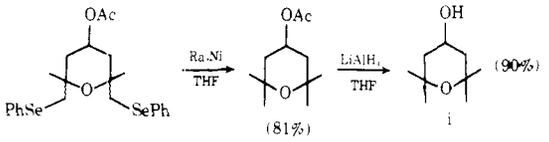
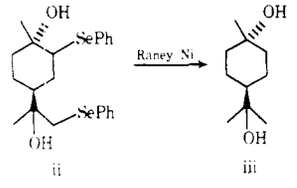
identification by high-resolution mass spectrometry.
(10) All yields recorded here were based on isolated material which was >95% pure.
(11) The following experimental procedure for the cyclization of 1,5-cyclooctadiene is representative of the reactions indicated in Table I. To a magnetically stirred, ice-cooled solution of diphenyl diselenide (312.1 mg, 1.0 mmol) in dry methylene chloride (7 mL) under argon was added dropwise chilled 30% hydrogen peroxide (110 μL, 1.0 mmol). After stirring vigorously at 0 °C for 30 min (white crystalls deposit), powdered anhydrous magnesium sulfate (200 mg) was added and the mixture was stirred for an additional 30 min at ice-bath temperature. The ice bath was removed, 1,5-cyclooctadiene (81.1 mg, 0.75 mmol) was added, and the mixture was stirred vigorously for 24 h at 25 °C. The reaction mixture was poured in ether (125 mL) and washed with 5% auqeous sodium carbonate (2 × 25 mL), water (10 mL), and brine (10 mL) successively. The dried ($MgSO_4$) solvents were removed and the residue was subjected to preparative layer chromatography, (E. Merck silica methylene chloride, R_f 0.45) to afford bis(phenylseleno)oxabicyclo[4.2.1]nonane (II) (294.5 mg, 90%) as colorless crystals recrystallized from petroleum ether; mp 95.5–96 °C; ^1H NMR (220 MHz, CCl_4) δ 1.88–2.16 (m, 8 H), 3.56 (m, 2 H, CH-Se), 4.48 (m, 2 H, CHO), 7.13 (m, 6 H), 7.35 (m, 4 H); ^{13}C NMR (100 Mz, $CDCl_3$) δ 28.5, 30.3, 49.2, (CSe), 80.9 (CO), 127.1, 129.1, 133.8. Anal. Calcd for $C_{20}H_{22}OSe_2$: C, 55.05; H, 5.08. Found: C, 55.28; H, 5.18.
(12) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, **97**, 5434 (1975); also see ref 3.
(13) N. Heap, G. E. Green, and G. H. Whitham, *J. Chem. Soc.*, 160 (1969).
(14) We are greatful to Dr. Ralph H. Obenauf and JEOL Analytical Instruments, Inc. for providing us with the ^{77}Se NMR spectrum of II; δ 7.57 relative to Et_2Se.
(15) F. G. Bordwell and M. L. Douglass, *J. Am. Chem. Soc.*, **88**, 993 (1966).
(16) Formation of cyclic ethers as reported here should be contrasted with the carbon–carbon bond formation reaction recently reported to occur upon treatment of 1,6-cyclononadiene with $PhSeO_2CCH_3$; see D. L. J. Clive, G. Chittattu, and C. K. Wong, *J. Chem. Soc., Chem. Commun.*, 441 (1978).
(17) Carbon skeletons were established rigorously by: (a) reductive removal (Raney Ni) of the phenylseleno groups to afford the known cyclic ethers; or (b) reductive fragmentation with *n*-Bu_3SnH to afford 2,4-dimethyl-4-penten-2-ol.
(18) The carbon skeleton of **7a** was established as illustrated below by conversion to the known alcohol (i); N. Nemeroff, M. M. Joullié and G. Preti, *J. Org. Chem.*, **43**, 331 (1978).



(19) Along with the cyclic product **10a**, the cyclization of limonene (**10**) produced considerable amounts (28%) of the dihydroxy diselenide ii as well as some monohydroxy selenide. The diselenide ii was efficiently converted to *cis*-terpin[20] (iii), a naturally occurring substance by Raney Ni reduction (70%).



