Journal of Organometallic Chemistry, 301 (1986) 257–267
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands

STERIC CONSEQUENCE OF THE DIASTEREOSELECTIVE ADDITION OF CHIRAL LITHIUM 2-(1-DIMETHYLAMINOETHYL)PHENYL CUPRATES TO SOME ENONES

STAFFAN ANDERSSON [a], SUSAN JAGNER [a]*, MARTIN NILSSON [b]* and FABIO URSO [b]

Departments of Inorganic Chemistry [a] and Organic Chemistry [b], Chalmers University of Technology, S-412 96 Göteborg (Sweden)

(Received August 2nd, 1985)

Summary

Conjugate addition of the mixed chiral species lithium [(*S*)-2-(1-dimethylaminoethyl)phenyl](2-thienyl)cuprate to (*E*)-4-phenyl-3-buten-2-one, 2-cyclohexenone or to 2-cyclopentenone proceeds with high diastereoselectivity. The first two enones gave crystalline adducts directly, while the non-crystalline cyclopentenone adduct was converted into a crystalline methiodide. The crystal structures of the compounds have been determined from single-crystal X-ray diffractometer data in order to reveal the configurations at the new chiral centres. In all three cases the configuration at the new asymmetric centre is *S*. (*S,S*)-4-[2-(1-Dimethylaminoethyl)phenyl]-4-phenyl-2-butenone, $C_{20}H_{25}NO$, crystallizes in space group $P2_1$ with a 7.604(2), b 9.398(5), c 12.290(6) Å, β 92.30(3)° and $Z = 2$. Full-matrix least-squares refinement of 273 structural parameters gave $R = 0.066$ for 1015 observed independent reflections. (*S,S*)-3-[2-(1-Dimethylaminoethyl)phenyl]-2-cyclohexanone, $C_{16}H_{23}NO$ crystallizes in space group $P2_12_12_1$ with a 12.499(4), b 6.645(3), c 17.568(7) Å and $Z = 4$. Full-matrix least-squares refinement of 142 structural parameters gave $R = 0.068$ for 1507 observed independent reflections. (*S,S*)-1-[2-(3-Oxocyclopentyl)phenyl]ethyltrimethylammonium iodide, $C_{16}H_{24}NOI$, crystallizes in space group $P4_1$, with a 10.569(3), c 30.895(7) Å and $Z = 8$; there are thus two crystallographically independent cations in the asymmetric unit. Full-matrix least-squares refinement of 342 structural parameters gave $R = 0.054$ for 2119 observed independent reflections.

The (*S,S*)-configuration observed in these adducts indicates that the conjugate addition gives the least crowded lithium enolate as the major product.

Introduction

We recently demonstrated the diastereoselective addition of the 2-(1-dimethylaminoethyl)phenyl group to some enones using optically active lithium bis[2-(1-di-

0022-328X/86/$03.50

TABLE 1

FRACTIONAL COORDINATES AND EQUIVALENT ISOTROPIC THERMAL PARAMETERS (Å^2) FOR THE NON-HYDROGEN ATOMS IN $C_{20}H_{25}NO$ [a]

Atom	x	y	z	B_{eq}
N	0.307(1)	0.246(1)	0.0275(5)	5.7(2)
C(1)	0.492(1)	0.250(2)	0.0576(9)	7.4(3)
C(2)	0.270(2)	0.365(2)	−0.0486(8)	8.3(4)
C(3)	0.001(1)	0.257(2)	0.0899(8)	7.1(3)
C(4)	0.194(1)	0.257(1)	0.1238(6)	4.8(2)
C(5)	0.235(1)	0.135	0.2009(5)	4.3(2)
C(6)	0.236(1)	−0.002(1)	0.1588(6)	5.4(3)
C(7)	0.258(1)	−0.121(1)	0.2210(7)	5.6(2)
C(8)	0.283(1)	−0.104(1)	0.3334(7)	5.6(3)
C(9)	0.285(1)	0.033(1)	0.3792(6)	5.1(2)
C(10)	0.255(1)	0.152(1)	0.3128(6)	4.4(2)
C(11)	0.262(1)	0.300(1)	0.3653(5)	4.3(2)
C(12)	0.227(1)	0.300(1)	0.4893(5)	4.7(2)
C(13)	0.183(1)	0.443(1)	0.5361(6)	4.8(2)
O	0.146(1)	0.546(1)	0.4785(4)	6.1(2)
C(14)	0.187(1)	0.455(1)	0.6552(7)	5.8(3)
C(15)	0.440(1)	0.373(1)	0.3465(5)	4.3(2)
C(16)	0.444(1)	0.509(1)	0.2997(6)	5.5(2)
C(17)	0.604(1)	0.571(1)	0.2801(8)	6.7(3)
C(18)	0.758(1)	0.503(1)	0.3060(7)	6.5(3)
C(19)	0.756(1)	0.372(1)	0.3550(7)	6.3(3)
C(20)	0.594(1)	0.306(1)	0.3742(6)	5.1(2)

[a] B_{eq} is defined as $8\pi^2/3\Sigma_i\Sigma_j U_{ij}a_i^{\star}a_j^{\star}\mathbf{a}_i\cdot\mathbf{a}_j$. Estimated standard deviations are given in parentheses.

