negative end of the dipole points away from the ring, which causes a severe deactivation in solution. Once trapped into the "electrostatic cage," the electrophile attacks the individual reaction centers according to competitive processes, characterized by activation energies determined by the electron density at the reaction site, which depends, in turn, on inductive and mesomeric factors analogous to those invoked to explain the selectivity of conventional electrophilic substitutions.

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Stereochemistry of the Nucleophilic Substitution of Vinylic Bromides with Copper

Sir:

Organometallic compounds undergo alkylation and it was shown[1] that Co(I) acts as a nucleophile in an S_N2 reaction which proceeds with inversion of configuration at the attacked carbon. The coupling of arylcopper,[2–5] vinylcopper,[3,4] and alkylcopper[3,5] compounds with alkyl and vinyl halides was explained[3,5] as involving the formation of "ate" complexes[6] by a nucleophilic substitution at carbon in the first step of the reaction, followed by a coupling of the carbons linked to the copper in the "ate" complex. Such a coupling was demonstrated[7] to proceed with retention of configuration in vinylic compounds.[7] The inversion of configuration observed in the coupling of diphenylcopper lithium with (−)-2-bromobutane was interpreted as an inversion during the process of the nucleophilic substitution of bromine with copper, followed by coupling with retention of configuration. There is, however, no proof for the nucleophilic substitution of bromine by copper, since the carbon linked to copper in the "ate" complex has enhanced nucleophilic character[4,8–11] and a direct substitution by carbon is possible.

We report now that nucleophilic substitution of a vinylic bromine with copper proceeds with retention of configuration.

Table I. Reactions of Dimethylcopper Lithium with Vinylic Bromides[a]

Substrate	Temp, °C (t, hr)[b]	Products (% of total product)
I	−80 (5)	III (23); V (77)
II	−80 (0.5)	IV (5); VI (95)
IX	−80 (3)	XI (13); XIII (87)
X	−80 (0.5)	XII (5); VI (95)
X[c,d]	−100 (0.5)	XIV (20); X (80)
I[e]	−80 (20)	III (25); V (13); VII (62)
IX[e]	−80 (3)	XI (11); XIII (12); XV (77)
IX[e]	−80 (3); 20 (18)	XI (15); XIII (6); V (6); VII (73)
XVII	−5 (1.5)	XIX (65)[f]
XVIII	−80 (1.5)	XX (90)[f]
XXI	−5 (0.5)	XIX (31); XXIII (41)[f]
XXI	−5 (2)	XIX (68); XXIII (5)[f]
XXII	−80 (0.5)	XX (83); XXIV (12)[f]
XVIII[e]	−80 (1.5)	XXV (90)[f]

[a] A 0.5 *M* ethereal solution (4.0 ml) of the substrate was injected slowly with a syringe into a 0.25 *M* ethereal solution (40 ml) of dimethylcopper lithium which was stirred in a bath kept at the temperature indicated. The reaction products were treated with acidified water at the reaction temperature. Analysis of the products was by nmr. The yields of the reactions were higher than 85% except for the reactions with methyl α-bromocrotonates (about 50% yield). [b] Temperature and duration of the reaction with $(CH_3)_2CuLi$. [c] The reaction was decomposed with methanol at the reaction temperature before being treated with acidified water. [d] This reaction was carried out using a ratio of $X/(CH_3)_2CuLi = 1/1.4$. [e] The reaction product was treated with acidified D_2O at the temperature of the reaction. [f] Other unidentified products were also formed.

trans-α-Bromocinnamic acid (I)[12] reacted with dimethylcopper lithium at −80° (Table I) to give, after treatment of the reaction product with acidified water, *trans*-α-methylcinnamic acid[13,14] (III) and *trans*-cinnamic acid (V). Similarly, methyl *trans*-α-bromocinnamate (II) gave methyl *trans*-α-methylcinnamate (IV) and methyl *trans*-cinnamate (VI). Treatment of the reaction mixture from I with acidified D_2O instead of water yielded the α-deuterated *trans*-cinnamic acid (VII). A similar reaction performed on *cis*-α-bromocinnamic acid (IX) gave the corresponding *cis*-α-methylcinnamic acid[15] (XI) and *cis*-cinnamic acid (XIII), both with retention of configuration. Again, treatment of the reaction mixture from IX with D_2O gave the α-deuterated *cis*-cinnamic acid (XV), proving that cinnamic acids are formed from organometallic intermediates. The organometallic compound XVI is not configurationally stable at room temperature in the presence of excess copper reagent. Such an isomerization of an α-vinylic copper derivative of a cinnamic acid has been observed before, with methyllithium.[9]

Treatment of methyl *cis*-α-bromocinnamate (X) with dimethylcopper lithium gave, under the conditions of the reaction used with the acid IX, methyl *trans*-cinnamate (VI) with inversion, and also the α-methyl derivative XII with retention of configuration. The trans ester resulted from an isomerization process, since at −100° some of the cis ester XIV was also obtained. Confirmation for this process was obtained on using a

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(1) F. R. Jensen, V. Madan, and D. H. Buchanan, *J. Amer. Chem. Soc.*, **92**, 1414 (1970).

