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Intermolecular Couplings between Vinyl Triflates and Allylic Cuprates: A Mild and Rapid Atypical Route to 1,4-Dienes

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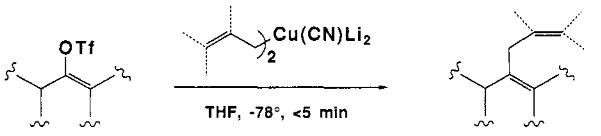
Summary: Treatment of vinyl triflates with several different cyanocuprates containing allylic ligands leads to coupling products in good yields. Cuprates containing allyl, methallyl, crotyl, and prenyl groups all participate in these reactions which take place instantly at low temperatures. Highly functionalized substrates may also be used.

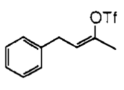
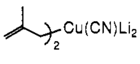
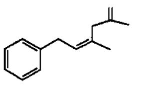
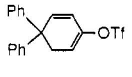
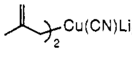
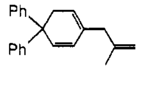
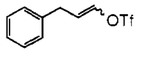
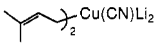
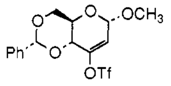
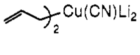
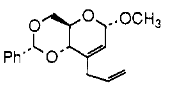
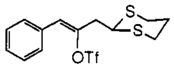
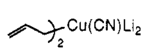
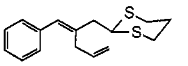
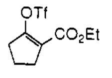
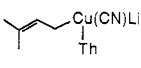
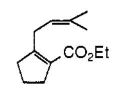
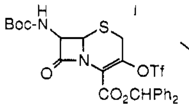
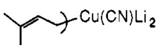
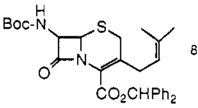
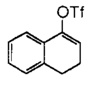
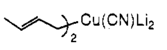
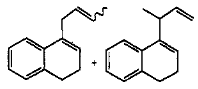
Retrosynthetic analysis as applied to a 1,4-diene logically suggests that the preferred disconnection leads to a vinylic nucleophile together with an allylic fragment bearing a leaving group. Indeed, many methods for arriving at such an array follow this line of thought.[2] Allylmetalations of suitably substituted alkynes are also well-known, although such processes can be plagued by acid–base and/or regiochemical issues.[3] Quite rare is the availability of an expedient alternative, that is, of a vinylic electrophile coupled with an allylic nucleophile (eq 1).



(1)

That few isolated examples have been reported involving nickel (both stoichiometric[4a] or catalytic[4b]), copper-catalyzed Grignard chemistry,[5] or palladium-mediated couplings[6] implies limited potential for transformations of this type with these reagents. We now report the first general method for preparing this valued functionality[7] which takes advantage of the remarkable reactivity of allylic higher order (H.O.) cyanocuprates toward vinyl triflates.[8]

Table I. Allylic Cyanocuprate Reactions in THF at –78 °C

entry	substrate	cuprate[a]	product(s)[b]	yield,[c] %
1				82
2				75
3	 (8:1 E:Z)		 (8:1 E:Z)	79
4		 [d]		76[e]
5		 [f]		74(85)[g]
6		 [h,i]		87
7	 [j]	 [k]		84(79)[l]
8			 (30% E, 10% Z) + (37%) [m]	77

[a] 1.5 equiv used unless stated otherwise. [b] All compounds were fully characterized by IR, NMR, MS, and HRMS. [c] Isolated yields. [d] 3.0 equiv were used. [e] Ca. 20% of the product of reduction was also isolated. [f] 2.5 equiv were used. [g] Yield based on recovered starting material. [h] 1.05 equiv were used. [i] Th = 2-thienyl; prepared from (Th)Cu(CN)Li (available from Aldrich). [j] Generously supplied by Dr. V. Farina of the Bristol-Myers Company. [k] 1.1 equiv were used. [l] Yield obtained using 1.1 equiv of (prenyl)Cu(CN)Li. [m] Ratio was determined by capillary GC.

Treatment of a vinyl triflate[9] with a H.O. cuprate prepared from lithium chloride solubilized CuCN[10] and either allyllithium, methallyllithium, crotyllithium, or prenyllithium[11] (2 equiv) in THF at -78 °C affords the corre-

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[1] A. P. Sloan Fellow, 1984–1988; Dreyfus Teacher–Scholar, 1984–1989.

