ble with the others. This is in contrast to the ring alkylation noted by other workers when *n*-butyllithium was used to metalate 4-picoline in ether.[13] The side-chain alkenylation of 4-alkylpyridines with isoprene in the presence of lithium gave no indication of polymerization, although lithium was reported to be highly stereoselective when used to polymerize isoprene in hydrocarbon solvents.[14]

The sodium-catalyzed addition of 4-ethylpyridine to ethylene has been studied in these laboratories.[15] Lithium-catalyzed reactions required longer reaction times and higher temperatures to get yields comparable with those obtained with sodium (Table II). In expt 2, under conditions for which sodium is known to catalyze the addition of ethylene, a lithium catalyst failed to yield any product.

Experimental Section[16]

Reagents.—4-Picoline and 4-ethylpyridine were obtained from Reilly Tar and Chemical Co. 4-Isopropylpyridine was purchased from Pfaltz and Bauer, Inc. The alkylpyridines were distilled, dried over Linde 5A Molecular Sieves, and redistilled immediately before use. Isoprene (Aldrich) was distilled before use and ethylene (Matheson) was used directly from the tank. Regular grade lithium metal (A. D. MacKay Inc.) was used.

General Procedure for Alkenylation Reactions.—The catalyst was prepared by dispersion of 15×10^{-4} g-atom of freshly cut alkali metal under predried *n*-pentane into 0.03 mol of 4-ethylpyridine or 4-isopropylpyridine for 5–10 hr to ensure complete dispersion. The reactions were performed under a slow stream of dry nitrogen in a three-necked flask equipped with reflux condenser, a rubber septum through which additions and withdrawals could be made with a syringe, and a specially designed high-speed stirrer. The active catalyst was a brown-black pseudohomogeneous solution. Isoprene (0.03–0.09 mol) was then added by a syringe to the catalyst solution, and the reaction carried out at room temperature. Samples were withdrawn periodically during the reaction, decomposed with methanol, and analyzed by vpc. At the conclusion of the reaction, the catalyst was decomposed with methanol. It was not possible to disperse lithium in 4-picoline at room temperature; so in this case the 4-picoline was heated to 130° and stirred for 3 hr before all of the lithium was dispersed. The catalyst solution was cooled and isoprepene added when the mixture was at 70°. The reaction was then followed as described above.

Ethylation of 4-Ethylpyridine.—The dispersion of lithium metal was carried out as described for the isoprene reactions. The lithium–4-ethylpyridine catalyst solution was transferred to a 100-ml-capacity Magne-Dash agitated autoclave. The autoclave was sealed, and after flushing with nitrogen it was charged with 40–70 atm of ethylene and heated to the desired temperature (see Table II). Stirring was started and continued for 8–12 hr until the pressure finished dropping. The stirring was then stopped and the autoclave removed from the heating jacket and allowed to cool. After the pressure was released, a few milliliters of methanol was added to the reaction mixture to decompose the organolithium compounds. The crude reaction mixture was then analyzed by vpc.

***n*-Butyllithium-Catalyzed Reactions.**—In a drybox 0.05 mol of 4-picoline was placed in a 30-dram vial, and 0.0025 mol of *n*-butyllithium (Alfa, 90% in hydrocarbon) was slowly added. An exothermic reaction occurred, giving a dark brown solution like that obtained when lithium metal was dispersed in the 4-alkylpyridines. A rubber septum was inserted and the catalyst solution was removed to the laboratory where the reactions were carried out at room temperature. Isoprene (0.015 mol) was then injected through the septum, and samples were removed with a syringe at various intervals, decomposed with methanol, and analyzed by vpc.

Registry No.—4-Isopropylpyridine, 696-30-0; 4-ethylpyridine, 536-75-4; 4-picoline, 108-89-4.