(2) H. Gilman and J. M. Straley, *Recl. Trav. Chim. Pays-Bas*, **55**, 821 (1936).

(3) E. J. Corey and G. H. Posner, *J. Amer. Chem. Soc.*, **89**, 3911 (1967); **90**, 5618 (1968); E. J. Corey, J. A. Katzenellbogen, and G. H. Posner, *ibid.*, **89**, 4245 (1967); E. J. Corey, J. A. Katzenellbogen, N. W. Gilman, S. A. Roman, and B. W. Erickson *ibid.*, **90**, 5618 (1968); E. J. Corey and I. Kuwajima, *ibid.*, **92**, 395 (1970).

(4) E. J. Corey and J. A. Katzenellbogen, *ibid.*, **91**, 1851 (1969).

(5) G. M. Whitesides, W. F. Fischer Jr., J. San Filippo, Jr., R. W. Bashe, and H. O. House, *ibid.*, **91**, 4871 (1969); G. N. Whitesides, J. San Filippo, Jr., C. P. Casey, and E. J. Panek, *ibid.*, **89**, 5302 (1967).

(6) W. Tochtermann, *Angew. Chem., Int. Ed. Engl.*, **5**, 351 (1966).

(7) G. M. Whitesides and C. P. Casey, *J. Amer. Chem. Soc.*, **88**, 4541 (1966).

(8) H. Gilman, R. G. Jones, and L. A. Woods, *J. Org. Chem.*, **17**, 1630 (1952).

(9) J. Klein and R. M. Turkel, *J. Amer. Chem. Soc.*, **91**, 6186 (1969).

(10) H. O. House and W. F. Fischer, Jr., *J. Org. Chem.*, **33**, 949 (1968); H. O. House, W. C. Respess, and G. M. Whitesides, *ibid.*, **31**, 3128 (1966).

(11) J. B. Siddal, M. Biskup, and J. H. Fried, *J. Amer. Chem. Soc.*, **91**, 1853 (1969).

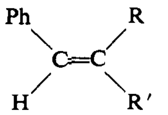
(12) J. J. Sudborough and K. J. Thompson, *J. Chem. Soc.*, **83**, 666 (1903).

(13) A. Psarrea, C. Sandris, and G. Tsatsas, *Bull. Soc. Chim. Fr.*, 2145 (1961).

(14) Nmr (CCl_4) δ 12.0 (COOH), 7.8 (=CH), 7.4 (C_6H_5), 2.15 (=CCH_3, doublet, J = 1.5 Hz).

(15) Nmr (CCl_4) δ 12.0 (COOH), 7.5 (C_6H_5), 6.8 (=CH), 2.15 (=CCH_3, doublet, J = 1.5 Hz). This compound was previously (ref 16) assigned the trans configuration.

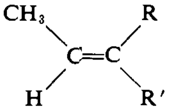
(16) J. Klein and S. Zitrin, *J. Org. Chem.*, **35**, 666 (1970).



V, R = H; R′ = COOH
VIII, R = Cu; R′ = COOCu
XI, R = COOH; R′ = CH_3
XIV, R = $COOCH_3$; R′ = H

I, R = Br; R′ = COOH
III, R = CH_3; R′ = COOH
VI, R = H; R′ = $COOCH_3$
IX, R = COOH; R′ = Br
XII, R = $COOCH_3$; R′ = CH_3
XV, R = COOH; R′ = D

II, R = Br; R′ = $COOCH_3$
IV, R = CH_3; R′ = $COOCH_3$
VII, R = D; R′ = COOH
X, R = $COOCH_3$; R′ = Br
XIII, R = COOH; R′ = H
XVI, R = COOZ; R′ = Cu



