spectrum, *m/z* 272. Anal. C, 70.32; H, 5.85. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92.

Acknowledgment. We thank Dr. Silvio Biali for discussions. This work was supported by The Israel Commission for Basic Research, The Israel Academy for Sciences and Humanities, to which we are grateful.

Registry No. 1, 20797-56-2; **2a**, 116437-29-7; **2b**, 4541-73-5; anisole, 100-66-3.

Parameterization of Cyano Group MM2 Constants in Peracetylated Aldononitriles

Josep Castells, Carlos Jaime,*,† Francisco López-Calahorra,*
Núria Santaló, and Dolores Velasco

Department Química Orgânica, Universitat de Barcelona,
Martí i Franquès, 1, 08028 Barcelona, Spain, and
Department Química, Unitat Química Orgânica, Universitat
Autônoma de Barcelona, 08193 Bellaterra (Barcelona),
Spain

Received February 19, 1988

Allinger's MM2 program[1] includes bending and torsional constants related to alkyl cyano groups; however, it does not permit the direct application to combinations of cyano and other functional groups. One of these is an acyloxy group α to the cyano group. This combination is typical in peracetylated aldononitriles, derivatives extensively used in the analysis of sugars.[2] Accordingly, the bending C_{sp}–C_{sp^3}–O_{sp^3} (type 4-1-6) and the torsional constants C_{sp}–C_{sp^3}–O_{sp^3}–C_{sp^2} (type 4-1-6-3) and C_{sp}–C_{sp^3}–O_{sp^3}–LP (type 4-1-6-20)[3] are here parameterized; PAAN compounds can be studied with the MM2 approach.

Experimentally determined structural data (bond lengths and angles and dihedral angles) have been reported for molecules **1**–**13**.[4–16] Molecules **4**–**13** were studied by X-ray diffraction, **1** was studied by electron diffraction,[4] and **2** and **3** by microwave spectroscopy.[5,6]

In general, good agreement was obtained between the reported experimental structural values and our own calculated values with the MM2(77) program;[17] however, the MM2 nitrogen(sp)–carbon(sp) bond lengths were appreciably and systematically longer than the experimental values (σ 0.0260). Readjustment of the reported 4-10 (C_{sp}–N_{sp}) stretching values led to the following parameters: l_0 = 1.135 Å and k_s = 18.500 mdyn/Å, in a better concordance with the experimental results (σ 0.0123). Experimental and calculated bond and angles related to the cyano group were in good agreement.

The correctness of torsional constants is confirmed by comparing experimental and calculated conformational energy (enthalpy) differences; in fact, the torsional contribution to the energy may overshadow all other energetic contributions. However, the experimental energy differences between conformers in acyclic molecules are scarce; indeed, experimental data were only available for **17**[18] and **21**.[19] The necessary values were obtained by following Allinger's practice[20] using MO calculations. The present study has been carried throughout within the MNDO approximation.[21] Our attention was centered on two groups of molecules: nitriles **17**–**20** (to evaluate the 4-1-1-1 (C_{sp}–C_{sp^3}–C_{sp^3}–C_{sp^3}) torsion parameters) and hydroxy nitriles **21**–**25** (to evaluate the 4-1-1-6 (C_{sp}–C_{sp^3}–C_{sp^3}–O_{sp^3}) torsion parameters).

Because of symmetry factors, molecules **17**, **19**, **20**, **23**, and **25** have only two energetically different conformers. The MNDO ΔH_f's of these conformers are collected in Table I; they lead directly to the conformational enthalpy differences shown in Table II. A correction factor of 0.84 kcal/mol was introduced to get acceptable agreement between experimental and theoretically[22] evaluated conformational enthalpy differences. The values $\Delta\Delta H_f$("exp") are the differences to be used in substitution of the experimentally unavailable ones when parameterization is done.

Empirical calculations on molecules **17**–**25** with the current MM2 values led to anti–gauche enthalpy differences smaller than they should be. The calculation of the standard deviation (root mean square, rms) with current MM2 values for the 4-1-1-1 and 4-1-1-6 torsion parameters gave the unsatisfactory values 0.68 and 0.61, respectively; consequently, a reparameterization process of 4-1-1-1 and 4-1-1-6 torsion values was undertaken.

