As is to be expected for the case of an exocyclic double bond on the three-membered ring[5], the C=N stretching vibration of the products **4** appears at relatively high wave-number (Table 1). An X-ray structure analysis has been carried out on **4f** (Fig. 1). Most striking, though also observed with other hetero-analogous methylenethiiranes[1], are the S—C2 bond length, which markedly exceeds the sum of the covalent radii, and the particularly small bond angle at the sulfur. The exocyclic C=N bond is somewhat shorter than in cyclic thioimidic esters[7].

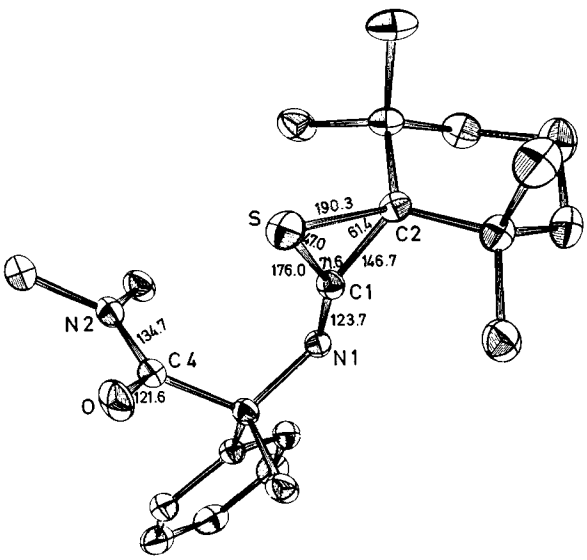

Fig. 1. Molecular structure of **4f** in the crystal, with most important bond lengths [pm] and angles [°] (ORTEP diagram).

The thiiranimines **4** are thermally relatively stable. **4a** cannot be desulfurized, even by heating (diethyl ether, 35 °C, 48 h) with tributylphosphane.

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Simple Transformation of the Azulene System into the Pentalene System**

By *Klaus Hafner** and *Michael Goltz*

Dedicated to Professor Hermann Stetter on the occasion of his 65th birthday

Cycloaddition reactions of the azulene system **1** with electron-poor and electron-rich alkynes provide a simple entry to derivatives of heptalene **2**[1] and cyclopentacyclononene **3**[2]. We have recently also been able to accomplish the transformation of **1** into the pentalene system **4**.

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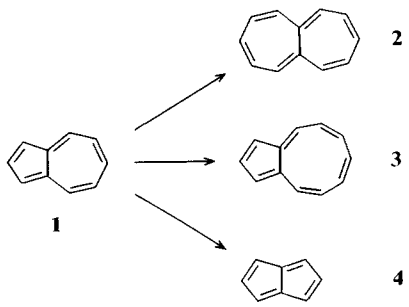
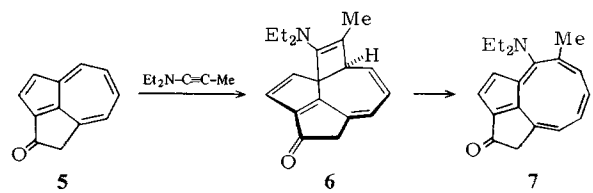
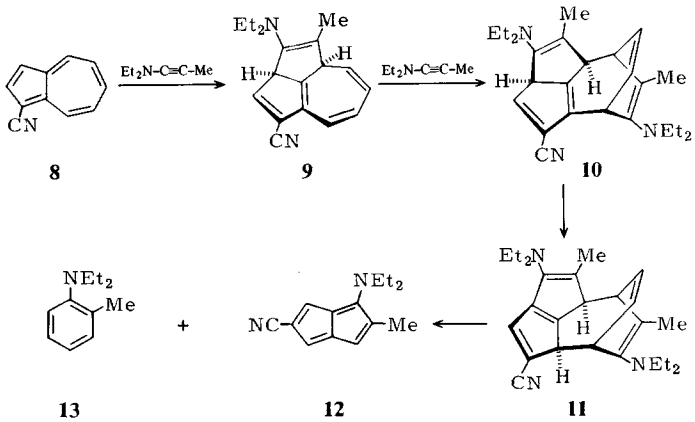
In the homologization of azulene with 1-diethylaminopropyne (**1**→**3**) electron-acceptors in the 1-position strongly influence both the rate as well as the course of the cycloaddition. 2-Oxo-1,2-dihydrocyclopenta[*cd*]azulene



