Two Different Structures for Copper and Lithium Derivatives of Vinylic Enolates.† The Effect of Structure on the Direction of Electrophilic Attack

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Copper derivatives of enolates derived from αβ-unsaturated esters. acids. or ketones have the copper linked covalently to an sp^2-hybridised carbon atom α to the carbonyl group. Their protonolysis or iodination proceeds with retention of configuration. Lithium derivatives of these compounds have the α-carbon *sp*-hybridised and the steric course of electrophilic attack does not depend on the configuration of the starting material. but on the ease of approach of the electrophile in the plane of the C(1)–C(2) double bond and the groups attached to the β-carbon atom.

SOME years ago[2] we advanced an explanation for the steric course of the decarboxylation of αβ-unsaturated malonic or cyanoacetic acids in quinoline, assuming the formation of a vinylic enol with an allenic structure [(I) or (II)] as an intermediate. The protonolysis of (I) or (II) was assumed to take place by attack at C(2) on the π-orbital linking it to C(1). This necessarily has to

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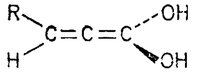
† We use the term ' metal derivative of an enolate ' to denote a derivative in which a hydrogen on a carbon atom α to a carbonyl group has been replaced,[1] regardless of whether the metal linkage is largely covalent and to the α-carbon atom, or largely ionic and to the oxygen atom. The term ' vinylic enolate ' thus refers to an enolate formed formally by abstraction of a vinylic proton from the α-carbon atom of an αβ-olefinic carbonyl compound.

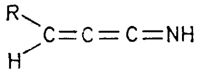
[1] H. O. House, ' Modern Synthetic Reactions,' 2nd edn., W. A. Benjamin, New York, 1972, pp. 492—3.

[2] J. Klein and A. Y. Meyer, *J. Org. Chem.*, 1964, **29**, 1038.

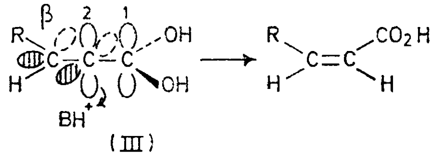
take place in the plane of the groups attached to the β-carbon and will preferentially be from the less hindered side (*i.e.* away from the R group) leading predominantly to the *cis*-acid [reaction (1)].



(I)



(II)



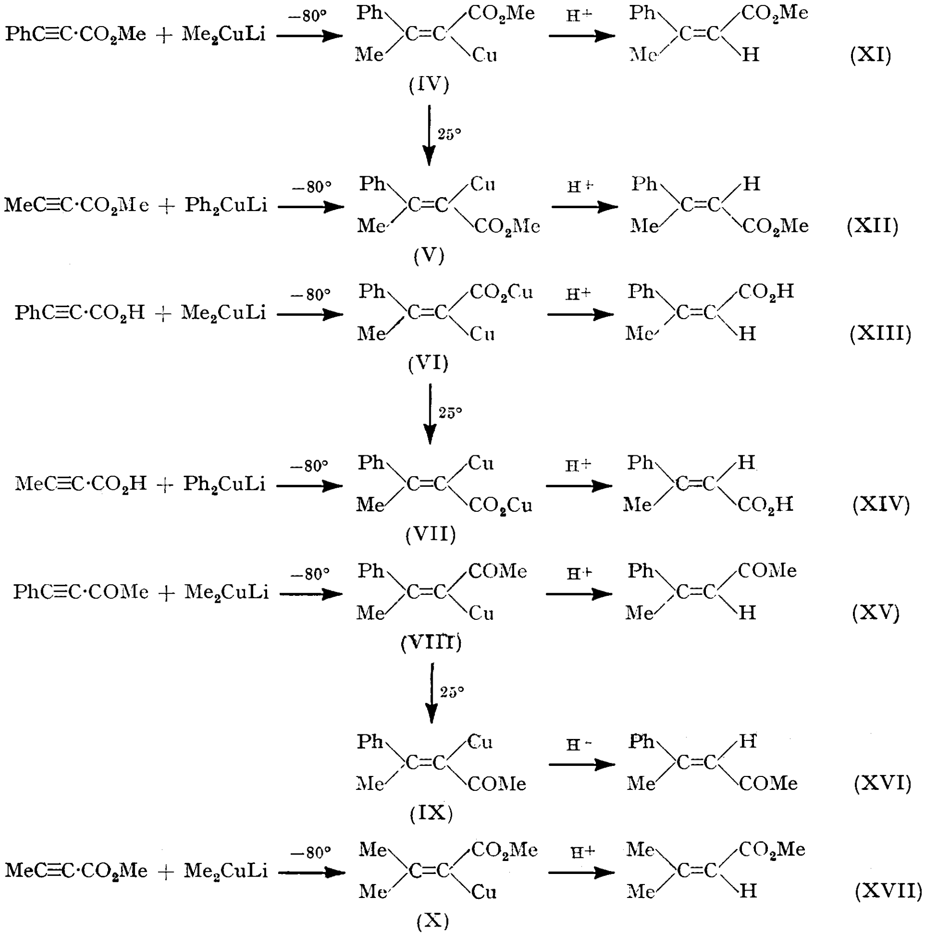
(III)