TABLE 2

FRACTIONAL COORDINATES AND ISOTROPIC THERMAL PARAMETERS (Å^2) FOR THE NON-HYDROGEN ATOMS IN $C_{16}H_{23}NO$ [a]

Atom	x	y	z	B
N	0.2068(4)	−0.255(1)	0.0338(3)	4.2(1)
C(1)	0.2840(7)	−0.357(1)	−0.0156(5)	5.6(2)
C(2)	0.1497(9)	−0.409(2)	0.0746(6)	6.7(2)
C(3)	0.3267(7)	0.038(1)	0.0435(5)	5.6(2)
C(4)	0.2563(5)	−0.112(1)	0.0855(4)	3.5(1)
C(5)	0.1729(5)	0.005(1)	0.1292(4)	3.3(1)
C(6)	0.0739(6)	0.042(1)	0.0967(4)	4.6(2)
C(7)	−0.0034(6)	0.154(1)	0.1340(4)	4.4(2)
C(8)	0.0155(6)	0.230(1)	0.2045(4)	4.4(1)
C(9)	0.1143(5)	0.196(1)	0.2382(4)	3.8(1)
C(10)	0.1930(4)	0.085(1)	0.2026(3)	3.1(1)
C(11)	0.2977(5)	0.053(1)	0.2446(4)	3.4(1)
C(12)	0.2834(6)	−0.097(1)	0.3101(4)	4.1(1)
C(13)	0.3820(6)	−0.121(1)	0.3568(4)	4.7(2)
O	0.4104(5)	−0.292(1)	0.3764(3)	7.3(2)
C(14)	0.4444(6)	0.058(1)	0.3768(5)	4.9(2)
C(15)	0.4562(6)	0.209(1)	0.3115(5)	4.9(2)
C(16)	0.3478(5)	0.248(1)	0.2729(4)	4.1(1)

[a] The temperature factor is $\exp[-(B\sin^2\theta)/\lambda^2]$. Estimated standard deviations are given in parentheses.

methylaminoethyl)phenyl]-cuprate, and, even more successfully, the mixed lithium [2-(1-dimethylaminoethyl)phenyl](2-thienyl)cuprate [1]. The configurations of the products have now been determined in order to ascertain the steric consequence of the reaction and to assist in mechanistic interpretation.

Results

Syntheses

By repeating the addition of lithium ((*S*)-2-dimethylaminoethyl)(2-thienyl)cuprate to (*E*)-4-phenyl-3-propene-2-one (benzalacetone) on a larger scale, we obtained the

TABLE 3

FRACTIONAL COORDINATES AND EQUIVALENT ISOTROPIC THERMAL PARAMETERS (Å^2) FOR THE NON-HYDROGEN ATOMS IN $C_{16}H_{24}NOI$ [a]

