Tetrahedron Letters,Vol.27,No.15,pp 1691-1694,1986 0040-4039/1986 $3.00 + .00
Printed in Great Britain

THE EFFECT OF CATIONS ON THE ASYMMETRIC CONJUGATE ADDITION OF ORGANOCOPPER REAGENTS TO CHIRAL VINYL SULFOXIMINES

Stephen G. Pyne
Department of Chemistry, University of Wollongong,
P.O. Box 1144, Wollongong, N.S.W. 2500, Australia.

Abstract: The chiral vinyl sulfoximines 1b and 4 have been prepared. The effect of cations (Li^+, Zn^{2+}) on the stereochemical outcome of their conjugate addition reactions with organocopper reagents is reported.

Recently we reported that chiral vinyl sulfoximines 1a underwent conjugate addition reactions with dialkylcopper lithium reagents (R_2CuLi. LiI) to yield a mixture of two diastereomeric adducts (2a, 3a) with modest diastereoselectivity (ratio 2a:3a, 81:19 - 86:14)[1] The stereochemical outcome of these reactions was readily rationalized in terms of first coordination of R_2CuLi with the nitrogen of the sulfoximine moiety of 1a, which then directed the organocopper reagent preferentially to one of the diastereotopic Π-faces of the vinyl group (Scheme I, RM=R_2CuLi). Thus the stereochemical outcome of these reactions seemed solely governed by the chirality at sulfur of 1a. The conjugate addition of 1a with monoalkylcopper reagents (RCu) in the presence of LiI, however, proceeded with high diastereoselectivity (90-93%) but with reverse Π-face selectivity (2a:3a $\leq$ 5:95). The stereochemical outcome of these reactions was consistent with attack of RCu on the lithium cation coordinated complex 1B (Met = Li^+(solvent)n) of 1a from the least encumbered Π-face (Scheme I). We report here on the results of a study on the effect of cations (Li^+,Zn^{2+}) on the stereochemical outcome of the conjugate addition reactions of the chiral vinyl sulfoximines 1b and 4b.

The chiral vinyl sulfoximines 1b and 4b were prepared as follows. Treatment of benzenesulfinyl chloride with (S)-(−)-1-phenylethylamine as previously described[1] gave the diastereomeric sulfinamides 7 and 8 (7:8, 2:1) as an inseparable mixture by TLC. This mixture was converted[1] to the chromatographically separable (SS)-sulfoximine 9 (42% overall)[2] and (SR)-(—)-sulfoximine 10 (33% overall)[2], which were stereospecifically (> 95%) converted to (SS)-sulfinamide 7 [2] and (SR)-sulfinamide 8 [2], respectively, upon reduction with aluminium amalgam[3]. The stereochemical identity of 7 was determined from its independent synthesis from (—)-menthyl(S)-benzenesulfinate[4] and lithium (S)-(—)-1-phenylethylamide[1,5] which yielded 7 contaminated with 16% of 8. The sulfoximines 9 and 10 were converted to (SS)-vinyl sulfoximines 4b and (SR)-vinyl sulfoximines 1b, respectively, by the previously reported method[1].

The reaction of vinyl sulfoximine 4b (R^1=CH_3,n-Bu) with $R_2CuLi.LiI$ [6] reagents (entries 1 and 6) proceeded with modest diastereoselectivity (52 - 76%) and produced preferentially the diastereomer predicted from the R_2CuLi complexed intermediate 4A (RM=R_2CuLi). No significant change in diastereoselectivity was observed when 2.5 or 5 equivalents of R_2CuLi was employed.

The stereochemistry of the newly created chiral carbon (C-2) of the major adduct 5b (R^1=n-Bu, R=CH_3 entry 1) was established by conversion to (S)-(—)-3-Methylheptanoic acid (71% ee).[1]

Notably, an enhanced diastereoselectivity, from 76% to 88% (entry 2) was observed in the reaction of 4b (R^1=n-Bu) with LiI 'free' $(CH_3)_2CuLi$.[8] A reversal of Π-face selectivity could be achieved when 4b (R^1=CH_3,n-Bu) was treated with $ZnBr_2$ (1.1 equiv.) solution prior to exposure to the organocopper reagent (entries 3 and 7). These results were consistent with attack of R_2CuLi on 4B (Met = Zn^{2+}),the Zn^{2+} complexed intermediate of 4b (Scheme I).

As expected, by analogy with 1a[1], the reactions of 4b (R^1=CH_3,nBu) with RCu.LiI reagents proceeded with reverse Π-face selectivity to that of $R_2CuLi.LiI$ reagents (entries 4 and 8). Only a marginal difference in product diastereoselectivity was observed in the absence of LiI (entry 5). We tentatively rationalize the stereochemical outcome of these reactions as arising from attack of RCu on 4B (Met = (RCu)n), the complex arising from coordination of 4b with a relative unreactive organocopper species.[10]

Table Conjugate Addition Reactions of Vinyl Sulfoximines 1b and 4b with Organometallic Reagents (RM).

