200. Triasteranetrione from Triasteranedione[1])

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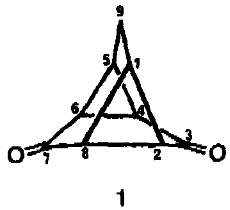
Zusammenfassung. Reaktion von Triasterandion (**1**) mit N-Bromsuccinimid ergab 44% 9-Brom-triasterandion (**5**), neben wenig 9,9-Dibrom-triasterandion (**6**). Substitution des Bromatoms in **5** durch eine Acetoxygruppe ergab 74% 9-Acetoxy-triasterandion (**10**). Umesterung mit Natriumäthylat und Oxydation des rohen Hydroxy-diketons **9** führte zu Triasterantrion (**2**). Versuche, Triasteranon (**11**) mit N-Bromsuccinimid in 3,5-Dibrom-triasteranon (**7**) umzuwandeln, waren ohne Erfolg.

Recently we reported syntheses of triasterane-dione (**1**) [1] and -trione (**2**) [2] from the intermediates bicyclo[3.3.1]nonane-3,7-dione (**3**) and bicyclo[3.3.1]nonane-3,7,9-trione-9-(ethylene)-acetal (**4**), respectively, with the trione **2** less readily available (7% from **4**) than the dione **1** (40% from **3**). The possibility of converting the dione **1** into the trione **2** was entertained; the results of this investigation are the subject of this report.



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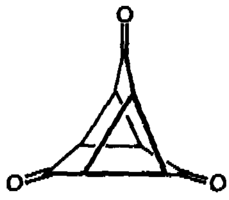

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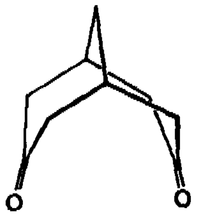

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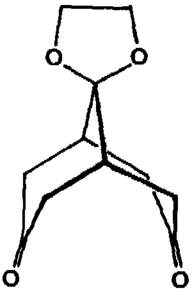

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[1] The systematic name for the triasterane skeleton is tetracyclo[3.3.1.$0^{2,8}$.$0^{4,6}$]nonane; its numbering is transferred to the trivial name.

[2] Post-doctoral fellow, University of Zürich 1972–1975.

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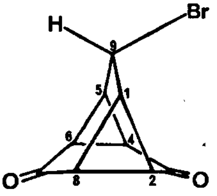
In alkyl-substituted cyclopropanes, it is known [3] that a vicinal carbonium ion (and presumably also a free radical) may be stabilised by interaction with the vicinal cyclopropane bonds. Studies by other workers have indicated that photosensitised bromination [4] and chlorination [5] of these systems usually lead to a mixture of rearranged and non-rearranged halides. Under carefully controlled conditions, however, halogenations have been observed [4] [5] to give mostly unrearranged products. The favourable geometry in triasteranedione (**1**), in which a *p*-orbital at C(9) would be orthogonal to two cyclopropane rings, prompted us to investigate the possibility of introducing a bromine atom at C(9).

Treatment of **1** with 1 mol-equiv. of recrystallised N-bromosuccinimide yielded 44% of 9-bromo-triasteranedione (**5**), m.p. 199°. When this reaction was carried out with technical grade N-bromosuccinimide the bromo-diketone **5** was accompanied by a minor amount (5%) of 9,9-dibromo-triasteranedione (**6**), m.p. 232°. The structure of **6** is evident from the spectral data, namely the *M*⁺*-peaks* at *m/e* 308/306/304 (nearly 1:2:1) in the MS. ($C_9H_6Br_2O_2$), the single IR.-band at 1700 cm^{-1} and the A_2X signal system (δ = 2.70 and 3.45 with J = 8) in the NMR.-spectrum. Attempts to improve upon the yield of the potentially useful dibromo-diketone **6** were unsuccessful.



