H), 2.2–2.0 (m, 8 H), 1.69 (s), 1.61 (s) (12 H)).

((4-Methyl-3-pentenyl)sulfonyl)(methylsulfonyl)methane (17). To a solution of 0.53 g (3.0 mmol) of **3** in 125 mL of THF was added 6.1 mL (9.4 mmol) of *n*-BuLi. The solution was stirred under Ar for 1 h, and then 0.12 mL (1.0 mmol) of prenyl bromide was added all at once. The mixture was stirred for 23 h, and then 1.5 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the 2.9 g of wet residue was purified by flash chromatography (1:1 EtOAc–hexane) to afford 0.11 (g (44% based on prenyl bromide) of a 6:1 mixture of **17** and **18**. Gradient flash chromatography (1:9–2:3 EtOAc–hexane) gave 0.087 g (35%) of **17** which, after crystallization from MeOH, had mp 62–63 °C: IR (KBr) 1310, 1125 cm^{-1}; ^1H NMR δ 5.20 (t, J = 7.3 Hz, 1 H), 5.01 (s, 2 H), 3.42 (m, 2 H), 3.26 (s, 3 H), 2.55 (m, 2 H), 1.69 (s, 3 H), 1.65 (s, 3 H); the multiplets at 3.42 (AA′) and 2.55 (BB′) could be simulated by use of the LAOCOON III program[19] with $J_{AA'} = J_{BB'} = 14.0$ Hz, $J_{AB'} = J_{A'B} = 7.1$ Hz, $J_{AB} = J_{A'B'} = 12.5$ Hz, and $J_{BvinylH} = J_{B'vinylH} = 7.3$ Hz; ^{13}C NMR (D_3CCOCD_3) δ 135.6, 120.6, 70.1, 54.0, 42.4, 25.7, 21.0, 17.7. Anal. Calcd for $C_8H_{16}S_2O_4$: C, 39.98; H, 6.71; S, 26.68. Found: C, 39.68; H, 6.65; S, 26.85.

1,1-Bis(methylsulfonyl)-4-methyl-3-pentene (18). To a solution of 4.0 g (23 mmol) of **3** in 200 mL of THF was added 30 mL (45 mmol) of *n*-BuLi. The solution was stirred under N_2 for 30 min, and 1.4 mL (12 mmol) of prenyl bromide was added all at once. The mixture was stirred for 15 h, and then 20 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the residue (5.5 g) was purified by flash chromatography (2:3 EtOAc–hexane) to afford 1.5 g (51% based on prenyl bromide) of **18** as a clear oil. Crystallization from 4:1 EtOH–H_2O afforded 1.4 g (48%) of **18**: mp 70.1–72.0 °C; IR (KBr) 1310, 1135 cm^{-1}; ^1H NMR δ 5.37 (t, J = 7.2 Hz, 1 H), 4.72 (t, J = 6.0 Hz, 1 H), 3.23 (s, 6 H), 2.98 (t, J = 6.6 Hz, 2 H), 1.72 (s, 3 H), 1.70 (s, 3 H); ^{13}C NMR (D_3CCOCD_3) δ 136.1, 119.7, 81.2, 41.3, 25.8, 23.8, 17.8. Anal. Calcd for $C_8H_{16}S_2O_4$: C, 39.98; H, 6.71. Found: C, 40.09; H, 6.72.

Alternatively, use of the detailed procedure described below for preparation of **20** on 0.53 g (3.1 mmol) of **3** under Ar afforded 47% of **18**. If the addition of *n*-BuLi were omitted from that procedure, 47% of **18** was obtained from 0.48 g (2.8 mmol) of **3**.

((4,8-Dimethyl-3,7-nonadienyl)sulfonyl)(methylsulfonyl)methane (19). To a solution of 0.50 g (2.9 mmol) of **3** in 250 mL of THF was added 7.8 mL (8.7 mmol) of *n*-BuLi. The solution was stirred under N_2 for 1 h, and 0.20 mL (1.0 mmol) of *trans*-geranyl bromide was added all at once. The mixture was stirred for 25 h, and then 25 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the residue (0.52 g) was purified by flash chromatography (2:3 EtOAc–hexane) to afford 0.094 g (30% based on *trans*-geranyl bromide) of a 9:1 mixture of **19** and **20**. Gradient flash chromatography (1:9–2:3 EtOAc–hexane) gave 0.078 g (25%) of **19** as a light yellow oil: IR (neat) 1335–1305, 1120 cm^{-1}; ^1H NMR δ 5.23 (t, J = 7.1 Hz, 1 H), 5.11 (t, J = 7.1 Hz, 1 H), 5.02 (s, 2 H), 3.44 (m, 2 H), 3.26 (s, 3 H), 2.57 (m, 2 H), 2.15–1.95 (m, 4 H), 1.68 (s, 3 H), 1.66 (s, 3 H), 1.60 (s, 3 H); ^{13}C NMR (D_3CCOCD_3) δ 139.2, 131.9, 124.7, 120.5, 70.1, 53.9, 42.3, 40.2, 27.1, 25.8, 20.9, 17.7, 16.1. Anal. Calcd for $C_{13}H_{24}S_2O_4$: C, 50.62; H, 7.84. Found: C, 50.60; H, 7.85.

