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STEROID SPIRO[2·4]HEPTAN-4-ONES: PRODUCTS OF THE REACTION BETWEEN DIPHENYLCYCLOPROPYLSULFONIUM YLIDE AND STEROID 4,6-DIENE-3-ONES

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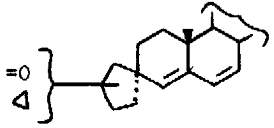
The reaction between the interesting new sulfur ylide reagent, diphenylcyclopropylsulfonium ylide, 1[1], and various steroidal saturated and unsaturated ketones was investigated. This reagent was shown by Trost and Bogdanowicz[2] to have considerable synthetic potential, e.g. with saturated ketones 1 gave spirocyclobutanones[2b] and with α,β-unsaturated ketones it gave spiropentanes[2c]. In this communication we report a new reaction path for this reagent which converts steroid 4,6-diene-3-ones to spiro[2·4]heptan-4-ones; the structure of one of these, 3, has been determined by X-ray crystallographic structure analysis.

Reaction of the 4,6-diene-3-one 2 with diphenylcyclopropylsulfonium ylide, 1[1,3], gave two products, in the ratio 5:1, both of which had incorporated two molecules of ylide reagent i.e. addition of a C_6H_8 unit had occurred. The major product 3 had m.p. 205-8° from acetone/hexane $[\alpha]^{26}_{D}$+102.2° ($CHCl_3$); $[\theta]^{286}$+3,600°, $[\theta]^{232}$+52,600° (MeOH); λ^{MeOH}_{max} 232, 240, 248 nm, ε 21,600, 23,100, 14,400; ν_{max} (CCl_4) 6,120 (cyclopropyl) cm^{-1}; ν_{max} ($CHCl_3$) 1760 (lactone), 1719 (>C=O) cm^{-1}; δ ($CDCl_3$), 0.97 (10-CH_3, s), 1.02 (13-CH_3, s), 5.14 (4-H, s), 5.53 (d,d J 10, 1.5 Hz), 5.95 (d,d J 10, 2 Hz) (6-H and 7-H) ppm. $C_{28}H_{36}O_3$ requires 420.2664: C, 79.96, H, 8.63%; found, 420.2671: C, 79.94, H, 8.59%, and the minor product 4 had m.p. 255-9° from acetone/hexane $[\alpha]^{26}_{D}$-32.2° ($CHCl_3$); $[\theta]^{285}$-4,100°, $[\theta]^{239}$+27,200° (MeOH); λ^{MeOH}_{max} 233, 240, 248 nm, ε 25,600, 27,500, 17,100; ν_{max} ($CHCl_3$) 1760 (lactone), 1719 (>C=O) cm^{-1}; δ($CDCl_3$), 0.90 (10-CH_3,s), 1.02 (13-CH_3,s), 5.10 (4-H, s), 5.53 (d,d J 10, 1.5 Hz), 5.94 (d,d J 10, 2 Hz) (6-H and 7-H) ppm. $C_{28}H_{36}O_3$ requires 420.2664: C, 79.96, H, 8.63%; found, 420.2666: C, 79.94, H, 8.81%.

Both compounds still contained the 4,6-diene grouping, as evidenced by the U.V. maxima[4] at 232, 240 and 248 nm and by the characteristic 3 proton vinyl multiplets in their pmr spectra, thus indicating that attack had occurred at the C_3 carbonyl group. The carbonyl absorption at 1719 cm^{-1} clearly ruled out the possible spiro[3·3]heptan-1-one structure 9 and suggested either a six-membered or a conjugated five-membered ring ketone[5]. The presence of a cyclopropyl group in the major product was shown by the absorption at 6120 cm^{-1} in the near infrared spectrum[6]. Since C_6H_8 had been added to the steroid, these data are consistent only with spiro[2·4]heptanes of the general formula

