that the $FlI^{-}\cdot/FlI$: reversible redox couple was observed in the cyclic voltammetric reduction of $FlIN_2$.[2] The chemical reductions of $FlIN_2$ and $FlIBr_2$ lead us to conclude that reduction of diazo compounds is the only efficient method presently available for producing these aryl carbene anion radicals in solution. As to the question of whether the reduction of carbene anion radicals → carbene dianions will be observed generally or will be strongly structure dependent, the answer must await the results of studies in progress.

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References and Notes

(1) R. N. McDonald, J. R. January, K. J. Borhani, and M. D. Hawley, *J. Am. Chem. Soc.*, **99**, 1268 (1977).
(2) R. N. McDonald, K. J. Borhani, and M. D. Hawley, *J. Am. Chem. Soc.*, **100**, 995 (1978).
(3) Lithium metal reductively cleaves $(Ph_2C{=}N{-})_2$ to Ph_2CHNH_2 (E. J. MacPherson and J. C. Smith, *Can. J. Chem.*, **48**, 1915 (1970)), while sodium and potassium give adducts which on hydrolysis yield *N*-benzhydrylbenzophenone hydrazone (*ibid.*, **48**, 1904 (1970)). See also H. Lund, *Acta Chem. Scand.*, **13**, 249 (1959), for the electrochemical reduction of benzalazine to the corresponding primary amines.
(4) The attack of FlH^{-} and $FlI^{-}\cdot$ on the terminal N of $FlIN_2$ supports the view that ethylidene anion radical reacts on the terminal N of N_2O in the gas phase: J. H. J. Dawson and N. M. M. Nibbering, *J. Am. Chem. Soc.*, **100**, 1928 (1978). Diazo compounds and N_2O are isoelectronic structures.
(5) The use of excess solvated electrons in the reduction of $FlIN_2$ produced some azine reduction along with considerable saturated C–H's in the ^1H NMR spectrum of the product. This was probably the result of Birch reduction of the fluorene nucleus.
(6) (a) G. A. Russell, A. J. Bemis, E. J. Geels, E. G. Janzen, and A. J. Moye, *Adv. Chem. Ser.*, **No. 75**, 174–202 (1968); (b) G. A. Russell, *IUPAC Int. Symp. Org. Chem. 1966*, 185–206 (1967).
(7) Both of these hydrocarbon dimers were indicated to be present as trace products by GLC in other reductions of $FlIN_2$.
(8) Percent compositions from ^1H NMR use the value of $FlIH_2$ determined for this species by ^{13}C NMR using relative integrals of two different aryl C's and C_9–H_2 of authentic $FlIH_2$ and of the deuterated sample. In the ^{13}C NMR analysis known relative integrals of these aryl C's to the triplet of authentic FlIHD were used to determine the percent of this species. The amount of $FlID_2$ was by difference.
(9) We thank Mr. Kevin Reid for this result.
(10) A. Lagu, H. B. Mark, and J. R. Jezorek, *J. Org. Chem.*, **42**, 1063 (1977), and references therein.
(11) In our gas-phase studies of related compounds in a flowing afterflow apparatus, we find no evidence for the parent molecular anion either by thermal electron attachment in the flow or at very low ionization energy (nominal 3.3 eV) directly in the mass spectrometer chamber. Thus, the process appears to be dissociative electron attachment in the gas phase with such reactants, and the same is indicated to be true in solution.[1,2]
(12) G. D. Sargent, C. M. Tatum, and S. M. Kastner, *J. Am. Chem. Soc.*, **94**, 7174 (1972). (b) G. D. Sargent, C. M. Tatum, and R. P. Scott, *ibid.*, **96**, 1602 (1974).
(13) See Y.-J. Lee and W. D. Closson, *Tetrahedron Lett.*, 1395 (1974), for similar reductions of benzhydryl and benzyl halides.

