and natural abundance *R*-II (poly(S^*/R^*-II) and poly(S^*/R-II)).[12] ^{13}C CP MAS NMR spectra of poly(S^*/R^*-II) and poly(S^*/R-II) gave imine carbon resonances (165 ppm) with widths at half-height at 493 and 327 Hz, respectively. This peak narrowing can be attributed to a reduction in the ^{13}C–^{13}C dipole–dipole relaxation mechanism in the singly labeled sample as opposed to the doubly labeled sample due to ^{13}C spin dilution along the individual polymer chains.[17] Hence, the singly labeled sample must have ^{13}C (*S*) carbons bound to ^{12}C (*R*) carbons, demonstrating that poly(*R*/*S*-II) is, in fact, a stereocopolymer.

Contrary to reports in the literature, we have shown that stereoselectivity is realized only to a limited degree in the polymerizations of II and III, with the $\Delta\Delta G^\ddagger$ values obtained representing an upper limit to this process. In light of the fact that poly(II) is the most widely studied polyisocyanide[18] and often serves as a point of reference for other polyisocyanides,[11,19] the absence of absolute stereoselectivity in polymerizations of II places the universally presumed absolute stereoselectivity of less sterically encumbered polyisocyanides in serious doubt.

Acknowledgment. This work was supported by University of California "Start-up Funds", the National Science Foundation (Grant No. CHE-9023253), and generous contributions from E. I. du Pont de Nemours and Company, the Exxon Corporation, Amoco, Kodak, and Chevron Research, T.J.D. gratefully acknowledges the NSF for a graduate fellowship. We thank Dr. David Duff for assistance with the ^{13}C CP MAS NMR spectra.

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[17] Sanders, J. K. M.; Hunter, B. K. *Modern NMR Spectroscopy*; Oxford University Press: New York, 1987.

[18] (a) See ref 6a. See p 112 in this review and ref 109 therein. (b) Millich, F.; Baker, G. K. *Macromolecules* **1969**, *2*, 122. (c) Millich, F. *Adv. Polym. Sci.* **1975**, *19*, 117. (d) Millich, F. *Macromol. Rev.* **1980**, *15*, 207. (e) Huang, S. Y.; Hellmuth, E. W. *Polym. Prepr.* (*Am. Chem. Soc., Div. Polym. Chem.*) **1974**, *15*, 499. (f) Huang, S. Y.; Hellmuth, E. W. *Polym. Prepr.* (*Am. Chem. Soc., Div. Polym. Chem.*) **1974**, *15*, 505.

[19] (a) van Beijnen, A. J. M.; Nolte, R. J. M.; Drenth, W.; Hezemans, A. M. F. *Macromolecules* **1980**, *13*, 1386. (b) King, R. B.; Borodinsky, L. *Macromolecules* **1985**, *18*, 2117. (c) King, R. B.; Greene, M. J. *J. Polym. Sci., Polym. Chem. Ed.* **1987**, *25*, 907.

(Trifluoromethyl)copper: A Useful CF_2 Transfer Reagent. A Novel Double Insertion of Difluoromethylene into (Pentafluorophenyl)copper

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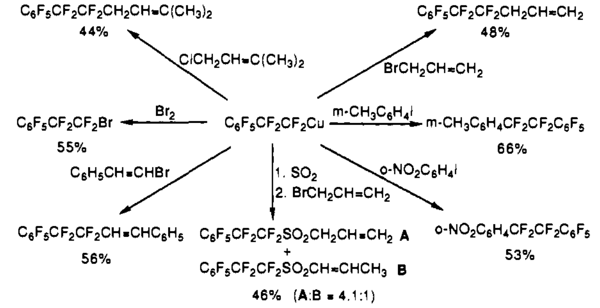
(Trifluoromethyl)copper has been demonstrated to be one of the most important reagents for the introduction of a trifluoromethyl group into organic molecules.[1] Previous preparations of this copper reagent have been achieved via the reaction of trifluoromethyl iodide, (trifluoromethyl)mercury, or iododifluoromethane sulfonyl fluoride with copper, but these methods have either employed expensive reagents or required high temperatures.