(1)

In order to confirm this hypothesis we tried to prepare the enols (I) or the corresponding enolates by an independent route consisting of the 1,4-addition of organometallic compounds to αβ-acetylenic esters or acids. However, addition of organocopper-reagents to acetylenic esters or acids was found by us[3] and others[4,5] to proceed stereospecifically at low temperatures. This shows that a covalent carbon–copper and not an oxygen–metal bond was formed, as expected for a derivative of enol (I). Addition of Grignard compounds led to different, but not conclusive, results.[3b] We undertook, therefore, a more detailed study of the structure and stereochemistry of protonolysis of these copper compounds and also those of lithium and magnesium vinylic enolates.

RESULTS

The α-copper derivatives (IV), (VI), (VIII), and (X) of the unsaturated carbonyl compounds were prepared in tetrahydrofuran (THF) by addition of dimethyl- or diphenyl-(lithio)copper at −80° to the acetylenic carbonyl compounds [reaction (2) and Scheme 1]. Their structures were determined by protonolysis at −80° which gave the products (XI), (XIII), (XV), and (XVII)



Scheme 1

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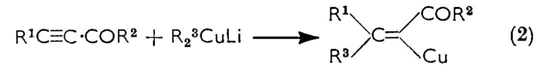
[3] (*a*) J. Klein and R. Turkel, *J. Amer. Chem. Soc.*, 1969, **91**, 6168; (*b*) J. Klein and N. Aminadav, *J. Chem. Soc.* (*C*), 1970, 1380.

[4] E. J. Corey and J. A. Katzenellenbogen, *J. Amer. Chem. Soc.*, 1969, **91**, 1851.

[5] B. Siddal, M. Biskup, and J. H. Fried, *J. Amer. Chem. Soc.*, 1969, **91**, 1853.

respectively. However, leaving the reaction mixture

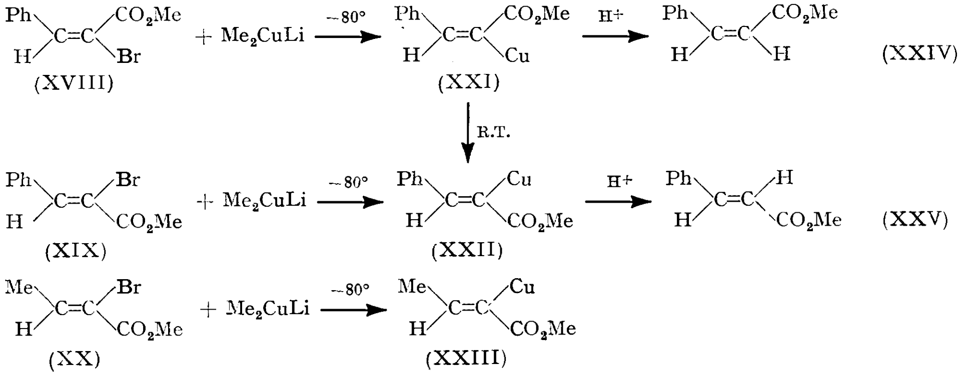


$$R^1C{\equiv}C{\cdot}COR^2 + R_2{}^3CuLi \longrightarrow (R^1)(R^3)C{=}C(COR^2)(Cu) \qquad (2)$$

at room temperature produced, after protonolysis, products consisting mainly or completely of the *trans*-isomers (XII), (XIV), and (XVI) formed from the copper derivatives (V), (VII), and (IX) (Scheme 1). The stereochemistry (*cis* or *trans*) is assigned according to the relative configurations of the phenyl and carbonyl groups. An alternative method of preparing α-copper derivatives of unsaturated carbonyl compounds[6] is by substitution of bromine by copper in the α-bromo-esters (XVIII)—(XX) [equation (3) and Scheme 2]. The THF

$$RCH{=}CBr{\cdot}CO_2Me + Me_2CuLi \longrightarrow RCH{=}CCu{\cdot}CO_2Me \quad (3)$$

solutions obtained after addition of dimethyl(lithio)-copper to the acetylenic carbonyl compounds were examined by i.r. (Table 1) in the 1500—2300 cm^{-1} region.



Scheme 2.

Table 1

I.r. spectra of copper derivatives (1500—2300 cm^{-1})

Compound	(V)	(VII)	(IX)	(X)	(XXII)	(XXIII)	(XXVI)	(XXXIII)
$\nu_{max.}/cm^{-1}$	1630s	1625s	1600s	1635s	1700w*	1715w*	1620s	1630s
	1580w	1550w	1575w	1590w	1620s	1640s	1710m	1550m
	1560w		1550w					

* Due to the formation of $RCH{=}CMe{\cdot}CO_2Me$.