1,1-Bis(methylsulfonyl)-4,8-dimethyl-3,7-nonadiene (20). To a mixture of 0.28 g (7.0 mmol) of KH and 200 mL of THF was added a solution of 2.4 g (9.1 mmol) of 18-crown-6 and 0.56 g (3.3 mmol) of **3** in 60 mL of THF. The mixture was stirred under N_2 for 2.5 h at 23 °C, and 2.5 mL (3.5 mmol) of *n*-BuLi was added. The mixture was stirred for 2 h, and 0.35 mL (1.8 mmol) of *trans*-geranyl bromide was added all at once. The mixture was stirred for 24 h, and then 25 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the residue (1.2 g) was purified by flash chromatography (2:3 EtOAc–hexane) to afford 0.31 g (56% based on geranyl bromide) of **20** as a light yellow oil. HPLC with H_3CCN–MeOH–H_2O (45:45:10) at a flow rate of 0.5 mL/min gave an analytical sample of **20** (retention time 8.7 min): IR (neat) 1310, 1125 cm^{-1}; ^1H NMR δ 5.40 (t, J = 7.2 Hz, 1 H), 5.11 (t, J = 7.2 Hz, 1 H), 4.72 (t, J = 6.0 Hz, 1 H), 3.23 (s, 6 H), 2.98 (t, J = 6.6 Hz, 2 H), 2.15–1.98 (m, 4 H), 1.70 (s, 3 H), 1.65 (s, 3 H), 1.60 (s, 3 H); ^{13}C NMR (D_3CCOCD_3) δ 139.8, 131.9, 124.8, 119.6, 81.3, 41.4, 40.2, 26.9, 25.8, 23.7, 17.7, 16.2. Anal. Calcd for $C_{13}H_{24}S_2O_4$: C, 50.62; H, 7.84. Found: C, 50.69; H, 7.89.

Alternatively, use of the detailed procedure described above for preparation of **18** on 0.180 g (1.00 mmol) of **3** under Ar afforded 53% of **20**.

((4,8,12-Trimethyl-3,7,11-tridecatrienyl)sulfonyl)(methylsulfonyl)methane (21). To a solution of 0.50 g (2.9 mmol) of **3** in 250 mL of THF was added 5.4 mL (8.9 mmol) of *n*-BuLi. The solution was stirred under N_2 for 5 h, and 0.21 g (0.74 mmol) of *trans,trans*-farnesyl bromide was added all at once. The mixture was stirred for 25 h, and then 25 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the residue (0.58 g) was purified by flash chromatography (2:3 EtOAc–hexane) to afford 0.090 g (32% based on *trans,trans*-farnesyl bromide) of a 9:1 mixture of **21** and **22**. Gradient flash chromatography (1:9–2:3 EtOAc–hexane) gave 0.063 g (23%) of **21** as a clear oil. HPLC with H_3CCN–MeOH–H_2O (37:37:26) at a flow rate of 2.0 mL/min gave an analytical sample of **21** (retention time 18.0 min): IR (neat) 1310, 1130 cm^{-1}; ^1H NMR δ 5.24 (t, J = 6.6 Hz, 1 H), 5.14 (t, J = 6.6 Hz, 1 H), 5.11 (t, J = 7.5 Hz, 1 H), 5.02 (s, 2 H), 3.44 (m, 2 H), 3.26 (s, 3 H), 2.58 (m, 2 H), 2.20–1.95 (m, 6 H), 1.69 (s, 3 H), 1.66 (s, 3 H), 1.61 (s, 3 H), 1.60 (s, 3 H); ^{13}C NMR (D_3CCOCD_3) δ 139.3, 135.7, 131.6, 125.1, 124.7, 120.6, 70.2, 54.0, 42.3, 40.2, 40.2, 27.4, 27.1, 25.8, 21.0, 17.7, 16.2, 16.1. Anal. Calcd for $C_{18}H_{32}S_2O_4$: C, 57.57; H, 8.59. Found: C, 57.70; H, 8.64.

