(±)-Dicranenone A from 1-Hydroxycyclopropanecarbaldehyde Derivatives

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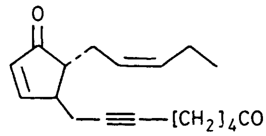
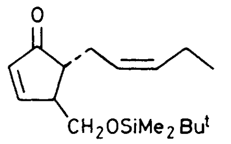
The five-membered ring compounds (**2**) and (**3**), precursors of dicranenones, have been prepared from 1-hydroxycyclopropanecarbaldehyde derivatives (**4**).

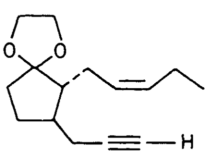
Dicranenones constitute a class of new fatty acids having a cyclopentenone ring structurally similar to prostanoids and jasmonoids. They have been isolated from Japanese mosses, and have been shown to possess antimicrobial activity.[1,2] The recent report of a total synthesis of (±)-dicranenone A (**1**), *via* the acetylenic cyclopentanone acetal (**3**) prepared from methyl jasmonate, prompts us to report our syntheses of the intermediates (**2**) and (**3**) from the readily available 1-hydroxycyclopropanecarbaldehyde derivatives (**4**).[3—5] We have previously reported that the tetrahydropyranyl ether (**4a**) and silylated derivative (**4b**) are convenient synthons for the total synthesis of jasmonoid[3] or spirovetivane[4] compounds, *via* the thermal $C_3 \rightarrow C_5$ ring enlargement of silylated 1-vinylcyclopropanol derivatives.



(1)



(2)



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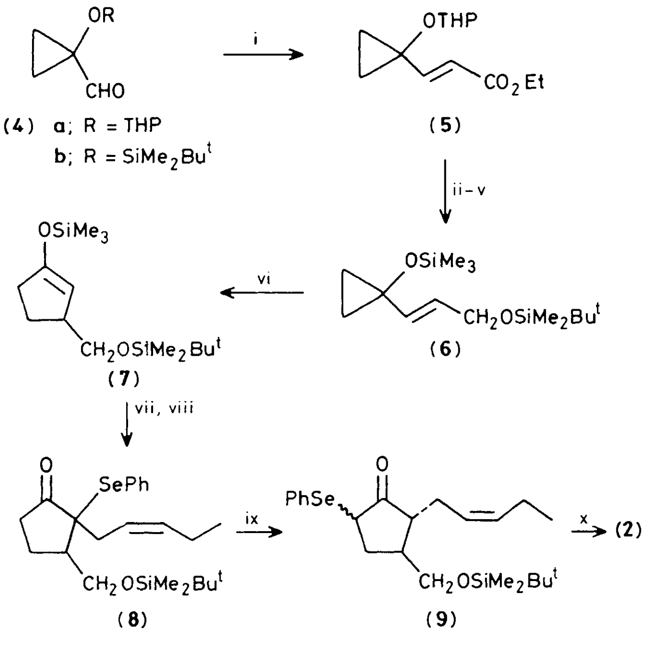
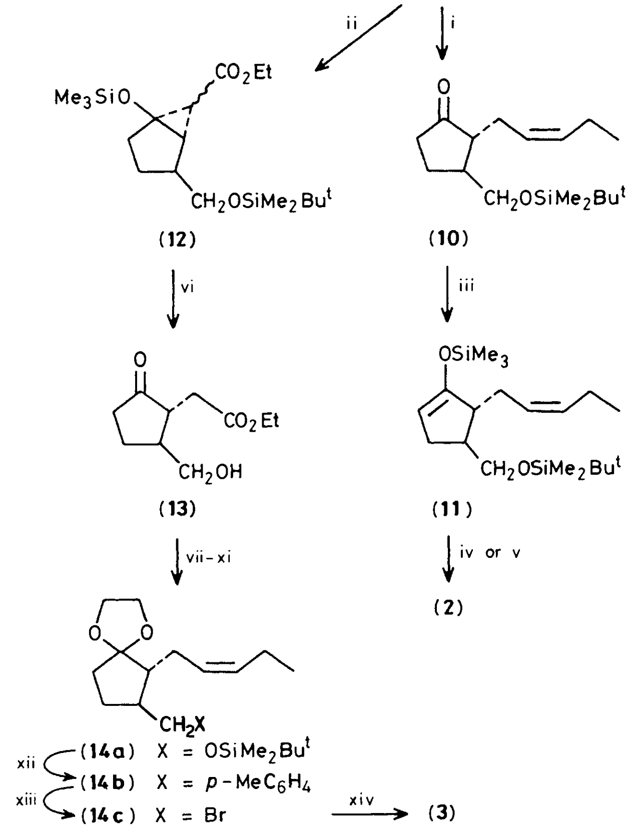
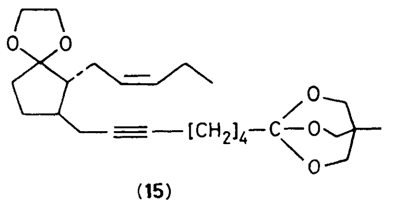