Atom	*x*	*y*	*z*	B_{eq}
I(1)	0.4082(1)	0.2082(1)	0.76034	4.24(3)
I(2)	0.7276(1)	0.2397(1)	0.38242(6)	4.81(4)
N(1)	0.350(1)	−0.094(1)	0.3741(4)	3.3(3)
C(2)	0.423(2)	−0.202(2)	0.3928(10)	5.6(7)
C(2)	0.304(2)	−0.142(2)	0.3306(7)	5.7(7)
C(3)	0.437(2)	0.015(2)	0.3675(7)	5.8(6)
C(4)	0.142(2)	−0.163(2)	0.4079(6)	4.6(5)
C(5)	0.237(1)	−0.050(1)	0.4012(5)	2.5(4)
C(6)	0.276(1)	0.008(2)	0.4429(5)	3.0(4)
C(7)	0.312(2)	−0.065(2)	0.4787(7)	4.4(5)
C(8)	0.352(2)	−0.024(2)	0.5171(6)	5.2(6)
C(9)	0.361(2)	0.117(2)	0.5230(6)	5.3(6)
C(10)	0.313(2)	0.197(2)	0.4892(6)	4.1(5)
C(11)	0.274(2)	0.143(2)	0.4492(6)	3.5(4)
C(12)	0.228(2)	0.236(1)	0.4157(6)	3.9(5)
C(13)	0.317(2)	0.353(2)	0.4079(6)	3.9(5)
C(14)	0.229(2)	0.447(2)	0.3841(6)	4.2(5)
O(1)	0.261(2)	0.535(1)	0.3644(5)	6.2(5)
C(15)	0.090(2)	0.403(2)	0.3930(8)	5.1(6)
C(16)	0.099(2)	0.296(2)	0.4271(7)	4.3(5)
N(2)	0.365(1)	0.443(1)	0.0075(5)	3.5(3)
C(17)	0.436(2)	0.508(3)	−0.0277(7)	5.5(7)
C(18)	0.438(2)	0.323(2)	0.0216(6)	4.5(5)
C(19)	0.372(2)	0.529(2)	0.0486(7)	5.1(6)
C(20)	0.147(2)	0.527(2)	−0.0104(7)	4.9(6)
C(21)	0.229(2)	0.406(2)	−0.0042(6)	3.9(5)
C(22)	0.224(2)	0.323(2)	−0.0431(6)	3.4(5)
C(23)	0.232(2)	0.375(1)	−0.0837(6)	3.3(4)
C(24)	0.224(2)	0.301(2)	−0.1217(7)	4.8(6)
C(25)	0.219(2)	0.177(2)	−0.1170(7)	4.4(5)
C(26)	0.210(2)	0.120(2)	−0.0773(7)	4.6(6)
C(27)	0.210(1)	0.190(1)	−0.0376(5)	2.9(4)
C(28)	0.188(1)	0.123(2)	0.0050(6)	3.6(4)
C(29)	0.243(2)	−0.014(2)	0.0079(10)	6.0(6)
C(30)	0.152(2)	−0.072(2)	0.0430(8)	5.4(6)
O(2)	0.178(2)	−0.181(1)	0.0580(4)	6.1(5)
C(31)	0.045(2)	0.007(2)	0.0523(8)	5.9(7)
C(32)	0.047(2)	0.095(2)	0.0135(9)	6.1(7)

[a] B_{eq} is defined as $8\pi^2/3\Sigma_i\Sigma_j U_{ij} a_i^\star a_j^\star \mathbf{a}_i \cdot \mathbf{a}_j$. Estimated standard deviations are given in parentheses.

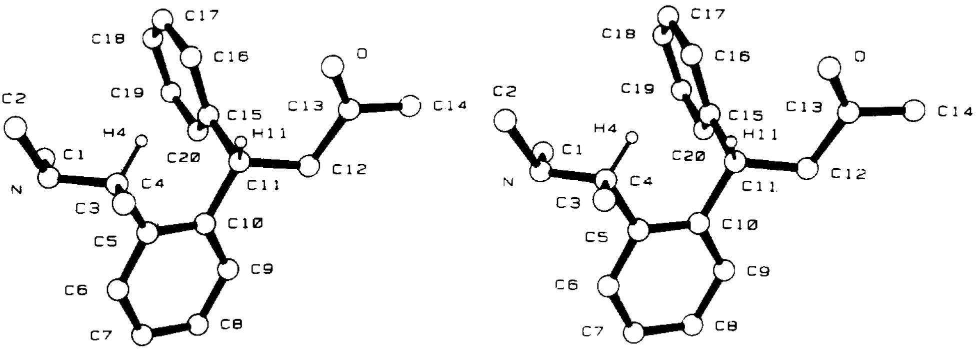
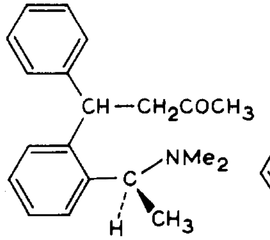
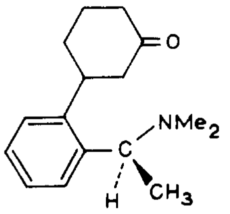


Fig. 1. Stereoscopic view [3] of the $C_{20}H_{25}NO$ molecule showing the atomic numbering. Non-hydrogen atoms are represented as spheres of radius 0.15 Å; the hydrogen atoms associated with the chiral centres are included as spheres of radius 0.08 Å.

conjugate addition product 4-phenyl-4-[2-(1-dimethylaminoethyl)phenyl]-butanone-2 (**1**), as crystals, m.p. 77–78°C, suitable for X-ray investigation.



(**1**)



(**2**)

Addition of the (*S*)-2-(1-dimethylaminoethyl)phenyl group to 2-cyclohexenone gave 3-[2-(1-dimethylaminoethyl)phenyl]-cyclohexanone (**2**) as a large hexagonal plate, m.p. 60–62°C. The reaction also gave minor amounts of *N*,*N*-dimethyl-1-(2-thienylphenyl)ethylamine and the symmetric biphenyl: *N*,*N*,*N*,*N*-tetramethylbiphenyl-2,2′-diyl-bis-(1-ethylamine) as by-products (GC-MS).