5[3] reacts with 1-diethylaminopropyne even at 25 °C in dichloromethane (14 h) or in benzene (4 d), presumably in a dipolar [2+2]-cycloaddition, to give the non-isolable adduct **6**; valence isomerization of **6** then affords 5-*N*,*N*-diethylamino-6-methyl-2-oxo-1,2-dihydrocyclonona[*cd*]-pentalene **7** (golden yellow crystals, m.p. 167—169 °C (dec)) in 60 or 80% yield, respectively[4,5a]. The analogous reaction of the 1,2-dihydrocyclopenta[*cd*]azulene yields only 43% of the corresponding ring-expansion product after about 20 d[2].



In contrast, 1-azulenecarbonitrile **8** reacts with the same ynamine at 25 °C in dichloromethane (15 min) to give the 4-(*N*,*N*-diethylamino)-5-methyl-2-pentalenecarbonitrile **12** (30%, olive-green crystals, m.p. >110 °C (dec))[5b], which is stable at room temperature and on exposure to air, together with 38% *N*,*N*-diethyl-*o*-toluidine **13**[5c]. In contrast to **5**, the azulene **8** apparently adds the ynamine in the 3,4-position to give the dihydrocyclopenta[*cd*]azulene deriva-



tive **9**, whereby the cycloaddition, as in the formation of **6**, may be initiated by a nucleophilic attack of the electron-rich alkyne in the 4-position of the azulene system. This presumably reacts in a subsequent Diels-Alder reaction with inverse electron-demand to give the 1:2 adduct **10**. Isomerization to **11** followed by cycloreversion finally

yields the pentalene **12**, stabilized by donor and acceptor groups, as well as **13**.

