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Photocatalyzed Reaction of Trifluoromethyl Iodide with Steroidal Dienones[1]

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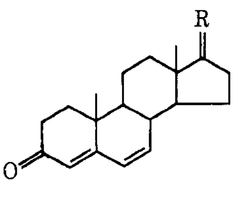
Received September 11, 1974

Ultraviolet irradiation (3500 Å) of pyridine solutions of 3-keto-$\Delta^{4,6}$-steroids in the presence of trifluoromethyl iodide gave 3-keto-4-trifluoromethyl-$\Delta^{4,6}$-steroids as the sole products of reaction. A similar reaction of using 7-oxo-3,5-androstadien-17β-yl acetate gave a mixture of 6-trifluoromethyl-7-oxo-$\Delta^{3,5}$-steroid and 3-trifluoromethyl-7-oxo-Δ^{5}-steroid indicating a steric as well as an electronic requirement for this reaction. An interesting reductive solvolysis of the 4-trifluoromethyl group has been observed.

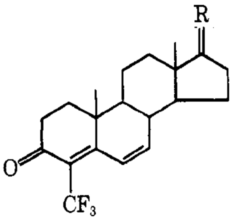
In the course of preparing trifluoromethylated steroids,[2] we attempted photochemical addition of trifluoromethyl iodide to the 3-keto-$\Delta^{4,6}$ system. Haszeldine has shown the trifluoromethyl group adds selectively to the terminal vinyl carbon when acrylic acid derivatives are exposed to trifluoromethyl iodide under photolytic conditions.[3] The position of addition in these cases was not dependent upon polarization of the double bond but on the stability of the intermediate radical. Accordingly, Godfredsen and Vangedal demonstrated that addition to the steroidal 3-alkoxy-$\Delta^{3,5}$ system resulted in substitution at the 6 position.[4] Wolff found addition to Δ^{3}-5α-steroids gives exclusively the axial 3α-trifluoromethylated product,[5] a result expected if one invoked steric considerations. We find trifluoromethyl substitution occurs preferentially α to the carbonyl function in linearly conjugated dienone systems. Both electronic and steric considerations must then be involved in the addition of the trifluoromethyl radical to these electron-deficient systems.

Irradiation of a solution of dienones **1a–d** in a mixture of pyridine and trifluoromethyl iodide with uv light (3500 Å) for 2–6 days at room temperature gave 4-trifluoromethylated steroids **2a–d** as the only products (32–42% conversion) found in addition to starting material. That the trifluoromethyl group was in the 4 position was evidenced by PMR absorption of vicinal vinyl hydrogens at C-6 and C-7 (complex doublets at about τ 3.7 and 3.3, $J \simeq 11$ Hz). This absorption disappeared when **2a** and **2b** were hydrogenated in ethyl acetate in the presence of palladium–barium sulfate catalyst to give 3-keto-Δ^{4} derivatives **3a** and **3b**. It is interesting that compounds **2** and **3**, with maxima at 283 and 233 nm, respectively, show no bathochromic shift on substitution of a trifluoromethyl group for a hydrogen α to the carbonyl.

The "reversed" linear dienone **4** when irradiated in the presence of trifluoromethyl iodide led to two products in addition to recovered starting material. The major product isolated was 6-trifluoromethyl-3,5-dien-7-one (**5**) formed in



1



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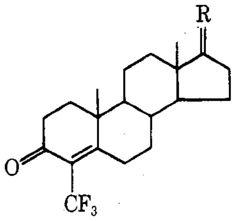

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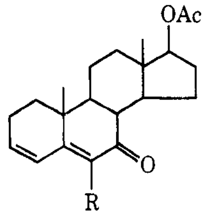
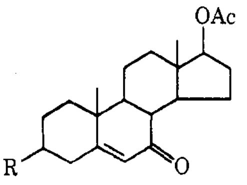
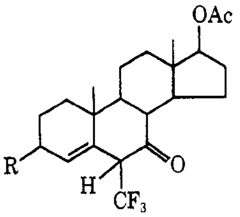