A strong bond at 1630—1640 cm^{-1} was found in the case of the esters, at 1625 cm^{-1} for the acid (copper salt) and at 1600 cm^{-1} for the ketone (IX). Similar bands were exhibited by the THF solutions of the copper derivatives (XXI)—(XXIII) prepared by reaction (3). The copper derivatives had mainly the *trans*-configuration in these samples, since the i.r. spectra were measured at room temperature.

The observed bands represent the C=O stretchings of the copper derivatives and are not due to a double bond or phenyl group, as was evidenced by the strong band at 1620 cm^{-1} for $CuCH_2{\cdot}CO_2Et$ (XXVI), prepared by a published procedure.[7] Also, similar bands were present in the aliphatic copper compounds (X) and (XXIII).

The position of the bands is unaltered when methyl-copper rather than dimethyl(lithio)copper is added to methyl phenylpropiolate and to 4-phenylbut-3-yn-2-one; residual methyl-lithium has no effect on the spectrum in the region measured.

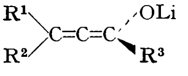
Addition of an ethereal solution of methyl-lithium to the THF solutions of the copper derivatives produced a profound change in the i.r. spectrum. The strong band at *ca.* 1630 cm^{-1} disappeared and a new, weaker band at 1900—1930 cm^{-1} became evident, reminiscent of an allenic band (Table 2). We assign to the lithium derivatives formed the structures (XXVII)—(XXXI), on the strength of the spectral change that occurred and the course of their protonolysis (see below).

Several equivalents of methyl-lithium (3—5) are needed to produce this spectral change. Though methyl-lithium is presumably formed by the addition of dimethyl(lithio)copper to methyl phenylpropiolate, according to reaction (2), no free methyl-lithium could be detected by Gilman's first test[8] on the reaction mixture. Methyl-lithium was not destroyed by 1 : 2 addition to the

Table 2

I.r. spectra of lithium enolates

Compound	(XXVII)	(XXVIII)	(XXIX)	(XXX)	(XXXI)
$\nu_{max.}/cm^{-1}$	1900	1900	1930	1920	1920



(XXVII) $R^1 = Ph, R^2 = Me, R^3 = OMe$
(XXVIII) $R^1 = Ph, R^2 = Me, R^3 = Me$
(XXIX) $R^1 = R^2 = Me, R^3 = OMe$
(XXX) $R^1 = Ph, R^2 = H, R^3 = OMe$
(XXXI) $R^1 = Me, R^2 = H, R^3 = OMe$

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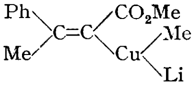
[6] J. Klein and R. Levene, *J. Amer. Chem. Soc.*, 1972, **94**, 2520.

[7] I. Kuwajima and Y. Doi, *Tetrahedron Letters*, 1972, 1163.

[8] G. E. Coates and K. Wade, ' Organometallic Compounds, vol. 1, Methuen, London, 1967, p. 31.

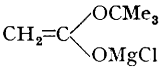
carbonyl group, since no sign of 1 : 2 addition products could be detected on protonolysis of the reaction mixture. It is probable that a cuprate complex (XXXII) exists in solution (which is more resistant to attack by methyl-lithium than is an ester without a metal atom at the α-position). The addition of one equivalent of methyl-lithium to the reaction mixture also produced no free



(XXXII)

$ClMgCH_2{\cdot}CO_2CMe_3$

(XXXIII)



$CH_2{=}C(OCMe_3)(OMgCl)$

(XXXIIIa)

methyl-lithium and the formation of a new complex is suspected. Free methyl-lithium was present after the addition of a further equivalent, but although the peak in the allenic region was now clearly apparent, the carbonyl band remained, though at reduced intensity. Such behaviour could be explained by an equilibrium between the copper and lithium enolates, but no quantitative evidence for this could be found. It is remarkable that, even in the presence of 3—5 equivalents of added methyl-lithium, very little 1 : 2 addition to the carbonyl group occurs. This may be attributed to the formation of the allenic structures (XXVII)—(XXXI).

When large amounts (up to 7 equivalents) of methyl-magnesium bromide or magnesium bromide were added to the copper enolate (V) a weak, broad peak was seen in the i.r. at *ca.* 1930 cm^{-1}, but a strong carbonyl peak remained. Copper was not precipitated from solution so it is possible that the absorption at 1630 cm^{-1} was due to residual copper compound. The magnesium enolate with magnesium bonded to the α-carbon is expected to absorb in the same region as the corresponding copper enolate, since the Grignard compound (XXXIII) prepared according to the method of Dubois,[9] absorbed at 1630 cm^{-1}. The spectrum of (XXXIII) in Nujol showed no peak at 3080 cm^{-1}, such as would be expected for the $=CH_2$ group of structure (XXXIIIa).

