are saturated *sec*-butyl esters.

The spectra of the high-boiling products II, IV and VII have a carbonyl peak at 1 772 cm^{-1} (5.64 μ), which is within the area reported [24] to be characteristic for saturated γ-lactones (1 780—1 760 cm^{-1}); there was no absorption found for saturated ester (1 750—1 735 cm^{-1}), saturated ketone (1 725—1 705 cm^{-1}), hydroxyl group or carbon-carbon double bond. Also an attempt at alkaline hydrolysis indicated a lactone structure: a very unsharp first end-point in the back-titration gave an equivalent weight of about 225 for II (calc. 254.4), but after some time more acid was required until eventually an amount of acid was used, which was equivalent to the amount of base employed.

The addition products from citraconic and mesaconic esters, III and VI, were saponified according to the saponification procedure previously described [20], except that the saponification time was prolonged to 24 h. The crude acids were obtained as oils, which in the case of VI slowly crystallized completely, whereas the acid-mixture from III only after long standing (a week or more) partially solidified. Crude crystalline products (m. p. range 85—110°) were obtained by recrystallization from ethanol-water. For identification purposes authentic samples of α-methyl-α-*n*-butylsuccinic acid, m. p. 86—88°, and α-methyl-α'-*n*-butylsuccinic acid, m. p. 121—132°, were prepared (see below). The infra-red spectra of these isomers could be distinguished from each other, especially by a difference in absorption around 1 190—1 330 cm^{-1}. Comparison of the spectra of the acids from III and VI with those of the authentic samples, showed the product from citraconic ester ($acid_{III}$) to be the α,α-isomer, whereas the product from mesaconic ester ($acid_{VI}$) was the α,α'-isomer.

By subsequent numerous recrystallizations from very diluted ethanol, the following melting points could indeed be obtained. $Acid_{III}$: m. p. 91—94° (neutr. equiv. 93.6); authentic α,α-isomer: m. p. 91—93° (neutr. equiv. 95.5); $acid_{VI}$: m. p. 132—137° (neutr. equiv. 95.5); authentic α,α'-isomer: m. p. 136—138° (neutr. equiv. 95.2). Mixed melting points of the two pairs of compounds showed no depressions; calc. neutr. equiv. 94.11.

In later experiments, however, also the α,α'-isomer was isolated from runs with citraconic ester, and both addition products (III and VI) might thus presumably be mixtures. The above-mentioned difference in the infra-red absorption groups around 1 190—1 330 cm^{-1} was utilized for estimating the approximate ratio of the isomers formed, by comparing the spectra of the crude acid-mixtures with spectra of suitable mixtures of authentic acids (Table 2).

The proportions of isomers in the mixtures were further checked by gas-liquid chromatography (Table 2), kindly performed and interpreted by Mr. Aage Jart, M.Sc., of the Danish Fat Research Institute, Copenhagen. The acids were transformed into their methyl esters by means of diazomethane. It was found that the retention time was rather strongly dependent on the size of the sample. Therefore, that mixture-component which was present in the smaller concentration was appearing first on the chromatogram in all cases. The ratios were estimated accurate to the nearest 5 %.

Preparations of authentic methyl-n-butylsuccinic acids. α-Methyl-α-*n*-butylsuccinic acid was prepared as described in literature [25]. The addition of hydrogen cyanide to ethyl α-cyano-β-*n*-butyl-β-methylacrylate (below) was followed by hydrolysis and decarboxylation of the dicyano-compound. The latter (ethyl α,β-dicyano-β-methylheptanoate) showed the b.p. 96—100°/1.5 mm (n_D^{23} 1.4399), whereas Miller and Long [25] report the b.p. 141—145°/2.3 mm. Ethyl α-cyano-β-*n*-butyl-β-methylacrylate, b.p. 142—144°/14 mm, n_D^{25} 1.4672, was obtained according to Cope *et al.*[26] by the condensation of methyl *n*-butyl ketone with ethyl cyanoacetate. The α-methyl-α-*n*-butylsuccinic acid had the m. p. 91—93° (rep.[25]: 93°) and the neutr. equiv. 95.5.

α-Methyl-α'-*n*-butylsuccinic acid was synthesized by the alkylation of ethyl *n*-butylmalonate [27] with ethyl α-bromopropionate, followed by hydrolysis and decarboxylation. The procedures used were those described in Organic Syntheses [28]. The α-methyl-α'-*n*-butylsuccinic acid had the m. p. 136—138° (rep.[11]: 85—105°) and neutr. equiv. 95.2.