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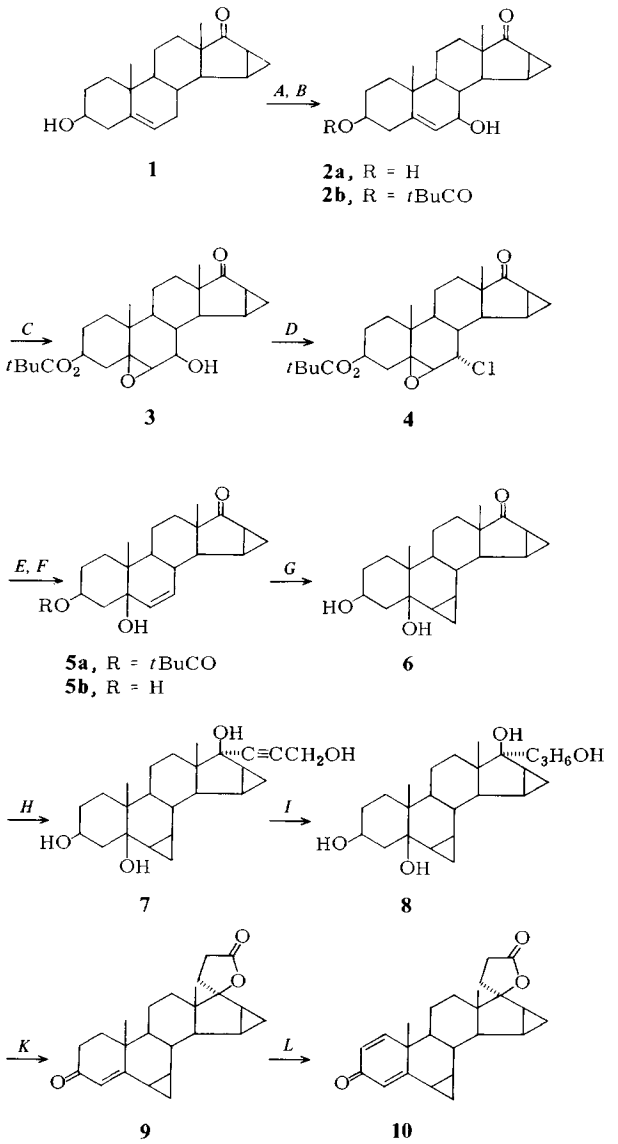
[3] K. Hafner, K.-P. Meinhardt, W. Richarz, *Angew. Chem. 86* (1974) 235; *Angew. Chem. Int. Ed. Engl. 13* (1974) 204.
[4] All the compounds isolated gave correct elemental analyses. The structure of 7 was confirmed by an X-ray structure analysis.
[5] a) 100 MHz-^{1}H-NMR spectrum ($CDCl_3$): $\delta = 1.4$ (2t, superimposed, $J = 7$ Hz, 6H, CH_2—CH_3); 1.71 (s, 3H, CH_3); 3.12 (d, $J = 20$ Hz, 1H, CO—HCH); 3.7 (m, 3H, CO—HCH + CH_2—CH_3); 4.16 (q, $J = 7$ Hz, 2H, CH_2—CH_3); 5.5, 5.95 (2m, 4H, H-6, H-7, H-8, H-9); 6.50 (s, 2H, H-2,3). 25.2 MHz-^{13}C-NMR spectrum ($CDCl_3$): $\delta = 12.2$ (CH_2—CH_3); 12.7 (CH_2—CH_3); 22.3 (CH_3); 44.7 (CH_2—CH_3); 45.3 (CH_2—CH_3); 50.4 (CO—CH_2); 109.0 (C—H); 109.3 (quart. C); 113.4 (C—H); 122.5 (C—H); 124.0 (C—H); 127.4 (C—H); 132.2 (C—H); 134.0 (quart. C); 136.7 (quart. C); 139.2 (quart. C); 151.3 (quart. C); 172.9 (quart. C); 194.2 (quart. C). UV/VIS spectrum (dioxane): λ_{max} ($\lg\varepsilon$) = 240 (4.06); 258 (4.09); 290 (sh, 4.09); 315 (4.15); 385 (4.23) nm.—b) 60 MHz-^{1}H-NMR spectrum ($CDCl_3$): $\delta = 1.35$ (t, $J = 7$ Hz, 6H, CH_2—CH_3); 1.93 (d, $J = 1.5$ Hz, 3H, CH_3); 3.3–3.9 (2q, superimposed, $J = 7$ Hz, 4H, CH_2—CH_3); 5.70 (s, 1H); 6.1 (m, 1H); 6.27 (s, 1H). 25.2-MHz ^{13}C-NMR spectrum ($CDCl_3$): $\delta = 10.4$ (CH_2—CH_3); 14.9 (CH_2—CH_3); 17.4 (CH_3); 46.8 (CH_2—CH_3); 50.1 (CH_2—CH_3); 98.1 (quart. C); 116.5 (quart. C); 118.9 (C—H); 120.7 (quart. C); 130.2 (C—H); 131.2 (quart. C); 136.2 (quart. C); 142.1 (C—H); 165.2 (quart. C, C—$N(C_2H_5)_2$). UV/VIS spectrum (dioxane): λ_{max} ($\lg\varepsilon$) = 273 (4.53); 398 (sh, 4.04); 411 (4.16); 431 (4.09); 630 (2.62) nm.—c) See M. Goltz, Diplomarbeit, Technische Hochschule Darmstadt 1981.