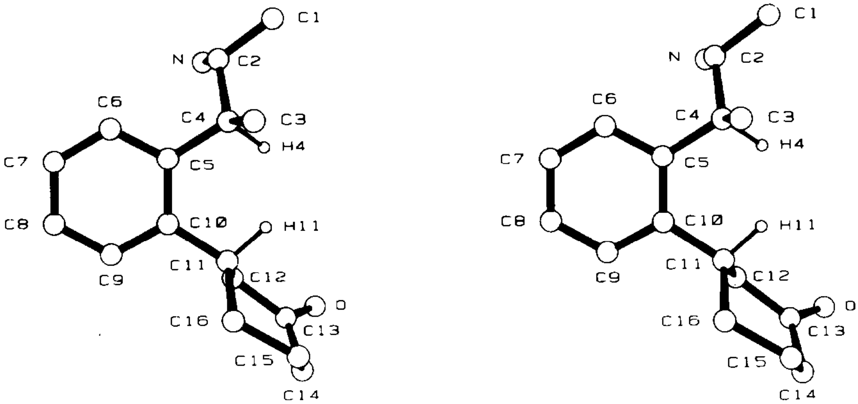
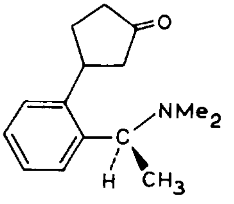
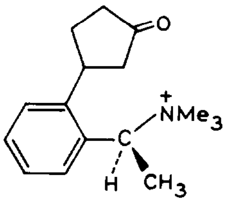


Fig. 2. Stereoscopic view [3] of the $C_{16}H_{23}NO$ molecule showing the atomic numbering. Non-hydrogen atoms are represented as spheres of radius 0.15 Å; the hydrogen atoms associated with the chiral centres are included as spheres of radius 0.08 Å.

The conjugate addition to 2-cyclopentenone was examined to check whether restricted mobility in the enone system would influence the diastereoselectivity. The product (**3**) was obtained in reasonable diastereoselectivity (84%) as an oil which did not crystallize. It was not possible to obtain suitable crystals of the picrate, hydrochloride or oxime, but suitable crystals of 1-[2-(3-oxocyclopentyl)phenyl]-ethyl-trimethylammonium iodide (**4**) were obtained on quaternization with methyl iodide.



(**3**)



(**4**)