TABLE 3 [a]

			Products of protonolysis (%)			
			with HCl		with Q,HCl [b]	
Substrate	Reagent (mol. equiv.)	Temperature/°C (time/min)	*cis*	*trans*	*cis*	*trans*
$PhC{\equiv}C{\cdot}CO_2Me$	Me_2CuLi(1·5)	−80 (30)	XI)(>99)			
	Me_2CuLi(1·5)	−80 (30); 20 (60)	(XI)(21)	(XII)(79)	(XI)(21)	(XII)(79) [c]
	Me_2CuLi(1·5)	−80 (30); 20 (60)				
	then MeLi (3)	−80 (30)	(XI)(50)	(XII)(50)	(XI)(58)	(XII)(42)
	Me_2CuLi(1·5)	−80 (30)				
	then MeLi(4)	−80 (30)	(XI)(54)	(XII)(46)		
$PhC{\equiv}C{\cdot}OMe$	Me_2CuLi(1·5)	−80 (30)	(XV)(60)	(XVI)(40)		
	Me_2CuLi(1·5)	−80 (30); 20 (60)	(XV)(8)	(XVI)(92)		
	Me_2CuLi(1·5)	−80 (30); 20 (60)				
	then MeLi(3)	−80 (30)	(XV)(51)	(XVI)(49)	(XV)(60)	(XVI)(40)
cis-PhCH : $CBr{\cdot}CO_2Me$	Me_2CuLi(5)	−80 (60)	(XXIV)(97)	(XXV)(3)		
	Me_2CuLi(5)	−80 (30); 20 (60)	(XXIV)(>99)		(XXIV)(>99)	
	Me_2CuLi(5)	−80 (30); 20 (60)				
	then MeLi(4·5)	−80 (30)	(XXIV)(50)	(XXV)(50)	(XXIV)(61)	(XXV)(39)
$PhC{\equiv}C{\cdot}CO_2Me$	CuI(1·1) + MeMgBr(5)	−80 (1100) [d]	(XI)(16)	(XII)(34)	(XI)(16)	(XII)(34)
$PhC{\equiv}C{\cdot}CO_2H$	Me_2CuLi(5)	−80 (240)	(XIII)(>99)			
$PhC{\equiv}C{\cdot}CO_2H$	Me_2CuLi(2·5)	20 (1200)	(XIII)(35)	(XIV)(65)	(XIII)(35)	(XIV)(65) [c]
	Me_2CuLi(2·5)	20 (120)				
	then MeLi(3·5)	20 (30)	(XIII)(21)	(XIV)(79)	(XIII)(21)	(XIV)(79) [c]
	MeCu(2·3)	20 (240)	(XIII)(98)	(XIV)(2)	(XIII)(98)	(XIV)(2) [c]
	MeCu(2·3)	20 (1200)	(XIII)(85)	(XIV)(15)		
cis-$PhCH{\cdot}CBr{\cdot}CO_2Me$	CuI(5) + MeMgBr(5)	−80 (60)	(XXIV)(10)	(XXV)(90)	(XXIV)(10)	(XXV)(90)
$PhC{\equiv}C{\cdot}CO_2Me$	Me_2CuLi(1·5)	−80 (30); 20 (60)				
	then $MgBr_2$(7)	−80 (60)	(XI)(35)	(XII)(65)	(XI)(40)	(XII)(60)
	Me_2CuLi(1·5)	−80 (30); 20 (60)				
	then $MgBr_2$(7)	0 (30)	(XI)(33)	(XII)(67)		
	CuI(7·5) + MeMgBr(7·5)	−80 (300)	(XI)(35)	(XII)(65)		
$PhC{\equiv}C{\cdot}CO_2H$	CuI(5) + MeMgBr(5)	20 (60)	(XIII)(22)	(XIV)(58)		
	CuI(5) + MeMgBr(5)	20 (1800)	(XIII)(22)	(XIV)(58)		
	MeCu(2·5)	20 (240)				
	then MeMgBr	20 (1800)	(XIII)(37)	(XIV)(63)		
	MeCu(2·5)	20 (240)				
	then $MgBr_2$(1·0)	20 (60)	(XIII)(52)	(XIV)(48)		

[a] The ratio of isomers was determined by n.m.r. The reactions were performed in THF with 0·1M concentration of substrate. [b] Q,HCl = quinoline hydrochloride. [c] Protonolysis with Q,HCl at 20°; in other cases at −80°. [d] 50% Unchanged starting material.

Table 3 shows the products of protonolysis of the compounds obtained according to reactions (2) or (3) under various conditions.

It can be seen that addition of dimethyl(lithio)copper to the conjugated triple bond proceeds in a *cis* manner and that the stereochemistry is retained at low temperatures. It is assumed that protonolysis is with retention of the configuration of the double bond (see below). At

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[9] J. E. Dubois and S. Molnafi, *Bull. Soc. chim. France*, 1963, 779.