1,1-Bis(methylsulfonyl)-4,8,12-trimethyl-3,7,11-tridecatriene (22). To a solution of 0.50 g (2.9 mmol) of **3** in 600 mL of THF was added 2.9 mL (4.4 mmol) of *n*-BuLi at 0 °C. The solution was stirred under N_2 for 2.5 h at 21 °C, and 0.28 g (1.0 mmol) of *trans,trans*-farnesyl bromide was added all at once. The mixture was stirred for 22 h, and then 0.5 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the residue (1.1 g) was purified by flash chromatography (2:3 EtOAc–hexane) to afford 0.18 g (49% based on farnesyl bromide) of **22** as a yellow oil: IR (neat) 1335–1305, 1145–1125 cm^{-1}; ^1H NMR δ 5.41 (t, J = 7.2 Hz, 1 H), 5.06–5.20 (m, 2 H), 4.72 (t, J = 6.0 Hz, 1 H), 3.23 (s, 6 H), 2.98 (t, J = 6.6 Hz, 2 H), 2.15–1.95 (m, 6 H), 1.70 (s, 3 H), 1.66 (s, 3 H), 1.61 (s, 3 H), 1.60 (s, 3 H); ^{13}C NMR (D_3CCN) δ 140.6, 136.1, 132.1, 125,2, 124.8, 119.2, 81.4, 42.0, 40.4, 40.2, 27.4, 27.0, 25.9, 23.9, 17.8, 16.4, 16.1. Anal. Calcd for $C_{18}H_{32}S_2O_4$: C, 57.57; H, 8.59. Found: C, 57.33; H, 8.57.

Acknowledgment. This research was supported by National Institutes of Health Grant HL23083. Some of the molecular modeling was performed by J. G. Rose, Jr.

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Preparation and Ring-Opening of Benzylic and Allylic Cyclopropyl Dianions

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Received December 17, 1991

There are several examples of substituted cyclopropyl anions rearranging to substituted allyl anions.[1] Although the ring-opening of cyclopropyl anion to allyl anion is not known for the parent compound, it has been studied by semiempirical and ab initio methods.[2] The reaction ap-

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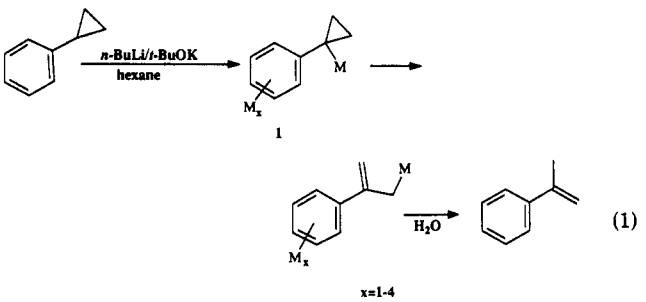
0022-3263/92/1957-3499$03.00/0

pears to be an example of an electrocyclic ring-opening.[3] There are apparent examples of cyclopropyl anions undergoing thermally allowed conrotatory ring-openings,[4] light-promoted disrotatory ring-openings,[5] and thermally forbidden disrotatory ring-openings.[6] Since the rate of rotation of the allyl bond in the allyl anion is fast relative to the ring-opening, the sense of the ring-opening is difficult to determine. It is not clear whether the rearrangement is concerted or proceeds through the known cyclopropyl radical or radical anion ring-opening reactions.[1] Although the exact pathway for the ring-opening is uncertain, it has been demonstrated that the first step must be the formation of a cyclopropyl anion in order for ring-opening to occur, not electron transfer from the base to the cyclopropane.[7]

A general requirement for the cyclopropyl anion ring-opening to occur is that the incipient allyl anion must have at least one group on the allyl termini which is capable of stabilizing the charge.[1] Both α-phenylcyclopropyl anion in the gas phase[8] and (α-phenylcyclopropyl)potassium in refluxing hexane[9] fail to undergo ring-opening. We have recently observed an example of a cyclopropyl anion ring-opening without benefit of stabilizing substituents on the resulting allyl anion.[9] Phenylcyclopropane was found to give α-methylstyrene on successive treatment with Lochmann's base and water. The metalation was shown to give polymetalated species 1, which ring-opened to the allyl anion product; quenching with water produced α-methylstyrene. The ring-opening is believed to result from the need for the charge in the benzylic position to be removed from the electron-rich polymetalated aryl ring, which this rearrangement accomplishes. The newly formed allyl anion is cross conjugated to the metalated phenyl ring, eq 1.



