Tetrahedron Letters No. 5, pp 475 - 478, 1978. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF ETHYL 3-ETHOXY-1.8-DIOXO-2-OXASPIRO [4.5] DECA-6.9-DIENE-3-CARBOXYLATE, AN INTERMEDIATE TO PREPHENATE

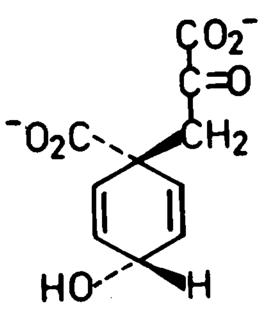
Walter Gramlich and Hans Plieninger*

Organisch-Chemisches Institut der Universität Heidelberg,
Im Neuenheimer Feld 270, D-6900 Heidelberg, West Germany

(Received in U K 5 December 1977; accepted for publication 8 December 1977)

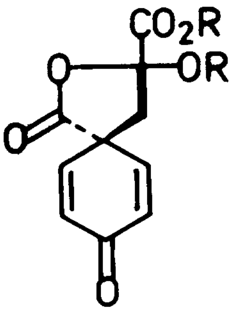
The unique structure of prephenate, the natural precursor of phenylpyruvic acid and many other aromatic compounds was proposed by U.Weiss[1] in a short but famous communication long before other cyclohexadienoles were known. By synthesizing the two stereoisomeric tetrahydroprephenic acids[2], not only the proposed constitution could be proved, but also the stereochemistry was established in which the hydroxylgroup is in cis position relative to the tert. carboxyl group[3]. All attempts to synthesize prephenate were more or less unsuccessful[4] because of the instability towards acids and strong bases[5].
By courtesy of S.Danishefsky, University of Pittsburgh, we have been informed of his most elegant and straightforward synthesis of prephenate via the cyclohexadienone 1a [6].