Scheme I



Recently, we reported a low-temperature pregenerative route to (trifluoromethyl)copper by the in situ metathesis of (trifluoromethyl)cadmium or -zinc reagents with cuprous halides.[2] The requisite cadmium and zinc reagents were prepared from the reaction of difluorodihalomethane with cadmium or zinc.[3] Although two different copper species can be formed in DMF solution, both slowly decompose at room temperature to afford (pentafluoroethyl)copper in quantitative yield.[2,4] The mechanism of the decomposition reaction has not been investigated in detail, but it is obvious that a CF_2 unit inserts into the carbon–copper bond. Since (trifluoromethyl)copper appeared to be a CF_2 transfer reagent, we were interested in determining whether (trifluoromethyl)copper could insert CF_2 units into other organometallic reagents or only insert into itself.

We report herein the preliminary results of a novel and efficient double insertion reaction of CF_2 into the carbon–copper bond of C_6F_5Cu generated from the metathesis of C_6F_5CdX with CuBr at room temperature. When a DMF solution of (pentafluorophenyl)copper was added to a DMF solution of (trifluoromethyl)copper at −30 °C and the resulting mixture was warmed to room temperature with stirring, $C_6F_5CF_2CF_2Cu$[5] was formed in 70–80% yields by ^{19}F NMR analysis of the reaction mixture. Since the exchange reaction of (perfluoroorgano)cadmium or -zinc reagents with cuprous halides occurs rapidly,[2] this insertion reaction could be simplified by in situ generation of the copper reagents. Thus, when 2 equiv of the (trifluoromethyl)cadmium or -zinc reagent and 1 equiv of C_6F_5CdX[6] were stirred with 3 equiv of CuBr in DMF at room temperature for 40 min, $C_6F_5CF_2CF_2Cu$ was observed in 70–80% yields.

$$C_6F_5Cu + 2CF_3Cu \xrightarrow[-30\ ^\circ\mathrm{C\ to\ RT}]{} \underset{70\text{–}80\%}{C_6F_5CF_2CF_2Cu}$$

$$\underset{M\,=\,Cd,\ Zn}{C_6F_5CdX + 2CF_3MX} \xrightarrow[RT]{CuBr} \underset{70\text{–}80\%}{C_6F_5CF_2CF_2Cu}$$

Multiple insertion of CF_2 units into C_6F_5Cu was not observed even when a large excess of CF_3Cu was utilized. When 3–9 equiv of CF_3Cu was slowly added to a solution of C_6F_5Cu, only $C_6F_5CF_2CF_2Cu$ and CF_3CF_2Cu were formed; no $C_6F_5(CF_2)_nCu$ ($n > 2$) was detected by ^{19}F NMR analysis of the reaction mixture. Insertion of CF_2 into the primary copper reagent, $C_6F_5CF_2CF_2Cu$, is slower than insertion into the more reactive CF_3Cu.

Previous reports have demonstrated that the formation of (trifluoromethyl)cadmium or -zinc reagents from difluorohalomethane involved difluorocarbene as an intermediate,[3] and $(CF_3)_2Cd$ has been used to produce difluorocarbene which can be trapped by alkenes.[7] Although the product was formed, apparently from the double insertion of difluoromethylene into the carbon–copper bond, no evidence was obtained for a free di-

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[1] (a) McLoughlin, V. C. R.; Thrower, J. *Tetrahedron* **1969**, *25*, 5921. (b) Kobayashi, Y.; Kumadaki, I. *Tetrahedron Lett.* **1969**, 4095. (c) Kobayashi, Y.; Kumadaki, I.; Sato, S.; Hara, N.; Chidami, E. *Chem. Pharm. Bull.* **1970**, *18*, 2334. (d) Kobayashi, Y.; Kumadaki, I.; Hanzawa, Y. *Chem. Pharm. Bull.* **1977**, *25*, 3009. (e) Kobayashi, Y.; Yamamoto, K.; Kumadaki, I. *Tetrahedron Lett.* **1979**, 4071. (f) Kobayashi, Y.; Kumadaki, I. *J. Chem. Soc., Perkin Trans. 1* **1980**, 661. (g) Kobayashi, Y.; Yamamoto, K.; Asai, T.; Nakano, M.; Kumadaki, I. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2755. (h) Kondratenko, N. V.; Vechirko, E. P.; Yagupolskii, L. M. *Synthesis* **1980**, 932. (i) Matsui, K.; Tobita, E.; Ando, M.; Kondo, K. *Chem. Lett.* **1981**, 1719. (j) Suzuki, H.; Yoshida, Y.; Osuka, A. *Chem. Lett.* **1983**, 135. (k) Carr, G. E.; Chambers, R. D.; Holmes, T. F. *J. Chem. Soc., Perkin Trans. 1* **1988**, 921. (l) Chen, Q.-Y.; Wu, S.-W. *J. Chem. Soc., Chem. Commun.* **1989**, 705. (m) Chen, Q.-Y.; Wu, S.-W. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2385. (n) Urata, H.; Fuchikami, T. *Tetrahedron Lett.* **1991**, *32*, 91. MacNeil, J. G.; Burton, D. J. *J. Fluorine Chem.*, in press.