TABLE 4

Products of the iodination of enolates [a]

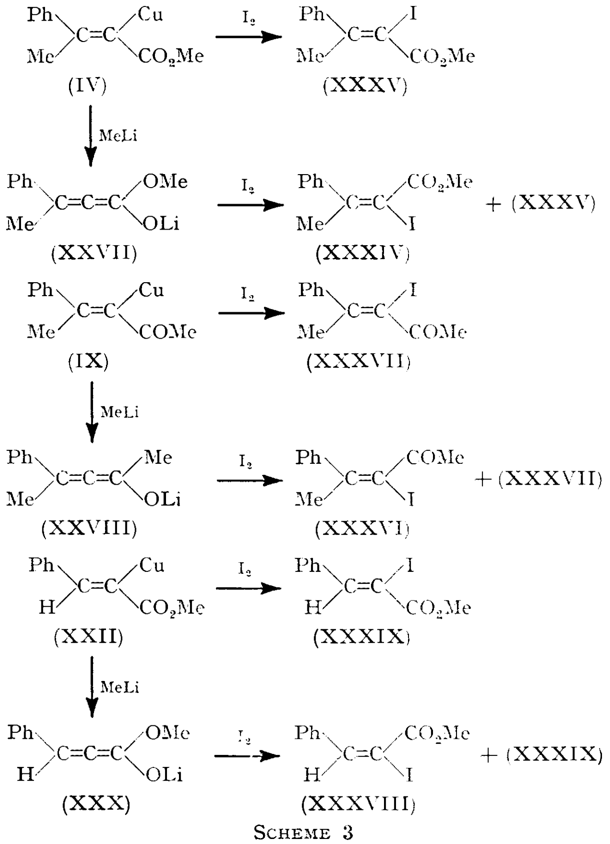
			Products of decomposition (%)			
			with HCl		with I_2	
Substrate	Reagent (mol. equiv.)	Temperature/°C (time/min)	*cis*	*trans*	*cis*	*trans*
$PhC{\equiv}C{\cdot}CO_2Me$	$Me_2CuLi(1{\cdot}5)$	−80 (30); 20 (60)	(XI)(21)	(XII)(79)	(XXXIV)(23)	(XXXV)(77)
	$Me_2CuLi(1{\cdot}5)$ then MeLi(3)	−80 (30); 20 (60) −80 (60)	(XI)(50)	(XII)(50)	(XXXIV) (68)	(XXXV)(32)
trans-$PhCH{:}CBr{\cdot}CO_2Me$	$Me_2CuLi(5)$	−80 (30); 20 (60)		(XXV) (>99)		(XXXIX) (>99)
	$Me_3CuLi(5)$ then MeLi(2·5) [b]	−80 (30); 20 (60) −80 (60)	(XXIV)(30)	(XXV)(70)	(XXXVIII) (51)	(XXXIX) (49)
$PhC{\equiv}C{\cdot}COMe$	$Me_2CuLi(1{\cdot}5)$	−80 (30); 20 (60)	(XV)(8)	(XVI)(92)		
	then MeLi(3)	−80 (30)	(XV)(51)	(XVI)(49)	(XXXVI) (62)	(XXXVII) (38)
$PhC{\equiv}C{\cdot}CO_2Me$	$MeMgBr(7{\cdot}5) + CuI(1{\cdot}5)$	−80 (300)	(XI)(35)	(XII)(65)	(XXXIV) (37)	(XXXV)(63)

[a] The ratio of isomers was determined by n.m.r. The reactions were performed in THF with 0·1M concentration of substrate. [b] Examination by i.r. showed the presence of a mixture of copper and lithium enolates.

room temperature an isomerisation to the *trans*-isomer occurs rapidly in the case of the ester or ketone and more slowly for the acid (salt). The isomerisation of both the ester and the acid is accelerated by the presence of MeMgBr or $MgBr_2$ [and also by the presence of excess dimethyl(lithio)copper [6]]. The use of methylcopper instead of Me_2CuLi leads to a configurationally more stable product from the acid. Similarly, replacement of bromine by copper in (XVIII) [reaction (3)] [6] occurs with retention at −80°, and protonolysis gives almost exclusively *cis*-methyl cinnamate (XXIV). Isomerisation to the *trans*-isomer is rapid and complete at room temperature.

The formation of predominantly or exclusively *trans*-products can be reversed to equal amounts of *cis*- and *trans*-isomers when MeLi is added before treatment with HCl. Similarly, it is possible to start from the *cis*-copper compound (IV), obtained at −80° and, by treatment with MeLi before decomposition with HCl, attain nearly equal amounts of the *cis*- and *trans*-isomers (XI) + (XII). The yield of *cis*-product can be increased to above 50% by protonolysis of the MeLi treated copper compound with quinoline hydrochloride instead of with HCl. The use of quinoline hydrochloride instead of HCl to decompose the copper derivatives untreated with MeLi did not effect the ratio of isomers.

A similar effect with methyl-lithium was observed when the enolates were treated with iodine (Scheme 3 and Table 4). Here again, protonolysis after treatment with methyl-lithium gives equal amounts of *cis*- and *trans*-isomers, whereas iodination gives *ca.* 60—70% of the *cis*-product. Without the addition of MeLi, nearly the same isomeric ratio is obtained from either protonolysis or iodination. When an insufficient amount of MeLi (2·5 mol. equiv.) was used, so as to convert the copper enolate (XXII) only partially into the lithium enolate, less than 50% of the *cis*-isomer (XXIV) was obtained on protonolysis; iodination of this mixture, instead of protonolysis, increased the yield of *cis*-isomer (XXXVIII) (Table 4).



