Zimmerman, H. G. C. Dürr, R. G. Lewis, and S. Bram, *Ibid.*, **84,** 4149 (1962); H. E. Zimmerman, H. G. C. Dürr, R. S. Givens, and R. G. Lewis, *ibid.*, **89,** 1863 (1967).

(5) It has been reported that on direct irradiation the nitrogen-hetero analogues, 1,3-dihydro-2*H*-azepin-2-ones, underwent exclusively cyclization to give 2-azabicyclo[3.2.0]hept-6-en-3-ones: O. L. Chapman and E. D. Hoganson, *J. Am. Chem. Soc.*, **86,** 498 (1964); L. A. Paquette, *ibid.*, **86,** 500 (1964); H.-D. Becker and K. Gustafsson, *Tetrahedron Lett.*, 1705 (1976).

(6) All new compounds except **6, 8,** and **18** in this communication gave satisfactory elemental analyses. Compounds **6** and **8** decomposed partially during purification by vacuum distillation or TLC on silica gel. Compound **18** was homogeneous on TLC, but still contained a trace of impurities as detected by NMR.

(7) IR ($CHCl_3$) 1718 (sh), 1707, and 1142 cm^{-1}; UV (EtOH) λ_{max} 225 (ϵ 8200) and 264 nm (ϵ 5200); ^1H NMR (100 MHz, C_6D_6) δ 1.31 (ddd, 1 H, $J = 6.9$, 5.5, and 4.9 Hz), 1.58 (dd, 1 H, $J = 4.9$ and 3.4 Hz), 1.77 (finely splitted s, 3 H), 4.06 (dd, 1 H, $J = 6.9$ and 3.4 Hz), 6.26 (finely splitted d, 1 H, $J = 5.5$ Hz), 6.54–6.70 (m, 2 H), and 6.98–7.12 (m, 3 H); ^{13}C NMR ($CDCl_3$, Me_4Si) 17.35 (q), 22.26 (d), 33.91 (d), 64.00 (d), 123.76 (s), 125.71 (d), 126.74 (d), 128.68 (d), 137.54 (s), 142.09 (d), and 161.87 ppm (s).

(8) G. W. Perold and H. K. L. Hundt, *J. Chem. Soc.*, 1924 (1966).

(9) For a review of cyclopropanol chemistry see: D. H. Gibson and C. H. DePuy, *Chem. Rev.*, **74,** 605 (1974).

(10) H. Weitkamp and F. Korte, *Tetrahedron*, **20,** 2125 (1964).

(11) O. A. Subbotin, A. S. Kozmin, Yu. K. Grishin, N. M. Sergeyev, and I. G. Bolesov, *Org. Magn. Reson.*, **4,** 53 (1972).

(12) G. L. Krueger, F. Kaplan, M. Orchin, and W. H. Faul, *Tetrahedron Lett.*, 3979 (1965).

(13) W. Skorianetz and G. Ohloff, *Helv. Chim. Acta*, **58,** 1272 (1975).

(14) Compound **16,** the original product formed by the photooxidation of 6-phenylfulvene, is unstable in solutions and isomerizes easily to the stable fully conjugated isomer. Hence, the sample separated from the photooxidation mixture by chromatography was immediately subjected to photolysis at low temperature.

(15) It was reported that decarbonylation is the main reaction pathway in the photochemical transformation of enol lactones: A. Yogev and Y. Mazur, *J. Am. Chem. Soc.*, **87,** 3520 (1965); C. D. Gutsche and B. A. M. Oude-Alink, *ibid.*, **90,** 5855 (1968); O. L. Chapman and C. L. McIntosh, *Chem. Commun.*, 383 (1971); B. A. M. Oude-Alink, A. W. K. Chan, and C. D. Gutsche, *J. Org. Chem.*, **38,** 1993 (1973); A. Padwa, D. Dehm, T. Oine, and G. A. Lee, *J. Am. Chem. Soc.*, **97,** 1837 (1975).

(16) S. S. Hixson, P. S. Mariano, and H. E. Zimmerman, *Chem. Rev.*, **73,** 531 (1973). See also ref 4a.

(17) This ring-forming step is formally a cycloheptatriene → norcaradiene type transfomation.