Molecular structures

Atomic coordinates and equivalent isotropic parameters ($C_{20}H_{25}NO$ and

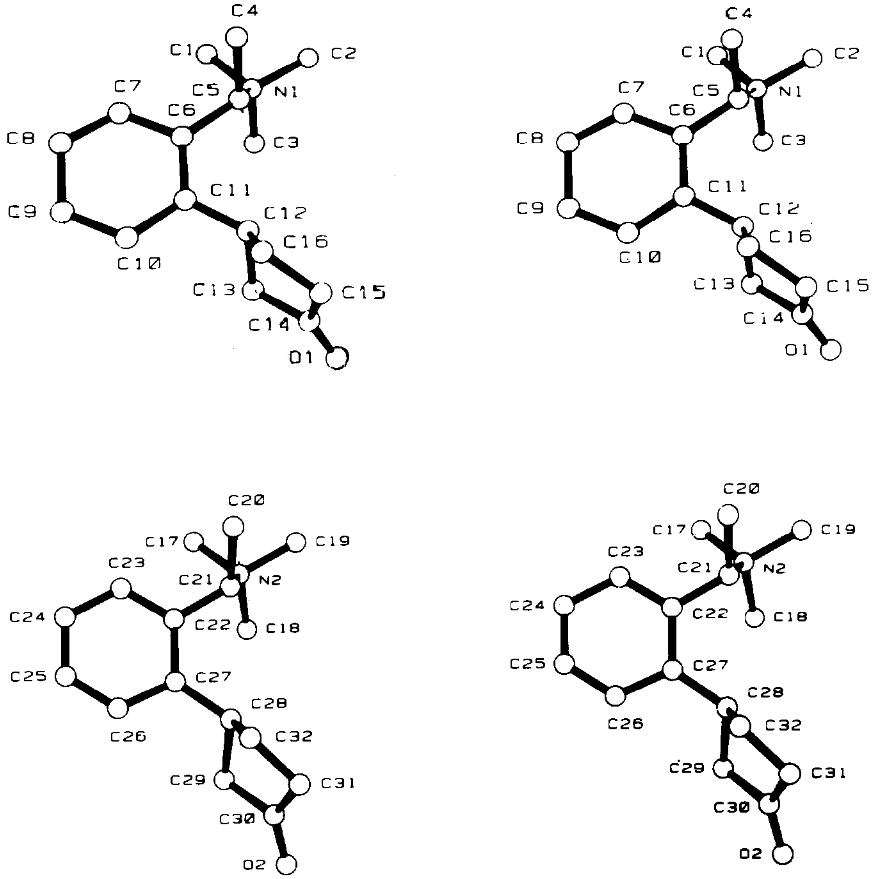


Fig. 3. Stereoscopic views [3] of the two crystallographically independent $C_{16}H_{24}NO^+$ ions in $C_{16}H_{24}NOI$, showing the atomic numbering. All atoms are represented as spheres of radius 0.15 Å.

$C_{16}H_{24}NOI$) or isotropic thermal parameters ($C_{16}H_{23}NO$) for the non-hydrogen atoms are given in Tables 1–3. Tables of structure factors, hydrogen-atom coordinates, anisotropic thermal parameters, bond distances and angles, and torsion angles may be obtained from the authors. The crystal data and details of the experimental procedure are summarized in Table 4.

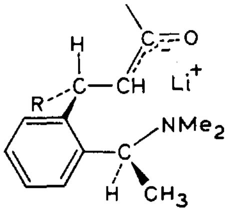
Since the absolute configuration of the starting amine, (*S*)-(−)-*N*,*N*-dimethyl-1-phenylethylamine is known [2], the configurations at the new asymmetric carbon atoms can be deduced from the molecular structures without having to determine the absolute configurations crystallographically. As is apparent from Figs. 1–3, all three new chiral centres have the same configuration, i.e. *S*. The geometries of the crystallographically independent cations in $C_{16}H_{24}NOI$ are essentially similar (Fig. 3), there being only barely significant differences in some of the torsion angles.

Discussion

There have been several attempts to bring about stereoselective conjugate addition of organocuprates to enones and enolates (for a briefly review see ref. 4). Attempts to bring about enantioselective additions using mixed chiral cuprates including a chiral auxiliary group have met with limited success. Interesting asymmetric inductions were obtained by Leyendecker and Lauchier [5], using tridentate auxiliary ligands with high affinity for copper and lithium. Studies of diastereoselective additions have been more fruitful, with the initial chirality located either in the substrate or in the cuprate.

It is noteworthy that the chiral (dimethylaminoethyl)phenyl group as an auxiliary ligand has only a slight influence on the addition of other groups whereas its own addition to the enone systems is highly diastereoselective. In retrospect this is not surprising, since the auxiliary ligand may point away from the reaction center.

In our systems the chiral organocuprates give the (*S*,*S*)-diastereomers. The primary stable product in the reaction should to be the lithium enolate since the reaction proceeds with precipitation of 2-thienylcopper. The chelated lithium enolate of an (*S*,*S*)-product is evidently less crowded than its diastereomer, and is shown in **5**. The cuprate reagent apparently gives the thermodynamically most stable product. The organolithium addition gives the other isomer (as well as 1,2-addition) [1], and thus appears to be kinetically controlled.



(5)

The importance of favourable chelation in the primary lithium enolate and obviously also in the transition state is further supported by the facile conjugate addition of the 2-pyridyl group to enones with lithium pyridylcuprates [6], which may involve some enantioselectivity when the (dimethylaminoethyl)phenyl group is used as a chiral auxiliary [7].

Interesting diastereoselectivities were observed by Yamamoto et al. in the addition of chiral lithium bis(azaenolato)cuprates to 2-cyclopentenone and 2-cyclohexenone [8]; their results can also be interpreted in terms of formation of the least crowded lithium enolate. Again, addition of a chiral, alkoxy-chelated *cis*-vinylcopper compound to 2-methyl-2-cyclopentenone is the diastereoselective first step in the double Michael addition reported by Takahashi et al. [9].

In all these reactions a fairly stable, chelated organocopper reagent attacks the enone. The chelation may control the geometry of orientation complexes, transition states and the final enolate, thus providing possibilities for stereoselectivity. The steric outcome is the same for our three substrates, and the diastereoselectivities are of the same order of magnitude, indicating that the chelation by the dimethylaminoethyl group in the entering group is more important than the steric differences between substrates.