Values of ΔH_f of gauche conformers more negative than those of the anti ones forces either V_1 or V_2 to be smaller or negative. Assigning negative values to V_1 is not convenient because it leads to a simultaneous stabilization for the eclipsed ($w = 0°$) conformer; consequently, values of V_2 more negative than the (already negative) current ones were studied. Best results were attained by making $V_2 = -1.1$ and readjusting the V_3 parameter. A larger V_3 value leads to a smaller σ but, simultaneously, to a higher energy for the eclipsed conformer and to an incorrectly high C_{sp^3}–C_{sp^3} rotation barrier. The compromise set of values provisionally adopted for the 4-1-1-1 torsional parameters was $V_1 = 0.2$, $V_2 = -1.1$ and $V_3 = 0.2$; this leads to a σ value of 0.20.

Hydroxy nitriles **21**–**25** were used to reparameterize the 4-1-1-6 constants and to refine the 4-1-1-1 constants, which also intervene in the empirical MM2 conformational energy calculations of those molecules. The *experimental* ΔH_f differences between the gauche and anti conformers in **17** (0.42 kcal/mol) and **21** ($\geq$0.72 kcal/mol) show that V_2-

---

† Universitat Autônoma de Barcelona.

(1) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. (b) Allinger, N. L.; Yuh, Y. H. *QCPE* **1980**, *12*, 395.

(2) Seymour, F. R.; Chen, E. C. M.; Bishop, S. H. *Carbohydr. Res.* **1979**, 19.

(3) MM2 program considers lone pairs of electrons as pseudoatoms.

(4) Danford, M. D.; Livinston, R. L. *J. Am. Chem. Soc.* **1955**, *77*, 2944.

(5) Lerner, R. G.; Dailey, B. P. *J. Chem. Phys.* **1957**, *26*, 678.

(6) Nugent, J.; Mann, E.; Licte, R. *J. Chem. Phys.* **1962**, *36*, 965.

(7) Viani, R.; Lapasset, J. *Acta Crystallogr., Sect. B* **1978**, *34*, 1190.

(8) Roques, R.; Guy, E. *Acta Crystallogr., Sect. B* **1976**, *32*, 602.

(9) Lynton, H.; Siew, Y. *Can. J. Chem.* **1975**, *53*, 192.

(10) Reck, G. *Cryst. Struct. Commun.* **1982**, *11*, 1815.

(11) Stanford, H.; Mckenzie, C. *Acta Crystallogr., Sect. B* **1974**, *30*, 421.

(12) Pêrez Salazsar, A.; Cano, F. H.; Martînez Carrera, S.; Garcîa Blanco, S. *Acta Crystallogr., Sect. B* **1977**, *33*, 2276.

(13) Viani, R.; Cossu, M.; Lapasset, J. *Acta Crystallogr., Sect. B* **1981**, *37*, 484.

(14) Cossu, M.; Viani, R.; Lapasset, J. *Acta Crystallogr., Sect. B* **1981**, *37*, 481.

(15) Beagley, B.; Morton, P.; Pritchard, G.; Ramage, P. *Acta Crystallogr., Sect. B* **1982**, *38*, 1393.

(16) Gassman, G.; Saito, K.; Talley, J. *J. Am. Chem. Soc.* **1980**, *102*, 7613.

(17) Some values of molecule **9** have not been taken into account in calculating the standard deviation (root mean square) because they belong to groupings with aromatic C atoms (4-1-2 and 4-1-2-2), which themselves await reparameterization.

(18) Fujiyama, T. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3317.