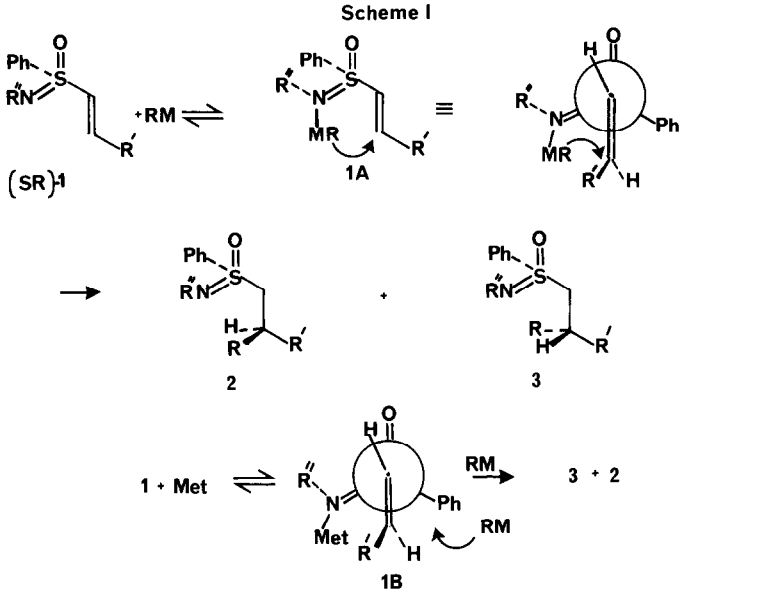
entry	substrate (R^1)	RM[c]	yield %[a]	ratio 5:6[b]	entry	substrate (R^1)	RM[c]	yield %	ratio 2:3
1	4b(n-Bu)	$(CH_3)_2CuLi$	60	88:12	9	1b(n-Bu)	$(CH_3)_2CuLi$	60	23:77
2	4b(n-Bu)	$(CH_3)_2CuLi$	72	94:6	10	1b(n-Bu)	$(CH_3)_2CuLi$	69	90:10
3	4b(n-Bu)	LiI 'free' $(CH_3)_2CuLi$ + $ZnBr_2$(1.1 equiv)	64	12:88	11	1b(n-Bu)	LiI 'free' $(CH_3)_2CuLi$ + $ZnBr_2$(1.1 equiv)	65	12:88
4	4b(n-Bu)	CH_3Cu	83	15:85	12	1b(n-Bu)	CH_3Cu	79	21:79
5	4b(n-Bu)	CH_3Cu, LiI 'free'	74	20:80	13	1b(n-Bu)	CH_3Cu, LiI 'free'	80	13:87
6	4b(CH_3)	nBu_2CuLi	80	24:76	14	1b(CH_3)	$n\text{-}Bu_2CuLi$	59	12:88
7	4b(CH_3)	nBu_2CuLi + $ZnBr_2$ (1.1 equiv)	82	78:22	15	1b(CH_3)	$n\text{-}Bu_2CuLi$ + $ZnBr_2$ (1.1 equiv)	62	56:44
8	4b(CH_3)	nBuCu	90	77:23	16	1b(CH_3)	n-BuCu	69	36:64

a. After purification by PTLC b. Determined on crude reaction mixtures by HPLC analysis [1]

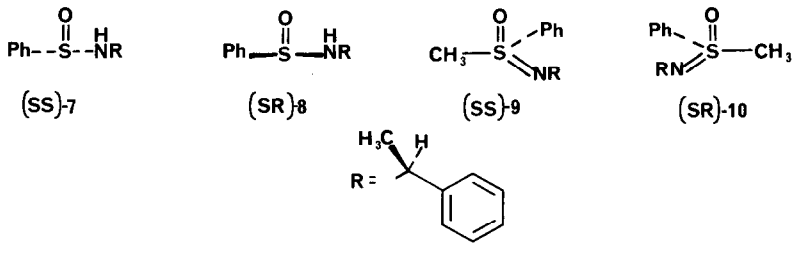
c. 5 equiv, at -25° (R=CH_3) and -40° (R=n-Bu)

The reaction of vinyl sulfoximine 1b (R^1=n-Bu) with $(CH_3)_2CuLi.LiI$, proceeded with modest diastereoselectivity (54%) and, as anticipated, gave 2b (R^1=n-Bu, R = CH_3) as the major diastereomeric product (entry 9). The stereochemical identity of 2b (R^1=n-Bu, R=CH_3) was disclosed by its conversion to (R)-(+)-3-Methylheptanoic acid (51% ee).[1] A

Scheme I



Scheme II



similar Π-face selectivity, but enhanced diastereoselectivity, was obtained when 1b (R^1=n-Bu) was pre-complex with $ZnBr_2$ prior to the addition of $(CH_3)_2CuLi$ (entry 11). Surprisingly, a reversal of Π-face selectivity was observed with $(CH_3)_2CuLi$ in the absence of LiI (entry 10), whereas CH_3Cu gave 2b (R^1=n-Bu, entry 12) as the major diastereomeric product. The diastereoselectivity of the later reaction was enhanced in the absence of LiI.