(1)

To better understand the reasons for this ring-opening we sought to understand the effect of substituents on the metalation and ring-opening of phenylcyclopropanes. Unfortunately, most electron-releasing substituents that come to mind will not survive these reaction conditions. In analogy to the metalation of the xylenes,[10] the metalation of o-, m-, and p-tolylcyclopropane with Lochmann's base should give the isoelectronic dicarbanions initially. We have studied the metalation of the tolylcyclopropanes with Lochmann's base. The methyl substituent reacts predictably with the base system, yielding a CH_2M as a substituent. These results are reported here.

Table I. Product Distribution for the Metalation/Ring-Opening Reaction Sequences

compd	product (yield, %)[a]			
2	3 (12%)	2 (44%)		
4	5 (53%)	6 (35%)	7 (8%)	
8	9 (25%)	10 (12%)	11 (4%)	12 (10%)
				8 (11%)
13	14 (19%)	13 (54%)		

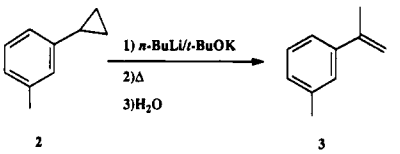
[a] The remainder of the material was found to be oligomeric.

Results

The tolylcyclopropanes used in this study are known compounds,[11] though none are commercially available. These are prepared by coupling cyclopropylmagnesium bromide with the appropriate tolyl bromide. The coupling is accomplished using dichloro[1,3-bis(diphenylphosphino)propane]nickel(II) as the catalyst.[12] 2-Cyclopropylpropene[13] is prepared similarly from the vinyl bromide and cyclopropylmagnesium bromide. Reaction of the cyclopropyl Grignard reagent is much more sluggish than typical Grignard reagents requiring THF, instead of ethyl ether, as solvent and prolonged reflux times. In contrast to similar coupling reactions, the reaction fails to proceed appreciably if the chlorotoluene isomer is substituted for a bromotoluene isomer.

These compounds are allowed to react with excess Lochmann's base (*n*-butyllithium/potassium *tert*-butoxide, a heterogeneous suspension in hexane)[14] by first allowing reaction at room temperature and then warming to reflux. Metalation gives rise to both mono- and polymetalated intermediates. The products and product distribution of the reaction open quenching with water are determined by ^1H NMR and gas chromatographic analysis. The product distributions for these reactions are shown in Table I. The sites of metalation are determined by studying the ^2H NMR spectra of the product mixtures obtained from quenching with CH_3CH_2OD or D_2O.

The reaction of *m*-tolylcyclopropane (2) with base followed by a H_2O quench gives 3, eq 2, a product similar to



(2)

what we observed previously for phenylcyclopropane. The observed product clearly comes from the protonation of the allyl anion resulting from the cleavage of the C2–C3 bond of the cyclopropane. ^2H NMR spectra of the ring-opened product after allowing it to quench with D_2O reveals deuterium incorporation on the benzylic methyl (δ 2.37) and the allylic methyl (δ 1.95). Starting material and

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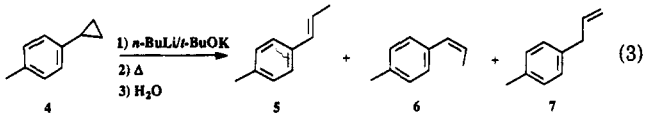
the ring-opened product account for approximately 50% of the material, the rest is isolated as an oil. Analysis of this oil by GPC reveals it to be oligomers, mainly dimers, trimers, and tetramers.

The products from metalation and quenching of *p*-tolylcyclopropane are entirely different than the products obtained for the meta isomer. The ortho isomer gives products that are common to both.

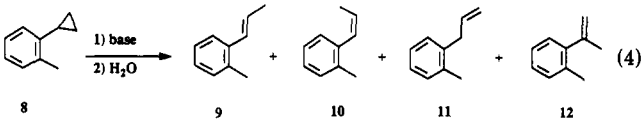
Treatment of *p*-tolylcyclopropane (**4**) under identical reaction conditions gives products **5**, **6**, and **7**, in eq 3. The



(3)

results are shown in Table I. These ring-opened products clearly result from the cleavage of the C1–C2 bond of the cyclopropane. This is in sharp contrast to the results observed for phenylcyclopropane and *m*-tolylcyclopropane. The D_2O quench of this reaction reveals deuterium to be incorporated into the products' benzylic methyls (δ 2.4), the allylic methyls (δ 1.9), and the allylic methylene (δ 3.41). ^2H NMR spectra showed little deuterium incorporated into the phenyl ring.