The detailed structure of lithium (*S*)-[2-(1-dimethylaminoethyl)phenyl](2-thienyl)cuprate is unknown, although it can be assumed to be dimeric. The structures of the tetramers of (2-dimethylaminoethyl)-phenylcopper or -lithium and of the dimeric lithium bis-2-(dimethylaminomethyl)phenylcuprate are known [10]. In the two latter structures the nitrogen atoms are coordinated to lithium. A similar preference for the nitrogen atoms to be coordinated to lithium is to be expected in the mixed thienylcuprate and in the lithium bis-[2-(1-dimethylaminoethyl)phenyl]cuprate.

The use of the 2-thienyl group as an auxiliary ligand has been further explored by us in mixed diorganocuprates for conjugate addition [11] and by Lipshutz et al. in mixed cuprates of higher order [12].

Experimental

Reactions were performed under an inert atmosphere with dry solvents and other chemicals. Mass spectra were recorded on a Finnigan 1200 GC-MS instrument and NMR spectra on a Bruker WH 270 spectrometer (deuteriochloroform, δ values in ppm).

The general procedure for conjugate addition was followed from [1]. We used (*S*)-*N*,*N*-dimethyl-1-phenylethylamine with an optical purity of 97%, purified via the picrate [13].

Adduct to E-4-phenyl-3-buten-2-one

(*S*)-2(1-Dimethylaminoethyl)phenyllithium was prepared from the reaction of (*S*)-(−)-*N*,*N*-dimethylphenylethylamine (82.5 mmol) with butyllithium (83 mmol, 1.6 *M* in hexane) in ether (210 ml) for 5 d. It was added to 2-thienylcopper in ether (made from thiophene (87.7 mmol), butyllithium (73.1 mmol), 40 min and purified copper(I) iodide [14] (73.1 mmol)) and the mixture was stirred for 10 min at 0°C to give the lithium [2-(1-dimethylaminoethyl)phenyl](2-thienyl)cuprate reagent as a dark-brown solution. 4-Phenyl-3-buten-2-one (60.9 mmol) in ether was added and the mixture was stirred for 60 h. The solid 2-thienylcopper was filtered off and washed with ether. The ether solution was shaken with an excess of saturated ammonia/ammonium chloride solution, washed with water, and extracted with 2 *M* hydrochloric acid. The extract was made alkaline with ammonia and the basic material re-extracted and dried (sodium sulfate). Evaporation of the solvent and the unchanged *N*,*N*-dimethyl phenylethylamine gave an oil which solidified in the

TABLE 4

CRYSTAL AND EXPERIMENTAL DATA FOR $C_{20}H_{25}NO$, $C_{16}H_{23}NO$ AND $C_{16}H_{24}NOI$

	$C_{20}H_{25}NO$	$C_{16}H_{23}NO$	$C_{16}H_{24}NOI$
M_r	295.4	245.4	373.3
M.p. (°C)	77–78	60–62	195–196
Unit-cell dimensions	*a* 7.604(2), *b* 9.398(5), *c* 12.290(6) Å, *β* 92.30(3)°	*a* 12.499(4), *b* 6.645(3), *c* 17.568(7) Å	*a* 10.569(3), *c* 30.895(7) Å
Space group	$P2_1$ (No. 4) [20]	$P2_12_12_1$ (No. 19) [20]	$P4_1$ (No. 76) [20]
Z	2	4	8
D_c (g cm^{-3})	1.12	1.12	1.44
μ(Mo-K_α) (mm^{-1})	0.0732	0.0741	1.87
Habit	Colourless plates	Colourless hexagonal plates	Colourless tetragonal bipyramids
Crystal size (mm)	0.27×0.27×0.24	0.40×0.33×0.35	0.28×0.20×0.18
Temperature (data collection) (K)	290	290	290
$2\theta_{max}$ (°)	55	50	60
Scan mode	$\omega-2\theta$	$\omega-2\theta$	ω
2θ scan rate (° min^{-1})	2.5–25	2.5–25	2.5–29
No. of independent reflections measured	2144	1507	5110
No. of observed independent reflections [$I > 3.0\sigma(I)$]	1015	800	2119
Method used to solve structure	Direct methods (MULTAN 80) [19]	Direct methods (MULTAN 80) [19]	Direct methods (MULTAN 80) [19]
No. of parameters refined	273	142	342
Anisotropic temperature factors for non-hydrogen atoms	Yes	No	Yes
Hydrogen atoms included	Yes	Yes	No
Reflections weighted according to	$w = [\sigma(F_o)^2 + 0.009(F_o)^2]^{-1}$	$w = [\sigma(F_o)^2 + 0.0009(F_o)^2]^{-1}$	$w = [\sigma(F_o)^2 + 0.0003(F_o)^2]^{-1}$
Final *R*	0.066	0.068	0.054
Maximum residual electron density (e Å^{-3})	0.17	0.21	0.51

refrigerator, m.p. 73–78°C. The product was dissolved in 30 ml pentane, and cooling gave crystals, m.p. 77–78°C; the yield of recrystallised product being 54% (8.56 g). NMR spectrum; 1.33 d (3H), 1.94 s (6H), 2.07 (3H), 2.17 dd (2H), 3.12 d (2H), 3.57 q (H), 5.03 t (H), 7.2–7.5 m (9H). Mass spectrum: 295 (M^+, 8%), 252 (17%), 207 (18%), 192 (100%) and 178 (42%).