(13) H. Gilman and H. S. Broadbent, *J. Amer. Chem. Soc.*, **82**, 4912 (1960).
(14) C. E. H. Bawn and A. Ledwith, *Quart. Rev.* (London), **16**, 361 (1962).
(15) H. Pines and B. Notari, *J. Amer. Chem. Soc.*, **82**, 2209 (1960).
(16) All compounds were identified by comparison with authentic samples from our laboratories.

Solvent Effects in the Base-Catalyzed Cyclization of 5-Chloro-2-pentanone

RICHARD A. BARTSCH AND DAVID M. COOK[1]

Department of Chemistry, Washington State University, Pullman, Washington 99163

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Cyclization of γ-substituted ketones is an important synthetic route to cyclopropylcarbonyl compounds.[2] The base-catalyzed cyclization of 5-halo-2-pentanones to cyclopropyl methyl ketones is well known.[3,4] The analogous formation of cyclopentanone, though conceivable, is not observed. It has been proposed that the preferred cyclization to a three-membered ring is due to solvation.[5] A high degree of solvation of the enolate anion produced by abstraction of the methyl proton would hinder intramolecular displacement, whereas only slight solvation of the enolate anion formed by removal of the methylene proton would be anticipated and intramolecular substitution would be more facile. If this is correct, the relative amounts of cyclopropyl methyl ketone and cyclopentanone should be strongly influenced by the anion-solvating properties of the reaction medium.

Successful cyclization of 5-halo-2-pentanones has been reported only with potassium or sodium hydroxide in water. Other base–solvent systems gave little or no yield of cyclopropyl methyl ketone.[4,6] Thus, only limited information is available concerning the effect of solvent.

Using gas–liquid partition chromatography (glpc), the cyclization of 5-chloro-2-pentanone in a number of base–solvent systems has been examined. Reaction of 5-chloro-2-pentanone with an excess of base produced the yields of cyclopropyl methyl ketone recorded in Table I. Although an estimated 0.2% yield of cyclopentanone would have been detected, no cyclization to form the five-membered ring was observed.

The results presented in Table I demonstrate that essentially quantitative cyclization of 5-chloro-2-pentanone to cyclopropyl methyl ketone can be induced by a variety of base–solvent systems. In view of the preferred cyclization to a three-membered ring even with wide variation of the anion-solvating capacity of the solvent, the solvation proposal is clearly inapplicable to this system. However, the results do not allow for

(1) National Science Foundation Undergraduate Research Participant.
(2) J. M. Conia, *Angew. Chem. Int. Ed. Engl.*, **7**, 570 (1968).
(3) G. W. Cannon, R. C. Ellis, and J. R. Leal, "Organic Syntheses," Coll. Vol. IV, John Wiley & Sons, Inc., New York, N. Y., 1963, p 597.
(4) L. I. Smith and E. R. Rogier, *J. Amer. Chem. Soc.*, **73**, 4049 (1951).
(5) E. Schmitz, *Angew. Chem. Int. Ed. Engl.*, **3**, 333 (1964).
(6) Reference 4 reports reaction of 5-chloro-2-pentanone with $LiNH_2$–Et_2O produces only traces of cyclopropyl methyl ketone. However, a 44% yield of 1-acetyl-2-methylcyclopropane is cited in the sodamide-catalyzed cyclization of 5-chloro-2-hexanone in ether.[7]
(7) G. W. Cannon, A. A. Santilli, and P. Shenian, *J. Amer. Chem. Soc.*, **81**, 1660 (1959).