[2] Wiemers, D. M.; Burton, D. J. *J. Am. Chem. Soc.* **1986**, *108*, 832.

[3] (a) Burton, D. J.; Wiemers, D. M. *J. Am. Chem. Soc.* **1985**, *107*, 5014. (b) Dolbier, W. R., Jr.; Wojtowicz, H.; Burkholder, C. R. *J. Org. Chem.* **1990**, *55*, 5420.

[4] Willert-Porada, M.; Burton, D. J.; Baenziger, N. C. *J. Chem. Soc., Chem. Commun.* **1989**, 1633.

[5] $C_6F_5CF_2CF_2Cu$: ^{19}F NMR (DMF, vs $C_6H_5CF_3$) −39.0 (t, J = 29.3 Hz, 2 F), −44.6 (s, 2 F), −77.2 (m, 2 F), −90.1 (m, 1 F), −101.1 (m, 2 F).

[6] Heinze, P. L.; Burton, D. J. *J. Fluorine Chem.* **1985**, *29*, 359.

[7] Krause, L. J.; Morrison, J. A. *J. Chem. Soc., Chem. Commun.* **1980**, 671.

J. Am. Chem. Soc. **1992**, *114*, 4403-4405

fluorocarbene intermediate. When the insertion reaction was carried out in the presence of an excess of tetramethylethylene, the sole product was $C_6F_5CF_2CF_2Cu$; no difluorocyclopropane derivative was observed. We propose that CF_3Cu is in equilibrium with a copper difluorocarbenoid complex,[8] followed by insertion into the C–Cu bond of C_6F_5Cu to form $C_6F_5CF_2Cu$, which is more reactive toward insertion than C_6F_5Cu. Consequently, only the double insertion product was formed. When the stoichiometry of C_6F_5Cu and CF_3Cu was 1:1, $C_6F_5CF_2CF_2Cu$ was formed in 55% yield and 45% of C_6F_5Cu remained. In the case of the addition of pregenerated $C_6F_5CF_2CdX$[9] to a solution of CF_3CdX in the presence of CuBr, $C_6F_5CF_2CF_2Cu$[10] was observed by ^{19}F NMR analysis.

$$CF_3Cu \rightleftharpoons CF_2{=}CuF$$

$$C_6F_5Cu + CF_2{=}CuF \xrightarrow{\text{slow}} C_6F_5CF_2Cu$$

$$C_6F_5CF_2Cu + CF_2{=}CuF \xrightarrow{\text{fast}} C_6F_5CF_2CF_2Cu$$

$C_6F_5CF_2CF_2Cu$ exhibits good thermal stability from room temperature to 55 °C. At higher temperatures (>85 °C) it undergoes decomposition.

Typical reactions of the (perfluoro-2-phenylethyl)copper reagent formed in situ are illustrated in Scheme I.

In conclusion, this work demonstrates that (trifluoromethyl)copper can be used for the insertion of CF_2 units into the carbon–copper bond of (pentafluorophenyl)copper and provides an unequivocal route to the (perfluoro-2-phenylethyl)copper reagent.[11] This reagent is also produced in high yield in situ from the (trifluoromethyl)cadmium or -zinc reagents and the (pentafluorophenyl)cadmium reagent in the presence of cuprous halide under mild conditions. Future work will focus on the applicability and generality of this novel difluoromethylene insertion process.

Acknowledgment. We thank the National Science Foundation for generous support of this work and Professor V. Platonov for a sample of $C_6F_5CF_2Br$.