The reaction of *o*-tolylcyclopropane (**8**) with Lochmann's base gives four products, eq 4. The product distribution



(4)

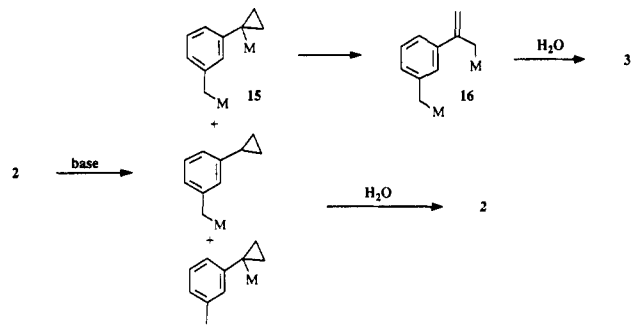
is shown in Table I. The ring-opened product **12** is similar to the ring-opened product observed from **2**. The ring-opened products **9**, **10**, and **11** are similar to the products observed from **4**. The deuterium quench of the reaction mixture shows incorporation of deuterium in the benzylic methyls (δ 2.3–2.5), allylic methyls (δ 1.8–2.0), and allylic methylene (δ 3.50). Stopping the reaction of **8** with Lochmann's base after 24 h by quenching with D_2O and before heating reveals no ring-opening. ^2H NMR spectra of this quenched product shows deuterium present in the following positions in these relative amounts: β-cyclopropyl (0.1), benzylic cyclopropyl (0.2), benzylic methyl (1.0), and aromatic (<0.05).

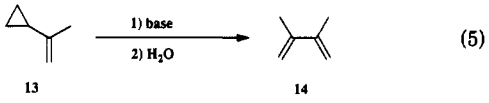
The D_2O quench of the unopened starting materials after heating in the above reactions shows predominate deuteration at the benzylic methyl much as expected, but there are also lesser amounts on the phenyl ring and the cyclopropyl ring. The majority of the deuterium incorporated at the site of the β-cyclopropyl hydrogens is trans to the phenyl (2:1). Since cyclopropyl anions generally retain their stereochemistry upon reaction,[15] this implies that the trans-metalated isomer is formed preferentially, as one might expect on the basis of steric considerations.

In an analogy to the work on the dimetalation of *p*-cresol[16] and the above tolylcyclopropane work, we have attempted to extend this metalation and ring-opening reaction to *p*-cyclopropylphenol and *p*-cyclopropylaniline. These reactions fail to give any detectable amounts of ring-opened products.

We are able to extend the metalation and ring-opening reaction observed for the *m*-tolylcyclopropane and phenylcyclopropane to 2-cyclopropylpropene (**13**). The treatment of **13** with Lochmann's base followed by treatment with ethanol gives rise to 2,3-dimethyl-1,3-butadiene (**14**) eq 5, Table I. Attempts to prepare the unknown isoprenyl anion[17] by metalation of vinylcyclopropane[18] fails to give any observable ring-opening.

Scheme I





(5)

Discussion

The ring opening observed for **2** is similar to the results observed for the phenylcyclopropane metalation ring-opening sequence. We propose a similar pathway, outlined in Scheme I. The species responsible for the ring-opened product is believed to be the dianion **16**. The ^2H NMR spectra of the D_2O quench of the reaction mixture reveal deuterium incorporation congruous with the proposed dianion **16**. In contrast to the metalation and ring-opening of phenylcyclopropane, little deuterium is found to be incorporated onto the aryl ring of **3**. The driving force for the ring-opening appears to be loss of ring strain in the cyclopropyl group and delocalization of charge onto the allyl moiety. The allyl anion is cross conjugated to the electron-rich phenyl ring. The mechanism by which dianion **15** goes to the ring-opened dianion **16** is not certain, either ring-opening of the dianion directly or indirectly by electron transfer from the dianion is possible. A ring-opened radical anion could accept an electron to give the corresponding ring-opened dianion.

The formation of oligomers may arise via a radical anion pathway, or from conjugate addition reactions of the anions to the alkene product formed during the quench of the reaction. Although the reaction mixture is full of electron donors for an electron-transfer reaction, there are no good electron accepters present.