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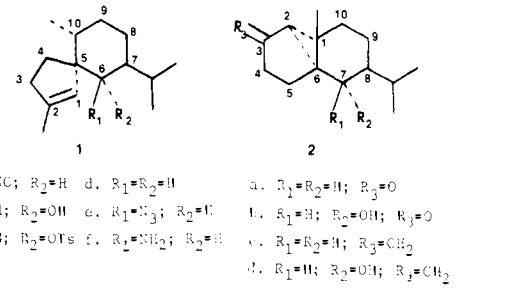
Total Synthesis of (−)-Axisonitrile-3. An Application of the Reductive Ring Opening of Vinylcyclopropanes

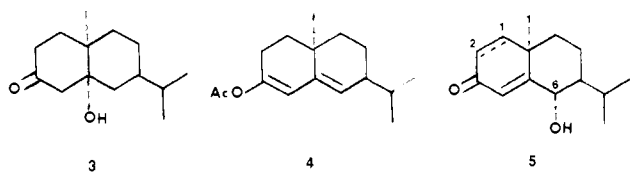
Sir:

Recently, Sica and co-workers isolated the isonitrile sesquiterpene (+)-axisonitrile-3 from the marine sponge *Axinella cannabina* and determined that it has a novel spiro[4.5]decane ring system by X-ray crystallography.[1] We report the total synthesis of (−)-axisonitrile-3 (**1a**) from (+)-dihydrocarvone. This synthesis establishes that the absolute configuration of the natural product is opposite to that shown in structure **1a**.

It is well known that reductive cleavage of 1-methyltricyclo[4.4.0.0^{2,6}]decan-3-ones provides a general method of synthesis of spiro[4.5]decanone derivatives.[2] Our recent work on the lithium/liquid ammonia cleavage of the tricyclodecanone **2a** demonstrated that opening of the cyclopropane ring to the corresponding spiro ketone occurred exclusively with inversion of configuration at the β carbon (C-1).[2c] We have now found that the related vinylcyclopropanes (cf. **2c,d**) undergo reductive ring opening with lithium in ethylamine to produce spiro[4.5]decenes such as **1b,d.** Again, exclusive inversion of configuration at C-1 was observed. This suggested that an *exo*-methylene compound of the type **2** having a substituent at C-7 which would allow elaboration to an isonitrile group would serve as a useful precursor of **1a.** From a number of possibilities, we selected a route which utilized the 7α-hydroxy compound **2d.**



The known ketol **3**,[3] which was prepared in 50% yield by annulation of (+)-dihydrocarvone[4] with methyl vinyl ketone followed by catalytic hydrogenation of the double bond of the isopropenyl group, was the starting material for the synthesis.



Treatment of **3** with acetic anhydride containing a catalytic amount of sulfuric acid (12 h, 25°C) gave the dienol acetate **4** (NMR δ_{Me_4Si} (CCl_4) 0.88 (d, J = 6 Hz, 3 H), 0.91 (d, J = 6 Hz, 3 H), 1.02 (s, 3 H), 2.03 (s, 3 H), 5.33 (d, J = 3 Hz, 1 H), 5.62 (d, J = 2 Hz, 1 H)) in 80% yield. Oxidation of **4** with *m*-chloroperbenzoic acid in 20:1 isopropyl alcohol-water[5] (4 h, 25 °C) gave a mixture of products containing 42% of the enone derived from dehydration of the ketol **3** and 56% (96% based upon unrecovered enone) of an ~6:1 mixture of the hydroxy enone **5a** and its 6β epimer. Hydroxy enone **5a**[6] (mp 116.0–118.0 °C (from benzene-hexane); NMR δ_{Me_4Si} (CCl_4) 0.93 (br m, 6 H), 1.40 (s, 3 H), 3.75 (s, 1 H), 4.20 (br s, 1 H), 5.67 (s, 1 H)) was isolated by chromatography by Florisil. The 6β epimer was not obtained completely pure, but the crude material showed NMR δ_{Me_4Si} (CCl_4) 0.92 (br m, 6 H), 1.25 (s, 3 H), 4.53 (br s, 1 H), 6.05 (d, J = 1.5 Hz, 1 H).