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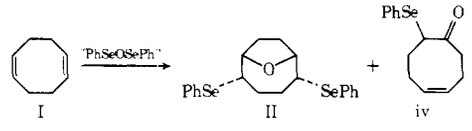
(21) H. J. Reich and F. Chow, *J. Chem. Soc. Chem. Commun.*, 790 (1975).
(22) K. C. Nicolaou, W. J. Sipio, R. L. Magolda, and D. A. Claremon, *J. Chem. Soc., Chem. Commun.*, 83 (1979).
(23) D. L. J. Clive, G. Chittattu, and C. K. Wong, *J. Chem. Soc., Chem. Commun.*, 41, (1978).
(24) Biological studies with this compound are currently in progress.
(25) **Note Added in Proof:** The recent introduction of "PhSeOSePh" as a useful synthetic reagent [see Shimizu, Takeda, and Kuwajima, *Tetrahedron Lett.*, 419 (1979)] prompted us to explore its reactivity with a 1,5-diene. To this end, reaction of 1,5-cyclooctadiene (I) with "PhSeOSePh" prepared according to Kuwajima afforded II and iv in 16 and 56% yield,[10] respectively. This experiment demonstrated not only that there is a difference in the reactivity of the two reagents, but also lends support to the proposed nature of the electrophilic species involved in our selenium-induced cyclizations as well as the reactions reported by Sharpless,[5] Reich,[6] and Kuwajima.



(26) We gratefully acknowledge financial support of this work from the National Institutes of Health [National Cancer Institute, CA-22807 (A.B.S.); Heart, Lung and Blood Institute, HV-E2931 (K.C.N.)] and the Donors of the Petroleum Research Fund, administered by the American Chemical Society (A.B.S. and K.C.N.). In addition we thank Mr. S. T. Bella of the Rockefeller University for the microanalysis and the Middle Atlantic Regional NMR Facility (NIH No. RR542) at the University of Pennsylvania where the 220 and 360 MHz NMR spectra were obtained.
(27) Camille and Henry Dreyfus Teacher–Scholar, 1978–1983.
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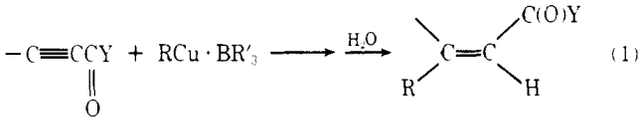
Stereocontrolled Cis Addition of Organocopper Reagents RCu·BR′$_3$ to α,β-Acetylenic Carbonyl Compounds

Summary: The reagent RCu·BR′$_3$ adds to α,β-acetylenic carbonyl compounds with a high stereospecificity at reasonably low temperatures (−70 to −20 °C), which cannot be achieved with reagents previously available.

Sir: Conjugate addition of organocopper reagents to α,β-acetylenic esters and acids is one of the most ubiquitous and useful methods to prepare various tri- and tetrasubstituted olefins[1] and is frequently employed for the natural product synthesis.[2] Since the reaction presumably proceeds through the carbon–copper enolate, the yield and the geometry of the products highly depend on temperature and duration of reaction before quenching.[2,3] No attempts have yet been made to control the stereochemistry of this reaction by developing a new reagent with wide applicability. We now wish to report that the use of organocopper–organoborane complexes (RCu·BR′$_3$) solves some of the inherent problems associated with these highly useful bond construction reactions (eq 1).



(1)

Y = OR″, OH, C, H

Previously, we reported that the alkenylborane–alkylcopper complexes underwent facile thermal dimerization to give the corresponding (*E,E*)-1,3-dienes with high stereospecificity.[4] The dimerization proceeded with greater stereospecificity than that of the free alkenylcoppers or the tri-*n*-butylphosphine complexes.[5] This observation suggested that the vinyl carbon–copper bond of the organocopper–organoborane complexes[6] might be more configurationally stable than that of normal organocopper reagents.[7] To test this idea and to develop a new methodology to influence the stereochemistry of the conjugate addition, we examined the reaction of various RCu·BR′$_3$ complexes with α,β-acetylenic esters, acids, ketones, and aldehyde. The results are summarized in Table I.