The para isomer, under these reaction conditions, ring-opens via scission of the C1–C2 bond. The products obtained suggest dianion **19** as an intermediate. The ^2H NMR data are consistent with what is expected for dianion **19** as an intermediate, deuterium incorporation at the allylic and benzylic sites of the products.

There are several reasonable ways the C1–C2 bond could cleave, electron transfer from the base to give a trimethylene radical anion,[19] ring-opening of a β-metalated cyclopropane, or ring-opening via a cyclopropylmethyl carbanion like intermediate. The radical anion pathway is ruled out since the reaction is nearly quantitative, virtually no coupling products are observed, and there is no

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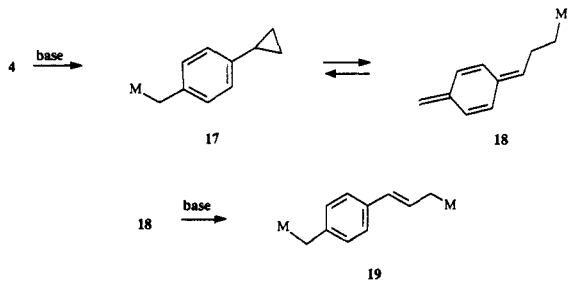
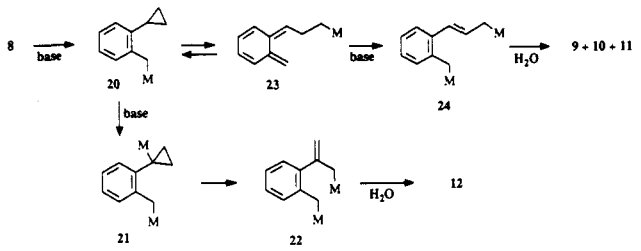
Scheme II



Scheme III

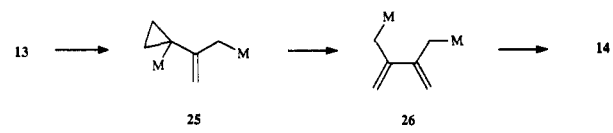


apparent reason why there should be a shift to a trimethylene radical anion intermediate on going from *m*-tolylcyclopropane to *p*-tolylcyclopropane. The ring-opening of a β-metalated intermediate is discounted since we found evidence for β-metalation in unopened **2** after reaction with Lochmann's base but detected no similar ring-opened products.[20]

It seems likely that these products arise through a several step sequence involving a cyclopropylmethyl carbanion intermediate, Scheme II. The isolated products from the protonation (or deuteration) of the reaction mixture are explained with the intermediacy of dianion **19**. The first step is the metalation of the methyl group, giving anion **17** which seems reasonable based on steric and statistical arguments and is the major metalated product found when the reaction is stopped before heating. This is in equilibrium with the ring-opened anion **18**.[21] Anion **18** reacts with a second equivalent of base to give dicarbanion **19**. The reaction of **19** with water gives rise to the products observed. Carbanion **18** could be formed in the same fashion that the cyclopropylmethyl carbanion rearranges to the 3-buten-1-yl carbanion.[22] Carbanion **17** could rearrange to **18** via a *p*-xylylene intermediate formed from a 1,6-elimination.[23]

With the ortho isomer both of the pathways are operative, Scheme III. These ring-openings come about in analogous ways; metalation of the benzylic methyl to give monoanion **20**, which is subsequently deprotonated at the second benzylic site to give **21**. Dianion **21** rearranges to dianion **22** and upon quenching with water, **12** is obtained. Products **9**, **10**, and **11** result from dianion **24**, analogous to the pathway that gave rise to the ring-opened products found with **4**. In a manner similar to **17**, **20** rearranges to give the ring-opened anion **23** and a second deprotonation

Scheme IV

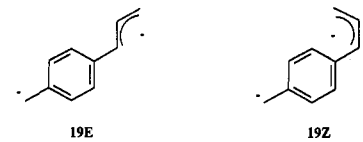


gives dianion **24** which on quenching would give products **9**, **10**, and **11**.

The ratio of [**9** + **10** + **11**]:**12**, (4:1), suggests that the metalation at the second benzylic position is comparable in rate to the ring-opening and metalation steps. This is what might be expected considering what is known about the directing ability of the first metalation in a polymetalation.[24] The initial metalated product is formed in a mixed aggregate with the metalating agent. The second benzylic hydrogen is held in close proximity to the base-accelerating deprotonation. This is observed in the metalation of the xylenes. The dimetalation of *o*-xylene is much faster and proceeds in higher yields than the metalation of *p*-xylene, where the second benzylic site is para and relatively far removed from the initially metalated site.[10,25]

The metalation and ring-opening of **13** gives products that are similar to those observed for phenylcyclopropane and **2**. This reaction, presumably, proceeds through the dianion **25** which then opens to give the well-known dianion **26**,[26] Scheme IV.