Conversion of **5a** to its MIP (methoxyisopropylidine) derivative,[7] followed by the introduction of a 1,2 double bond using the phenylselenenylation-selenoxide elimination procedure,[8] gave **5b**[6] (mp 92.5–93.5 °C (from benzene-hexane); NMR δ_{Me_4Si} (CCl_4) 0.83 (d, J = 5 Hz, 3 H), 0.93 (d, J = 5 Hz, 3 H), 1.41 (s, 3 H), 4.38 (br s, 1 H), 5.93 (dd, J = 1.6, 10 Hz, 1 H), 5.97 (d, J = 1.6 Hz, 1 H), 6.57 (d, J = 10 Hz, 1 H)) in 85% yield. Irradiation of a 0.04 M solution of **5b** in anhydrous dioxane at room temperature gave a single crude tricyclodecenone[9] (NMR δ_{Me_4Si} (CCl_4) 0.81 (d, J = 6 Hz, 3 H), 0.93 (d, J = 6 Hz, 3 H), 1.17 (s, 3 H), 4.03 (d, J = 7 Hz, 1 H), 5.73 (d, J = 6 Hz, 1 H), 7.33 (d, J = 6 Hz, 1 H)) which was catalytically reduced (Pd/C, ethanol) to the hydroxy ketone **2b**[6] (mp 70.5–72.0 °C (from hexane); NMR δ_{Me_4Si} (CCl_4) 0.78 (d, J

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= 6.5 Hz, 3 H), 0.90 (d, J = 6.5 Hz, 3 H), 1.17 (s, 3 H), 3.60 (d, J = 7 Hz, 1 H)) in 52% yield from **5b**.

Treatment of the hydroxy ketone **2b** with triphenylmethylenephosphorane in dimethyl sulfoxide (12 h, 55 °C)[10] gave the *exo*-methylene compound **2d**[6] (mp 68.0–69.0 °C (from hexane); NMR δ_{Me_4Si} (CCl_4) 0.74 (d, J = 7 Hz, 3 H), 0.87 (d, J = 7 Hz, 3 H), 0.98 (s, 3 H), 3.60 (d, J = 7.5 Hz, 1 H), 4.63 (br s, 1 H), 4.75 (br s, 1 H)) in 92% yield. Reductive cleavage of **2d** with lithium in ethylamine (1 min, 16 °C) gave a single alcohol, **1b**, in 90% crude yield.[11] There was no evidence that any of the 10β epimer of **1b** (retention of configuration in the ring opening) was obtained in this reaction. Without purification **1b** was converted into the tosylate **1c**[6] (mp 81–82 °C (from hexane); NMR δ_{Me_4Si} (CCl_4) 0.75 (d, J = 6 Hz, 3 H), 0.78 (d, J = 6 Hz, 3 H), 0.86 (d, J = 6 Hz, 3 H), 1.63 (br s, 3 H), 2.45 (s, 3 H), 4.52 (d, J = 8 Hz, 1 H), 5.13 (br s, 1 H), 7.23 (d, J = 8 Hz, 2 H), 7.72 (d, J = 8 Hz, 2 H)) using tosyl chloride in pyridine (96 h, 25 °C) in 60% overall yield from **2d**.

We also carried out the conversion of the model tricyclodecanone **2a** into (+)-spiroaxene (**1d**)[1] in a similar manner. Methylenation of **2a** as above gave **2c** (NMR δ_{Me_4Si} (CCl_4) 0.82 (d, J = 6 Hz, 6 H), 0.97 (s, 3 H), 4.64 (br s, 1 H), 4.47 (br s, 1 H)) which upon reaction with lithium in ethylamine gave **1d**[6] (NMR δ_{Me_4Si} (CCl_4) 0.75 (d, J = 6 Hz, 3 H), 0.83 (d, J = 6 Hz, 6 H), 1.72 (br s, 3 H), 5.28 (br s, 1 H); $[\alpha]^{25}_D$ +11.6° (c 2.0, ether).[11]