Completely stereospecific addition to α,β-acetylenic esters and acids can be realized by using RCu·BR′$_3$ (entries 1–3 and 10–14). Such a high specificity at the reasonably low temperatures cannot be achieved with reagents previously available. *Since the stereospecificity via methylcopper reagents is generally greater than that via n-butylcopper re-*

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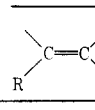
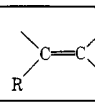
Table I. Conjugate Addition of RCu·BR'$_3$ to α,β-Acetylenic Carbonyl Derivatives[a]

entry	acetylenic carbonyl deriv –C≡CC(O)Y	RCu·BR'$_3$ R	BR'$_3$	temp, °C	product, %[b] 		yield,[c] % (isolated)
1	$MeO_2CC{\equiv}CCO_2Me$	*n*-Bu	*n*-Bu_3B	−70	>99	<1	93
2	$MeO_2CC{\equiv}CCO_2Me$	*n*-Bu	Et_3B	−70	>99	<1	(85)
3	$MeO_2CC{\equiv}CCO_2Me$	*n*-Bu	*n*-Bu-9-BBN[d]	−70	~100	ND[e]	92
4	$MeO_2CC{\equiv}CCO_2Me$	*n*-Bu	*n*-Bu-9-BBN[d]	0	90	10	90
5	$MeO_2CC{\equiv}CCO_2Me$	*n*-Bu	BF_3	−70	87	13	85
6	$MeO_2CC{\equiv}CCO_2Me$	*n*-Bu	$B(OMe)_3$	−75	91	9	92
7	$MeO_2CC{\equiv}CCO_2Me$	*n*-BuCu·PBu_3[f]		−75	93	7	90
8	$MeO_2CC{\equiv}CCO_2Me$	*n*-BuCu[f]		−70	85	15	95
9	$MeO_2CC{\equiv}CCO_2Me$	*n*-Bu_2CuLi		−70	60	40	98
10	$MeO_2CC{\equiv}CCO_2Me$	Me	Et_3B	−60	~100	ND[e]	95(88)
11	$HC{\equiv}CCO_2Et$	*n*-Bu	Et_3B	−55	98	2	67(52)[g]
12	$PhC{\equiv}CCO_2H$[h]	*n*-Bu	Et_3B	20[i]	96	4	96(85)
13	$PhC{\equiv}CCO_2H$[h]	*n*-Bu	*n*-Bu-9-BBN[d]	20[i]	~100	ND[e]	85
14	$HC{\equiv}CCO_2H$[h]	*n*-Bu	Et_3B	−70	~100	ND[e]	(50)[g]
15	PhC≡CC(O)Me	*n*-Bu	Et_3B	−70	77	23	(90)
16	PhC≡CC(O)Me	*n*-Bu	*n*-Bu-9-BBN[d]	−70	88	12	72
17	PhC≡CC(O)Me	*n*-Bu_2CuLi		−70	55	45	95
18	HC≡CC(O)Me	*n*-Bu	Et_3B	−70	~100	ND[e]	(78)
19	PhC≡CC(O)H	*n*-Bu	Et_3B	−60	89	11	(30)
20	PhC≡CC(O)H	*n*-Bu_2CuLi		−60	50	50	60

[a] All reactions were performed on a 1-mmol scale with the same procedure as described in the text. The α,β-acetylenic derivatives were added to the copper reagents in ether at −75 °C. The resulting mixture was slowly warmed up to the temperature indicated above, and then quenched with MeOH. It took 30 min except where otherwise indicated. [b] Identified by ^1H NMR and IR spectroscopy, GC–MS, elemental analysis, and/or comparison with authentic materials. The isomer ratio was determined by ^1H NMR spectra. [c] By GLC analysis, based on the carbonyl derivatives. [d] *n*-Butyl-9-borabicycl3.3.1]nonane. [e] Not detected. [f] Prepared from *n*-BuLi and CuI. [g] The addition compound of the alkenylcopper intermediate to the starting acetylene was formed as a major byproduct. [h] Two equivalents of the copper reagent were used. [i] The reaction mixture was stirred overnight at room temperature.