The product distribution, Table I, for the products of C1–C2 bond cleavage gives a clue to the structure and energies of the dianions **19** and **24**. It is clear from the product distribution that there is a nonequilibrium quench of the dianions. An equilibrium quench would give *E*/*Z* ratios of greater than 99. The large proportion of the *Z* alkene suggests that the cisoid and transoid dianions, **19E** and **19Z**, are both present and close in energy. This is not surprising considering the S shape of solid hexadienyldilithium as determined by X-ray crystallography[27] and the cisoid/transoid equilibrium known for crotyl anion.[28]



Conclusions

The *m*-tolylcyclopropane, *o*-tolylcyclopropane, and 2-cyclopropylpropene upon treatment with Lochmann's base give rise to ring-opened products via scission of the C2–C3 bond. We believe that this ring-opening proceeds through dimetalated intermediates. The ring-opened products arise from the benzylic cyclopropyl anion being pushed open from the electron-rich ring rather than being pulled by electron-withdrawing groups on the incipient allyl anion termini. With *p*- and *o*-tolylcyclopropane two different ring-opening reactions are possible; scission of the C1–C2

(20) We observed formation of the β-phenylcyclopropylanion in the reaction of Lochmann's base with phenylcyclopropane and no products from scission of the C1–C2 bond were observed.[9]

(21) MNDO calculations suggest that the monomeric lithium salts of anions **17** (ΔH_f = 28.0 kcal/mol) and **18** (ΔH_f = 33.6 kcal/mol) are close in energy. MOPAC: version 6.00, J. J. P. Stewart, QCPE, 455.

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bond via a cyclopropylmethyl anion type rearrangement or scission of the C2–C3 bond via a dianion intermediate. The *p*-tolylcyclopropane opens exclusively at C1–C2. The *o*-tolylcyclopropane gives products from both ring-opening pathways.

Experimental Section

All organic reagents were obtained from Aldrich Chemical Co. The [1,3-bis(diphenylphosphino)propane]nickel(II) dichloride was obtained from Strem Chemicals. The *n*-butyllithium was obtained from FMC Corp. The potassium *tert*-butoxide was used without further purification. The hexane used in metalation reactions was washed with concentrated sulfuric acid and then distilled from calcium hydride. Tetrahydrofuran was distilled from sodium/benzophenone. NMR spectra were obtained on a 7.1-T, broadband QE300 NMR instrument operating at 300.2 MHz for proton, 75.4 MHz for ^{13}C, and 46.1 MHz for deuterium. Chemical shifts are reported relative to TMS except in the case of the deuterium NMR, where the samples were run in chloroform and the shifts were obtained relative to CD_2Cl_2. Gas chromatographic analysis was carried out on a Hewlett-Packard chromatograph Model 5890A with a wide bore methylphenylsilicone capillary column, 30 m in length. Product yields were determined by both ^1H NMR and gas chromatography.

Preparation of the Tolylcyclopropanes 2, 4, and 8. Cyclopropylmagnesium bromide (0.18 mol in 125 mL of THF) was added via syringe to a stirred mixture of the bromotoluene (16.5 g, 0.097 mol), [1,3-bis(diphenylphosphino)propane]nickel(II) dichloride (0.25 g), and THF (125 mL) in a nitrogen-charged 250-mL round-bottom flask equipped with reflux condenser and septum. Upon completion of addition, the mixture was allowed to stir at room temperature for 2 h before the flask was placed in an oil bath and allowed to reflux for 72 h. The reaction was monitored by gas chromatography and shown to be complete by the disappearance of the bromotoluene. The reaction mixture was worked up by adding 100 mL of ether and washing with 5% HCl followed by several water washings. The organic layer was dried with magnesium sulfate. The solvent was removed using a rotary evaporator. The residue was vacuum distilled to give the tolylcyclopropane.

Compound **2** was isolated in 70% yield (bp 80–83 °C/18 Torr, lit.[11] bp 75–77 °C/12 Torr; 97% pure). ^1H NMR ($CDCl_3$): δ 0.68 (m, 2 H); 0.91 (m, 2 H); 1.86 (m, 2 H); 2.31 (s, 3 H); 6.87 (d, J = 9.1 Hz, 1 H); 6.88 (s, 1 H); 6.95 (d, J = 9.1 Hz, 1 H); 7.15 (t, J = 9.1 Hz, 1 H).