4, R = H
5, R = CF_3

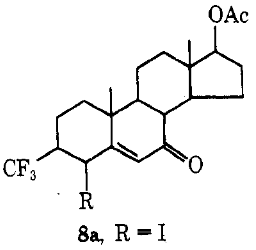
a, R = β-OAc, α-H
b, R = β-$COCH_3$, α-OAc
c, R = β-$OCH_2CH_2CH_2$-α
d, R = β-$CH(CH_3)CH_2CH_2CH_2CH(CH_3)_2$, α-H



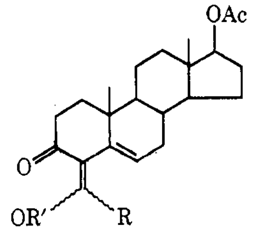
6a, R = CF_3
b, R = OAc



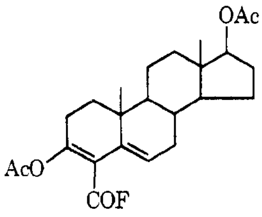
7a, R = I
b, R = radical



8a, R = I
b, R = radical



9a, R = F, R' = Ac
b, R = OCH_3, R = Ac
c, R = H, R' = H



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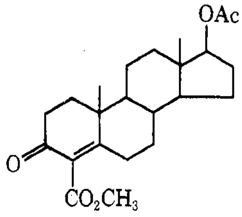

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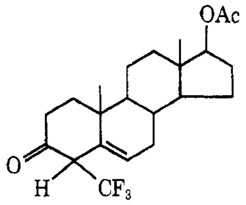
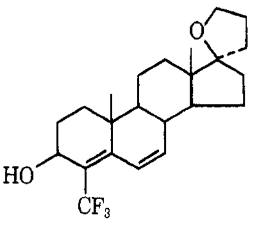


12



13

a manner similar to that described above. The second product had a molecular weight of 398 (mass spectrum), this being two units higher than for **5**. Ultraviolet (λ_{max} 237 nm), infrared (5.79 and 5.96 μm), and proton magnetic resonance (τ 4.26, vinyl hydrogen) spectra indicate the Δ^5,7-one system remained intact. Comparison of the PMR spectrum of this material with 3β-acetoxy-7-oxo-Δ^5-steroid **6b** showed only slight differences in their respective 19-CH_3 and 6-H shifts. Structure **6a** is favored over the 4-substituted isomer whose PMR spectrum would be expected to show some change at one or both of those resonances. Configuration of the trifluoromethyl group remains unknown.

Interestingly, under these reaction conditions, addition α to the carbonyl affords dienone **5** whereas addition at the terminal δ position results in reduced product **6a**. It may be intermediate iodo compounds **7a** and **8a** are formed. Elimination would occur readily with **7a** due to the acidity of the proton α to the carbonyl group. The C-3 proton of **8a** is not as acidic and thus the allylic iodine atom could be removed reductively with hydrogen iodide generated within the reaction mixture.

If Haszeldine's conclusions are correct, these results imply the radical generated by attack α to the carbonyl (i.e., **7b**) is more stable than that generated by terminal attack on the dienone system (**8b**). Another factor is electron density in the dienone system is highest at the α position and the trifluoromethyl radical, being electrophilic, would be most disposed to attach to that point. Steric factors certainly must be considered, for δ addition occurred only when the α position was placed in a more hindered environment and the terminal end was more exposed as in **4**.

Hydrogenation of **2a** in methanol in the presence of a Pd/C catalyst resulted in the rapid uptake of greater than 1 equiv of hydrogen and formation of a mixture of products. When sodium acetate was added to moderate the rate and reaction was stopped after uptake of 1 equiv of hydrogen, a product containing an additional acetoxy group was formed. Depending on the manner of work-up, the major product (isolated yield, 24–50%) showed a molecular ion at either 418 or 430. Material of mol wt 418 had a proper elemental analysis for $C_{24}H_{31}FO_5$ and showed five absorption peaks in the range 5.50–6.14 μm of its infrared spectrum. These data would accommodate structures **9a** or **10**. Structure **9a** is favored as its uv maximum at 229 nm is near that of the similar cross-conjugated system **9c** (231 nm).[6] The compound of mol wt 430 is the corresponding methoxy steroid **9b**. This material when heated in wet methanol containing sodium acetate was transformed into 4-carbomethoxytestosterone acetate **11**.[7]