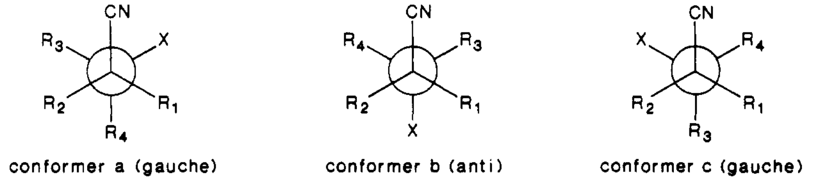
(19) Schneider, M.; Giguère, A. *Can. J. Chem.* **1969**, *47*, 4685.

(20) (a) Allinger, N. L.; Hickey, M. J. *Tetrahedron* **1972**, *28*, 2157. (b) See ref 62 in Osawa, E.; Müsso, H. *Top. Stereochem.* **1982**, *22*, 117.

(21) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899. (b) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4907.

(22) Unpublished results.

Table I. Calculated MNDO Values of the Formation Enthalpy for the Different Conformers Looking through the Angle NC–C–C–X (Related Dihedral Angles Are Also Given)



molecule	conformer	X	R_1	R_2	R_3	R_4	$\theta_{NC-C-C-X}$, deg	ΔH_f, kcal/mol
18	a	CH_3	CH_3	H	H	H	63.26	8.16
	b	CH_3	CH_3	H	H	H	−165.24	8.09
	c	CH_3	CH_3	H	H	H	−66.05	7.64
19	a	CH_3	CH_3	CH_3	H	H	59.97	10.60
	b	CH_3	CH_3	CH_3	H	H	−179.91	11.00
20	a	CH_3	H	H	CH_3	H	64.76	8.28
	b	CH_3	H	H	CH_3	H	−166.57	8.29
22	a	OH	CH_3	H	H	H	63.01	−30.60
	b	OH	CH_3	H	H	H	168.89	−30.47
	c	OH	CH_3	H	H	H	−63.04	−30.64
23	a	OH	CH_3	CH_3	H	H	58.76	−28.49
	b	OH	CH_3	CH_3	H	H	179.99	−28.42
24	a	OH	H	H	H	CH_3	63.21	−30.81
	b	OH	H	H	H	CH_3	168.49	−30.33
	c	OH	H	H	H	CH_3	−60.83	−30.48
25	a	OH	H	H	CH_3	CH_3	57.51	−28.74
	b	OH	H	H	CH_3	CH_3	179.94	−28.25
26	a	$COCH_3$	H	H			180.04	−57.27
	b	$COCH_3$	H	H			80.67	−57.27
27	a	$COCH_3$	CH_3	H			59.80	−58.65
	c	$COCH_3$	CH_3	H			−80.83	−60.32
28	a	$COCH_3$	CH_3	CH_3			54.54	−57.87
	b	$COCH_3$	CH_3	CH_3			179.92	−56.90
29	a	$COCH_3$	CH_2CH_3	H			57.17	−62.74
	c	$COCH_3$	CH_2CH_3	H			−81.00	−64.54

Table II. Calculated Conformational Enthalpy Differences for Molecules in Table I

molecule	$\Delta\Delta H_{MNDO}$, kcal/mol	$\Delta\Delta H_{\text{"exp"}}$,[a] kcal/mol	molecule	$\Delta\Delta H_{MNDO}$, kcal/mol	$\Delta\Delta H_{\text{"exp"}}$,[a] kcal/mol
18b–18a	−0.07	0.77	**24b–24a**	0.48	0.48
18b–18c	0.45	1.29	**24b–24c**	0.15	0.99
19b–19a	0.40	1.24	**25b–25a**	0.49	0.49
20b–20a	0.01	0.85	**26b–26a**	0.00	0.84
22b–22a	0.13	0.97	**27a–27c**	1.67	1.67
22b–22c	0.17	1.01	**28b–28a**	0.97	1.81
23b–23a	0.07	0.91	**29a–29c**	1.80	1.80

[a] $\Delta\Delta H_{\text{"exp"}} = \Delta\Delta H_{MNDO} + \Delta H_{correc}$.