[2] Methods based on Li: Corey, E. J.; Williams, D. R. *Tetrahedron Lett.* **1977**, 3847. Cu: Normant, J. F.; Bourgain, M. *Ibid.* **1971**, 2583. Corey, E. J.; Cane, D. E.; Libit, L. *J. Am. Chem. Soc.* **1971**, *93*, 7016. Swenton, J. S.; Raynolds, P. W.; Manning, M. J. *J. Chem. Soc., Chem. Commun.* **1977**, 499. Pd/Zr: Schwartz, J.; Temple, J. S. *J. Am. Chem. Soc.* **1980**, *102*, 7381. Pd/Zr/Al: Negishi, E.; Matsushita, H. *Ibid.* **1981**, *103*, 2882. Pd/Sn: Stille, J. K.; Sheffy, F. K.; Godschalx, J. P. *J. Am. Chem. Soc.* **1984**, *106*, 4833. Stille, J. K.; Tueting, D. R.; Echavarren, A. M. *Ibid.* **1988**, *110*, 4039. Pd/Hg: Larock, R. C.; Bernhardt, J. C.; Driggs, R. J. *J. Organomet. Chem.* **1978**, *156*, 45. Larock, R. C.; Takagi, K. *J. Org. Chem.* **1988**, *53*, 4329.

[3] Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841 and references therein. Negishi, E. *Acc. Chem. Res.* **1987**, *20*, 65 and references therein.

[4] (a) Corey, E. J.; Semmelhack, M. F. *J. Am. Chem. Soc.* **1967**, *89*, 2755. Hegedus, L. S.; Waterman, E. L.; Catlin, J. *Ibid.* **1972**, *94*, 7155. (b) Kumada, M. *Pure Appl. Chem.* **1980**, *52*, 669 and references therein. Oppolzer, W.; Bedoya-Zurita, M.; Switzer, C. Y. *Tetrahedron Lett.* **1988**, *29*, 6433.

[5] (a) Normant, J. F.; Commercon, A.; Villieras, J. *J. Organomet. Chem.* **1977**, *128*, 1. (b) Blanchette, M. A.; Malamas, M. S.; Nantz, M. H.; Roberts, J. C.; Samfai, P.; Whritenour, D. C.; Masamune, S.; Kageyama, M.; Tamura, T. *J. Org. Chem.* **1989**, *54*, 2817.

[6] (a) Stille, J. K.; Scott, W. J.; Crisp, G. T. *J. Am. Chem. Soc.* **1984**, *106*, 4630. (b) Scott, W. J.; Stille, J. K. *Ibid.* **1986**, *108*, 3033. (c) Larock, R. C.; Gong, W. H. *J. Org. Chem.* **1989**, *54*, 2047.

[7] Henrick, C. A. *Tetrahedron* **1977**, *33*, 1845. Green, R. H.; Lambeth, P. F. *Ibid.* **1983**, *39*, 1687. *The Leukotrienes; Chemistry and Biology*; Chakrin, L. W., Bailey, D. M., Eds.; Academic Press: New York, 1984. For a recent innovative method that involves nucleophilic fragmentation of 1-[(trimethylsilyl)alkyl]cyclopropanes, see: Wilson, S. R.; Zucker, P. A. *J. Org. Chem.* **1988**, *53*, 4682.

[8] Coupling reactions of vinyl triflates with most types of cuprates, except for allylic reagents, have been reported; cf.: McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1980**, *21*, 4313. See also: McMurry, J. E.; Mohanraj, S. *Ibid.* **1983**, *24*, 2723. Scott, W. J.; McMurry, J. E. *Acc. Chem. Res.* **1988**, *21*, 47.

[9] Vinyl iodides led to mixtures of substitution and reduction products,[5a] for methods to prepare vinyl triflates, see: Schleyer, P. v. R.; Stang, P. J.; Summerville, R. H.; Senkler, C. A.; Duever, T. E. *J. Am. Chem. Soc.* **1974**, *96*, 1100. Stang, P. J.; Treptow, W. *Synthesis* **1980**, 283. McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1983**, *24* 979. Yamamoto, H.; Naruse, Y.; Esaki, T. *Ibid.* **1988**, *29*, 1417 and reference 6b.