Kazuhiro Sato, Hisahiro Hagiwara, Hisashi Uda*
Masaji Sato, Nobuyuki Harada
Chemical Research Institute of Nonaqueous Solutions
Tohoku University
Katahira 2-1-1, Sendai 980, Japan

Received April 2, 1976

The Chemospecific, Homogeneous, Ambient Temperature Ullmann Coupling of *o*-Haloarylimines

Sir:

The classical Ullmann reaction allows for the coupling of aryl halides to form biaryls at elevated temperatures (100-250 °C). In the case of unsymmetrical couplings, three products (AA, AB, BB) are formed in varying amounts.[1] We wish to report a method for the homogeneous, chemospecific coupling of ortho-halogenated arylimines at ambient temperature[2] as illustrated in Scheme I.

Scheme I

(L = $(C_2H_5O)_3P$)

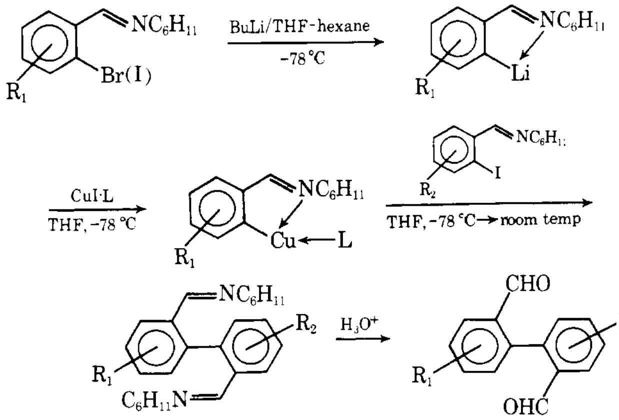
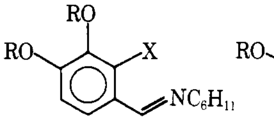


Table I

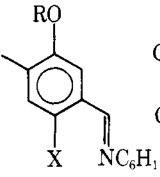
Entry	Cu reagent	Iodide	Biaryl	Yield % NMR[a]	Yield % isolated[b]
1	1a	1b	5a	60	44
2	2a	2b	5b	65	59
3	1a	2b	5c	70	54
4	2a	1b	5c	86	58
5	2c	2d	5d	—	62
6	3	2b	5e	77	63
7	4	2b	6	—	54[c]

[a] Aldehyde proton integrated against benzaldehyde standard. [b] Crystallized yields.[4] [c] Isolated as oxazoline-imine.

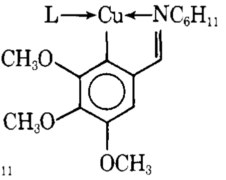
The biaryl formed in each case is determined by the position of the halogen atom in each of the starting imines and is formed by the union of the preformed copper reagent and the aryl iodide. The specific couplings which were investigated are listed in Table I.[3]



1

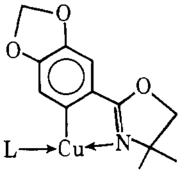


2

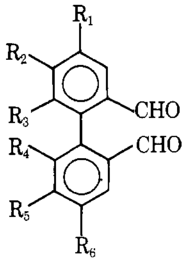


3

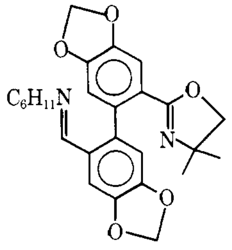
a, R = $-CH_2-$; X = Cu←L
b, R = $-CH_2-$; X = I
c, R = CH_3; X = Cu←L
d, R = CH_3; X = I



4



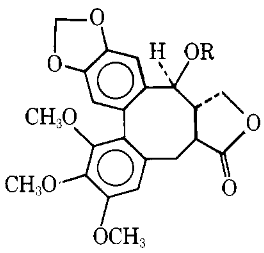
5



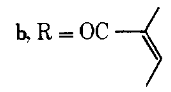
6

a, $R_1 = R_6 = H$; $R_2, R_3 = R_4, R_5 = OCH_2O$
b, $R_3 = R_4 = H$; $R_1, R_2 = R_5, R_6 = OCH_2O$
c, $R_1 = R_4 = H$; $R_2, R_3 = R_5, R_6 = OCH_2O$
d, $R_3 = R_4 = H$; $R_1 = R_2 = R_5 = R_6 = OCH_3$
e, $R_3 = H$; $R_1, R_2 = OCH_2O$; $R_4 = R_5 = R_6 = OCH_3$

The sequence has the advantage over traditional Ullmann conditions in that (a) the reaction can be conducted homogeneously at ambient temperature; (b) both symmetrical and unsymmetrical dimers can be produced; (c) unsymmetrical biaryls can be prepared in either of two modes (Table I, entries 3 and 4); (d) both biaryl aldehydes and oxazolines (latent ester or carboxylic acid[5]) can be produced. While nickel(0) biscyclooctadiene,[6] nickel(0) tetrakistriphenylphosphine,[7] and nickel(0) tristriphenylphosphine[8] have been utilized to couple aryl halides, halides flanked by two ortho-substituents fail to dimerize.[7,8] Entry 6 reveals that this effect is not significant in this reaction, a fact of critical importance in synthetic approaches to the antileukemic biaryls, steganacin **7a** and steganagin **7b**,[9] which depend upon initial formation of the biaryl system.