This compound has been tested by the National Cancer Institute under the NSC number 600079-S and found to be inactive in a leukemia screen (3PS31) test [15].

2-Cyclohexenone adduct

Freshly distilled 2-cyclohexenone (10 mmol) was added to the lithium [2-(1-dimethylaminoethyl)phenyl](2-thienyl)cuprate reagent (10 mmol) at 0°C in ether. The mixture was stirred for 30 min then treated with saturated ammonia/ammonium chloride solution (100 ml) and extracted three times with ether. The ether layer was washed with 2.5 *M* hydrochloric acid and the aqueous extract made alkaline with sodium carbonate. Re-extraction with ether, followed by drying of the ethereal extract with magnesium sulfate and evaporation, gave a crude oil (1.90 g) containing the conjugate adduct (79%), *N*,*N*-dimethyl-1-phenylethylamine (19%), and small amounts of *N*,*N*,*N*,*N*-tetramethylbiphenyl-2,2′-diyl-bis(1-ethylamine) (ca. 1%) and *N*,*N*-dimethyl-1-(2-thienylphenyl)-ethylamine (0.2%) (GC-MS). The *N*,*N*-dimethylphenylethylamine was distilled off in a Kugelrohr apparatus (b.p. below 90°C at 700 Pa) and the addition product then distilled at ca. 150°C and 25 Pa. The product was soluble in pentane and in ethanol, and was recrystallized from methanol in a refrigerator, m.p. 60–62°C. NMR spectrum: 1.30 d (3H), 1.9 m (6H), 2.14 s (6H), 2.49 m (4H), 3.43 q (2H), 3.5 m (1H), 7.2 m + 7.5 m (4H). Mass spectrum: (M^+, 8%), 230 (15), 200 (54), 185(40), 143(92) and 129 (100).

Cyclopentenone adduct

2-Cyclopentenone (10 mmol) was added to lithium 2-[(1-dimethylaminoethyl)-phenyl]-(2-thienyl)cuprate (10 mmol in 25 ml ether) at 0°C and the mixture was stirred for 30 min. (After longer reaction times the yield of the desired product decreased.) The mixture was treated with aqueous ammonia/ammonium chloride and work up was as above. The product mixture was shown by GC-MS to contain the desired addition product, together with *N*,*N*-dimethylphenylethylamine, the symmetric biphenyl, 2-thienyl-*N*,*N*-dimethylphenylethylamine, and a dimerisation product from cyclopentenone. The diastereomeric excess in the crude product was 84% as estimated from the mass spectrum. The crude material was distilled in a Kugelrohr apparatus to give the starting amine and the crude addition product, b.p. 90–150°C at ca. 2 Pa. Flash chromatography and thick layer chromatography (silica gel, hexane with 0.3 *M* triethylamine) eventually removed the symmetric biphenyl and gave the pure adduct as an oil, which did not crystallize. Mass spectrum: 231 (M^+, 5%), 216 (17%), 186 (22%), 158 (18%), 143 (100%), 129 (53%) and 46 (100%).

Quaternization with excess methyl iodide and repeated crystallization from ethanol gave colourless tetragonal bipyramids of the pure methiodide, melting at 195–196°C, (partly) resolidifying at 198°C, and finally melting with decomposition at 240–248°C. NMR: 1.71 quintet (1H), 1.78 s (1H), 1.90 d (3H), 2.05 s (1H), 2.4 m (3H), 2.7 dd (1H), 2.90 q (1H), 3.40 s (9H), 4.53 broad p (1H), 5.81 q (H), 7.47 m (4H).

Crystal and intensity data

Intensities of reflections were measured with a Syntex $P2_1$ diffractometer using graphite-monochromated Mo-K_α radiation. For $C_{16}H_{23}NO$ a fragment was cut from the single crystal described above. 96-Step ($C_{20}H_{25}NO$ and ($C_{16}H_{24}NO$) or 19-step $C_{16}H_{24}NOI$) profiles were recorded for each reflection and the Lehmann and Larsen profile-analysis method [16] was used to calculate the intensities [17]. Data were corrected for Lorentz and polarisation effects. An empirical correction for the effects of absorption [18] was made for $C_{16}H_{24}NOI$ after solution of the structure. No absorption corrections were applied to the data for $C_{20}H_{25}NO$ and $C_{16}H_{23}NO$. Unit-cell parameters were determined from diffractometer setting angles for 15 reflections. Crystal data and further details of the collection of intensity data are given in Table 4.