SCHEME 3

DISCUSSION

The presence of a carbon–copper covalent bond in the products of addition of copper compounds to acetylenes [3-5,10] [reaction (2)] or in the substitution of vinylic bromides [6] [reaction (3)] was firmly established by the stereospecificity relations between the starting materials

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[10] J. F. Normant and M. Borgain, *Tetrahedron Letters*, 1971, 2583.

and their protonolysis products. Thus, addition of dimethyl(lithio)copper (or methylcopper in the case of the acid) to phenylpropiolic acid or its ester led to the *cis*-products (XIII) or (XI), but a similar reaction between but-2-ynoic acid or its ester and diphenyl(lithio)-copper gave (XIV) or (XII) respectively (Scheme 1). Similarly,[6] *cis*-α-bromocinnamic acid or its ester when reacted with dimethyl(lithio)copper gave after protonolysis, *cis*-cinnamic acid or its ester, whereas *trans*-α-bromocinnamic acid or its ester led to the respective *trans*-isomers (Scheme 2).

The stereospecifity of the formation of olefinic acids or esters in the reaction of organocopper compounds with triple bonds can be explained in two ways. Either the addition occurs stereospecifically in a *cis* manner and acidolysis is with retention, or addition is *trans* and acidolysis is with inversion. It is reasonable to assume that electrophilic substitution of copper by a proton proceeds with retention of configuration.[11] Further support for this assumption is gained from the fact that only those copper compounds which give a *cis*-product on protonolysis [(IV), (VI), (VIII), and (XXI)] undergo thermal isomerisation, whereas those that give a *trans*-product [(V), (VII), (IX), and (XXII)] are unaffected by a rise in temperature. The retention of configuration during acidolysis of the copper compounds requires *cis* addition in reaction (2) and retention of configuration in reaction (3).

The addition of MeLi to the copper derivatives produces lithium derivatives (XXVII)—(XXXI) with different structures from the starting materials. The strong carbonyl absorption of the copper compound at 1600—1630 cm^{-1} is no longer present and a band at 1900—1930 cm^{-1} appears. In addition to this i.r. evidence, the allenic structures for the lithium derivatives are supported by the protonolysis and iodination reactions. These are no longer stereospecifically linked with the starting material and give mixtures of the two possible geometrical isomers. Thus, a copper compound that gives almost exclusively the *trans*-product on protonolysis or iodination yields, after treatment with MeLi and then HCl, 50% of the less stable *cis*-product. Moreover, the stereochemistry of electrophilic attack is now somewhat dependent on the size of the electrophile, quinoline hydrochloride or iodine giving more of the *cis*-isomer than does HCl. The i.r. absorption and the changes in the course of electrophilic attack are accommodated by the structures (XXVII)—(XXXI) and by the mechanism (1) for protonolysis of the vinylic enol of allenic structure. There is no steric effect on the course of the protonolysis of the allenic enol by HCl; equal amounts of *cis*- and *trans*-isomers result. However, with a bulky electrophile, the course of protonolysis or iodination depends on the ease of approach to the enol in the plane containing the β-substituents and this will be easier on the side opposite the larger group on the β-carbon. Another explanation involving a fast equilibrium (4) could be also considered for the course of

(4)

protonolysis. This is not, however, consistent with the i.r. absorption.

Structures similar to (XXVII)—(XXXI) were proposed by Walborsky[12] for vinylic enolates * on the basis of the course of racemisation and H/D exchange of optically active unsaturated ketones or nitriles. These reactions could, however, be accommodated by equilibrium (4), particularly when the anions are hydrogen bonded to the protonating agent. Our system is different from that of Walborsky, since the vinylic enolates are formed as entities which can be identified and, in principle, isolated. No internal return and memory effects play a role in the reactions of the vinylic enolates prepared by our method. Since these effects are not present and also the enolates are not symmetrical, the steric course of their reactions can be determined.

It is of interest that magnesium enolates are apparently present in solution largely in the form with a C–Mg bond. The absorption at 1630 cm^{-1} does not disappear after addition of even large amounts of MeMgBr or MgBr$_2$ to the copper derivative (V), although a weak band at approximately 1930 cm^{-1} is exhibited by these compounds. However, since copper remains in solution, it is possible that the absorption at 1630 cm^{-1} is due to residual copper derivatives and the above conclusion must remain tentative. In the conjugate addition (in THF) of methylmagnesium bromide to 4-phenylbut-3-yn-2-one, catalysed by 0·05 mole of copper(I) chloride, the reaction solutions also showed a weak allenic band and a strong carbonyl one. However, the yield of conjugate addition product was only 15%, so that again, a relatively high proportion of copper enolate could have been present. The spectrum of the Grignard compound (XXXIII) supports the tentative conclusion that magnesium is largely attached to carbon.

EXPERIMENTAL

Proton n.m.r. measurements were taken in CCl$_4$ solutions on a Varian T60 machine and chemical shifts are given with respect to Me$_4$Si. I.r. spectra were measured on a Perkin-Elmer 257 grating spectrophotometer. The measurements

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* The name 'vinyl anion' given to these compounds[12] is misleading, since it implicitly attributes to the real vinyl anion a structure similar to the enolates, which is probably not correct for the free anion and certainly not for the lithium derivatives[13] of the anions with a localised charge.