(4-1-1-6) must be more negative than for the V_2(4-1-1-1). Parameterization in a combined and iterative manner afforded the following final set of values, for which the σ value is 0.25 now, 4-1-1-1: $V_1 = 0.2$, $V_2 = -0.95$, $V_3 = 0.2$; 4-1-1-6: $V_1 = 0.0$, $V_2 = -1.1$, $V_3 = 0.2$.

The α-acyloxy substituent to a cyano group introduces three structural features that are not parameterized into the MM2 program: the 4-1-6 (C_{sp}–C_{sp^3}–O_{sp^3}) bond angle and the 4-1-6-3 (C_{sp}–C_{sp^3}–O_{sp^3}–C_{sp^2}) and 4-1-6-20 (C_{sp}–C_{sp^3}–O_{sp^3}–LP) dihedral angles.

Parameterization of the 4-1-6 bending constants was done with reference to the experimental values of the C_{sp}–C_{sp^3}–O_{sp^3} angle in the cyano-containing molecules **14**–**16**.[23-26] The current values for the 2-1-6 (C_{sp^2}–C_{sp^3}–O_{sp^3}) bending constants[27] were taken as starting values in the parameterization process. However, values for the 4-1-6-20 (in molecules **14**,–**16**), 4-1-6-1 (in molecules **14** and **15**), and 4-1-6-3 (in molecule **16**) torsional constants were needed; since they are unavailable, zero was provisionally used in all cases. The use of the 2-1-6 bending values gives an unsatisfactory σ value of 3.06. After a series of adjustments, the set $k_b = 0.9$ mdyn Å/rad^2 and $\theta_o = 105.0°$, for which σ is 0.89, was considered to be a convenient one.

As experimental energy differences for conformers of molecules including the 4-1-6-3 unit are not available, molecules ^{2}6–^{2}9 were theoretically studied as before; the results are included in Table I and II. No correction factor (0.84 kcal/mol) was applied in calculating the **27a**–**c** and **29a**–**c** energy differences because the CH_3CO substituent is always in a gauche position relative to the cyano group in these conformers.[22] After several trial-and-error adjustments, the best 4-1-6-3 and 4-1-6-20 torsional parameters were considered to be $V_1 = 0.3$, $V_2 = -2.5$, $V_3 = -0.4$ and $V_1 = 1.0$, $V_2 = -0.2$, $V_3 = 0.0$ kcal/mol, respectively. With these constants, a σ of 0.64 ensued. It is worth pointing out that the global standard deviation for the conformational energy $\sigma = 0.38$ for the complete set of studied molecules (**17**–**25** and **26**–**29**). Finally, the whole

---

[23] Foces-Foces, C.; Cano, F. H.; García-Blanco, S. *Acta Crystallogr., Sect. B* **1976**, *32*, 964.