THP = tetrahydropyran-2-yl

Scheme 1. *Reagents and conditions:* i, $(EtO)_2P(O)CHCO_2Et$, tetrahydrofuran (THF), 88% yield; ii, pyridinium toluene-*p*-sulphonate, EtOH, 55 °C, 95%; iii, Me_3SiCl, NEt_3, dimethyl sulphoxide (DMSO), 98%; iv, Bu^i_2AlH; v, $ClSiBu^tMe_2$, imidazole, dimethylformamide (DMF), 20 h, 93%; vi, 600 °C; vii, PhSeBr; viii, *cis*-$EtCH{=}CHCH_2Br$, lithium di-isopropylamide (LDA), hexamethylphosphoramide (HMPA); ix, LDA (0.5 equiv.), THF–HMPA, −78 °C; x, 30% H_2O_2, CH_2Cl_2, 90%.





(15)

Scheme 2. *Reagents and conditions:* i, *cis*-$EtCH{=}CHCH_2Br$, $ZnBr_2$, 20—40%; ii, $Cu(MeCOCHCOMe)_2$, C_6H_6, 80 °C, ethyl diazoacetate, 75%; iii, LDA, Me_3SiCl; iv, $Pd(OAc)_2$ (0.5 equiv.), *p*-benzoquinone (0.5 equiv.), MeCN, room temp., 78%; v, PhSeBr, oxidation; vi, $ClSiMe_3$, MeOH, room temp., 30 min, 97%; vii, $HOCH_2CH_2OH$, C_6H_6, *p*-$MeC_6H_4SO_2OH$, 80 °C; viii, $ClSiBu^tMe_2$; ix, $LiAlH_4$, THF, 65 °C, 1 h; x, DMSO, $(COCl)_2$; xi, $EtCH{=}PPh_3$; xii, *p*-$MeC_6H_4SO_2Cl$, pyridine, 0 °C, 82%; xiii, LiBr, Me_2CO reflux, 12 h, 92%; xiv, $LiC{\equiv}CH\text{-}NH_2CH_2CH_2NH_2$ (1.5 equiv.), DMSO.

Addition of the triethylphosphonoacetate carbanion in THF to aldehyde (**4a**) gave the *trans*-vinylcyclopropane (**5**).[5] Deprotection of the THP group,[6] silylation of the cyclopropanol,[7] reduction of the ester group, and silylation of the resulting allylic alcohol[8] led to the *trans*-disiloxyvinylcyclopropane (**6**).[6] On flash thermolysis (**6**) underwent ring expansion into the regiospecific cyclopentanone silyl enol ether (**7**).[9] Addition of phenylselenenyl bromide[10] and alkylation of the resulting α-selenocyclopentanone with *cis*-pent-2-enyl bromide[11,12] provided the cyclopentanone (**8**) in 76% yield. Base induced selenium shift[12] gave the isomeric α′-selenocyclopentanone (**9**) which underwent oxidative elimination[13] to provide the expected cyclopentenone (**2**). Introduction of hex-5-ynecarboxylic acid to obtain dicranenone A (**1**) from (**2**) required protection of the carbonyl group. However in spite of many attempts, for example, using 1,2-ethanedithiobis(trimethylsilane),[14] selective protection of (**2**) could not be achieved. To overcome this problem, we introduced the conjugated bond only in the final stage. First of all, we determined that it was possible to trap the kinetic enol ether (**11**) of the cyclopentanone (**10**) upon treatment with lithium di-isopropyl amide and trimethylsilyl chloride.[15] Then (**11**) underwent either dehydrosilylation with palladium acetate[16] or regioselective phenylselenylation[10] and oxidation[13] to give the cyclopentenone (**2**) with the double bond in the required position. The cyclopentanone (**10**) was prepared by zinc catalysed alkylation of (**7**)[17] with *cis*-pent-2-enyl bromide. In an alternative approach copper salt-catalysed cyclopropanation of (**7**) with ethyl diazoacetate[18] gave (**12**). Desilylation of (**12**) and regiospecific opening of the cyclopropane ring by treatment with MeOH containing a drop of $ClSiMe_3$[19] afforded the γ-ketoester (**13**) (97%). Protection of the carbonyl and hydroxy groups[8] of (**13**), followed by reduction and oxidation[20] gave, after Wittig reaction of the corresponding aldehyde with salt-free n-propylidenetriphenylphosphorane,[21] the acetal (**14a**) in 73% overall yield from (**13**). Then sulphonation and treatment with lithium bromide (acetone reflux 12 h, 92%) provided (**14b**) and (**14c**) successively. Acetylenation of (**14c**)[22] led to the expected cyclopentanone acetal (**3**) in 85% yield. Our first attempts at alkylation of the terminal acetylenic carbon of (**3**) with the ortho-ester prepared from 5-iodopentanoic acid chloride and 3-methyl-3-hydroxymethyloxetane[23] gave the α,β-disubstituted cyclopentanone acetal (**15**) in 23% yield. However more successful alkylation of the triple bond of (**3**) with tris[5-(tetrahydropyran-2-yloxy)pentyl]borane (61% yield), as well as the final step toward dicranenone A have been reported.[2] 1-Hydroxycyclopropanecarbaldehyde derivatives such as (**4**) can be considered as convenient synthons to enter this class of compounds.