agents, the comparison of the previously known reagents with the organocopper–organoborane complexes is made with the *n*-butyl derivatives (entries 1–6 vs. 7–9). The alkylborane complexes are most effective among the complexes examined; RCu·BF_3[8] does not give a satisfactory result. The high stereospecificity via the 9-BBN complex suggests the important role of the steric factor around boron. Surprisingly, the vinylcopper–9-BBN complex derived from phenylpropiolic acid retains completely its configuration at room temperature for prolonged periods (entry 13, cf. ref 3a). The reaction of the internal acetylenic ketone and aldehyde proceeds smoothly, but small amounts of the undesirable isomer are formed at the temperature indicated above (entries 16 and 19). This result is consistent with the previous observation that the control of the stereochemistry in α,β-acetylenic ketones is quite difficult.[1,3c,9] On the other hand, the terminal acetylenic ketone undergoes completely stereospecific addition (entry 18). The reactivity of the organocopper reagents decreases along the series R_2CuLi > RCu > RCu·BEt_3 > RCu·Bu-9-BBN.

The following procedure for the synthesis of dimethyl (*Z*)-1-*n*-butymaleate is representative. In a 50-mL flask, equipped with a magnetic stirrer and maintained under N_2, were placed 5 mL of dry ether and 0.2 g (1 mmol) of CuI.[10] *n*-BuLi in hexane (1.3 M, 1 mmol) was slowly added at −30 to 40 °C and the resulting dark brown suspension was cooled to −75 °C. BEt_3 (1 mmol, 0.14 mL) was added. After the resulting viscous mixture was stirred for a while, dimethyl acetylenedicarboxylate (1 mmol, 0.13 mL) was added. The color immediately changed to reddish-brown. The temperature was raised to −70 °C for 30 min. MeOH (1 mL) was added and the mixture was allowed to warm to room temperature. Oxidation of the borane was accomplished by H_2O_2–NaOH at 0 °C. Separation of the ether layer, drying, and distillation yielded the desired olefin: 0.17 g; 85%; bp 130–135 °C (5 mmHg, Kugelrohr).

The products arising from the transfer of ethyl group are not observed in the reaction via *n*-BuCu·BEt_3,[11] indicating that the copper borate complex, *n*-$BuB^-Et_3Cu^+$, is not involved as an intermediate.[12] As an alternative possibility, the formation of the complex between BR'_3 and LiI, which is present in the reaction mixture, might suppress the conversion of the copper enolate to the lithium enolate.[3] However, the ^1H NMR spectra of the mixture of BEt_3 and LiI did not indicate the presence of such a complex. Moreover, when *n*-BuCu·PBu_3 complex free from LiI[5] was treated with 4-phenyl-3-butyn-2-one at −70 °C, the undesirable isomer was produced as a major product. Consequently we assume that the reactive species is depicted as RCu·BR'_3 where some weak interaction between the organocopper and the organoborane is operating. Although we do not have yet a clear understanding of the real intermediate, the present development clearly provides an attractive synthetic approach to control the stereochemistry of the conjugate addition to the acetylenic derivatives. We are currently studying the extension of RCu·BR'_3 to the synthesis of optically active organocopper compounds.[13]

Acknowledgment. Financial support from Ministry of Education, Science, and Culture (Grant 247020, 321709, 334029) is gratefully acknowledged.