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REFERENCES

1. Munch-Petersen, J. *Acta Chem. Scand.* **12** (1958) 967.
2. Purdie, T. and Arup, P. S. *J. Chem. Soc.* **97** (1910) 1537.
3. Tarbell, D. S. *J. Am. Chem. Soc.* **60** (1938) 215.
4. Weizmann, C. and Bergmann, F. *J. Am. Chem. Soc.* **60** (1938) 2647.
5. Scholtis, K. *Ann.* **557** (1947) 82.
6. Marvel, C. S., Myers, R. L. and Saunders, J. H. *J. Am. Chem. Soc.* **70** (1948) 1694.
7. Munch-Petersen, J. *Acta Chem. Scand.* **12** (1958) 2007.
8. Cason, J. *J. Org. Chem.* **13** (1948) 231; Cason, J. and Smith, R. D. *J. Org. Chem.* **18** (1953) 1202.
9. Michael, A. *Ber.* **29** (1896) 1791.
10. Hsing, C. and Li, L. *J. Am. Chem. Soc.* **71** (1949) 774.
11. Marvel, C. S. and Fuller, J. A. *J. Am. Chem. Soc.* **74** (1952) 1508.
12. Munch-Petersen, J. *Acta Chem. Scand.* **12** (1958) 2046.
13. Brändström, A. and Forsblad, I. *Arkiv Kemi* **6** (1954) 561; *cf.* Hook, W. H. and Robinson, R. *J. Chem. Soc.* **1944** 152.
14. Lutz, R. E. and Reveley, W. G. *J. Am. Chem. Soc.* **63** (1941) 3180; *cf.* Johnson, J. R. in Gilman, *Organic Chemistry*, Vol. **II**, John Wiley & Sons, 2nd. ed. 1943, p. 1881—1882; Royals, E. E. *Advanced Organic Chemistry*, Prentice-Hall, 1954, p. 699 ff.; Alexander, E. R. *Principles of Ionic Organic Reactions*, John Wiley & Sons, 1950, p. 193—194.
15. For a review, see Douglas, B. E. in Bailar, *The Chemistry of the Coordination Compounds*, Reinhold Publishing Corp. 1956, p. 494; Basolo, F. and Pearson, R. G. *Mechanisms of Inorganic Reactions*, John Wiley & Sons 1958, p. 350 ff. For references see also Slade, P. E. and Jonassen, H. B. *J. Am. Chem. Soc.* **79** (1957) 1277.
16. Atkinson, E. R., Rubinstein, D. and Winiarczyk, E. R. *Ind. Eng. Chem.* **50** (1958) 1553 and further references given therein.
17. Keefer, R. M., Andrews, L. J. and Kepner, R. E. *J. Am. Chem. Soc.* **71** (1949) 2381, and further references given therein.
18. Mosher, H. S. and La Combe, E. *J. Am. Chem. Soc.* **72** (1950) 3994; *cf.* Swain, C. G. and Boyles, H. B. *J. Am. Chem. Soc.* **73** (1951) 870.
19. *cf.* Gilman, H. and Straly, J.M. *Rec. trav. chim.* **55** (1936) 821.
20. Munch-Petersen, J. *J. Org. Chem.* **22** (1957) 170.
21. Walton, W. L. and Hughes, R. B. *Anal. Chem.* **28** (1956) 1388.
22. Wideqvist, S. *Acta Chem. Scand.* **3** (1949) 303.
23. Cope, A. C. and Hancock, E. M. *J. Am. Chem. Soc.* **60** (1938) 2645.
24. Bellamy, L. J. *The Infra-Red Spectra of Complex Molecules*, Methuen, 2nd. ed. 1958, p. 179.
25. Miller, C. A. and Long, L. M. *J. Am. Chem. Soc.* **75** (1953) 375.
26. Cope, A. C., Hofmann, C. M., Wyckoff, C. and Hardenbergh, E. *J. Am. Chem. Soc.* **63** (1941) 3452.
27. Adams, R. and Kamm, R. M. *Organic Syntheses* Coll. Vol. **I** (1941) 250.
28. Adkins, H., Isbell, N. and Wojcik, B. *Organic Syntheses* Coll. Vol. **II** (1943) 262; Vliet, E. B., Marvel, C. S. and Hsueh, C. M. *Organic Syntheses* Coll. Vol. **II** (1943) 416.

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