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(7) A medium-pressure preparative liquid chromatography unit fitted with a 2.5 × 100 cm column packed with 32–63 μm Woelm silica gel. The system utilized a single-stage constant flow pump with a flow of approximately 22 mL/min. The eluent was directed to a Gilson fraction collector.
(8) Plates (10 × 20 or 20 × 40 cm) of Merck (Darmstadt) silica gel PF 254 of 1.5–2.0-mm thickness were employed.
(9) Analysis performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

Communications

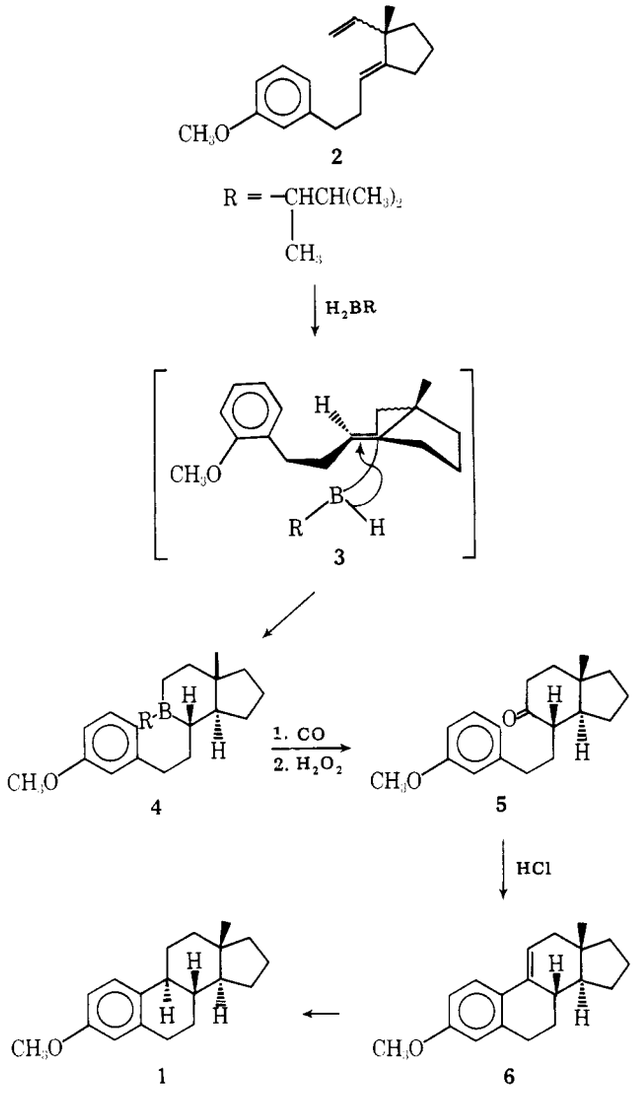
Synthesis of (±)-3-Methoxyestra-1,3,5(10)-triene: Stitching and Riveting as a Tool for Steroid Synthesis

Summary: (±)-3-Methoxyestra-1,3,5(10)-triene has been prepared from 1-chloromethylcyclopentene and 2-(*N*,*N*-dimethylamino)-4-(*m*-methoxyphenyl)butyronitrile.

Sir: We have been exploring the synthetic strategy of stitching and riveting,[1] hydroboration–carbonylation, as a means of preparing steroids and other stereochemically demanding natural products. Described herein are some of the initial results from our investigations directed toward the synthesis of 3-methoxyestra-1,3,5(10)-triene (**1**). This well-characterized steroid[2] was chosen as our first synthetic objective due to the presence of the natural configuration of the ring junctures along with its lack of complicating functional groups, and we envisioned it as evolving from diene **2** through the hydroboration–carbonylation procedures of Brown (Scheme I).[3] The well-documented theory of selectivity in the addition of alkylboranes to olefins led us to the proposition that thexylborane[4] would regioselectively add to the monosubstituted double bond in **2**, boron becoming bonded to the least-substituted end of that double bond, generating carborane **3**. This compound (**3**) would then be predisposed to deliver boron and hydrogen (cis addition) to the trisubstituted olefin (*E* geometry) of compound **3** in an intramolecular process that is stereochemically guided by attachment of these groups to the steroidal "*D* ring" as illustrated in Scheme I. Realization of this stitching process would force formation of all trans tricyclic carborane **4**. Carbonylation and oxidation of **4** would then form hydrindanone **5**, a structure analogous to compounds previously converted to estrone derivatives by Cohen and Smith.[5]