We have synthesized the ethyl derivative 1b independently in the

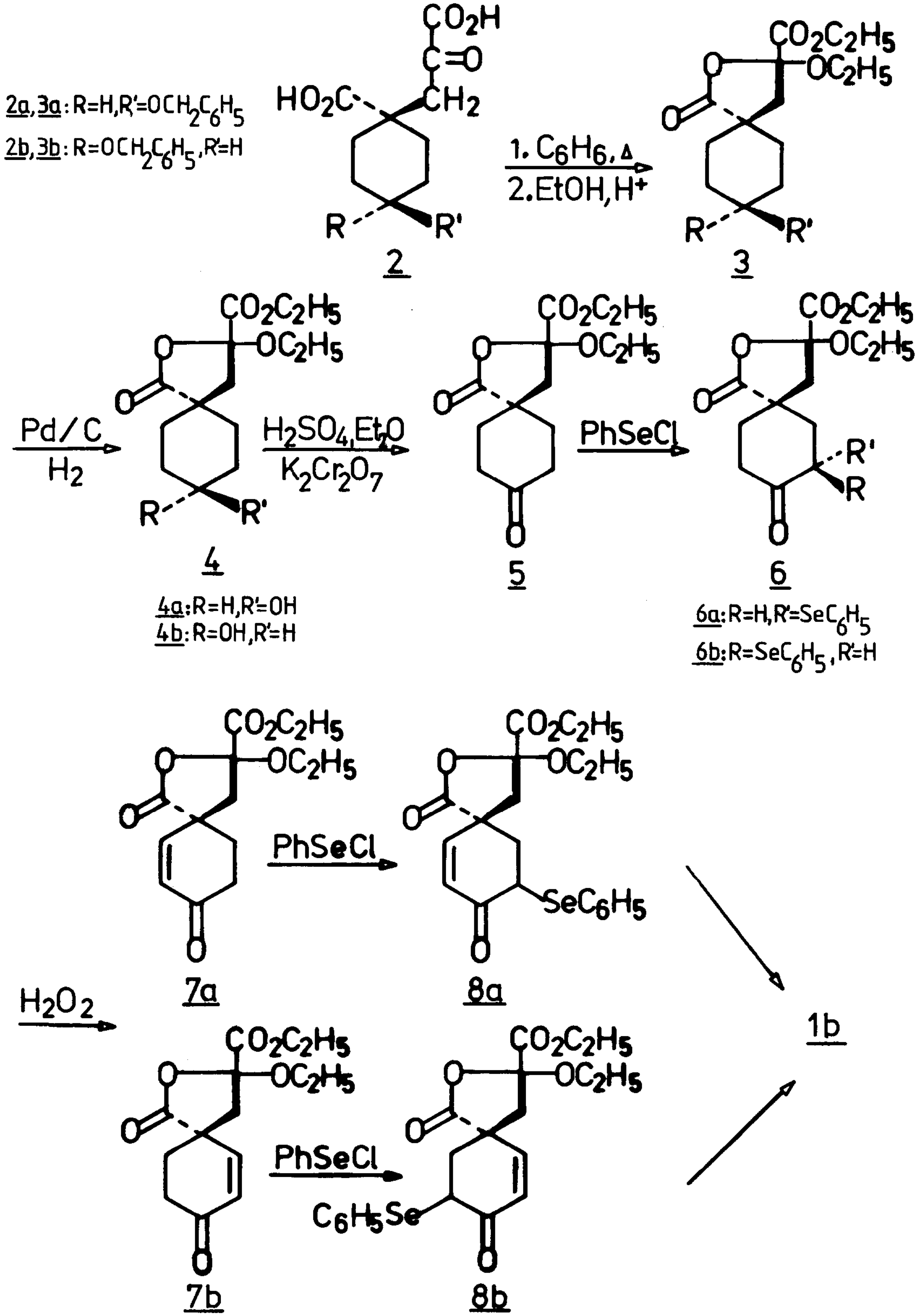


prephenate

1a: R= CH_3
1b: R= C_2H_5



1


2a,3a: R=H,R'=OCH2C6H5
2b,3b: R=OCH2C6H5,R'=H
CO2H
C=O
CH2
HO2C
R
R'
2
1. C6H6, Δ
2. EtOH, H+
CO2C2H5
OC2H5
O
O
R
R'
3
Pd/C
H2
4
4a: R=H,R'=OH
4b: R=OH,R'=H
H2SO4, Et2O
K2Cr2O7
5
PhSeCl
6
6a: R=H,R'=SeC6H5
6b: R=SeC6H5,R'=H
7a
PhSeCl
SeC6H5
8a
H2O2
7b
PhSeCl
C6H5Se
8b
1b

following way using the method of Sharpless and co-workers[7)] to introduce the double bonds of dienone 1. The ester lactones 3a, 3b were prepared from the keto diacids 2a, 2b analogous to earlier experiments[8)].

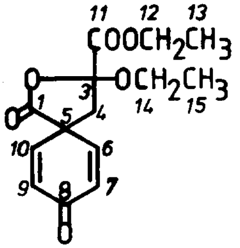
All the above compounds were well characterized by ^1H, ^{13}C-NMR, IR and UV spectra. Either high resolution mass spectra or combustion analyses were in accordance with the structural formulas[9)]. Similar to the synthesis of 1b, ten other 4,4-disubstituted 2,5-cyclohexadienones have been prepared in pure form via the phenylseleno-enones[10)].