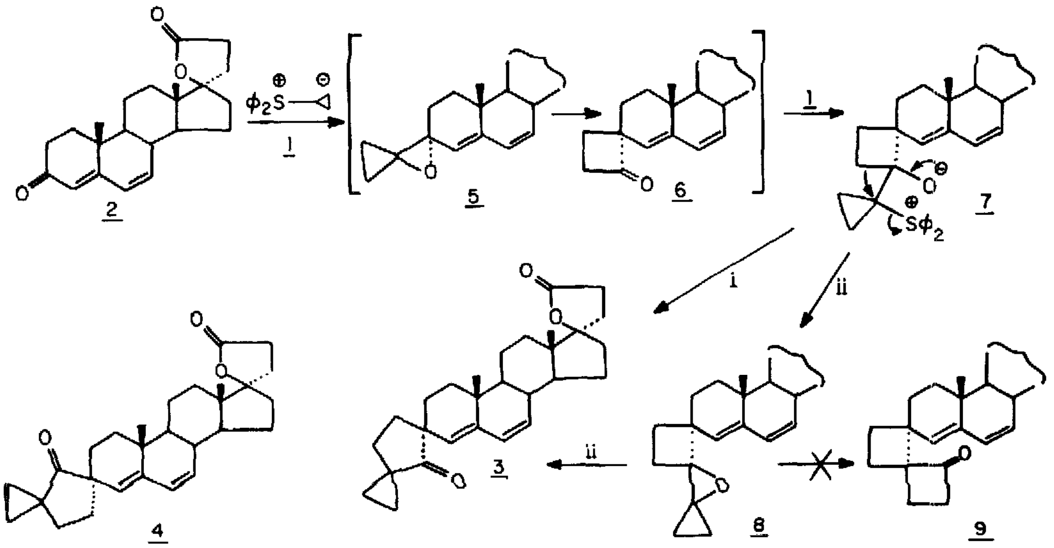


where the carbonyl and cyclopropyl groups are on adjacent carbon atoms.

In order to determine which of these compounds had been formed, the major product was subjected to single-crystal X-ray analysis and shown to be 3. The steroid spiro[2·4]heptan-4-one, 3, crystallizes in the orthorhombic system, space group $P2_12_12_1$, a = 12.79(1), b - 23.01(1), c = 7.98(1) Å, U = 2349 $Å^3$, D_m (flotation) = 1.20, Z = 4, D_c = 1.189 $g.cm^{-3}$. The structure was solved by direct non-centrosymmetric phase-determining methods using the "magic integer" approach[7] in combination with MULTAN[8]. The positional and anisotropic thermal parameters of the non-hydrogen atoms have been refined by full-matrix least-squares calculations to R 0.128 over 1538 statistically insigificant [$I > 2.0\sigma(I)$] *reflections measured on an Enraf-Nonius CAD 3* automated diffractometer (Ni-filtered Cu-K_{α}, λ = 1.5418 Å radiation) operating in the θ-2θ scanning mode.

The structure 3 can be readily explained by postulating the intermediacy of a C_3 spirocyclobutanone 6 as shown in the scheme. That initial attack of the ylide occurs at C_3 rather than at C_7 can be accounted for by the large bulk of the reagent and to the relatively hindered nature of the C_7-position. Also, the rearrangement of the oxaspiropentane 5 to the spirocyclobutanone 6 under the basic conditions of the reaction is reasonable since the spiro carbon atom C_3 is allylic and therefore can stabilize the partial positive charge formed on it during the rearrangement. Similar *uncatalyzed rearrangements have been noted where the incipient carbonium ion* is stabilized by two phenyl groups or a cyclopropyl group[2a,b,d]. Further reaction of the spirocyclobutanone 6 with 1 then gives the observed product 3 either directly (route i) or via the oxaspiropentane 8 (route ii). The latter route is unlikely since rearrangement of 8 to 3 would require the cyclopropyl carbon to develop, at least a partial positive charge[2a,b]. Also, there seems to be no a priori reason why 8 should not rearrange normally[9] to give the spiro[3·3]heptan-1-one 9. We consider *that the oxaspiropentane 8 is not an intermediate in the rearrangement and that* route i is the correct mechanism. An inspection of Dreiding Models shows that the antiperiplanar arrangement of the $C-\overset{\ominus}{O}$ and the $C-\overset{\oplus}{S}\emptyset_2$ bonds necessary for closure to 8 *is sterically hindered whereas this arrangement for the migrating bond and the* $C-\overset{\oplus}{S}\emptyset_2$ bond appears to be unhindered.

SCHEME



The minor product is tentatively assigned the C_3 epimeric structure 4 since the only major spectral difference between the two products is in the C.D. spectra where the carbonyl cotton effects are equal in magnitude but opposite in sign.

Further work to support the postulated mechanism and to determine the scope and utility of this reaction is currently underway in the laboratory at Schering Corporation.

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