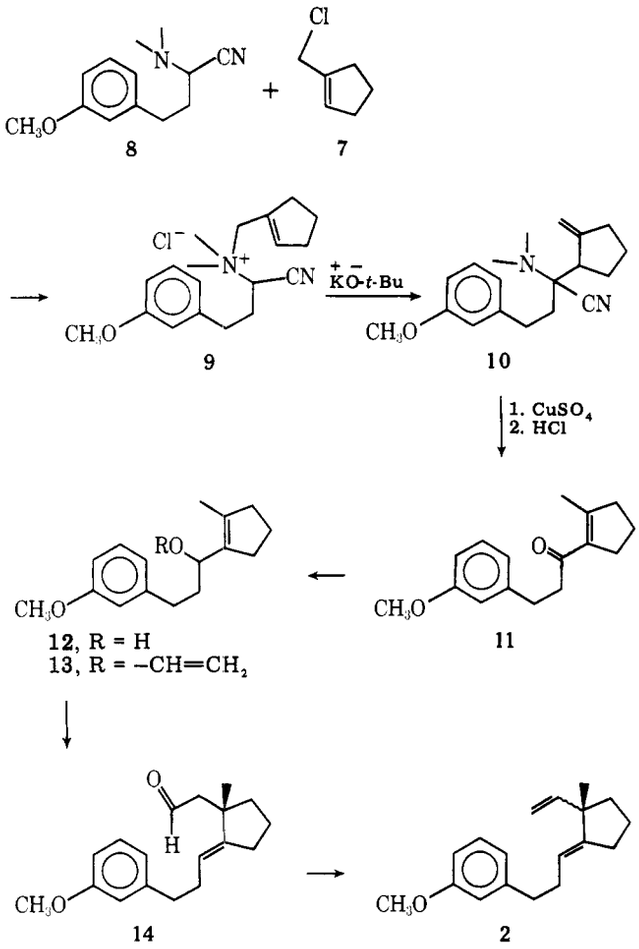
Pursuing these considerations, compound **2** was prepared and added to a solution of thexylborane (BH_3 was generated in situ, $LiAlH_4/BF_3OEt_2$, −78 °C; then 2,3-dimethyl-2-butene was added at 0 °C) forming crude carborane **4** (vinyl proton resonances of **2** absent in ^1H NMR of **4**). This material was immediately treated with carbon monoxide (1200 psi, 50 °C, 5 h) and then oxidized (NaOAc, H_2O_2, aqueous THF) affording **5** (53% from **2**). Studies on **5** have been strongly suggestive of the all trans structure shown in Scheme I.[6,7] Acid-catalyzed cyclization of **5** (10 N HCl/methanol)[5] gave 3-methoxyestra-1,3,5(10),9(11)-tetraene (**6**, mp 82–85 °C),[8] which forms the desired 3-methoxyestra-1,3,5(10)-triene (**1**) via reduction (1 atm H_2, Pd/C; mp 78 °C from methanol).[2] Chromatographic and spectroscopic comparison of this (±)-steroid with optically active 3-methoxyestra-1,3,5(10)-triene (**1**) prepared from natural 3-methoxyestra-1,3,5(10)-trien-17-one via deoxygenation (tosylhydrazone, NaH_3BCN)[9] confirmed the structural identity of these two substances.

Scheme I



Bicyclic diene **2** is accessible (Scheme II) through two sigmatropic rearrangements starting with 1-chloromethylcyclopentene (**7**)[10] and the *N*,*N*-dimethylaminonitrile **8**,[11] the latter of which is derived from *m*-methoxyhydrocinnamaldehyde. These two reagents (**7** and **8**) react to form amorphous salt **9**,[12] which was rearranged to amino nitrile **10** by the action of base (potassium *tert*-butoxide, Me_2SO/THF, −30 °C).[13] Copper sulfate (pentahydrate) assisted hydrolysis[13] (refluxing EtOH, 10 min) and acid-catalyzed bond migration (HCl

Scheme II



aqueous in THF, 8 h) forms enone 11 [46% from 8: IR 1680, 1650 cm^{-1}; ^1H NMR δ 2.05 (allylic CH_3)]. Reduction (11 to 12, $LiAlH_4$, ether, 15 min), vinyl ether exchange [12 to 13, ethyl vinyl ether, $Hg(OAc)_2$], and Claisen rearrangement affords aldehyde 14 [55% from 11; IR 2740, 1725 cm^{-1}; ^1H NMR δ 9.51, 5.12 (aldehyde and vinyl H's)] with the transoid geometry of the trisubstituted olefin in 14 (Scheme II) resulting from this rearrangement. Diene 2 was cleanly formed by reduction ($LiAlH_4$, THF) and dehydration using the multiple step procedure of Sharpless (MsCl, o-$NO_2C_6H_4SeNa$, H_2O_2, Δ).[14]

The ease with which we have been able to prepare steroid 1 with the all trans natural configuration starting from simple starting materials via stitching and riveting has encouraged us to pursue more complex natural products, the report of which will be forthcoming.