Lability of an olefinic trifluoromethyl group under such mild conditions is surprising. The trifluoromethyl groups of **2a** and **3a** were stable to refluxing methanolic sodium acetate indicating the catalyst and/or a reactive intermediate (i.e., **12**) play a part in formation of **9**.[8] Each trifluoromethyl dienone **2a** and **2b** when hydrogenated in ethyl acetate in the presence of fresh, but not pre-reduced palladium on barium sulfate catalyst gave an unidentified by-product in addition to a low yield of the dihydro product **3**. Reduction of **2c** with sodium borohydride in methanol gave alcohol **13** in good yield.

Experimental Section[9]

17β-Acetoxy-4-trifluoromethyl-4,6-androstadien-3-one (2a). A solution of 2.40 g of 17β-acetoxy-4,6-androstadien-3-one (**1a**) in a mixture of 10 ml of pyridine and 8 g of trifluoromethyl iodide was irradiated in a sealed Pyrex tube for 3.5 days at room temperature. The tube containing the dark mixture was then cooled and opened. The mixture was acidified by addition to excess 2.5 *N* HCl. The product was extracted into chloroform and was washed successively with water, 5% aqueous $NaHSO_3$, and water. After drying ($CaSO_4$) and concentration, the residue (~3 g) was chromatographed on 150 g of silica gel. The trifluoromethyl compound **2a** (1.157 g) which eluted with benzene was recrystallized from heptane to give 0.990 g of heavy, pale yellow needles: mp 156–158°; $[\alpha]^{25}\mathrm{D}$ +94.3°; uv max (CH_3OH) 283 nm (ε 2.3 × 10^4); ir 5.78, 5.97, 6.17, and 6.39 μm; PMR τ 3.29 (complex doublet, 1, *J* = 11 Hz, 7-CH), 3.69 (complex doublet, 1, *J* = 11 Hz, 6-CH), 7.96 (s, 3, CH_3CO), 8.87 (s, 3, 19-CH_3) and 9.10 (s, 3, 18-CH_3); *m/e* 396, 354, 336, 321, and 133.

Anal. Calcd for $C_{22}H_{27}F_3O_3$: C, 66.65; H, 6.87; F, 14.38. Found: C, 66.88; H, 6.70; F, 14.30.

Continued elution of the column afforded 0.330 g of material identified as the starting dienone **1a** by its infrared spectrum and thin layer chromatography behavior.

4-Trifluoromethyl-4,6-cholestadien-3-one (2d). A solution of 1.00 g of 4,6-cholestadien-3-one (**1d**) in 4 ml of pyridine and 3.4 g of trifluoromethyl iodide was irradiated as described above for 6 days. Workup and chromatography afforded 0.450 g of the trifluoromethylated steroid **2d**. Recrystallization of this material from hexane gave yellow prisms: mp 107–108°, $[\alpha]^{25}\mathrm{D}$ +84.1°.

Anal. Calcd for $C_{28}H_{41}F_3O$: C, 74.63; H, 9.17; F, 12.65. Found: C, 74.38; H, 9.15; F, 13.06.

2′,3′α-Tetrahydrofuran-2′-spiro-17-(4-trifluoromethyl-4,6-androstadien-3-one) (2c). A solution of 1.00 g of the dienone **1c** in 6 ml of pyridine and 4.0 g of trifluoromethyl iodide was irradiated as described above for 2.5 days. Work-up and chromatography afforded 0.397 g of **2c**. Recrystallization from hexane gave 0.305 g, mp 122–125°. An analytical sample from methanol separated as pale yellow, heavy needles: mp 123–124°; $[\alpha]^{25}\mathrm{D}$ +61.3°; uv max (CH_3OH) 285 nm (ε 2.4 × 10^4).