7a, R = COCH$_3$



b, R = OC

$\mathrm{R = OC{-}C(CH_3){=}CH_2}$

It has been demonstrated[10] that phenylcopper and deuterioiodobenzene in a coordinating solvent such as pyridine or quinoline give a nearly statistical distribution of labeled and unlabeled biphenyl, whereas, in a weakly coordinating solvent (DMF), biphenyl forms by phenylcopper disproportionation.

We have found that it is necessary for the intramolecular stabilizing ligands to be present.[11] When aryl Cu^I **1a** was treated with an equivalent of iodobenzene, unsymmetrical coupling was repressed in favor of symmetrical coupling, **5a**, by aryl Cu^I disproportionation.[12] The biaryls **5a** and **5b** were found to be by-products (<5% of the crude hydrolyzed reaction mixture, HPLC analysis) in entries 3 and 4, respectively.

The mechanism is viewed as an oxidative addition[13] of the arylimine iodide to the copper reagent to form an intermediate (arylimine)$_2$Cu^{III}I-d_8 species which collapses to product and CuI·L.[14]

Typical reaction conditions are as follows (entry 3). In a flame-dried flask equipped with a serum cap and N$_2$ inlet is dissolved 310 mg (1 mmol) of 6-bromopiperonalcyclohexylimine[15] in 5 ml of THF (from sodium benzophenone ketyl) followed by cooling to −78 °C (CO$_2$-acetone bath). To the magnetically stirred solution was added via syringe 0.52 ml (1.10 mmol) of 2.1 M BuLi in hexane (Ventron). After the yellow solution had been stirred for 15 min, addition of 535 mg (1.5 mmol) of solid CuI·(C$_2$H$_5$O)$_3$P[16] formed a homogeneous orange-red solution. After an additional 15 min, 357 mg (1 mmol) of 2-iodopiperonalcyclohexylimine[15] was added as a solid, the bath was removed, and the reaction mixture allowed to warm to room temperature while stirring was continued for 5 h. The reaction mixture was diluted with methylene chloride and washed continuously with concentrated NH$_4$OH (until the aqueous washes were no longer blue) followed by successive washing with water and saturated brine. The organic layer was dried over anhydrous MgSO$_4$, filtered, and concentrated providing 623 mg of oil which was subsequently hydrolyzed in 10 ml of CH$_2$Cl$_2$ and 10 ml of 10% aqueous HCl at reflux for 1 h. Separation of the layers followed by workup (vide supra) gave 356 mg of foam. Integration (NMR) of the aldehyde resonances (δ 9.67 and 9.73) against a known quantity of freshly distilled benzaldehyde (δ 10.00) indicated a yield of 86%. The residue was percolated through a short column of silica gel (1:1 THF/hexane) followed by HPLC purification (40% THF/hexane, E. Merck Silica Gel 60H). The combined biaryl fractions (253 mg) were crystallized from ethanol to provide 148 mg (58%) of **5c**, mp 146.5–148.5 °C (corr.).

Acknowledgment. We wish to thank the National Institutes of Health (CA 16432) and Hoffmann-La Roche for financial support of this work.

References and Notes

(1) For a recent review of the Ullmann reaction and related copper chemistry, see (a) J. F. Normant, *Synthesis*, 63 (1972), and (b) P. E. Fanta, *ibid.*, 9 (1974).

(2) For related biaryl forming reactions under mild conditions, see (a) A. I. Meyers and E. D. Mihelich, *J. Am. Chem. Soc.*, **97**, 7383 (1975), and (b) T. Cohen and I. Cristea, *ibid.*, **98**, 748 (1976).

(3) Reagent **2a** failed to couple with 6-iodopiperonal and 3,4-methylenedioxy-6-iodoacetophenone. A coupling with methyl 3,4-methylenedioxy-6-iodobenzoate was partially successful (30% of aldehydo-ester isolated). The *anti-O*-methyloxime of 3,4-methylenedioxy-6-iodoacetophenone coupled efficiently on the basis of the NMR spectrum of the crude reaction mixture.