Quite unexpectedly the reaction of 1b (R^1=CH_3) with n-Bu_2CuLi and n-BuCu reagents also gave 2b (R^1=n-Bu, R=CH_3) as the major diastereomeric product. The product of the former reaction was converted to (R)-(+)-3-Methylheptanoic acid (71% ee).[1]

The reasons for the apparent opposite Π-face selectivity in the reactions of 1b with $(CH_3)_2CuLi$ and n-Bu_2CuLi reagents remain unclear. Inspection of molecular models indicates that conformation 1A should be energetically much less favourable than conformation 4A because of severe non-bonded interactions between the methyl group of the auxillary chiral ligand and the S-phenyl group. Possibly, the phenyl group of the auxillary ligand may be responsible for the observed stereoselectivity.[11] At this point it is not possible to ascertain the importance of these and other conformational factors, especially when the exact nature of the reactive organocopper species is unclear.[9]

These results demonstrate the potential of controlling the Π-face selectivity in reactions involving chiral vinyl sulfoximines by complexing metal cations. The application of these concepts to asymmetric synthesis is currently under investigation.

References and Notes

1. S.G. Pyne, J. Org. Chem., 51,81,(1986)
2. 7: ^{1}H NMR ($CDCl_3$) δ 7.8-7.0 (m, 10H), 4.7-4.2 (m,2H), 1.62 (d, J=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$; in part) δ 51.64 (d), 23.87 (q); 8: ^{1}H NMR ($CDCl_3$) δ 7.8-6.9 (m,10H), 4.9-4.3 (m,2H), 1.42 (d, J=6.4Hz, 3H); ^{13}C NMR ($CDCl_3$ in part) 53.15 (d), 24.06(q); 9: $[\alpha]^{21}_D$ 0 ± .16° ($CHCl_3$, C 0.10); Rf 0.35 (EtoAc,hexane, 1:1); ^{1}H NMR ($CDCl_3$) δ 8.13-6.80 (m,10H), 4.21 (q, J=6.4Hz, 1H), 3.00 (S,3H), 1.46 (d, J=6.6Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 146.2, 139.2 131.9, 128.4, 127.9, 127.4, 125.5, 53.4, 44.9, 27.2, 10: $[\alpha]^{21}_D$ - 15.3° ($CHCl_3$, C 0.11); Rf 0.25 (EtoAC, hexane, 1:1); ^{1}H NMR ($CDCl_3$) δ 8.4-6.8 (m,10H), 4.32 (q, J=6.6Hz, 1H), 2.91 (S, 3H), 1.38 (d, J=6.6Hz,3H); ^{13}C NMR ($CDCl_3$) δ 146.9, 140.0, 132.1, 128.6, 127.6, 127.4, 125.7, 125.5, 52.9, 44.2, 26.5.
3. C.W. Schroeck and C.R. Johnson, J. Amer. Chem. Soc. 93, 5305 (1971)
4. H.F. Herbrandson and R.T. Dickerson, Jr., J. Amer. Chem. Soc. 81, 4102 (1959)
5. C.R. Johnson, E.V. Jonsson and A. Wambsgans, J. Org. Chem., 44 2061 (1979)
6. Prepared from RLi (2 equivalents) and CuI (1 equivalent) in ether as previously reported (2RLi + CuI → R_2CuLi + LiI)[1]
7. Prepared from LiI 'free' CH_3Cu and CH_3Li according to E.C. Ashby and J.J. Watkins, J. Amer. Chem. Soc., 99, 5312 (1977)
8. No enhancement of diastereoselectivity was observed in the reaction of 1b (R^1=CH_3) with LiI 'free' Bu_2CuLi, whereas, a decrease in diastereoselectivity was observed with 4b (R^1=CH_3, 12% de)
9. S.R. Krauss and S.G. Smith, J. Amer. Chem. Soc., 103 141 (1981)
10. Experiments in which 1-2 equivalents of RCu were employed were inconclusive due to the poor yields of adducts (10-20%). Competing side reactions, presumably between the anion of 6 and 4 were a major problem.
11. G.H. Posner, C.M. Lentz, J. Amer. Chem. Soc.101, 934 (1979)

Acknowledgement. Financial support by the Australian Research Grants Scheme is gratefully acknowledged.

(Received in UK 26 February 1986)