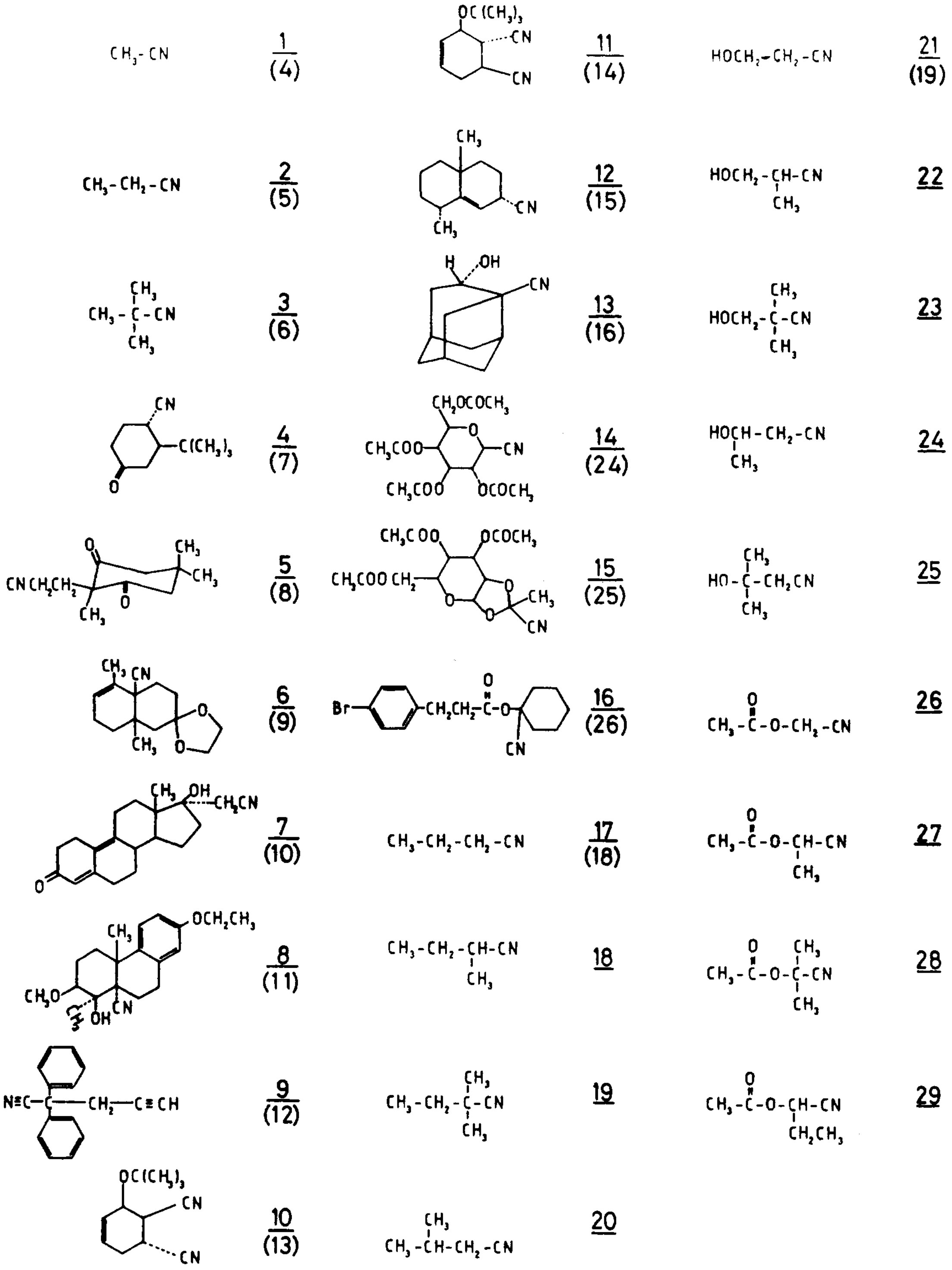
[24] Foces-Foces, C.; Cano, F. H.; García-Blanco, S. *Acta Crystallogr., Sect. B* **1976**, *32*, 3029.

[25] Sova, V. *Zh. Strukt. Khim.* **1971**, *12*, 1032.

[26] For the sake of simplicity, the Br atom in molecule **16** (located at several bonds from the cyano group) was considered to be an H atom.

[27] $k_B = 0.7$ mdyn Å/rad^2, $\theta_o = 109.5°$.

Chart I[a]



[a] References in parentheses.

set of reparameterized and parameterized constants (including the 4-1-6 bending constants) were checked by reproducing the experimental structural data for molecules 1–13[4–16] and 14–16,[23–26] and excellent agreement was obtained.[28] The significant results of this work are summarized in Table III.

Table III. New Set of Constant Parameters Related to Cyano Group

structural features	constants parameters
N_{sp}–C_{sp}	$l_0 = 1.135$, $k_s = 18.500$
C_{sp}–C_{sp^3}–O_{sp^3}	$\theta_0 = 105.0$, $k_b = 0.9$
C_{sp}–C_{sp^3}–C_{sp^3}–C_{sp^3}	$V_1 = 0.2$, $V_2 = -0.95$, $V_3 = 0.2$
C_{sp}–C_{sp^3}–C_{sp^3}–O_{sp^3}	$V_1 = 0.0$, $V_2 = -1.1$, $V_3 = 0.2$
C_{sp}–C_{sp^3}–O_{sp^3}–C_{sp^2}	$V_1 = 0.3$, $V_2 = -2.5$, $V_3 = -0.4$
C_{sp}–C_{sp^3}–O_{sp^3}–LP	$V_1 = 1.0$, $V_2 = -0.2$, $V_3 = 0.0$