(4) All new compounds gave satisfactory combustion analyses and spectra. Known compounds were in accord with literature data.

(5) Reference **2a** and earlier papers in the series.

(6) M. F. Semmelhack, P. M. Helquist, and L. D. Jones, *J. Am. Chem. Soc.*, **93**, 5908 (1971).

(7) M. F. Semmelhack and L. S. Ryono, *J. Am. Chem. Soc.*, **97**, 3875 (1975).

(8) A. S. Kende, L. S. Liebeskind, and D. M. Braitsch, *Tetrahedron Lett.*, 3375 (1975).

(9) Isolation and structure: S. M. Kupchan, R. W. Britton, M. F. Ziegler, C. J. Gilmore, R. J. Restivo, and R. F. Bryan, *J. Am. Chem. Soc.*, **95**, 1335 (1973). Synthesis: A. S. Kende and L. S. Liebeskind, *ibid.*, **98**, 267 (1976); L. R. Hughes and R. A. Raphael, *Tetrahedron Lett.*, 1543 (1976).

(10) M. Nilsson and O. Wennerström, *Tetrahedron Lett.*, 3307 (1968), and *Acta Chem. Scand.*, **24**, 482 (1970).

(11) For related examples, see A. C. Cope and R. N. Gourley, *J. Organomet. Chem.*, **8**, 52 (1967), and G. van Koten and J. Noltes, *ibid.*, **104**, 127 (1976).

(12) A. H. Lewin and T. Cohen, *Tetrahedron Lett.*, 4531 (1965).

(13) J. P. Collman, *Acc. Chem. Res.*, **1**, 136 (1968).

(14) Cohen and Cristea[2b] have demonstrated that the formation of biaryl from *o*-bromonitrobenzene with cuprous triflate (excess) in aqueous ammonia obeys the rate equation $d[\mathrm{Ar_2}]/dt = k_{\mathrm{Ar_2}}[\mathrm{ArBr}]^2[\mathrm{Cu^I}]$, indicating that an initially formed ArCu^{III}Br species is not reduced to the Cu^I state prior to reacting with a second molecule of ArBr. This is an isoelectronic equivalent of the Ni(0) coupling of aryl halides.[6] This observation does not preclude oxidative addition to a Cu^I species from occurring when the opportunity arises.

(15) F. E. Ziegler and K. W. Fowler, *J. Org. Chem.*, **41**, 1564 (1976).

(16) Y. Nishizawa, *Bull. Soc. Chim. Jpn.*, **34**, 1170 (1961).

(17) National Institutes of Health Career Development Awardee, 1973–1978.

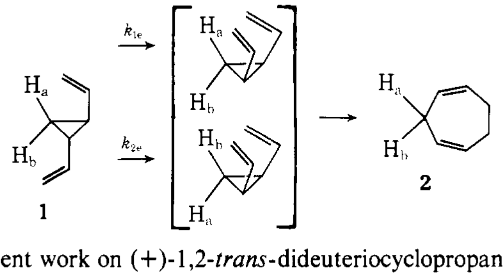
Frederick E. Ziegler,*[17] Kerry W. Fowler, Sheldon Kanfer
Sterling Chemistry Laboratory, Yale University
New Haven, Connecticut 06520

Received July 13, 1976

Thermal Isomerization of (−)-(1*R*,5*R*)-6-*exo*-Vinylbicyclo[3.1.0]hex-2-ene to (−)-(1*R*,5*R*)-Bicyclo[3.2.1]octa-2,6-diene: One-Center Thermal Epimerization of a Cyclopropane

Sir:

trans-1,2-Divinylcyclopropane at 190 °C gives rise to 1,4-cycloheptadiene;[1] this net result and related data for other *trans*-1,2-dialkenylcyclopropanes have been interpreted in terms of geometrical isomerization to give short-lived *cis*-1,2-dialkenylcyclopropanes which in turn suffer rapid Cope rearrangements.[2-4] Whether the geometrical isomerization is a one-center epimerization or a two-center process has not been addressed experimentally. For *trans*-divinylcyclopropane (**1**), a two-center epimerization leading to racemization is kinetically competitive with the trans-to-cis geometrical isomerization,[4] but the latter could well be either a one-center or a two-center event.



1

2

Recent work on (+)-1,2-*trans*-dideuteriocyclopropane[5] and both antipodes of *trans*-1-phenyl-2-deuteriocyclopropane[5] indicated exclusive or nearly exclusive epimerization through two-center processes. Kinetic work on deuterium labeled and