TABLE I
REACTION OF 5-CHLORO-2-PENTANONE WITH VARIOUS BASE–SOLVENT SYSTEMS

Base-solvent	Yield[a,b] of cyclopropyl methyl ketone, %	Base-solvent	Yield[a,b] of cyclopropyl methyl ketone, %
NaOH[c,d]	85	t-BuOK–DMSO[e]	84
NaOH–H_2O[d,e]	98	t-BuOK–Et_2O[d,e]	100
NaOH–(50% (DMSO–50% H_2O)[e]	96	PhOK–MeOH[f]	40
MeOK–MeOH[e]	93	K_2CO_3–H_2O[d,e]	7
EtOK–EtOH[e]	100	NaOAc–MeOH[g]	0
t-BuOK–t-BuOH[e]	98	Et_3N–C_6H_6[e]	0

[a] Measured by glpc. [b] Estimated uncertainty ±2%. [c] No solvent. Conditions: 120 min at 100°. [d] Heterogeneous. [e] Conditions: 15 min at 30°. [f] Conditions: 15 min at 25°. [g] Conditions: 120 min at reflux.

assessment of the relative importance of stabilizing conjugation of the carbonyl group with the developing three-membered ring,[8] transition state entropy effects, or other factors which might be responsible for preferential cyclization to cyclopropyl methyl ketone.

Experimental Section

The base (3 mmol) in 10 ml of solvent was added to 5-chloro-2-pentanone[3] (2 mmol) and isobutylbenzene (Ethyl Corp., internal standard), and the reaction mixture was magnetically stirred for the desired reaction time. A 1-μl sample was injected directly[9] into a Varian Aerograph flame ionization gas chromatograph using a 20 ft × 1/8 in. column of 20% XF-1150 on Chromosorb P operated at 150°. When the solvent was water or 50% DMSO–50% H_2O, 20 ml of t-butyl alcohol was added to make the reaction mixture homogeneous before injection. Peak areas were measured with a Disc integrator.

Registry No.—5-Chloro-2-pentanone, 5891-21-4.

(8) A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc., B*, 808 (1967).
(9) A glass insert filled with glass wool prevented column contamination.

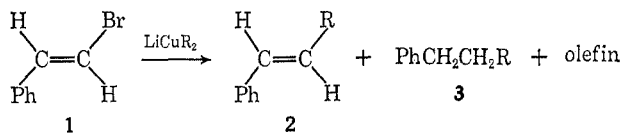
Reduction and Elimination as Side Reactions in the Replacement of Vinylic Bromine Atoms by Means of Lithium–Copper Organometallics

ALLAN T. WORM AND JAMES H. BREWSTER

Department of Chemistry, Purdue University, Lafayette, Indiana 47907

Received July 28, 1969

The reaction of vinyl halides with lithium dialkylcopper compounds[1–3] appeared promising as a method for the stereochemical correlation of certain chiral olefins. A pilot study with β-bromostyrene (90% *trans*, 10% *cis*) (**1**) has shown that the bromine atom can be replaced by secondary, tertiary, and phenyl groups by this method. Several side reactions, of potential mechanistic interest, were noted. Thus, when the R group was isopropyl, the reduced compound (**3**, R = i-C_3H_7) was obtained as 40% of the C_{11} product. With R as t-butyl, half of the C_{12} product was **3**, R = t-C_4H_9; isobutylene, recovered and identified as the dibromo derivative, was formed during the reaction in this case. Another reduction product, styrene, was always obtained, often as a major by-product. Reaction of the pure stereoisomers of **1** with lithium diphenylcopper gave much biphenyl and styrene. Stilbenes were formed in small amounts, with predominating, but not exclusive, retention of configuration, *trans*-**1** giving 18% *cis*- and 84% *trans*-**2**, and *cis*-**1** giving 70% *cis*- and 30% *trans*-**2**.



Experimental Section[4]