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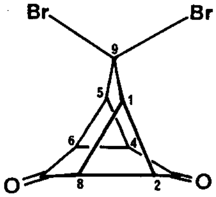

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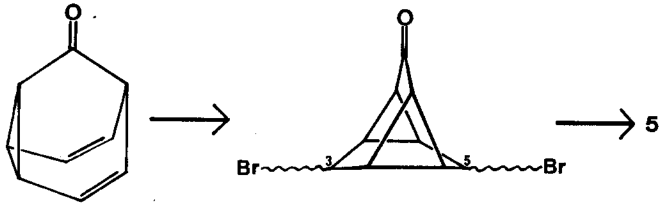
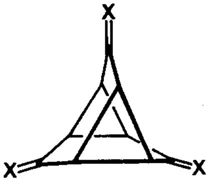
The monobromo-diketone **5** has been previously described by *Vedejs et al.* [6] who observed the rearrangement product 3,5-dibromo-triasteranone (**7**) during the bromination of barbaralone; they found that a *Kornblum*-type oxidation converted **7** to **5**, but efforts to convert the latter to triasteranetrione (**2**) were unsuccessful.



Barbaralone **7**

In our earlier work [2] we noted that an over-reduced triasterane derivative, presumably a hydroxy-triasteranone (**8**), could readily be oxidised to triasteranetrione (**2**). Thus we anticipated that the oxidation of 9-hydroxy-triasteranedione (**9**), potentially available from the bromo-dione **5**, would be a feasible synthetic approach.



X=O or H,OH

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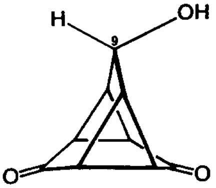
Nucleophilic displacement of the bromine atom in **5** by an acetoxy group occurred with sodium acetate in acetic anhydride to give 74% of the 9-acetoxy-triasterane-dione (**10**), m.p. 167°. The IR.-spectrum shows two types of carbonyl absorptions, at 1750 and 1700 cm^{-1}, the former supporting the presence of an acetoxy group,



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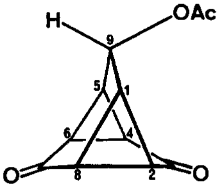

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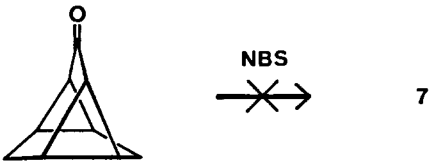
which is confirmed by a singlet at $\delta = 2.14$ in the ^{1}H–NMR.-spectrum of **10**. As in the corresponding bromide **5** H–C(9) appears as a triplet with a coupling of 3 Hz but at a lower field ($\delta = 5.71$ in **10** as compared with $\delta = 5.08$ in **5**).

Because of the reported [6] instability of triasteranols, the acetate **10** was subjected to a mild solvolysis with a catalytic amount of sodium in ethanol and the crude hydroxy dione **9** was immediately oxidised with *Jones'* reagent [7] to give triasteranetrione (**2**) in 64% yield from **10**. The overall yield from triasteranedione (**1**) was 25%; triasteranetrione (**2**), therefore, can be prepared from bicyclo[3.3.1]nonane-3,7-dione (**3**) in 10% yield, only a moderate improvement on the alternate synthetic route [2].



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Preliminary attempts to prepare a 3,5-dibromo-triasteranone (**7**) by N-bromo-succinimide bromination of triasteranone (**11**)[4]) were unsuccessful; the spectra of the crude products suggested the absence of **7** and the possible presence of unsaturated compounds.

This work was supported by the *Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung* and by *Sandoz AG* Basel. We thank Dr. B. *Szechner* for interesting discussions on this problem and Mr. *H. Hilpert* for technical assistance.

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[4]) We thank Prof. *H. Musso*, University of Karlsruhe, for a sample of triasteranone (**11**).

Experimental Part

The abbreviations used in the following text have been described previously [8].