[11] D. J. Cram, 'Fundamentals of Carbanion Chemisty,' Acedemic Press, New York, 1965, p. 131; A. N. Nesmeyanov and E. A. Borisov, *Tetrahedron*, 1957, **1**, 158; D. Y. Curtin, H. W. Johnson, and E. C. Steiner, *J. Amer. Chem. Soc.*, 1955, **77**, 4560; P. M. Treichel and F. G. A. Stone, *Adv. Organometallic Chem.*, 1964, **1**, 192; B. L. Booth and R. G. Hargreaves, *J. Chem. Soc.* (*A*), 1970, 308.

[12] H. M. Walborsky and L. M. Turner, *J. Amer. Chem. Soc.*, 1972, **94**, 2273; J. F. Arnett and H. M. Walborsky, *J. Org. Chem.*, 1972, **37**, 3678.

[13] D. Y. Curtin and E. E. Harris, *J. Amer. Chem. Soc.*, 1951, **73**, 4519.

were made on *ca.* 0·1M-solutions in THF in a 0·1 mm cell, balanced by a reference cell containing THF (THF does not absorb between 2500 and 1500 cm^{-1} except for a weak absorption at 1970 cm^{-1}).

Phenylpropiolic acid,[14] methyl phenylpropiolate, 4-phenylbut-3-yn-2-one,[15] methyl but-2-ynoate,[16] methyl *cis*- and *trans*-α-bromocinnamate (XVIII) and (XIX),[17] methyl *trans*-α-bromocrotonate (XX) [17] and *cis*-methyl cinnamate (XXIV) [18] were prepared by known and standard methods. Methyl *cis*-α-bromocinnamate [17] contained 14% *trans*-isomer (n.m.r.).

cis- and *trans*-β-Methylcinnamic acid (XIII) and (XIV) and methyl *cis*- and *trans*-β-methylcinnamate (XI) and (XII) were prepared as described previously.[3b]

cis-4-*Phenylpent*-3-*en*-2-*one* (XV).—*cis*-β-Methylcinnamic acid (XIII) (162 mg) was stirred in ether (5 ml) at 0 °C and methyl-lithium (1·9M; 1·6 ml) was added. After 30 min at 0 °C the solution was poured onto ice and HCl. Work-up and p.l.c. gave the *cis*-enone (XV), $\nu_{max.}$ 1670, 1620, and 1610 cm^{-1}, δ 7·19 (m, Ph), 6·94 (m, =CH), 2·09 (d, *J* 1 Hz, =CMe), and 1·60 (s, O=CMe).

trans-4-*Phenylpent*-3-en-2-*one* (XVI).—This was prepared as described before,[3b] and had δ 7·10br (s, Ph), 6·21 (m, =CH), 2·35 (d, *J* 1 Hz, =CMe), and 2·06 (s, O=CMe).

cis-α-*Iodo*-β-*methylcinnamic Acid and Methyl* cis-α-*Iodo*-β-*methylcinnamate* (XXXIV).—Phenylpropiolic acid (0·876 g, 6 mmol) was stirred for 5 h at −80° with Me_2CuLi (30 mmol) in ether (65 ml). A solution of iodine (8·0 g) in THF (20 ml) was then added at −80°. After 15 min at −80° the mixture was poured onto ice and HCl. The organic layer was washed with aqueous sodium thiosulphate, then extracted with aqueous sodium hydrogen carbonate. The aqueous layer was acidified to give the yellow acid (65%), m.p. 85—88°, δ 10·1 (s, OH), 7·30br (s, Ph), and 2·40 (s, =CMe) (Found: C, 42·2; H, 3·2; I, 43·0. Calc. for $C_{10}H_9IO_2$: C, 41·8; H, 3·1; I, 44·0%). Esterification gave the methyl ester (XXXIV), δ 6·9br (s, Ph), 3·22 (s, OMe), and 2·23 (s, =CMe).

trans-α-*Iodo*-β-*methylcinnamic Acid and Methyl* trans-α-*Iodo*-β-*methylcinnamate* (XXXV).—The previous reaction was repeated, but with stirring overnight at room temperature with Me_2CuLi (2·5 mol. equiv.). The mixture was cooled to −80°, treated with iodine and worked up as previously, to give the acid (70%), m.p. 146—149°, δ 10·1 (s, OH), 7·1—7·6 (m, Ph), and 2·50 (s, =CMe) (Found: C, 41·8; H, 3·1; I, 43·8. Calc. for $C_{10}H_9IO_2$: C, 41·8; H, 2·1; I, 44·0%). Esterification gave the methyl ester (XXXV), δ 7·1 (m, Ph), 3·65 (s, −OMe), and 2·20 (s, =CMe).