[10] Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.

[11] Prepared from the corresponding tributylstannanes by treatment with MeLi in THF at -78 °C; cf.: Seyferth, D.; Weiner, M. A. *J. Org. Chem.* **1961**, *26*, 4797.

0022-3263/90/1955-1695$02.50/0

sponding 1,4-dienes virtually upon mixing.[12] A portion of our results are summarized in Table I. Yields in all cases are good to excellent. Several noteworthy features of these couplings are apparent; firstly, stereochemical integrity about the olefinic center of the educt is completely maintained. Equally impressive is the range of functionality which is tolerated. Hence, branched chain sugars are readily prepared (entry 4), sulfur-containing substrates do not interfere (entry 5), and highly reactive centers of electrophilicity, as with an ethyl ester (entry 6)[13] or a fully functionalized cephem (entry 7), are compatable.

Although regiochemical issues in the allyl and methallyl cases do not apply, it is important to note that prenyl couplings occur with >99% α-attack, which is completely opposite to what is expected in Lewis acid promoted couplings with electrophiles.[14] Crotyl cuprates, which give quite efficient displacements under these conditions, unfortunately appear to react both regio- and stereorandomly, as 2-3:1 mixtures of *Z*:*E* products result, along with ca. 1-2:1 ratios of $\alpha:\gamma$ attack.

In summary, an extremely facile route to 1,4-dienes has been uncovered utilizing allylic cyanocuprate technology together with both relatively simple and complex vinyl triflate reaction partners.

Acknowledgment. Financial support provided by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the NSF (Grant CHE 87-03757) is gratefully acknowledged. We warmly express our gratitude to the 3M Company (St. Paul, MN) for a generous sample of trifluoromethanesulfonic acid.

Registry No. (*Z*)-$\mathrm{PhCH_2CH{=}C(CH_3)OTF}$, 123994-43-4; (*E*)-$\mathrm{PhCH_2CH{=}CH(OTF)}$, 123994-45-6; (*Z*)-$\mathrm{PhCH_2CH{=}CH(OTF)}$, 123994-46-7; $\mathrm{(CH_2{=}C(CH_3)CH_2)_2Cu(CN)Li_2}$, 122700-72-5; $\mathrm{[(CH_3)_2C{=}CHCH_2]_2Cu(CN)Li_2}$, 122700-73-6; $\mathrm{(CH_2{=}CHCH_2)_2Cu(CN)Li_2}$, 91328-60-8; $\mathrm{(CH_3)_2C{=}CHCH_2Cu(Th)(CN)Li_2}$, 124020-71-9; (*E*)-$\mathrm{(CH_3CH{=}CHCH_2)_2Cu(CN)Li_2}$, 124020-72-0; (Th)Cu(CN)Li, 112426-02-5; 5,5-diphenyl-2-[[(trifluoromethyl)sulfonyl]oxy]-1,3-cyclohexadiene, 123994-44-5; methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-[[(trifluoromethyl)sulfonyl]oxy]-α-D-*erythro*-hex-2-enopyranoside, 123994-47-8; (*E*)-3-(1,3-dithian-2-yl)-1-phenyl-2-[[(trifluoromethyl)sulfonyl]oxy]-1-propene, 123994-48-9; ethyl 2-[[(trifluoromethyl)sulfonyl]oxy]-1-cyclopentanecarboxylate, 122539-74-6; diphenyl 7-(*tert*-butylcarbonylamino)-3-[[(trifluoromethyl)sulfonyl]oxy]-3-cepham-4-carboxylate, 123054-32-0; 1-[[(trifluoromethyl)sulfonyl]oxy]-3,4-dihydronaphthalene, 123994-49-0; ((*Z*)-3,5-dimethyl-2,5-hexadienyl)benzene, 123994-50-3; 5,5-diphenyl-2-(2-methylpropenyl)-1,3-cyclohexadiene, 123994-51-4; (*E*)-(6-methyl-2,5-heptadienyl)benzene, 123994-52-5; (*Z*)-(6-methyl-2,5-heptadienyl)benzene, 123994-53-6; methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-(2-propenyl)-α-D-*erythro*-hex-2-enopyranoside, 123994-54-7; (*E*)-2-[methyl(1,3-dithianyl)]-1,4-pentadienylbenzene, 123994-55-8; ethyl $\Delta^{1,2}$-2-(3-methyl-2-butenyl)cyclopentenecarboxylate, 123994-56-9; diphenyl 7-(*tert*-butylcarbonylamino)-3-(3-methyl-2-butenyl)-3-cepham-4-carboxylate, 123994-57-0; (*E*)-1-(2-butenyl)-3,4-dihydronaphthalene, 123994-58-1; (*Z*)-1-(2-butenyl)-3,4-dihydronaphthalene, 123994-59-2; 1-(1-methyl-2-propen-1-yl)-3,4-dihydronaphthalene, 57256-49-2; tributyl(3-methyl-2-butenyl)stannane, 53911-92-5; methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside, 65530-27-0.