Bromination of triasteranedione (**1**). A solution of 0.17 g (1.14 mmol) triasteranedione (**1**) in 30 ml carbon tetrachloride was refluxed with 0.207 g (1.16 mmol) of freshly recrystallised N-bromosuccinimide over a *150 watt light bulb for 1 h, after which time* another 0.207 g (1.16 mmol) of the N-bromosuccinimide was added and reflux continued for another 1 h. The reaction mixture was diluted with chloroform, washed with 10% hydrochloric acid, with very dilute sodium hydrogensulphite solution and with water, dried and evaporated to leave a brown oil. Purification by preparative TLC. on silica gel with ethyl acetate/hexane 1:1 gave 0.03 g (17%) of recovered starting material (**1**) and 0.095 g (44%) of *9-bromo-triasteranedione* (**5**) as colourless crystals, m.p. 190–195°, after recrystallisation from benzene/petroleum ether as colourless needles, m.p. 197–199°. – Lit. [6] IR. and NMR-spectra identical as far as reported. – MS. (70 ev): 228/226 (20/20, M^+); 147 (100, $M^+ - \mathrm{Br}$); 119 (5); 103 (10); 92 (6); 91 (70); 90 (6). – The NMR.-spectrum (100 MHz, $CDCl_3$) can be interpreted as follows: $\delta = 5.08/t$ ($J = 3$), 1H (H–C(9)); 2.99–2.68/*m*, 2H (H–C(1), H–C(5)); 2.52/*d* ($J = 8$), 4H (H–C(2), H–C(4), H–C(6), H–C(8)).

When the bromination was repeated with technical grade N-bromosuccinimide the purification by preparative TLC. (see above) gave 0.061 (27%) of **5** and 0.014 (5%) of *9,9-dibromo-triasteranedione* (**6**), m.p. 228–232° (dec.). – The latter had: IR. (KBr): 3075*m*; 1700*s*; 1368*w*; 1340*m*; 1225*m*; 1070*w*; 1030*s*; 935*s*; 910*m*; 875*m*; 830*m*; 722*m*. – MS. (70 ev): 308/306/304 (2/5/3, M^+), 280/278/276 (1/2/1, $M^+ - \mathrm{CO}$), 227/225 (85/85, $M^+ - \mathrm{Br}$), 199/197 (3/3, $M^+ - \mathrm{Br} - \mathrm{CO}$), 161 (10), 159 (9), 147 (20), 146 (45, $M^+ - 2 \times \mathrm{Br}$), 135 (5), 133 (6), 119 (16), 118 (100, $M^+ - 2 \times \mathrm{Br} - \mathrm{CO}$), 117 (7), 92 (11), 91 (30), 90 (64). – ^{1}H-NMR. (100 MHz, $CDCl_3$): $\delta = 3.45/t$ ($J = 8$), 2H (H–C(1), H–C(5)); 2.70/*d* ($J = 8$), 4H (H–C(2), H–C(4), H–C(6), H–C(8)). – Variation of reaction time and the amount of either technical grade or recrystallised N-bromosuccinimide did not result in an improved yield of the dibromo-dione **6**.

9-Acetoxy-triasteranedione (**10**). A solution of 0.130 g (0.56 mmol) 9-bromo-triasteranedione (**5**) in 20 ml freshly distilled acetic anhydride was treated with 0.45 g (5.49 mmol) of freshly dried sodium acetate and the mixture was heated with stirring under reflux for 24 h. Most of the acetic anhydride was then removed under reduced pressure and the residue was diluted with aqueous sodium carbonate solution and extracted with chloroform. The combined extracts were dried and evaporated to leave 0.170 g of a brown oil which was purified by crystallisation from chloroform/petroleum ether to give 0.088 g (74%) of *9-acetoxy-triasteranedione* (**10**) as colourless needles, m.p. 165–167°. – IR. ($CHCl_3$): 3020*m*; 1750*s*; 1700*s*; 1372*m*; 1350*w*; 1330*w*; 1320*w*; 1265*w*; 1235–1200*s*; 1145*w*; 1020*m*; 982*m*; 915*m*. – MS. (70 ev): 206 (32, M^+); 164 (32, $M^+ - \mathrm{CH_2{=}C{=}O}$); 163 (16); 147 (29); 146 (70, $M^+ - \mathrm{CH_2{-}C{=}O} - \mathrm{H_2O}$); 136 (52, $M^+ - \mathrm{CH_2{=}C{=}O} - \mathrm{CO}$); 135 (18); 122 (5); 120 (5); 119 (28); 118 (75); 108 (16); 107 (62); 103 (18); 95 (41); 94 (14); 92 (17); 91 (100). – ^{1}H-NMR. (100 MHz, $CDCl_3$): $\delta = 5.71/t$ ($J = 3$), 1H (H–C(9)); 2.8–2.5/*m*, 2H (H–C(1), H–C(5)); 2.38/*d* ($J = 8$, with the 2.34 portion of the signal showing fine splitting), 4H (H–C(2), H–C(4), H–C(6), H–C(8)); 2.14/*s*, 3H (OAc).