Bose, Kistner, and Farber[12] have reported the conversion of menthyl tosylate into neomenthylamine via S_N2 reaction with sodium azide in aqueous dimethylformamide followed by lithium aluminum hydride reduction of the azide. However, attempted conversion of **1c** to the azide **1e** using their procedure led primarily to the formation of elimination products as did the use of potassium azide in acetonitrile containing 18-crown-6. It was clear that it would be necessary to carry out the tosylate displacement under conditions which would be more favorable to an S_N2 reaction. This was accomplished by treating **1c** with 3 equiv of potassium azide in benzene containing 5 equiv of 18-crown-6 (48 h, 80 °C).[13] The azide **1e** showed NMR δ_{Me_4Si} (CCl_4) 0.71 (d, J = 6 Hz, 3 H), 0.93 (d, J = 6 Hz, 3 H), 0.97 (d, J = 6 Hz, 3 H), 1.77 (br s, 3 H), 3.47 (s, 1 H), 5.20 (br s, 1 H); mass spectrum (70 eV), no M^+, m/e 219 ($M - N_2$, weak), 204 ($M - HN_3$, strong). Reduction of **1e** with $LiAlH_4$ in ether at reflux gave the amine **1f** (NMR δ_{Me_4Si} (CCl_4) 0.71 (d, J = 6 Hz, 3 H), 0.87 (d, J = 5 Hz, 6 H), 1.73 (br s, 3 H), 2.63 (br s, 1 H), 5.27 (br s, 1 H)) in 30% overall yield[14] from **1c**.

Using a procedure analogous to that of Hertler and Corey,[15] **1f** was converted into (−)-axisonitrile-3 (**1a**) in 85% overall yield by treatment with a 2:1 mixture of formic acid in acetic anhydride at reflux for 2 h followed by reaction with tosyl chloride in pyridine at 25 °C for 1 h. (The formamide derivative, presumably (+)-axamide-3,[1,16] was isolated as an intermediate in this sequence.) The synthetic material[6] showed mp 97–99 °C (from hexane); NMR δ_{Me_4Si} (CCl_4) 0.75 (d, J = 6.5 Hz, 3 H), 0.93 (br d, J = 6.5 Hz, 6 H), 1.75 (br s, 3 H), 3.52 (br s, 1 H), 5.14 (br s, 1 H); IR (CCl_4) 2120 cm^{-1}; $[\alpha]^{25}_D$ −71° (c 0.35, $CHCl_3$).

These physical properties generally agreed with those reported for (+)-axisonitrile-3,[1] the enantiomer of **1a**, except for the sign of the optical rotation.[1] However, there were small discrepancies between the observed NMR chemical shifts, particularly for the methyl groups of the isopropyl group, and those reported by Sica and co-workers.[1] Therefore, verification of the structure of the synthetic material was desirable. Unfortunately, a direct comparison of the synthetic material with the natural product could not be made since neither a pure authentic sample nor copies of the original spectral data were available to us. In order to confirm the structure of the synthetic compound, a single crystal X-ray study was carried out using a Syntex $P2_1$ four-circle diffractometer. A complete data set was collected; the published coordinates[1] were refined using Sheldrick's SHELX-76 least-squares program. The refinement converged, with a residual of 0.13, using isotropic thermal parameters and without the hydrogen atoms being included. A difference Fourier synthesis showed no peaks of electron density greater than 0.5e/Å^3. This conclusively demonstrated that the synthetic material was in fact (−)-axisonitrile-3 (**1a**).[17]