Computational Methods

All MM2 and MNDO calculations were carried out with local IBM/CMS versions of MM2[1] and MOPAC[29] program with

---

(28) Standard deviation (root mean square) for the different structural features: N_{sp}–C_{sp}, 0.014; C_{sp}–C_{sp^3}, 0.0016; N_{sp}–C_{sp}–C_{sp^3}, 2.32 (This value σ 2.32, significantly reduces to 1.71 if the reported 172.594° value for the molecule[25] 16 is excluded; in fact, value is questionable because it differs greatly from the "normal" 180° value.); C_{sp}–C_{sp^3}–X ($X = C_{sp^3}$, C_{sp^2}, O_{sp^3}, H), 1.79; C_{sp}–C_{sp^3}–X–Y (X = C_{sp^3}, C_{sp^2}, O_{sp^3}; Y = C_{sp^3}, C_{sp^2}, O_{sp^3}, H), 3.79.

standard parameters. Optimized structures were determined by minimizing the energy with respect to all geometrical parameters without imposing molecular symmetry constraints.

Supplementary Material Available: Tables comparing experimental and MM2 calculated structural features (2 pages). Ordering information is given on any current masthead page.

---

[29] (a) Stewart, J. J. P. *QCPE Bull.* **1983**, *3*, 101. (b) Olivella, S. *QCPE Bull.* **1984**, *4*, 109.

Dilithium (Trimethylstannyl)(2-thienyl)(cyano)cuprate, a Synthetically Useful Higher Order Cuprate Reagent

Edward Piers* and Richard D. Tillyer

Department of Chemistry, University of British Columbia, Vancouver, B.C., Canada V6T 1Y6

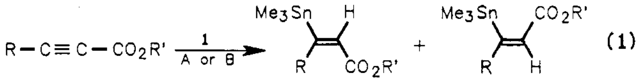
Received May 4, 1988

Recently, we described, inter alia, the preparation of lithium (trimethylstannyl)(phenylthio)cuprate (1) and showed that this lower order cuprate reagent readily transfers the Me_3Sn moiety to the β carbon of a variety of α,β-unsaturated carbonyl compounds.[1] Subsequently,

$[Me_3SnCuSPh]Li$

1

it was shown that 1 can be used effectively for the conversion of α,β-acetylenic esters 2 into either alkyl (E)- or (Z)-3-(trimethylstannyl)-2-alkenoates (3, 4, respectively).[2] Thus, treatment of substrates 2 with reagent 1 in tetrahydrofuran (THF) at -78 °C in the presence of methanol (conditions A, eq 1) provides, stereoselectively, the E products 3, while reaction of 2 with 1 under conditions B, eq 1, gives largely the Z products 4.[2a,c] Interestingly, of the various (trimethylstannyl)copper(I) reagents employed thus far in our work,[1,2] a number of them may be used for the stereoselective transformation of 2 into 3,[2] while only 1 effects the efficient, stereocontrolled conversion of 2 into 4.[2a,c]



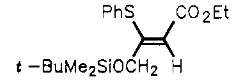
(1)

2	3		4
A: THF, MeOH, −78°C	≥96	:	≤ 4
B: THF, −48°C; MeOH	≤ 7	:	≥93

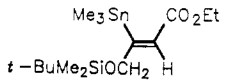
It was found, however, that the reactions of 1 with α,β-acetylenic esters containing an ether function on the γ carbon were anomalous. For example, reaction of 1 with 5 under conditions B outlined in eq 1 gave 6 as the major product (35%).[2b,c] The expected, desired product 7 was produced in only 29% yield.[2b,c] The preferred transfer of the phenylthio group was also observed in the reaction of reagent 1 with other α,β-acetylenic esters of general structure 8. Since, in connection with other research projects, we required compounds of general structure 9, we were interested in finding a (trimethylstannyl)copper(I) reagent that would convert 8 into 9 in a clean, efficient manner.