Anal. Calcd for $C_{23}H_{29}F_3O_2$: C, 70.03; H, 7.41; F, 14.45. Found: C, 69.91; H, 7.54; F, 14.67.

A solution of 30 mg of the above compound, **2c**, in 2.0 ml of methanol was treated at 0° with 10.0 mg of sodium borohydride with stirring. After 20 min, a drop of glacial acetic acid was added and the mixture was diluted with water. The product was worked up in ether solution to give 30 mg of a crystalline residue. Recrystallization from acetonitrile afforded 20.5 mg of the 3-ol **13** as small prisms: mp 194–195°; devoid of carbonyl absorption in its infrared spectrum; uv max (CH_3OH) 245 nm (ε 2 × 10^4); *m/e* 396 (M^+), 378, 319, 97.

Anal. Calcd for $C_{23}H_{31}F_3O_2$: C, 69.67; H, 7.88. Found: C, 69.25; H, 7.92.

17α-Acetoxy-4-trifluoromethyl-4,6-pregnadiene-3,20-dione (2b). A solution of 300 mg of the dienone **1b** in 2 ml of pyridine and 1.2 g of trifluoromethyl iodide was irradiated as described above for 4 days. Work-up and chromatography resulted in 149 mg of crystalline **2b** which separated from methanol as heavy prisms: mp 226–227°; $[\alpha]^{25}\mathrm{D}$ +47.4°; uv max (CH_3OH) 283 nm (ε 2.4 × 10^4).

Anal. Calcd for $C_{24}H_{29}F_3O_4$: C, 65.75; H, 6.67; F, 13.00. Found: C, 65.50; H, 6.68; F, 12.81.

4-Trifluoromethyltestosterone Acetate (3a). A solution of 100 mg of the 4,6-dienone **2a** in 35 ml of ethyl acetate was hydrogenated at atmospheric pressure and room temperature in the presence of 60 mg of 5% palladium on barium sulfate catalyst. The reaction was stopped after theoretical uptake had occurred. The catalyst was separated and the solution concentrated to give 106 mg of a crystalline residue. Recrystallization from heptane gave 52 mg of fine needles, mp 130–144°. Concentration of the filtrate left crystalline material which when recrystallized twice from hexane amounted to 20 mg and had mp 138–144°. The infrared spectrum and thin layer mobility of this material was identical with that of the 130–144° melting material. It had uv max (isooctane) 233 nm (ε 1.3 × 10^4); PMR τ 5.36 (doublet of doublets, 1, 17-CH), 7.96 (s, 3, CH_3CO), 8.73 (s, 3, 19-CH_3), and 9.14 (s, 3, 18-CH_3).

Anal. Calcd for $C_{22}H_{29}F_3O_3$: C, 6.31; H, 7.33; F, 14.30. Found: C, 66.29; H, 7.55; F, 14.16.

A second material (mp 225–229°) isolated by thin layer chromatography (silica gel) of residues from work-up of the hydrogenation was analyzed by high resolution mass spectrometry and found to have an intense (molecular?) ion measured at 412.18409 mass units and corresponds best with an empirical formula of $C_{22}H_{27}F_3O_4$.

17α-Acetoxy-4-trifluoromethylprogesterone (3b). A solution of 438 mg of dienone **2b** in 35 ml of ethyl acetate was hydrogenated in the presence of 200 mg of 5% palladium on barium sulfate catalyst. The hydrogenation was stopped after uptake of 1 equiv. The catalyst was removed and the filtrate concentrated to a slowly crystallizing gum. Recrystallization in three steps using acetonitrile, benzene–hexane, and then methanol gave 47 mg of **3b**, mp 241–243°. The filtrates were combined and concentrated. The residue was eluted with 4:1 benzene–ethyl acetate on 78 g of Silica Gel H using the dry column technique. The eluent was collected in 5-ml fractions using a fraction collector. Additional **3b** (108 mg) was obtained in the early fractions. Recrystallization of this material gave 57 mg: mp 241–244°; uv max (MeOH) 241 nm (ε 1.1 × 10^4); PMR τ 7.91 (s, 3, CH_3CO_2), 7.99 (s, 3, 21-CH_3), 8.76 (s, 3, 19-CH_3), and 9.33 (s, 3, 18-CH_3); *m/e* 440 (M^+) 398, 397, 380, 355, and 337.