Registry No. A, 140468-37-7; B, 140468-38-8; $C_6F_5CF_2CF_2Br$, 140468-34-4; C_6F_5CdBr, 104698-12-6; CF_3ZnBr, 97571-13-6; $C_6F_5CF_2CF_2Cu$, 140468-35-5; $C_6F_5CF_2CF_2SO_2Cu$, 140468-36-6; CF_3CdBr, 97571-11-4; $C_6F_5CF_2CF_2CH_2CH{=}CH_2$, 140468-39-9; $ClCH_2CH{=}C(CH_3)_2$, 503-60-6; $C_6F_5CF_2CF_2CH_2CH{=}C(CH_3)_2$, 140468-40-2; $C_6F_5CF_2CF_2CH{=}CHC_6H_5$, 140468-41-3; $C_6H_5CH{=}CHBr$, 103-64-0; *m*-$CH_3C_6H_4CF_2CF_2C_6F_5$, 140468-42-4; *m*-$CH_3C_6H_4I$, 625-95-6; *o*-$NO_2C_6H_4CF_2CF_2C_6F_5$, 140468-43-5; *o*-$NO_2C_6H_4I$, 609-73-4; $C_6F_5CF_2Br$, 35523-39-8; $C_6F_5CF_2Cu$, 140468-44-6; $C_6F_5CF_2CdCF_2C_6F_5$, 140468-45-7; $C_6F_5CF_2CdBr$, 140468-46-8.

Supplementary Material Available: Experimental procedures, characterization data, and NMR spectra for all compounds described in Scheme I, as well as ^{19}F NMR spectra of $C_6F_5CF_2CdX$ (X = Br, $CF_2C_6F_5$), $C_6F_5CF_2Cu$, and $C_6F_5CF_2CF_2Cu$ and ^{113}Cd NMR spectra of $C_6F_5CF_2CdX$ (X = Br, $CF_2C_6F_5$) (55 pages). Ordering information is given on any current masthead page.

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(8) Transition metal trifluoromethyl complexes (CF_3–M) exhibit strong M–C and weak C–F bonds. Clark and Tsai have proposed a hyperconjugation argument that employs "no-bond" resonance structures $(M{=}CF_2)^+F^-$. See: Clark, H. C.; Tsai, J. H. *J. Organomet. Chem.* **1967**, *7*, 515. Also see: Cotton, F. A.; McCleverty, J. A. *J. Organomet. Chem.* **1965**, *4*, 490. Cotton, F. A.; Wing, R. M. *J. Organomet. Chem.* **1967**, *9*, 511. Lichtenberger, D. L.; Fenske, R. F. *Inorg. Chem.* **1974**, *13*, 486. Hall, M. B.; Fenske, R. F. *Inorg. Chem.* **1972**, *11*, 768. Brothers, P. J.; Roper, W. R. *Chem. Rev.* **1988**, *88*, 1293.

(9) $C_6F_5CF_2CdX$ could be readily prepared from the reaction of $C_6F_5CF_2Br$ and cadmium in DMF at room temperature. Metathesis of the cadmium reagent with CuBr at −35 °C gave a (perfluorobenzyl)copper reagent. ^{19}F NMR (DMF, vs $C_6H_5CF_3$) indicated two species of the copper reagent in a 7:1 ratio: **A**, −24.1 (t, *J* = 22.0 Hz, 2 F), −82.8 (m, 2 F), −97.7 (m, 1 F), −102.4 (m, 2 F); B, −28.0 (t, *J* = 22.0 Hz, 2 F), −82.8 (m, 2 F), −97.7 (m, 1 F), −102.4 (m, 2 F). Addition of allyl bromide to the copper reagent solution caused the disappearance of both species and resulted in the formation of $C_6F_5CF_2CH_2CH{=}CH_2$.

(10) The enhanced reactivity of $C_6F_5CF_2Cu$ relative to C_6F_5Cu correlates with the stability of these reagents. $C_6F_5CF_2Cu$ decomposes readily at room temperature, whereas C_6F_5Cu is stable indefinitely at room temperature.

(11) The insertion process is not specific for C_6F_5Cu. Other fluorinated copper reagents exhibit similar behavior. Preliminary work with *p*-XC_6F_4Cu (X = H, CH_3O) yields *p*-$XC_6F_4CF_2CF_2Cu$. Similarly, $\overline{C_2F_2NC_2F_2C}Cu$ gives $\overline{C_2F_2NC_2F_2C}CF_2CF_2Cu$ and (*Z*)-$CF_3CF{=}CFCu$ gives (*E*)-$CF_3CF{=}CFCF_2CF_2Cu$ under similar conditions. In related work,[12] $(EtO)_2P(O)CF_2Cu$ inserted CF_2 to produce $(EtO)_2P(O)CF_2CF_2Cu$.