Triasteranetrione (**2**). To a stirred solution of 0.036 g (0.17 mmol) 9-acetoxy-triasteranedione (**10**) in 3 ml abs. ethanol was added a small amount of sodium metal (~0.002 g). After 1 h at RT. 20 ml water was added and the solution was saturated with sodium chloride and extracted with chloroform six times. The combined extracts were dried and evaporated to leave 0.033 g of impure *9-hydroxy-triasteranedione* (**9**) as an off-white solid. An alternative procedure for the extraction of the hydroxy-dione **9** was to evaporate the aqueous solution to dryness and then to extract the product with acetone. Evaporation of the acetone gave the same amount of off-white solid as above. The hydroxy-dione **9** was dissolved in 3 ml acetone and *Jones'* reagent was added with stirring and cooling until the orange colour persisted. After 1 h at RT. 20 ml water was added and the solution was saturated with sodium chloride. Extraction with chloroform followed by drying of the extracts and evaporation gave 0.03 g of a crystalline residue which was recrystallised from ethyl acetate to leave 0.018 g (64%) of *triasteranetrione* (**2**), m.p. 302–305° (Lit. [2] m.p. 303–306°). – The NMR.- and MS.-spectra of this sample were identical to those already reported [2] for the trione **2**.

Bromination of triasteranone (**11**). – Two bromination reactions of 0.07 g and 0.035 g of triasteranone (**11**) with 4 and 2 mol equivalents of freshly recrystallised N-bromosuccinimide, respectively, under the conditions reported for the bromination of the dione **1** yielded crude products, which were impure, as seen from the thin layer chromatograms. Of the three possibly expected 3,5-dibromo-triasteranones (**7**), two isomers are known [6]. The ^{1}H-NMR.-spectra of our two products did not contain some of the signals described for these isomers. Furthermore, the IR.-spectra of the two crude products showed major C–O bands at 1710–1720 cm^{-1}, whereas the known triasterane systems with a C=O group have IR.-bands in the range of 1660–1700 cm^{-1} (for example, both isomers of **7** have 1685 cm^{-1}). From these data we conclude that neither of the two known isomers of **7** is present in our products. The presence of the third possible isomer of **7** in appreciable quantities is made unlikely by the IR.-spectra. The IR.- and the ^{1}H-NMR.-spectra of both of our crude products also showed reasonably strong bands at 1625–1635 cm^{-1} and signals at δ ≈ 6.7–6.0 ppm, suggesting the presence of compound(s) with double bonds.

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201. Synthèse de *spiro*-pyrazolines par cycloaddition du diazométhane sur des sucres insaturés ramifiés.

Influence de l'isomérie géométrique sur l'orientation de la réaction 1)

Communication préliminaire 2)

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Summary. The orientation of the cycloaddition of diazomethane on unsaturated branched-chain sugars has been studied. For 3-*C*-cyanomethylidene-3-deoxy-1,2-*O*-isopropylidene-α-D-*glycero*-tetrofuranose the orientation was 'normal' and did not depend on the configuration at the double bond. The same situation prevailed with derivatives of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methylidene-α-D-*xylo*-hexofuranose. For the 3-*C*-acylmethylidene- and the 3-*C*-cyanomethylidene-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranoses, the *trans*-(H–C(3')–C(2))-isomer gave the 'normal' cycloadduct whereas the *cis*-isomer gave predominantly the 'abnormal' *spiro*-pyrazoline. This observation represents the first instance where the regioselectivity of a cycloaddition reaction is affected by the geometrical isomerism of the dipolaro-

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1) Dérivés *C*-glycosyliques. Partie XXVII. Pour la 26ème communication voir [1]. Une partie des résultats rapportés ont été présentés au «VIIth International Symposium on Carbohydrate Chemistry», Bratislava 1974, résumé des communications p. 66.

2) Une publication plus détaillée paraîtra ultérieurement.