Reaction of Lithium Diisopropylcopper with β-Bromostyrene.—To a suspension of 7.6 g (0.04 mol) of cuprous iodide in 20 ml of ether at −15° was added 0.40 ml (0.076 mol) of commercial 1.9 *M* isopropyllithium in pentane.[5] The solution was cooled to −78°, and 1.5 g (0.008 mol) of β-bromostyrene[6] in 10 ml of ether was added. The mixture was stirred at −78° for 1 hr, warmed to about −15°, and worked up as above to give 0.8 g of a mixture containing (vpc isolation) styrene (trace), 1-phenyl-3-methylbutane (40%), and *trans*-1-phenyl-3-methylbutene (60%). The 1-phenyl-3-methylbutane had nmr ($CDCl_3$) δ 0.95 (d, 6, *J* = 5 cps, CH_3), 1.50 (m, 3, $-CH_2CH-$), 2.60 (m, 2, $ArCH_2$), and 7.17 (m, 5, phenyl); mass spectrum (75 eV) *m/e* (relative intensity) 148 (19) ($C_{11}H_{16}^+$), 92 (100) ($C_7H_8^+$), 91 (64). *trans*-1-Phenyl-3-methylbutene had nmr ($CDCl_3$) δ 1.06 (d, 6, *J* = 6 cps, CH_3), 2.41 (m, 1, ≥CH), 6.17 (m, 2, vinyl), and 7.2 (m, 5, phenyl); ir (film) 1370, 1385 [*sym* doublet, $-CH(CH_3)_2$], 968 (*trans* -CH=CH-), and 745, 694 cm^{-1} ($-C_6H_5$); mass spectrum (75 eV) *m/e* (relative intensity) 146 (34) ($C_{11}H_{14}^+$), 131 (100) ($M^+ - 15$), and 91 (49) ($C_7H_7^+$).

Reaction of Lithium Di-t-butylcopper with β-Bromostyrene.—To a suspension of 9.5 g (0.05 mol) of cuprous iodide in 20 ml of anhydrous ether at −15° was added 50 ml (0.10 mol) of commercial 2.0 *M* t-butyllithium in pentane.[5] The solution was cooled to −78°, 2.0 g (0.011 mol) of β-bromostyrene[6] in 15 ml of ether was added, and the solution was stirred at −78° for 1 hr. It was allowed to warm slowly to 0° with a stream of nitrogen passing through the flask and into a test tube (protected from light) containing bromine in carbon tetrachloride. The bromine solution warmed and decolorized; the solvent was removed; and the residue was distilled to give 1,2-dibromo-2-methylpropane: bp 50° (10 mm); nmr ($CDCl_3$) δ 1.88 (s, 6, CH_3) and 3.88 (s, 2, CH_2Br), comparable with literature values.[7] The main reaction mixture was worked up in the usual way and distilled to give 1.2 g, bp 75–78° (6 mm), of a mixture of 1-phenyl-3,3-dimethylbutane (50%) and *trans*-1-phenyl-3,3-dimethylbutene (50%). The two

(1) E. J. Corey and G. H. Posner, *J. Amer. Chem. Soc.*, **89**, 3911 (1967); **90**, 5615 (1968).
(2) H. O. House, W. L. Respess, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966).
(3) G. M. Whitesides, W. F. Fischer, Jr., J. S. Filippo, Jr., R. W. Bashe, and H. O. House, *J. Amer. Chem. Soc.*, **91**, 4871 (1969).

(4) All melting points were determined on a Fisher-Johns apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on a Varian A-60A instrument and reported in δ units from tetramethylsilane. Mass spectra were obtained on a Hitachi RMU-6A mass spectrometer. Infrared spectra were recorded on a Perkin-Elmer Infracord. Unless otherwise stated, vapor phase chromatography (vpc) was carried out on a 25% QF-1 column; analytical compositions have not been corrected for thermal conductivity differences. All reaction vessels were flamed out; anhydrous ether was distilled from an ethereal solution of lithium aluminum hydride.
(5) Obtained from Alfa Inorganics, Inc.
(6) Obtained as a mixture of 90% *trans* and 10% *cis* isomers by action of aqueous sodium carbonate on the dibromide of *trans*-cinnamic acid; see C. Dufraisse, *Ann. Chim.* (Paris), **17**, 133 (1922).
(7) N. S. Bhacca, D. P. Hollis, L. F. Johnson, E. A. Pier, and J. N. Shoolery, "Varian NMR Spectra Catalog," Vol. II, National Press, 1963, Spectrum 412.