(12) Work in progress with H. K. Nair.

Synthesis of Strychnine via the Wieland–Gumlich Aldehyde

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The synthesis of strychnine (**1**) by Woodward[1] not only confirmed its structure but also was the first total synthesis of a complicated natural product. Considering the extensive synthetic efforts devoted to indole alkaloids, the original Woodward report (1953) still stands as the only synthesis of strychnine.[2]

As part of our studies on the synthesis of heptacyclic indole alkaloids,[3] we report the synthesis of the hexacyclic relay compound **2**, Scheme I, which has been correlated by degradation of strychnine, and its conversion into strychnine.

The tetracyclic amine **3**[4] (Scheme II) was treated with β,β,β-trichloroethyl chloroformate to give a mixture of **4** (38%) and **5** (25%). Exposure of **4** to NaOMe/MeOH gave **5** (62% from **3**). Protection of the indole nitrogen and reductive removal of the β,β,β-trichloroethyl carbamate (Zn/AcOH/THF) gave the secondary amine **7**. Acetylation of **7** with $PhSCH_2CO_2H$/BOPCl gave the amide **8**, which was directly oxidized to the diastereomeric sulfoxides **9**. Treatment of **9** with NaH/THF resulted in intramolecular conjugate addition to give the tetracyclic lactam **10** (as a mixture of stereoisomers at the C–S and S–O bonds). Similarly the sulfide **8** gave the corresponding tetracyclic lactam sulfide **10a** (X-ray). The mixture of sulfoxides **10** was subjected to Pummerer-type conditions followed by mercuric ion assisted hydrolysis to give the dione **11** as a single stereoisomer which exists in

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(1) Woodward, R. B.; Cava, M. P.; Ollis, W. D.; Hunger, A.; Daeniker, H. U.; Schenker, K. *J. Am. Chem. Soc.* **1954**, *76*, 4749. Woodward, R. B.; Cava, M. P.; Ollis, W. D.; Hunger, A.; Daeniker, H. U.; Schenker, K. *Tetrahedron* **1963**, *19*, 247.

(2) Most recent published synthetic approaches: Fevig, J. M.; Marquis, R. W., Jr.; Overman, L. E. *J. Am. Chem. Soc.* **1991**, *113*, 5085. Kuehne, M. E.; Frasier, D. A.; Spitzer, T. D. *J. Org. Chem.* **1991**, *56*, 2696. Grotjahn, D. B.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1990**, *112*, 5653. Kraus, G. A.; Thomas, P. J.; Bougie, D.; Chen, L. *J. Org. Chem.* **1990**, *55*, 1624. Legseir, B.; Henin, J.; Massiot, G.; Vercauteren, J. *Tetrahedron Lett.* **1987**, *28*, 3573. Bonjoch, J.; Casamitjana, N.; Quirante, J.; Rodriquez, M.; Bosch, J. *J. Org. Chem.* **1987**, *52*, 267. There are numerous other reports of synthetic endeavors, and these are referred to in the following: Massiot, G.; Delaude, C. African *Strychnos* Alkaloids. In *The Alkaloids*; Brossi, A., Ed.; Academic Press: New York, 1988; Vol. 34, p 211. Bosch, J.; Bonjoch, J. Pentacyclic *Strychnos* Alkaloids. In *Studies in Natural Products Chemistry*; Rahman, A., Ed.; Elsevier: Amsterdam, 1988; Vol. 1, p 31.

(3) Magnus, P.; Katoh, T.; Matthews, I.; Huffman, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 6707. Magnus, P.; Gallagher, T.; Brown, P. *J. Am. Chem. Soc.* **1984**, *106*, 2105. Gallagher, T.; Huffman, J. C.; Magnus, P. *J. Am. Chem. Soc.* **1983**, *105*, 2086. Magnus, P.; Gallagher, T.; Brown, P.; Pappalardo, P. *Acc. Chem. Res.* **1984**, *17*, 35.

(4) Magnus, P.; Ladlow, M.; Elliott, J.; Kim, C.-S. *J. Chem. Soc., Chem. Commun.* **1989**, 518. Ethyl ester of **3**: Wenkert, E.; Garratt, S.; Dave, K. G. *Can. J. Chem.* **1964**, *42*, 489.

0002-7863/92/1514-4403$03.00/0