We obtained the dienone 1b as a colourless oil, which is very sensitive to acids and bases. Especially the purification process by chromatography on silica gel was always accompanied by big losses due to dienone-phenol rearrangement. The dienone 1b shows the following spectral data: IR(film):3040(C=C-H), 1788 (-O-C=O), 1750(O=C-OEt),1688(-C=O),1630(C=C), 1605 cm^{-1}.- UV(methanol):$\lambda_{max}(\log\varepsilon)$=229nm(3.9).- ^1H-NMR($CDCl_3$)[11)]: δ=7.1 (1H, dd, J=10.6Hz, J=2.5Hz, olefin H at C_6 or C_{10}); 6.8(1H, dd, J=10.6Hz, J=2.5Hz, olefin H at C_{10} or C_6);6.45(2H, d, olefin hydrogens at C_7 and C_9);4.32 (2H, q, J=7.2Hz, RCO_2-$C\underline{H}_2$-CH_3); 3.75 (2H, m, RO-$C\underline{H}_2$-CH_3); 2.68 (2H, s, hydrogens at C_4);1.28(3H, t, J=7.2Hz, RCO_2CH_2-$C\underline{H}_3$); 1.20 ppm (3H, t, J=7.2Hz, $ROCH_2$-$C\underline{H}_3$). - The dienone 1b gives no molecular ion m/e 280 in the high resolution mass spectrum under conditions of electron impact (E.I.):m/e=236 (M^+-CO_2,41%;236.1048 calc. 236.1049 for $C_{13}H_{16}O_4$); 207 (M^+-CO_2Et,52%; 207.0651 calc. 207.0657 for $C_{11}H_{11}O_4$). Only the chemical ionisation mass spectrum (C.I.)[12)] with isobutane as reagent gas gives the expected quasi-molecular ion MH^+ (m/e 281) with a relative abundance of 45%. The fragmentation pattern of the E.I. and C.I. mass spectra are quite different.

The signals of the ^{13}C-NMR spectrum could be assigned by proton off-resonance decoupling and by comparison with the spectra of other spirocyclic lactones and dienones[13)]. The ^{13}C chemical shift of the carbonyl carbon C-8 (δ_C=184.18 ppm) is typical for 2,5-cyclohexadienones.

TABLE. ^{13}C Chemical Shifts of 1b in $CDCl_3$

(δ_C in ppm, TMS=0)



C-1	C-3	C-4	C-5	C-6	C-7	C-8
170.60	103.68	43.44	50.45	144.77^{+}	130.78^{++}	184.18

C-9	C-10	C-11	C-12	C-13	C-14	C-15
132.07^{++}	144.37^{+}	166.33	62.79	14.09	63.02	15.34

$^{+,++}$ These signal assignments may be reversed

References and Notes

1. U.Weiss,C.Gilvarg,E.S.Mingioli and B.D.Davis,Science 119,774(1954).
2. (a) H.Plieninger and H.J.Grasshoff,Chem.Ber. 90, 1973 (1957).
   (b) H.Plieninger and G.Keilich,Chem.Ber. 92, 2897 (1959).
3. H.Plieninger and G.Keilich,Z.Naturforsch. 16b, 81 (1961).
4. H.Plieninger,L.Arnold,R.Fischer and W.Hoffmann,Chem.Ber. 98, 1774 (1965).
5. For a review of prephenate: H.Plieninger,Angew.Chem. 74,423 (1962).
6. S.Danishefsky, personal communication; S.Danishefsky and M.Hirama, J.Am.Chem.Soc. in press.
7. K.B.Sharpless,R.F.Lauer and A.Y.Teranishi,J.Am.Chem.Soc. 95, 6137 (1973).
8. H.Plieninger,L.Arnold,A.vor der Brück,W.Hoffmann,W.Kaden and R. Mündnich,Chem.Ber. 108, 159 (1975).
9. W.Gramlich and H.Plieninger, full paper in preparation.
10. H.Plieninger and W.Gramlich, submitted to Chem.Ber.
11. 8b exhibits a strong solvent dependent splitting of the ß-olefinic signals of the dienone-system, apparently due to the appropriate center of chirality. Similar observations were made with other dienone lactones, see ref.9.
12. M.S.B.Munson and F.H.Field,J.Am.Chem.Soc. 88, 2621 (1966).
13. W.Gramlich and H.Plieninger, results to be published.