$t\text{-}BuMe_2SiOCH_2-C{\equiv}C-CO_2Et$

5



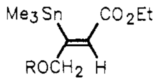
6



7

$ROCH_2C{\equiv}C-CO_2R'$

8



9

$Me_3SnCu(2\text{-}Th)(CN)Li_2$

10

Although intermediates derived from the interaction of various (trimethylstannyl)copper(I) reagents with α,β-acetylenic esters 1 are readily protonated to afford 3 and/or 4 (eq 1), we[3] and others[4] have shown that these intermediates cannot be trapped with electrophiles other than a proton. Consequently, another goal of the present work was to search for a reagent that, upon transfer of the Me_3Sn group to the β carbon of substrates 1, would produce intermediates that would be amenable to reaction with other electrophiles, particularly alkylating agents.

Important recent work in organocopper chemistry has shown that higher order alkyl, alkenyl, and aryl cuprates are readily prepared and possess very useful chemical reactivity.[5] In many instances, these reagents are synthetically superior to the corresponding lower order cuprates. Consequently, it seemed worthwhile to investigate the possibility that a higher order (trimethylstannyl)cuprate might serve our purposes in connection with the problems outlined above. We summarize herein the results of a brief study on the synthesis and chemistry of one such reagent, dilithium (trimethylstannyl)(2-thienyl)(cyano)cuprate (10).[6]

Results and Discussion

(a) Preparation of Reagent 10. A convenient method for preparing the higher order cuprate 10 involved the following procedure. Ethereal MeLi (2 equiv) was added to a THF solution (-20 °C) of a mixture of $(Me_3Sn)_2$ (1 equiv) and thiophene (1 equiv). After the solution had been stirred at -20 °C for 50 min, it was cooled to -78 °C and solid CuCN (1 equiv) was added. Warming of the resultant suspension to -48 °C afforded a bright yellow solution of reagent 10, which was used immediately.

(b) Reaction of 10 with α,β-Unsaturated Carbonyl Compounds. In order to acquire information regarding the chemical reactivity of reagent 10, its reaction with a number of α,β-unsaturated carbonyl compounds was carried out. Treatment of the enones 11 and 12 with 1.5 equiv of 10 in THF at -20 °C gave the corresponding conjugate addition products 18 (90%) and 19[1b] (87%), respectively. A similar reaction involving (R)-(+)-pulegone (13) afforded

---

[1] (a) Piers, E.; Morton, H. E. *J. Chem. Soc., Chem. Commun.* **1978**, 1034. (b) Piers, E.; Morton, H. E.; Chong, J. M. *Can. J. Chem.* **1987**, *78*, 65.

[2] (a) Piers, E.; Morton, H. E. *J. Org. Chem.* **1980**, *45*, 4263. (b) Piers, E.; Chong, J. M.; Morton, H. E. *Tetrahedron Lett.* **1981**, *49*, 4905. (c) Piers, E.; Chong, J. M.; Morton, H. E., submitted for publication in *Tetrahedron*.

[3] Piers, E.; Chong, J. M. *J. Org. Chem.* **1982**, *47*, 1602.

[4] Cox, S. D.; Wudl, F. *Organometallics* **1983**, *2*, 184.

[5] (a) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *24*, 5005. (b) Lipshutz, B. H. *Synthesis* **1987**, 325.

[6] 2-Th refers to the 2-thienyl group. This moiety has been shown to be an excellent nontransferable ligand for mixed organocuprates and has been employed by Lipshutz and co-workers[5,7] in the preparation of versatile higher order cuprates. The formulation shown in 10 is not meant to represent an actual structure, but is used for convenience and to show stoichiometry. Analogous formulations have been used for higher order alkylcuprates.[5,7]

[7] Lipshutz, B. H.; Koerner, M.; Parker, D. A. *Tetrahedron Lett.* **1987**, *28*, 945.

0022-3263/88/1953-5366$01.50/0