Synthesis of Spirorenone—A Novel Highly Active Aldosterone Antagonist

By *Dieter Bittler, Helmut Hofmeister, Henry Laurent, Klaus Nickisch, Robert Nickolson, Karl Petzoldt,* and *Rudolf Wiechert**

Spironolactone (7α-acetylthio-3-oxo-17α-pregn-4-ene-21,17-carbolactone)[1] is a competitive antagonist of aldosterone, the most active natural mineralocorticoid. It has been used therapeutically for approximately twenty years to treat edamatous diseases and essential hypertonia. As a side effect—particularly when used over longer periods of time and at higher doses—endocrinological disorders have been observed, which can be attributed to antiandrogenic and to progestational properties of the compound. In the search for an aldosterone antagonist having increased main activity without relevant side effects, we synthesized 6β,7β:15β,16β-dimethylene-3-oxo-17α-pregna-1,4-diene-21,17-carbolactone, **10**, spirorenone.

The starting material **1**[2], which was hydroxylated microbiologically in the 7β-position using the fungal strain *Botryodiplodia malorum,* was obtained from 3β-hydroxy-5,15-androstadien-17-one by Corey cyclopropanation. Selective esterification of the 3β-hydroxy group of **2a** was performed using pivalic anhydride. According to *Hanson et al.*[3], 7β-hydroxy-Δ^5-steroids react stereospecifically with *tert*-butyl hydroperoxide under vanadium(IV) oxide-acetylacetonate catalysis to afford 5β,6β-epoxides, which can be converted by treatment with Ph_3P/CCl_4 in pyridine into 7β-chloro derivatives. Applying this reaction sequence



Scheme 1. *A: Botryodiplodia malorum,* substrate concentration 1 g/L, fermentation time 40 h; *B:* $[(CH_3)_3CCO]_2O$, dimethylaminopyridine in pyridine, RT, 72 h; *C: tert*-butyl hydroperoxide, $VO(C_5H_7O_2)_2$ in toluene, 80 °C, 2 h; *D:* $P(C_6H_5)_3$ in CCl_4/CH_2Cl_2/pyridine, 0 °C→RT, 2 h; *E:* Zn powder in Ac_2O/tetrahydrofuran (THF), 70 °C, 1.5 h; *F:* KOH, $NaClO_4$ in THF/MeOH, RT, 2.5 h; *G:* ZnCu, CH_2I_2 in ethylene glycol dimethyl ether, 55 °C, 5 h; *H:* HC≡CCH_2OH, KOEt in THF, RT, 2 h; *I:* $Pd/CaCO_3$, H_2 in THF/2-propanol, RT, 1 bar, 2 h; *K:* pyridinium dichromate in DMF, 70 °C, 24 h; L: DDQ in dioxane, 100 °C, 1.5 h.—Yields [%], melting points [°C] (Mettler FP11, 2 °C/min), and $[\alpha]_D^{22}$ values [°] ($c = 0.5$ in $CHCl_3$): **2a**: 55, 229.5, −51; **2b**: 65, 336.0, −45; **3**: 98, 220.0, −12; **4**: 79, 228.3, −100; **5a**: 75, 247.5, −24; **5b**: 94, 202.4, −78; **6**: 88, 210.9, −34 ($c = 0.5$ in EtOH); **7**: 69, 198.5 −87 ($c = 0.5$ in EtOH); **8**: 95, 181.3, −25; **9**: 62, 201.3, −182; **10**: 59, 259.8, −159.

to **2b** gave the chloro epoxide **4**, which yielded the 5β-hydroxy-Δ^6-derivative **5a** upon reductive elimination of the chlorine atom (Zn/CH_3CO_2H). Saponification with KOH/$NaClO_4$ in methanol results in formation of the 3β,5β-diol **5b**, the key compound for stereospecific cyclopropanation using the Simmons-Smith method (**5b**→**6**)[4]. To form the spirolactone ring, propargyl alcohol was added to the ketone **6**. Hydrogenation of the triple bond followed by oxidation of the tetrol **8** with pyridinium dichromate in dimethylformamide (DMF) led, *via* formation of the α,β-unsaturated ketone and the lactone ring, to compound **9** [UV

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