Supplementary Material Available: Experimental data and spectra for all products in Table I (14 pages). Ordering information is given on any current masthead page.

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[12] A representative procedure (Table I, entry 3) is as follows: To a −78 °C solution of 705 mg (1.87 mmol) of tributyl(3-methyl-2-butenyl)stannane[11] in 2.0 mL of anhydrous tetrahydrofuran (THF) was added 1.20 mL of methyllithium (1.55 M in diethyl ether, 1.86 mmol) via syringe. The resulting golden solution was stirred 15 min at −78 °C. Independently, a 10-mL two-necked flask was charged with 84 mg (0.93 mmol) of CuCN and 40 mg (0.93 mmol) of LiCl, gently flame-dried in vacuo, and then purged three times with Ar. Anhydrous THF (1.20 mL) was introduced via syringe, and the solubilized Cu(I) salt was cooled to −78 °C, whereupon, the solution of prenyllithium was immediately and rapidly charged into the two-necked flask via cannula, and the resulting pale yellow solution was stirred 10 min at −78 °C. The reagent was treated with 165 mg (0.62 mmol, as an 8:1 mixture of *E*:*Z* isomers, respectively) of 3-phenyl-1-(((trifluoromethyl)sulfonyl)oxy)propene dissolved in 0.5 mL of dry THF. A reddish color ensued and persisted for 15 min, at which time the reaction was quenched with 2 mL of 10% NH_3/saturated NH_4Cl aqueous solution, diluted with 10 mL of hexanes, and allowed to warm to ambient temperature. Following ethereal extraction, the organic extract was washed with brine and dried over Na_2SO_4. The volatiles were removed with a rotary evaporator and purification by flash chromatography (ICN Silica 32-63, 60A, eluting with petroleum ether boiling range 38–50 °C) afforded 91 mg (79%) of (6-methyl-2,5-heptadienyl)benzene as an 8:1 mixture of *E*:*Z* isomers.

[13] Attempts to effect this coupling with prenyltributylstannane under the influence of $Pd(PPh_3)_4$/LiCl in refluxing THF[6a,b] afforded ca. 10–20% yields of the desired material after 3 days. Considerable amounts of starting material were recovered (ca. 55%), with only trace quantities of the β-chloro enoate being detected by capillary GC analyses (comparison with an authentic sample).

[14] See, for examples: Yamamoto, Y.; Maruyama, K.; Matsumoto, K. *J. Chem. Soc., Chem. Commun.* **1984**, 548. Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, *21*, 2595.

An Efficient Screen for Determining Solid-State Hydrogen-Bonding Patterns in Carboxylic Acids

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Summary: Simple crystalline keto carboxylic acids adopt hydrogen-bonding modes that are either intra- or intermolecular, with the latter, far larger, class including carboxyl dimers and carboxyl-to-ketone catemers; it is demonstrated that symmetry-based differences between solid-state infrared and Raman spectra may be reliably used to differentiate those with dimeric H-bonding from those with noncentrosymmetric H-bonding patterns.

With few exceptions, simple carboxylic acids in their pure condensed phases exist as mutually hydrogen-bonded pairs.[1] However, when other functional groups capable

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[1] Leiserowitz, L. *Acta Crystallogr.* **1976**, *B32*, 775-802.