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Formation of Intramolecular Oxetanes in the Photolysis of *N*-2-Alkenyl Alicyclic Imides

Summary: On irradiation in acetonitrile, *N*-(2-methylallyl)-succinimide (1) underwent intramolecular ring closure to give oxetane 4. On the other hand, in weakly acidified methanol (or water) 1 gave the corresponding ring-enlarged compound 7 (or 5) via oxetane 4.

Sir: We wish to report on the first example of intramolecular oxetane formation in the photolysis of imides.[1,2] *N*-(2-Methylallyl)succinimide (1), *N*-allylsuccinimide (2), and *N*-allylglutarimide (3) were examined in this work.

Irradiation of 1 (0.05 M) in acetonitrile with a 120-W low-pressure Hg-arc lamp for about 120 h gave, after evaporation of the solvent, an oily product 4 almost quantitatively. After a prolonged heating at about 100 °C, 4 decomposed into the starting material 1. The structure of 4 (oxetane) is assigned on the basis of its ^{13}C and ^1H NMR spectra.[3] The ^{13}C NMR spectrum of 4 revealed the presence of eight different carbon atoms: δ ($CDCl_3$) 14, 15, 27, 30, 50 (NCC), 59 (OCC), 79 (NCO), 181 (NC=O). In the ^1H NMR spectrum the observed long-range coupling between H_a and H_c, which is confirmed by the spin decoupling, clearly demonstrates the fixed W configuration (H_aCCCH_c) for 4: δ ($CDCl_3$) 1.32 (s, 3 H, CH_3), 1.9–2.9 (m, 4 H, $-CH_2CH_2-$), 3.68 (dd, J = 2, 9 Hz, 1 H, H_a), 4.10 (d, J = 9 Hz, 1 H, H_b), 4.36 (dd, J = 2, 6 Hz, 1 H, H_c), 4.69 (d, J = 6 Hz, 1 H, H_d). By treatment with aqueous acid, 4 was converted to 5 (oil), then to acetate 6: mp 111.0–112.5 °C; ^1H NMR ($CDCl_3$) δ 1.02 (s, 3 H, CH_3), 2.04 (s, 3 H, OAc), 2.4–3.0 (m, 4 H), 3.24 (dd, J = 6, 16 Hz, 1 H), 3.44 (dd, J = 6, 16 Hz, 1 H), 4.20 (br s, 2 H, CH_2OAc), 7.20 (br t, 1 H, NH); IR (KBr) 3320, 3090 (NH), 1737 (ester), 1706 (keto), 1663 (amide) cm^{-1}. Irradiation of 1 in water acidified with a trace of hydrochloric acid also gave 5 in a good yield. On the other hand, irradiation of 1 (0.05 M) in acidic methanol acidified with a trace of hydrochloric acid for about 20 h afforded a ketal 7 (88%): mp 160.0–161.0 °C; ^1H NMR ($CDCl_3$) δ 0.98 (s, 3 H, CH_3), 1.8–2.6 (m, 4 H, $-CH_2CH_2-$), 3.34 (s, 3 H, OCH_3), 3.39 (s, 3 H, OCH_3), 2.8–4.0 (m, 5 H), 6.80 (br t, 1 H, NH); IR (KBr) 3400 (OH), 3240, 3070 (NH), 1655 (amide) cm^{-1}. Acetate of 7 (8): mp 124.0–126.0 °C; ^1H NMR ($CDCl_3$) δ 1.02 (s, 3 H, CH_3), 2.06 (s, 3 H, OAc), 1.8–2.6 (m, 4 H, $-CH_2CH_2-$), 3.28 (s, 3 H, OCH_3), 3.34 (s, 3 H, OCH_3), 2.8–3.5 (m, 2 H), 4.02 (d, J = 12 Hz, 1 H), 4.23 (d, J = 12 Hz, 1 H), 6.36 (br t, 1 H, NH); IR (KBr) 3200, 3080 (NH), 1735 (ester), 1670 (amide) cm^{-1} (Scheme I).