Compound **4** was isolated in 70% yield (bp 80–83 °C/18 Torr, lit.[11] bp 80–81 °C/14 Torr; 99% pure). ^1H NMR ($CDCl_3$): δ 0.72 (m, 2 H); 0.98 (m, 2 H); 1.92 (m, 1 H); 2.37 (s, 3 H); 7.03 (d, J = 7.8 Hz, 2 H); 7.12 (d, J = 7.8 Hz, 2 H).

Compound **8** was isolated in 65% yield (80–83 °C/18 Torr, lit.[11] bp 70–71 °C/18 Torr; 98% pure). ^1H NMR ($CDCl_3$): δ 0.62 (m, 2 H); 0.90 (m, 2 H); 1.86 (m, 1 H); 2.41 (s, 3 H); 6.95 (m, 1 H); 7.04–7.14 (m, 3 H). NMR data for these compounds are consistent with that reported in the literature.[11]

Preparation of 2-Cyclopropylpropene (13). A 1-L three-necked flask charged with nitrogen was equipped with a magnetic stirrer, a pressure equalizing dropping funnel containing cyclopropylmagnesium bromide (385 mL, 1.3M in THF), a reflux condenser, 2-bromopropene (40.0 g, 0.33 mol), dichloro[1,3-bis-(diphenylphosphino)propane]nickel(II) (0.30 g), and anhydrous THF (185 mL). The Grignard reagent was added over 15–20 min to the ice-cooled mixture. The reaction mixture was then allowed to warm to room temperature. An exothermic reaction beings after about 30 min and the mixture starts to reflux. External heat was applied to allow the reflux to continue for 8 h. After removing the heat source and allowing the mixture to cool to room temperature, water was carefully added to discharge the excess Grignard reagent. Dilute HCl was added to help form a discrete organic layer. The organic layer was washed with water until it was nearly free of THF. The organic layer was then distilled (bp 73–77 °C; lit.[13] bp 70–80 °C) to give 2-cyclopropylpropene (17 g, 70%, 96% pure).

^1H NMR ($CDCl_3$): δ 0.47 (m, 2 H); 0.59 (m, 2 H); 1.39 (m, 1 H); 1.62 (m, 3 H); 4.65 (m, 1 H); 4.69 (m, 1 H). Spectral data are consistent with literature values.[13]

Metalation of the Tolylcyclopropanes. In a typical metalation reaction, potassium *tert*-butoxide (2.50 g, 22.4 mmol), *n*-butyllithium (13.8 mL of 1.6 M *n*-butyllithium), the tolylcyclopropane (0.66 g, 5 mmol), and 20 mL of dry hexane were combined under nitrogen in a Schlenk flask equipped with a magnetic stirring bar. The heterogeneous reaction mixture was stirred at room temperature under nitrogen for at least 24 h before quenching or heating. If the reaction mixture was heated, the stopper was replaced by a reflux condenser and gas tube. The flask was placed in an oil bath, and the solvent was allowed to reflux with stirring while being kept under nitrogen.

Acknowledgment. We would like to thank the UNCC foundation for partial financial support of this work and the Lithium Division of FMC Corporation for their generous donation of alkyllithium reagents.

Registry No. **2**, 19714-73-9; **3**, 1124-20-5; **4**, 6921-43-3; **5**, 2077-30-7; **6**, 2077-29-4; **7**, 3333-13-9; **8**, 27546-46-9; **9**, 2077-34-1; **10**, 2077-33-0; **11**, 1587-04-8; **12**, 7399-49-7; **13**, 4663-22-3; **14**, 513-81-5; cyclopropylmagnesium bromide, 23719-80-4; 3-bromotoluene, 591-17-3; 4-bromotoluene, 106-38-7; 2-bromotoluene, 95-46-5; 2-bromopropene, 557-93-7.

Luffariolides A–E, New Cytotoxic Sesterterpenes from the Okinawan Marine Sponge *Luffariella* sp.

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Received December 30, 1991

Manoalide is an antimicrobial sesterterpene first isolated from the Palauan sponge *Luffariella variabilis*[2] that has proven to have analgesic and antiinflammatory activities[3] and inhibit the action of phospholipase A_2.[4] Recent studies have revealed that marine sponges of the genus *Luffariella* are a rich source of manoalide-related sesterterpenoids, and most of them possess useful bioactivities.[5] During our investigations of pharmacologically active substances from Okinawan marine organisms,[6] we recently examined extracts of the Okinawan sponge *Luffariella* sp.

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