Anal. Calcd for $C_{24}H_{31}F_3O_4$: C, 65.44; H, 7.09; F, 12.94. Found: C, 65.51; H, 7.00; F, 12.83.

Continued elution gave 41 mg of starting dienone **1b** identified by its TLC mobility and infrared spectrum. Another crystalline component (121 mg) eluted next. This material was recrystallized from ether by addition of hexane to give prisms: mp 195–198°; uv max (CH_3OH) 236 nm (E% 220); ir 2.85 and 3.02 (OH), 5.80 (acetate), 5.90 (unsatd C=O?) and 6.26 μm (C=C); PMR τ 4.76 (narrow m, 1), 7.98 (s, 3, CH_3CO_2), 8.03 (s, 3, 21-CH_3), 8.60 (s, 3, 19-CH_3), and 9.35 (s, 3, 18-CH_3); *m/e* (no $M\cdot^+$), 455 (highest *m/e*), 410, 369, 353, 351, and 335.

Anal. Found: C, 61.15; H, 6.43; F, 12.43.

17α-Acetoxy-4-trifluoromethylprogesterone (3b). A suspension of 200 mg of 5% palladium on barium sulfate catalyst was prereduced in 10 ml of degassed ethyl acetate. A solution of 436 mg of the dienone **2b** in 25 ml of degassed ethyl acetae was added under hydrogen. Hydrogen uptae ceased after 30-min stirring at 25° and atmospheric pressure. The catalyst was removed and the filtrate concentrated to a crystalline residue. Recrystallization from ethanol gave 239 mg of **3b**, mp 236–240°, identical with the material described above in its spectral properties.

Photolysis of Trifluoromethyl Iodide in the Presence of 7-oxo-3,5-androstadien-17β-yl Acetate. A mixture of 0.800 g of the dienone **4** in 6.0 ml of pyridine and 6.2 g of trifluoromethyl iodide was irradiated as described above for 7 days. The material went into solution gradually and the mixture became dark. Workup in ethyl acetate resulted in ~1.0 g of dark residue. Vapor phase chromatography (VPC) indicated the mixture to contain three major components in the approximate ratio of 2:4:3 (order of elution). The last eluted major component corresponded to the starting dienone **4**. The residue was chromatographed on a column prepared from a mixture of 100 g of Stahl Silica Gel and 75 g of diatomaceous earth. Elution with benzene (4 l.) and then 2% ether in benzene (25-ml fractions using a fraction collector) gave after a small forerun 268 mg of crystalline **5**. After separation from heptane and then methanol, 135 mg was obtained, mp 148–152°. This material corresponded to the second eluted material by VPC. An analytical sample had mp 149–151°, $[\alpha]\mathrm{D}$ −351°; uv max (CH_3OH) 278 nm (ε 1.98 × 10^4); PMR τ 3.28 (complex doublet, *J* = 11 Hz, 3-CH), 3.58 (complex doublet, *J* = 11 Hz, 4-CH), 7.96 (s, CH_3CO), 8.82 (s, 19-CH_3) and 9.15 (s, 18-CH_3), *m/e* 396 (M^+), 336, 320, 255 (base), 242, and 229.

Anal. Calcd for $C_{22}H_{27}F_3O_3$: C, 66.65; H, 6.87; , 14.38. Found: C, 66.24; H, 6.78; F, 14.74.