References and Notes

(1) Posner, G. H. *Org. React.* **1972**, *19*, 1.
(2) For example: (a) Siddall, J. B.; Biskup, M.; Fried, J. H. *J. Am. Chem. Soc.* **1969**, *91*, 1853. (b) Corey, E. J.; Katzenellenbogen, J. A. *ibid.* **1969**, *91*, 1851, (c) Obayashi, M.; Utimoto, K.; Nozaki, H. *Tetrahedron Lett.* **1977**, 1807.
(3) (a) Klein, J.; Turkel, R. M. *J. Am. Chem. Soc.* **1969**, *91*, 6186. (b) Klein, J.; Aminadav, N. *J. Chem. Soc. C*, **1970**, 1380. (c) Klein, J.; Levene, R. *J. Chem. Soc., Perkin Trans. 2*, **1973**, 1971.
(4) Yamamoto, Y.; Yatagai, H.; Moritani, I. *J. Am. Chem. Soc.* **1975**, *97*, 5606. Yamamoto, Y.; Yatagai, H.; Maruyama, K.; Sonoda, A.; Murahashi, S-I. *ibid.* **1977**, *99*, 5652.
(5) Whitesides, G. M.; Casey, C. P. *J. Am. Chem. Soc.* **1966**, *88*, 4541. Whitesides, G. M.; Casey, C. P.; Krieger, J. K. *ibid.* **1971**, *93*, 1379. The isomeric purity in the case of the alkenylcoppers and their tri-*n*-butylphosphine complexes is <98%.

(6) Previously we thought that the free alkenylcopper derived from the ate complexes underwent dimerization.[4] However, there is a possibility that some interaction between the alkenylcopper (RCu) and the borane ($RBBu_2$) is operating and the dimer is produced from this complex ($RCu{\cdot}BRBu_2$).
(7) (a) Bergbreiter, D. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974,** *96,* 4937; only one type of configurationally stable sp^3-hybridized R group has been reported (RCu·R'HgX). (b) Posner, G. H. *Org. React.* **1975,** *22,* 253; Normant, J. F. *Synthesis,* **1972,** 63; many examples of configurationally stable sp^2-hybridized R groups are known in which R is not enolizable.
(8) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1978,** *100,* 3240; *J. Organomet. Chem.* **1978,** *156,* C9.
(9) It is recently reported that α,β-acetylenic nitriles[9a] and sulfoxides[9b] undergo the stereospecific conjugate addition; (a) Westmijze, H.; Kleijn, H.; Vermeer, P. *Synthesis,* **1978,** 454. (b) Truce, W. E.; Lusch, M. J. *J. Org. Chem.* **1978,** *43,* 2252.
(10) CuI was purified by the standard procedure; Posner, G. H.; Whitten, C. E.; Sterling, J. J. *J. Am. Chem. Soc.* **1973,** *95,* 7788.
(11) If trace amounts of air were introduced into the reaction mixture, the conjugate addition of ethyl group was observed and the olefin thus obtained was stereochemically homogeneous. See also, Suzuki, A.; Nozawa, S.; Itoh, M.; Brown, H. C.; Kabalka, G. W.; Holland, G. W. *J. Am. Chem. Soc.* **1970,** *92,* 3503.
(12) The copper boron ate complex, $R_3B^-Me\ Cu^+$, transfers both R and Me groups to ethyl propiolate; Yamada, K.; Miyaura, N.; Itoh, M.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1977,** *50,* 3431.
(13) For a stable chiral copper reagent, see Periasamy, M. P.; Walborsky, H. M. *J. Am. Chem. Soc.,* **1975,** *97,* 5930.

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New Method for Direct Conversion of Amides to Amines

Summary: The reagent *I,I*-bis(trifluoroacetoxy)iodobenzene is found to bring about the conversion of carboxylic acid amides to amines under extremely mild conditions (room temperature, 2–5 h, 1:1 acetonitrile–water) without the necessity of isolating or trapping the intermediate isocyanate.

Sir: We wish to report a new reagent for carrying out the Hofmann rearrangement ($RCONH_2 \rightarrow RNH_2$) without the necessity of trapping the intermediate isocyanate.

The decarboxylative rearrangement of organic compounds at the carboxylic acid level of oxidation has been carried out in a number of ways, including the Hofmann rearrangement, Curtius rearrangement, Schmidt rearrangement, or various modifications of these.[2] In particular, the direct rearrangement of amides to isocyanates has been typically carried out by the Hofmann hypobromite reaction or, more recently, by the rearrangement brought about by lead tetraacetate.[3] In the latter reaction, it is obligatory for best results that the isocyanate which results from the rearrangement be trapped as an intermediate carbamate by running the reaction in benzyl alcohol or *tert*-butyl alcohol. In addition, $Pb(OAc)_4$ sometimes reacts with other functionality.[3b]

