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THE CHEMICAL TRANSFORMATION TO PULCHELLON FROM PULCHELLIN*[1]

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A novel pseudotwistane named pulchellon(1a) was first isolated from a collection of Gaillardia pulchella as a minor constituent[2a] along with the pseudoguaianolide alkaloids such as pulchellidine(2a)[2a] and neopulchellidine (2b)(11αH)[2b]. The complete stereostructure of pulchellon(1a) has been established as depicted in Fig. 1 based on its chemical and spectral evidences together with the biogenetic consideration as well as the direct three dimensional X-ray crystallographic analysis of pulchellon itself[1].

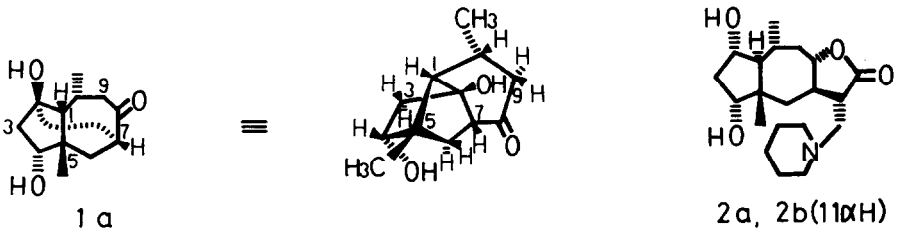
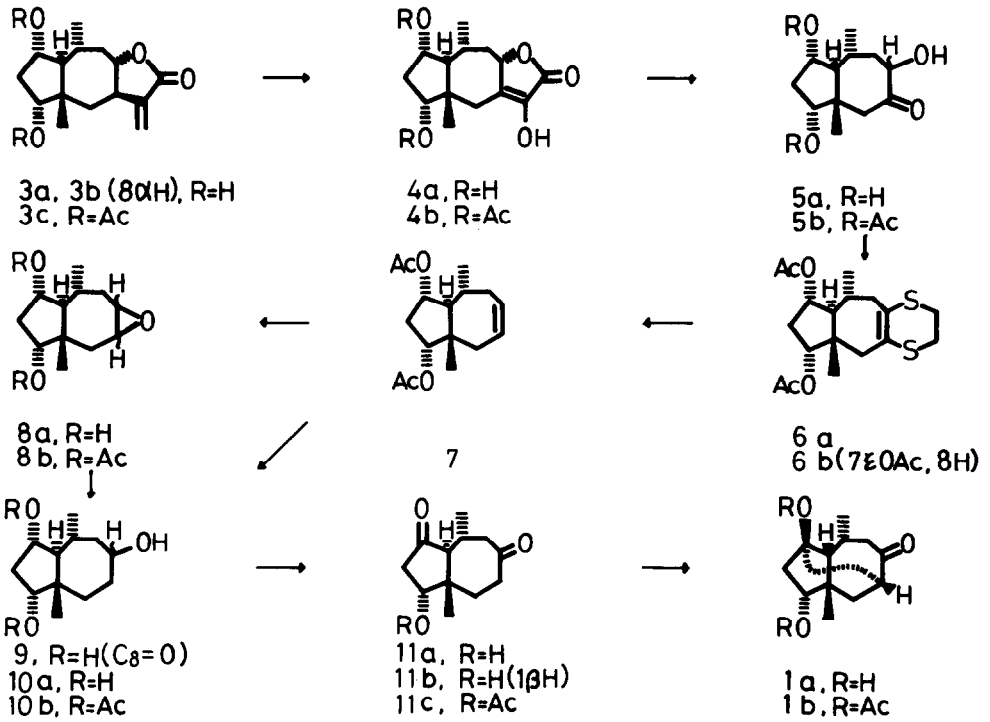


FIG. 1

The present paper concerns a convenient partial synthesis of pulchellon(1a) developed on the basis of the biogenetic assumption proposed earlier[3]. In another word, this successful transformation of pulchellin(3a)[2a,2c] or neopulchellin(3b)[2b] to pulchellon(1a), whose absolute structures have all been established[4][1], implicates a substantiation of the possibility by a chemical means.

Since the possible biogenetic pathway[3][1] is considered similarly as shown in Scheme 1 except in the presence of 6 and 7, a biomimic synthesis of 1a has been virtually executed starting from 3a as a precursor through the hypothetical route. The C-3 isopropyl unit in the original constituent pseudoguaianolide,

e.g. 3a, can be eliminated by the following degradative manner. The ozonolysis of diacetylpulchellin(3c) obtainable from 3a afforded in nearly quantitative yield diacetylnorpulchellone(4b), mp 217-220°[5]. The oxidation of 4b with $KMnO_4$ and $MgSO_4$ in 50% aqueous acetone under a carefully defined condition (-3 to -4°, 4 hr) led in good yield to the ketol(5a), which could not be induced to crystallize. The acetate mixture prepared by pyridine-acetic anhydride gave, on silica gel chromatography, a crystalline acetate(5b). $C_{18}H_{26}O_7$*2 (M^+ 354), mp 127-130.5°, $[\alpha]_D^{20}$ +55.8° (EtOH), ν(KBr) 1754, 1736($OCOCH_3$), 1714(C=O)(cm^{-1}). The AB patterned PMR signal of the methylene neighboring to the carbonyl (J =16.5 Hz at 2.61 ppm) reveals the C(7)-ketonic structure designated in 5b.



