Counterion Influence on the Stereochemistry of Cyclopropane Formation *via* Organocopper and Organosodium Intermediates

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Summary Cyclopropanes are formed from methyl α-chloropropionate and methacrylonitrile using $Bu^tOCu{\cdot}PBu_3{}^n$ or NaH, *via* organocopper or organosodium intermediates; a counterion effect on the *cis/trans* stereochemistry of cyclopropane formation is observed.

ORGANOCOPPER compounds are known to exhibit a high carbanionic reactivity when complexed with organometallics such as organolithiums or Grignard reagents, or with inorganic salts, *e.g.*, LiI.[1] Versatility of lithium organocuprates in organic synthesis has been established.[1,2] Recently, a contrasting counterion influence on alkylation regioselectivity of lithium and copper dienolates has been reported.[3] We now report a characteristic difference between an organocopper-phosphine complex and an organosodium intermediate in the stereochemistry of cyclopropane formation from an α-chloro compound and an α,β-unsaturated cyano compound.

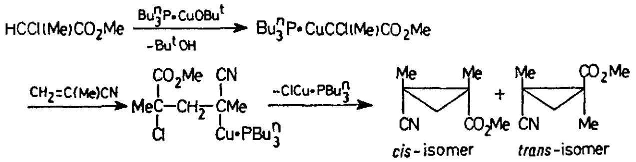
Using $Bu_3{}^nP{\cdot}CuOBu^t$ [4] the cyclopropane derivative was readily formed from methyl α-chloropropionate and methacrylonitrile at 30°, *via* the proposed organocopper intermediates (Scheme). The organocopper co-ordinated

TABLE Yields and *cis*/*trans* ratios in cyclopropane formation

Metallation reagent[a]	NaH		NaOBu^t		Bu^{t}OCu·PBu$^n_3$	
Solvent	Yield/%	*cis*/*trans* ratio	Yield/%	*cis*/*trans* ratio	Yield/%	*cis*/*trans* ratio
Dimethylformamide	89	0·88			61	0·50
Tetrahydrofuran	52	2·5	31	2·7	54	0·39
Benzene	48	4·5	41	4·6	50	0·43

[a] Metallation reagents of 0·50—1·0 mM were used. A mixture of an equimolar amount of each component was heated at 30° for *ca.* 2·5 h in a 10-fold excess of solvent (relative to the volume of methacrylonitrile).

with PBu$_3{}^n$ showed a high carbanionic reactivity (addition to the carbon–carbon double bond and intramolecular cyclization) which is comparable with that of organosodium intermediates generated from NaH and NaOBu^t.



PBu$_3{}^n$ was an indispensable component and CuOBu^t alone did not cause the reaction. Bu^{t}NC, P(OMe)$_3$ and pyridine ligands were not effective. A yellow Bu^{t}NC·Cu-OBu^t complex[5] slowly precipitated from the reaction mixture of CuOBu^t, Bu^{t}NC, methyl α-chloropropionate and methacrylonitrile in dimethylformamide, indicating no metallation of methyl α-chloropropionate at 30° using Bu^{t}NC ligand. The effectiveness of the PBu$_3{}^n$ ligand may be ascribed to its high σ-donor strength which may increase the basicity of Bu^{t}O group and also the carbanionic reactivity of organocopper.[6]

A characteristic difference in the *cis*/*trans* stereochemistry of cyclopropane formation between the organocopper and organosodium systems is interesting (Table). In the organosodium system, the *cis*:*trans* ratio increased with decrease in the polarity of solvent, but the ratio of cyclopropane formation *via* the organocopper intermediate was not varied by the polarity of solvent and the *trans*-isomer predominated even in benzene.

Previously, the solvent effect on the stereochemistry of the NaH-methyl α-chloropropionate-methyl methacrylate system has been explained in terms of chelation of a free sodium cation with two functional groups.[7] In the present system, the chelation involving cyano group, methoxycarbonyl group and a free sodium cation may preferentially give the *cis*-isomer in a less polar solvent where the chelation is favoured. Based on this explanation, a hypothesis for the stereochemical result in the copper system may be suggested, which assumes that the carbanionic group of the organocopper-phosphine complex firmly co-ordinates to copper, *i.e.*, the copper atom is not free even in a polar solvent. Thus, with the organocopper intermediate, intramolecular cyclization would occur without chelation involving copper, producing the more favoured *trans*-isomer due to non-bonded interactions between substituents. An additional observation which supports this suggestion is the insensitivity of the *cis*:*trans* ratio of the copper system to the change of functional substituents. The ratios obtained in dimethylformamide were 0·46 (Bu^{t}OCu·PBu$_3{}^n$) and 0·33 (NaH) using methyl α-chloropropionate-methyl methacrylate, and 0·52 (Bu^{t}OCu·PBu$_3{}^n$) and 0·67 (NaH) using α-chloropropionitrile-methacrylonitrile.

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[1] J. F. Normant, *Synthesis*, 1972, 63.

[2] Conjugate addition of organocuprates has been explained in terms of the currently more accepted hypothesis of electron transfer, *e.g.*, G. H. Posner, *Org. Reactions*, 1972, **19**, 1.

[3] J. A. Katzenellenbogen and A. L. Crumrine, *J. Amer. Chem. Soc.*, 1974, **96**, 5662.

[4] T. Tsuda, T. Hashimoto, and T. Saegusa, unpublished result, see also *J. Amer. Chem. Soc.*, 1972, **94**, 658.

[5] T. Tsuda, H. Habu, S. Horiguchi, and T. Saegusa, *J. Amer. Chem. Soc.*, 1974, **96**, 5930.

[6] T. Tsuda, K. Ueda, and T. Saegusa, *J.C.S. Chem. Comm.*, 1974, 380; T. Tsuda, H. Habu, and T. Saegusa, *ibid.*, p. 620.

[7] Y. Inoue, M. Horiike, M. Ohno, and H. M. Walborsky, *Tetrahedron*, 1968, **24**, 2907.