XXI, R = COOH; R′ = Br
XXIV, R = $COOCH_3$; R′ = H

XVII, R = Br; R′ = COOH
XIX, R = H; R′ = COOH
XXII, R = $COOCH_3$; R′ = Br
XXV, R = D; R′ = $COOCH_3$

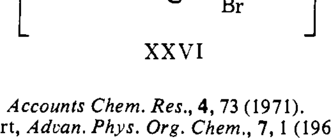
XVIII, R = Br; R′ = $COOCH_3$
XX, R = H; R′ = $COOCH_3$
XXIII, R = COOH; R′ = H

smaller ratio of dimethylcopper lithium to X. In this case only the cis ester XIV was obtained. The ester XVI (Z = CH_3) is apparently more prone than the acid copper derivative XVI (Z = Cu) to isomerization by the reagent, or possibly by methyllithium that is in equilibrium with the copper compound.

trans-α-Bromocrotonic acid (XVII) and its methyl ester XVIII gave, with dimethylcopper lithium, replacement of the halogen with copper and finally crotonic acid (XIX) and its ester XX, respectively. The cis isomers XXI and XXII yielded a mixture of cis and trans crotonic acids and esters, respectively.

Nucleophilic vinylic substitution has been reviewed[17–21] several times and it is assumed generally that these reactions consist of two steps. Only an addition–elimination sequence could apply in our case, since elimination–addition with both I and IX would give *cis*-β-methylcinnamic acid.[9] On the other hand, addition as the first step should occur by attack of the nucleophile at the carbon β and not α to the carboxyl. The reaction of *trans*-α-bromocrotonic acid and its ester with phenylmagnesium bromide gave 2-bromo-3-phenylbutyric acid[16] by a 1,4 addition. The stereoselectivity of the reaction eliminates also the possibility of a radical reaction by electron transfer.[22]

It seems to us that our reaction and many other nucleophilic vinylic substitutions proceed by an SN2 mechanism with retention of configuration with a transition state depicted by XXVI. The nucleophile approaches perpendicularly to the plane of the molecule, then begins to rotate together with the leaving group in such a manner that there is a continuous partial overlap of the orbitals of both the forming and breaking bonds with the p orbital of the β-trigonal carbon, until bromine leaves perpendicularly to the plane of the molecule. Other accepted explanations involving differences of angles of rotation in two directions before the second step (elimination) occurs,[23–26] or fast inversion–rotation,[20] cannot explain the regiospecificity and the steric course of our reaction. It is not the angle of rotation which should determine the ease of rotation in a particular direction, but rather the height of the potential barrier to the rotation in each direction. Consideration of the reactions of the isomeric bromo acids shows that no correlation can be found between reasonable barriers and the stereochemistry of the reaction.



XXVI

The retention of configuration in vinylic nucleophilic substitution is in agreement with the rules[27,28] for concerted reactions with the participation of six electrons (including those of the double bond). A four-electron reaction with retention is also possible[28] in the case of a π-type electron donor. However, inversion of configuration in the reaction with saturated alkyl halides[5] supports the six-electron reaction course.

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(17) G. Modena, *Accounts Chem. Res.*, **4**, 73 (1971).
(18) Z. Rappaport, *Advan. Phys. Org. Chem.*, **7**, 1 (1969).
(19) M. I. Rybinskaya, *Zh. Vses. Khim. Obshch.*, **12**, 11 (1967).
(20) S. I. Miller, *Advan. Phys. Org. Chem.*, **6**, 185 (1968).
(21) B. P. De La Mare, *Progr. Stereochem.*, **2**, 165 (1958).
(22) G. M. Whitesides and C. P. Casey, *J. Amer. Chem. Soc.*, **88**, 4541 (1966).
(23) D. E. Jones, R. O. Morris, C. A. Vernon, and R. F. M. White, *J. Chem. Soc.*, 2349 (1960).
(24) S. I. Miller and P. K. Yonan, *J. Amer. Chem. Soc.*, **79**, 5931 (1957).
(25) W. E. Truce and M. M. Boudakian, *ibid.*, **78**, 2748 (1956).
(26) F. Montanari, *Gazz. Chim. Ital.*, **86**, 406 (1956).
(27) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 78 (1969).
(28) R. G. Pearson, *Accounts Chem. Res.*, **4**, 152 (1971).

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Electrochemical Irreducibility of the Cyclooctatetraene Radical Anion

Sir:

We have recently reexamined the electrochemical behavior of two benzo-fused derivatives of cyclooctatetraene, and found that the radical anion product of electron addition to the neutral hydrocarbon is not electroreducible in water-free ($<10^{-5}$ *M* H_2O) tetrahydrofuran (THF) solutions.[1] This implies that it is considerably more difficult to form the dianion species in these cases than had been reported previously.[2] On the basis of this evidence, we therefore turned to a study

(1) L. B. Anderson and L. A. Paquette, *J. Amer. Chem. Soc.*, in press.
(2) T. J. Katz, M. Yoshida, and L. C. Siew, *ibid.*, **87**, 4516 (1965).