We have found that *I,I*-bis(trifluoroacetoxy)iodobenzene (1) [iodobenzene bis(trifluoroacetate), or bis(trifluoroacetato)-*O*-phenyliodine] is a superb reagent for carrying out the amide-to-amine conversion to yield the amine directly in high yield without the need for isolation or trapping of the intermediate isocyanate (eq 1). Some results are presented in Table I.

$$R\text{-}\overset{O}{\overset{\|}{C}}\text{-}NH_2 + C_6H_5\text{-}I(O\text{-}\overset{O}{\overset{\|}{C}}\text{-}CF_3)_2 + H_2O \xrightarrow[\underset{\sim}{1}]{} R\text{-}NH_3^+ + CO_2 + C_6H_5I + 2CF_3CO_2^- + H^+ \quad (1)$$

$$R\text{-}\overset{O}{\overset{\|}{C}}\text{-}NH_2 \rightleftharpoons R\text{-}N{=}C{=}O \xrightarrow{H_2O} R\text{-}NH_2 + CO_2 \quad (2)$$

$$R\text{-}NH\text{-}\overset{O}{\overset{\|}{C}}\text{-}NH\text{-}R$$

In some methods, the isocyanate will be trapped by the amine produced in the reaction to give a symmetrical urea (eq 2). Indeed, the use of the commercially available *I,I*-diacetoxyiodobenzene (iodobenzene diacetate, or phenyliodosyl acetate) in this conversion resulted in mixtures of amines and ureas.[4] The production of trifluoroacetic acid in this reaction (eq 1) can both catalyze the attack of water on the isocyanate[5] and protonate the product amine, thereby removing it from participation in the side reaction of eq 2.[6]

Only primary amides are affected during reaction with 1; secondary and tertiary amides do not react. In particular, the reagent has been used to prepare *N*-(aminomethyl)benzamide (2) in excellent yield from hippuramide (eq 3). Compounds

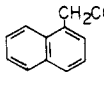
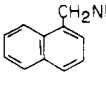
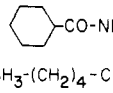
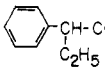
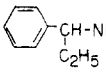
$$C_6H_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}NH\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}NH_2 \xrightarrow[\underset{\sim}{2}]{1} C_6H_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}NH\text{-}CH_2\text{-}NH_3^+\ Cl^- \quad (3)$$
$$(87\%)$$

of the *N*-(1-aminoalkyl)amide type, 3, are extremely interesting in the context of the development of the retro-inverso peptide concept[7] as well as in the evolution of a carboxyl-terminal sequential peptide degradation.[8]

$$R^1\text{-}\overset{O}{\overset{\|}{C}}\text{-}NH\text{-}\underset{\underset{\sim}{3}}{\underset{|}{CH}}\text{-}NH_3^+ \qquad R^2$$

Because reagent 1 seems to be a weaker oxidizing agent than lead tetraacetate,[9] it is expected to be compatible with a wide variety of functionality. The last two entries in Table I are our initial realizations of this expectation. One limitation both anticipated[4,10] and realized in practice, however, is that the reagent cannot be used in the Hofmann rearrangement of aromatic carboxylic acids to the corresponding amines, since

Table I. Results of the Reaction of Carboxylic Acid Amides with *I,I*-Bis(trifluoroacetoxy)iodobenzene

amide	product (yield, %)[a]
	 (85)
	 (96)
$CH_3\text{-}(CH_2)_4\text{-}CO\text{-}NH_2$	$CH_3\text{-}(CH_2)_4\text{-}NH_3^+\ Cl^-$ (86)
	 (92)
	 (92)
	 (55)[b]
$C_6H_5\text{-}CO\text{-}NH\text{-}CH_2\text{-}CO\text{-}NH_2$	$C_6H_5\text{-}CO\text{-}NH\text{-}CH_2\text{-}NH_3^+\ Cl^-$ (87)

[a] The yields reported are those of isolated, recrystallized material, except for the entry described by footnote *b*. The melting points and NMR spectra of all compounds agree with those of authentic material. [b] Yield by gas chromatography.

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