Continued elution (fractions 220–275) afforded 76 mg of crystalline material corresponding to the first VPC eluted major product. Recrystallization from heptane gave 27.5 mg of **6a**, mp 225–228° with crystal modification >200°; ir 5.80, 6.00, and 6.13 (shoulder) μm; uv max (CH_3OH) 236 nm (ε 1.28 × 10^4); PMR τ (HR-100) 4.25 (partially resolved doublet, width at half-height, 3.5 Hz), 7.98 (s, CH_3CO), 8.78 (s, 19-CH_3) and 9.19 (s, 18-CH_3); *m/e* 398 (M^+, base), 338, 323, 257, 244, and 231. The PMR (HR-100) of 3β-acetoxy-17-hydroxy-5-androsten-7-one had τ 4.28 ($w_{1/2}$ = 3.2 Hz) and 8.78 (s, 19-CH_3).

Anal. Calcd for $C_{22}H_{29}F_3O_3$: C, 66.31; H, 7.33. Found: C, 66.74; H, 7.13.

Continued elutions (fraction 315–350) afforded 151 mg of crystalline starting dienone, identified by its melting point and ir spectrum.

Hydrogenation of 2a in Methanolic Potassium Acetate. A solution of 100 mg of the trifluoromethyl dienone **2a** and 1.00 g of potassium acetate in 30 ml of methanol was hydrogenated at room temperature and atmospheric pressure in the presence of 25 mg of 10% palladium on charcoal catalyst. One equivalent of hydrogen (5.9 cm^3) was quickly absorbed and the reaction was stopped. The catalyst was removed and the filtrate was concentrated at room temperature to a small volume. After dilution with water, the product was separated by filtration, washed with water, and dried under reduced pressure. Preparative thin layer chromatography of the residue (silica gel eluted with 4:1 benzene–ethyl acetate) resulted in the isolation of 25 mg of the major component. When quickly recrystallized from methanol, fine crystalline material was obtained, mp 180–193° slow decomposition, then rapid gas evolution: uv max 229 nm (ϵ 1.1 × 10^4) and shoulder 260 nm (ϵ 5 × 10^3); ir 5.51, 5.69, 5.81, 6.00, and 6.15 μm; PMR (T-60) τ 4.16 (narrow m, 6-CH), 7.93 (s, CH_3CO), 7.97 (s, CH_3CO), 9.18 (s, 19-CH_3), and 9.42 (s, 18-CH_3); *m/e* 418, 376, 356 (base), 328, 164, 162, and 133; metastable peaks at *m/e* 335 and 302 confirmed the fragmentation sequence, *m/e* 376 → 356 → 328.

Anal. Calcd for $C_{24}H_{31}O_5F$: C, 68.87; H, 7.47; F, 4.54. Found: C, 68.64; H, 7.72; F, 4.96.

In an attempt to repeat the above experiment with 0.5 g of **2a**, the same conditions were used except heat (bath temperature ~50°) was used when concentrating the filtrate after removal of the catalyst. In this case, the major product isolated, **9b** (250 mg, preparative TLC), was different from that described above in that it had mp 155–160°; *m/e* 430 (M^+), 388, 356 (base), 328, 164, 162, and 133; uv max 230 nm (ϵ 1.8 × 10^4); ir 5.62 and 5.73 μm; PMR (T-60) τ 4.55 (m, 6-CH), 6.29 (s, OCH_3), 7.90 (s, O_2CCH_3), 7.99 (s, O_2CCH_3), 8.99 (s, 19-CH_3) and 9.20 (s, 18-CH_3).

Anal. Calcd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 68.95; H, 8.03.

A solution of 200 mg of this material (**9b**) in a mixture of 10 ml of methanol, five drops of water, and 200 mg of potassium acetate was heated at reflux for 16 hr under nitrogen. The mixture was concentrated and then the residue was extracted with ethyl acetate. After drying and concentration, the residue was eluted on a thick layer (1000 μ) silica gel-coated plate. The major component **11** was extracted and crystallized from methanol, 70 mg: mp 147–149°; *m/e* 388 (M^+), 356 (base), 332, and 328; uv max 244 (ϵ 1.08 × 10^4) and 287.5 nm (ϵ 1.72 × 10^3); ir 5.77, 5.97, and 6.19 μm; PMR τ 6.21 (s, OCH_3), 7.98 (s, O_2CCH_3), 8.77 (s, 19-CH_3), and 9.17 (s, 18-CH_3).