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References

1 T. Ichikawa, M. Namikawa, K. Yamada, K. Sakai, and K. Kondo, *Tetrahedron Lett.*, 1983, **24**, 337.
2 K. Sakai, T. Fujimoto, M. Yamashita, and K. Kondo, *Tetrahedron Lett.*, 1985, **26**, 2089.
3 J. Salaün and Y. Almirantis, *Tetrahedron*, 1983, **39**, 2421.
4 J. P. Barnier and J. Salaün, *Tetrahedron Lett.*, 1984, **25**, 1273.
5 J. Ollivier and J. Salaün, *Tetrahedron Lett.*, 1984, **25**, 1269.
6 N. Miyashita, A. Yoshikoshi, and P. A. Grieco, *J. Org. Chem.*, 1977, **42**, 3772.
7 R. G. Visser, H. J. T. Boss, and L. Brandsma, *Recl. Trav. Chim. Pays-Bas*, 1980, **99**, 70.
8 E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, 1972, **94**, 6190.
9 J. Salaün, *Chem. Rev.*, 1983, **83**, 619 and references cited therein.
10 H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, 1975, **97**, 5434.
11 G. Zima, C. Barnum, and D. Liotta, *J. Org. Chem.*, 1980, **45**, 2737.
12 D. Liotta, C. S. Barnum, and M. Saindane, *J. Org. Chem.*, 1981, **46**, 4301; D. Liotta, M. Saindane, and D. Brothers, *ibid.*, 1982, **47**, 1598.
13 H. J. Reich, S. Wollowitz, J. E. Trend, F. Chow, and D. F. Wendelborn, *J. Org. Chem.*, 1978, **43**, 1697.
14 D. A. Evans, L. K. Truesdale, K. G. Grimm, and S. L. Nesbitt, *J. Am. Chem. Soc.*, 1977, **99**, 5009.
15 E. J. Corey and A. W. Gross, *Tetrahedron Lett.*, 1984, 495.
16 Y. Ito, T. Hirao, and T. Saegusa, *J. Org. Chem.*, 1978, **43**, 1011.
17 I. Paterson, *Tetrahedron Lett.*, 1979, 1519.
18 H. V. Reissig and E. Hirsch, *Angew. Chem.*, 1980, **92**, 839; *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 813.
19 The use of F^- was not necessary to open the three-membered ring as reported by J. P. Marino, R. Fernandez de la Pradilla, and E. Laborde, *J. Org. Chem.*, 1984, **49**, 5280.
20 A. J. Mancuso, S. L. Huang, and D. Swern, *J. Org. Chem.*, 1978, **43**, 2480.
21 H. Tanaka and S. Torri, *J. Org. Chem.*, 1975, **40**, 462.
22 W. N. Smith and O. F. Beumel, Jr., *Synth. Commun.*, 1974, 441.
23 E. J. Corey and N. Raju, *Tetrahedron Lett.*, 1983, **24**, 5571.