References and Notes

(1) B. DiBlasio, E. Fattorusso, S. Magno, L. Mayol, C. Pedone, C. Santacroce, and D. Sica, *Tetrahedron*, **32**, 473 (1976).
(2) (a) W. G. Dauben and E. J. Deviny, *J. Org. Chem.*, **31**, 3794 (1966); (b) E. Piers and P. M. Worster, *J. Am. Chem. Soc.*, **94**, 2895 (1972); (c) D. Caine, W. R. Pennington, and T. L. Smith, Jr., *Tetrahedron Lett.*, 2663 (1978).
(3) J. A. Marshall, W. I. Fanta, and H. Roebke, *J. Org. Chem.*, **31**, 1016 (1966); J. A. Marshall, G. L. Bundy, and W. I. Fanta, *ibid.*, **33**, 3913 (1968).
(4) SMC Corp., Glidden Organics, Jacksonville, Fla.
(5) D. N. Kirk and J. M. Wiles, *Chem. Commun.*, 518 (1970).
(6) A correct combustion analysis has been obtained for this compound.
(7) A. F. Kluge, K. G. Untch, and J. H. Fried, *J. Am. Chem. Soc.*, **94**, 7827 (1972). We suggest the abbreviation MIP (i.e., methoxyisopropylidine) for this derivative.
(8) (a) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, **97**, 5434 (1975). (b) K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *ibid.*, **95**, 6137 (1973). (c) D. L. J. Clive, *J. Chem. Soc., Chem. Commun.*, 695 (1973). (d) For the specific application of this sequence to conversion of an octalone to a cross-conjugated dienone, see D. Caine, A. A. Boucugnani, and W. R. Pennington, *J. Org. Chem.*, **41**, 3632 (1976).
(9) (a) For reviews covering the photochemical conversion of bicyclic cross-conjugated dienones into tricyclodecenones, see P. J. Kropp, *Org. Photochem.*, **1**, 1 (1967); K. Schaffner, *Adv. Photochem.*, **4**, 81 (1966). (b) A Hanau NK-20 low-pressure mercury lamp was used as the light source.
(10) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).
(11) In general, the cyclopropane ring of simple vinylcyclopropanes is not cleaved by metals in liquid ammonia (see S. W. Staley, *Sel. Org. Transform.*, **2**, 97 (1972)). Compound **2c** was found to be stable to excess lithium in liquid ammonia at −33 °C for 2 h. However, **2c** and **2d** were rapidly cleaved by lithium in ethylamine and extreme care had to be exercised to prevent overreduction. To our knowledge the conversions of **2c** and **2d** into **1d** and **1b**, respectively, represent the first examples of reductive cleavages of vinylcyclopropanes with lithium in ethylamine. However, cleavages of strained divinylcyclopropanes such as octamethylsemibullavene with lithium in liquid ammonia have been reported (W. T. Borden, A. Gold, and S. D. Young, *J. Org. Chem.*, **43**, 486 (1978)).
(12) A. J. Bose, J. F. Kishner, and L. Farber, *J. Org. Chem.*, **27**, 2925 (1962).
(13) We are indebted to Professor Charles L. Liotta for discussions on this point and for a gift of 18-crown-6.
(14) The yield of the amine **1f** obtained in the reduction of the azide **1e** with $LiAlH_4$ in ether was surprisingly low. Other methods for accomplishing this conversion are being explored.
(15) W. R. Hertler and E. J. Corey, *J. Org. Chem.*, **23**, 1221 (1958).
(16) Spectral data for (−)-axamide-3 were not reported in ref 1.
(17) We are very grateful to Dr. Donald G. VanDerveer for his assistance in carrying out the X-ray work.

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Stereospecific Total Synthesis of Gibberellic Acid. A Key Tricyclic Intermediate

Sir:

Since the recognition of the central biological role of gibberellic acid (gibberellin A_3, GA_3) (**1**) in the plant kingdom,[1] the clarification of its chemical structure,[2] and commercial production on a large scale from the fungus *Gibberella fujikuroi*, this substance has occupied a major position in the field of natural products.[3] The biosynthesis of gibberellic acid from prenyl units, though long and involved, is known in considerable detail.[1,3,4] Despite extensive efforts (some 150 published papers from about 25 different laboratories), the total chemical synthesis of gibberellic acid has not previously been achieved,[5] largely because the combination of overall molecular complexity, centers of high sensitivity toward many reagents, and

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