Anal. Calcd for $C_{23}H_{32}O_5$: C, 68.56; H, 8.25. Found: C, 68.16; H, 8.27.

Stability of the Trifluoromethyl Steroids 2b and 3b to Methanolic Sodium Acetate. A solution of 20 mg of each of the steroids **2b** and **3b** was dissolved with 200 mg of sodium acetate in 5 ml of methanol. These solutions were heated at reflux for 30 min, then cooled and concentrated. The ethyl acetate extracts of the respective residues were concentrated to a crystalline material which, after recrystallization, were identified by mixture melting point, ir spectra, and TLC mobilities with their corresponding starting materials.

Acknowledgment. The authors wish to thank Dr. Byron Arison and Mr. Jack L. Smith for their assistance in interpreting the NMR and mass spectra discussed in this paper.

Registry No.—**1a,** 2352-19-4; **1b,** 425-51-4; **1c,** 6693-79-4; **1d,** 566-93-8; **2a,** 53821-28-6; **2b,** 53821-29-7; **2c,** 53821-30-0; **2d,** 53821-31-1; **3a,** 53821-32-2; **3b,** 53821-33-3; **4,** 13583-12-5; **5,** 53821-34-4; **6a,** 53821-35-5; **9a,** 53821-36-6; **9b,** 53821-37-7; **11,** 53821-38-8; **13,** 53835-06-6; trifluoromethyl iodide, 2314-97-8.

References and Notes

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(9) Melting points were determined on a Kofler hot-stage and are uncorrected. Infrared spectra were determined with a Perkin-Elmer spectrometer, Model 137, as chloroform solutions and are in accord with the assigned structures. PMR spectra were obtained from deuteriochloroform solutions with a Varian Model A-60A spectrometer unless otherwise noted. Mass spectra were obtained on either a CEC Model 21-110 or an LKB Type 9000 spectrometer by the direct probe technique. Rotational data were obtained from 1% chloroform solutions. Irradiations were carried out in a Rayonet photochemical reactor, Type RS, using lamps with peak intensity at 3500 Å. All isolated products were analyzed by thin-layer chromatography on silica gel-coated glass plates eluted with an appropriate benzene–ethyl acetate system.

Total Syntheses of Optically Active 19-Norsteroids. (+)-Estr-4-ene-3,17-dione and (+)-13β-Ethylgon-4-ene-3,17-dione

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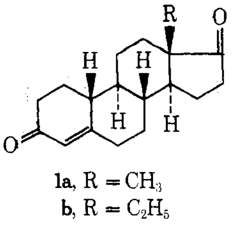
Received October 9, 1974

Highly efficient total syntheses of the title 19-norsteroids are described in which the chirality is introduced early in the synthetic scheme *via* an asymmetric synthesis of the bicyclic intermediates **4a** and **4b**. These substances are then converted in five stages into the key α-methylene ketones **9a** and **9b**. Michael addition of the β-keto ester **17** (prepared starting from diketene and formaldehyde) to the enones **9** followed by cyclization, saponification, and decarboxylation then affords the tricyclic compounds **20a** and **20b** which are readily transformed into the title diones in three additional stages. The efficiency of this approach is demonstrated by the production of **1a** and **1b** in overall yields of 27 and 18%, respectively, based on the starting 2-alkyl-1,3-cyclopentanediones.

In a previous publication,[2] two of us described a convergent, stereo-controlled total synthesis of racemic 19-norsteroids in which the synthetic strategy involved initial construction of a bicyclic C,D-ring synthon followed by elaboration of ring B and finally ring A. We now wish to present the results of a team effort directed toward the application of this scheme to the production of optically active 19-norsteroids of biological and commercial significance.[3] In particular, we wish to describe highly efficient and practical syntheses of diones (+)-**1a**[3,4] and (+)-**1b**[5] in which all carbon atoms of the final steroid molecule are derived from readily available building blocks. Furthermore, the crucial problem of introduction of chirality is solved *via*



1a, R = CH_3
b, R = C_2H_5