Structure determination and refinement

The structures of $C_{20}H_{25}NO$ and $C_{16}H_{23}NO$ were solved by direct methods (MULTAN 80, [19]); in the case of $C_{16}H_{24}NOI$ the positions of the iodine atoms were obtained by direct methods [19], and those of the remaining non-hydrogen atoms from a subsequent electron-density map. Details of the full-matrix least-squares refinements are given in Table 4. Isotropic thermal parameters were refined for the non-hydrogen atoms of $C_{16}H_{23}NO$, while anisotropic thermal parameters were included for those of $C_{20}H_{25}NO$ and $C_{16}H_{24}NOI$. For $C_{20}H_{25}NO$ and $C_{16}H_{23}NO$ hydrogen atoms were located from difference maps and their coordinates included in the refinement, the isotropic thermal parameters of the hydrogen atoms being set equal to B_{eq} or B of the carrying carbon atoms in the two structures, respectively. Hydrogen-atom coordinates were not included in the refinement of $C_{16}H_{24}NOI$. Atomic scattering factors were taken from the International Tables for X-Ray Crystallography [20]. The computer programs are described in [21].

Acknowledgements

The work was supported by the National Swedish Board of Technical Development. We thank Dr. Hans Malmberg for friendly discussions and Mr. L. Larsson and Mr. S. Stevancevic for some experimental assistance in the synthetic work. We acknowledge the testing of one compound by the National Cancer Institute, Bethesda, Md.

References

1 H. Malmberg, M. Nilsson and C. Ullenius, Tetrahedron Lett., (1982) 3823.
2 D.J. Cram, L.K. Gaston and H. Jager, J. Am. Chem. Soc., 83 (1961) 2183.
3 C.K. Johnson, ORTEP, ORNL Report 3794, Oak Ridge National Laboratory, Oak Ridge, Tennessee, U.S.A., 1965.
4 M. Nilsson, Chemica Scripta, 25 (1985) 79.
5 F. Leyendecker and D. Laucher, Tetrahedron Lett., (1983) 3517.
6 H. Malmberg and M. Nilsson, Tetrahedron, 38 (1982) 1509.
7 H. Malmberg and M. Nilsson, J. Organomet. Chem., 243 (1983) 241.
8 K. Yamamoto, M. Iijima and Y. Ogimura, Tetrahedron Lett., (1982) 3711.
9 T. Takahashi, H. Okumoto and J. Tsuji, Tetrahedron Lett., (1984) 1925.
10 G. van Koten and J.G. Noltes in G. Wilkinson, F.G.A. Stone, E.W. Abel (Eds.), Comprehensive Organometallic Chemistry, Pergamon Press, Oxford, 1982, Ch. 14, p. 709.
11 E.-L. Lindstedt and M. Nilsson, manuscript in preparation.
12 B.H. Lipschutz, J.A. Kozlowski, D.A. Parker, S.L. Nguyen and K.E. McCarthy, J. Organomet. Chem., 285 (1985) 437.

13 H. Malmberg, M.Nilsson and C. Ullenius, Acta Chem. Scand., B 35 (1981) 625.
14 G.B. Kauffman and L.A. Teter, Inorg. Synth., 7 (1963) 9.
15 Screening performed under the auspices of the Developmental Therapeutics Program, Division of Cancer Treatment, National Cancer Institute, Bethesda, Maryland.
16 M.S. Lehmann and F.K. Larsen, Acta Crystallogr. A, 30 (1974) 580.
17 O. Lindqvist and E. Ljungström, J. Appl. Crystallogr., 12 (1979) 134.
18 N. Walker and D. Stuart, Acta Crystallogr. A, 39 (1983) 158.
19 P. Main, S.J. Fiske, S.E. Hull, L. Lessinger, G. Germain, J.-P. Declerq and M.M. Woolfson, MULTAN 80: A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Data, Universities of York, U.K. and Louvain, Belgium 1980.
20 International Tables for X-ray Crystallography, Vol. I, Kynoch Press, Birmingham, U.K. 1952 and Vol. IV, 1974.
21 O. Lindgren, An Integrated Set of Computer Programs, On the Oxygen Coordination of Cerium in Some Sulfates and Chromates, Ph.D. Thesis, (Department of Inorganic Chemistry, Chalmers University of Technology and University of Göteborg, Göteborg, Sweden 1977).