SCHEME I. A BIOMIMETIC CHEMICAL TRANSFORMATION FROM PULCHELLIN(3) TO PULCHELLON(Ia).

Since attempted ketol exchange reactions from 5a to the corresponding 8-keto-7-ol isomer in the presence of Al_2O_3 or dil. HCl failed, our attention was directed to the thioketalization of 5b with 1, 2-ethanedithiol/BF_3-etherate resulting in formation of the unexpected diacetyl dithiane(6a). $C_{18}H_{26}O_4S_2$ (M^+ 370), mp 143-144°, $[\alpha]_D^{21}$ +4.8° (EtOH). ν(KBr) 1729, 1741($OCOCH_3$), 1605(C=C) (cm^{-1}). It is also of interest to note that there obtained a small amount of a triacetate(6b) along with 6a instead of the normal triacetyl thioketal. This

dithiane derivative was found to be a suitable synthetic precursor for the postulated key intermediate, ketodiol(9) and its triol analogue(10a) being derivable from the corresponding olefine(7). Desulfurization of 6a with deactivated Raney nickel in boiling acetone afforded almost quantitatively olefine(7), whose PMR spectrum showed the olefinic two proton signals centred at 5.72 ppm as a multiplet. $C_{16}H_{24}O_4$ (M^+ 280), bp_2 143-144°, $[\alpha]_D^{20}$ +1.7° (EtOH). ν(KBr) 1739, 1745($OCOCH_3$), 1635(C=C)(cm^{-1}). Hydroboration of 7 with diborane in THF followed by treatment of the borate with alkaline hydrogenperoxide and subsequent hydrolysis with 5% KOH/MeOH gave a triol mixture(10a), whose structure was identified by Mass spectrum of the corresponding triacetate(10b), $C_{18}H_{28}O_6$ (M^+ 340). The triol was smoothly converted by oxidation with more than 3 moles of Jones reagent to diketool, i.e. trans-4α-hydroxy-5β, 10α-dimethylbicyclo[5.3.0]decane-2, 8-dione(11a) without formation of the undesired trione. ν(KBr) 3375(OH), 1745(cyclopentanone), 1720(cycloheptanone)(cm^{-1}), which on acetylation by the usual manner gave an oily diketoacetate(11c), $C_{14}H_{20}O_4$ (M^+ 252). On the other hand, epoxidation of 7 with m-chloroperbenzoic acid in CH_2Cl_2 afforded, on silicic acid chromatography, an epoxide(8b). $C_{18}H_{24}O_5$ (M^+ 296), mp 84-86°, ν(KBr) 1739, 1732($OCOCH_3$)(cm^{-1}). Reduction of the epoxide with $LiAlH_4$ in ether followed by hydrolysis with 5% KOH/MeOH gave triol(10a) mentioned above.

The final stage of the transformation is an intramolecular aldol condensation between C(2) and C(7) from the trans fused bicyclic diketool(11a) to form 2β, 4α-dihydroxy-5β, 10α-dimethyltricyclo[5.3.0.$0^{2,7}$]decane-8-one, i.e. pulchellon(1a). Several trials of the required bond formation in the intermediary cis fused bicyclic system(11b) being equilibrated from 11a[cf.2c] using a catalytic amount of conc. HCl in acetone, Al_2O_3 in acetone and $SnCl_4$ in benzene were not successful. Consequently, treatment of 11a with BF_3-etherate in Ac_2O/HOAc at room temperature for 2 days followed by silica gel chromatography yielded the desired diacetylpulchellon(1b). This spontaneous bridging is evidently due to effective sequential reactions, namely, irreversible epimerization at the ring juncture from C(1)-αH to C(1)-βH, favorable condensation between C(2)-carbonyl and C(7)-methylene and simultaneous acetylation of the newly born C(2)-β-hydroxy group wherefore the reversion of the foregoing two reactions should be probably difficult to occur.

The synthetic diacetylpulchellon(1b) indicates the two peaks at Rf 6.5 and 8.1 on a micro high pressure liquid chromatography(HPLC) [Familic-100, HP-01 (0.5 ϕ x 200 mm), MeOH], the former of which is coincident with that of the authentic acetate[2a] derived from the natural pulchellon(1a). Further supports were supplied by the GC-Mass spectrometry with GC Rt at 2.8 and 3.2 [OV-17/Chromosorb W], in which the latter GC peak is again identical with that of 1b and also reveals the exactly same mass fragmentation pattern as that of the authentic sample. Though the conversion of diacetylpulchellon(1b) to pulchellon(1a)

using a trace of conc. H_2SO_4 or conc. HI in acetone and 5% KOH/MeOH at different temperatures gave no promising results, it was finally achieved by hydrolysis under a rather strictly controlled condition using 2.5% KOH/MeOH at 0° for 15 min. Pulchellin(3a) has now been transformed to pulchellon(1a) by means of a biomimic chemical synthesis mentioned above.

Acknowledgements

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References and Notes

*1 The present communication is dedicated to Professor R.B. Woodward on the occasion of his sixtieth birthday in 1977, wherein presented at the 26th IUPAC Congress, Tokyo, Sep., 4-10, 1977. See Abstracts (Section IV and V), p. 1112.

*2 All new compounds described in this paper gave satisfactory elemental analyses and proper PMR spectral data.

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