The following *cis*- and *trans*-compounds were prepared similarly: methyl *cis*-α-iodocinnamate (XXXVIII), δ 7·1 (m, Ph and =CH) and 3·55 (s, OMe); methyl *trans*-α-iodocinnamate (XXXIX), δ 7·95 (s, =CH), 7·7—6·9 (m, Ph), and 3·70 (s, OMe); *cis*-3-iodo-4-phenylpent-3-en-2-one (XXXVI), δ 7·1 (m, Ph), 2·32 (s, =CMe), and 1·78 (s, O=CMe); *trans*-3-iodo-4-phenylpent-3-en-2-one (XXXVII), δ 7·15 (m, Ph), 2·45 (s, =CMe), and 2·15 (s, O=CMe).

Quinoline Hydrochloride.—This was prepared similarly to the method for pyridine hydrochloride.[19] The product was separated and washed with ether by decantation. Finally quinoline (~10%) was added to eliminate free HCl, and the residual ether was evaporated off. All the work was performed under nitrogen. Quinoline deuteriochloride was prepared using DCl (obtained from $POCl_3$ and dried over P_2O_5).

Reactions using Copper Reagents.—Ether and THF were dried over $LiAlH_4$. CuI (B.D.H.) was not further purified. A stock solution of MeLi was prepared in ether from MeBr. Thus in reactions using MeLi, 1 mol. equiv. of LiBr was present for each mol. equiv. of MeLi used. MeLi and MeMgBr solutions were standardised against HCl. MeLi solutions were also standardised by addition under N_2 to a suspension of a weighed amount of pulverised CuI in ether until a colourless solution was just obtained. In the preparation of MeCu and Me_2CuLi,[20] a 5% excess of CuI was used to ensure the absence of free MeLi. Reactions were performed under N_2 and reagents were added and samples withdrawn with a syringe *via* a side arm capped with a rubber septum. The procedures and apparatus described by Shriver [21] were used to evaporate solvents, to add quinoline hydrochloride, and to add a solution of I_2 under N_2. The overall yields of the reactions have been previously reported.[3a,6]

The following is representative of the experimental procedure. MeLi (1·9M; 3·2 ml) was injected into a flask purged with N_2 and the ether was removed under vacuum. THF (20 ml) was then added and a clear solution was obtained. CuI (600 mg) was added at 0° under a stream of N_2 and the mixture was stirred at 0° until a clear, slightly coloured solution was obtained. This solution was cooled to −80° and a solution of methyl phenylpropiolate (320 mg, 2 mmol) in THF (0·5 ml) was added. A yellow colour developed immediately. Stirring was continued at −80° for 30 min and then for 1 h at room temperature. A small sample was withdrawn, introduced into a N_2 purged i.r. cell and the spectrum was recorded between 2300 and 1500 cm^{-1} (Table 1). A sample (7 ml) was withdrawn, added to ice–HCl and the mixture extracted with dichloromethane. The extract was washed with aqueous sodium thiosulphate and dried ($MgSO_4$). The solvent was evaporated, carbon tetrachloride was added, and evaporation was repeated. The residue was examined by n.m.r. to determine the ratio of the isomers (XI) and (XII) (Table 3). The residual solution was cooled to −80° and an ethereal solution of MeLi (1·9M; 2·1 ml, 3 mol. equiv.) was added. After 30 min at −80° the solution was again examined by i.r.; the carbonyl peak had disappeared and an allenic absorption was apparent (Table 2). Half the reaction solution was withdrawn, decomposed on ice–HCl, and treated as before to determine the new ratio of isomers. Quinoline hydrochloride (1·5—2·0 g) was added to the residual mixture. Stirring was continued for 2—3 h at −80° followed by 1 h at room temperature. The mixture was acidified and then treated as before to determine the ratio of isomers. (In the cases indicated in Table 3, treatment with quinoline hydrochloride was at room temperature.) For iodination, the experiment was repeated and the residual reaction solution was treated with an excess of iodine in THF at −80°.

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[16] J. C. Kauer and M. Brown, *Org. Synth.*, 1962, **42**, 97.

[17] J. Klein and S. Zitrin, *J. Org. Chem.*, 1970, **35**, 666.

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[19] L. F. Fieser and M. Fieser, 'Reagents for Organic Synthesis,' Wiley, New York, 1967, p. 964.

[20] H. Gilman, R. G. Jones, and L. A. Woods, *J. Org. Chem.*, 1952, **17**, 1630; G. M. Whitesides, W. F. Fischer, J. San Filippo, R. W. Bashe, and H. O. House, *J. Amer. Chem. Soc.*, 1969, **91**, 4871.

[21] D. F. Shriver, 'The Manipulation of Air-sensitive Compounds,' McGraw-Hill, New York, 1969, ch. 7.

After stirring for 15 min at −80° the reaction mixture was treated as before (Table 4). In an additional experiment, quinoline deuteriochloride was added after the reaction mixture hod been stirred for one hour at room temperature (and without treatment with MeLi). Examination by n.m.r. showed that 80% deuteriation was achieved.

Copper in the reaction solution was determined by a standard procedure.[22]

[3/650 *Received*, 28*th March*, 1973]

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