

## A Novel 11-Enolate Ion of a Pregna-1,4-diene-3,11-dione from Sodium Bistrimethylsilylamide

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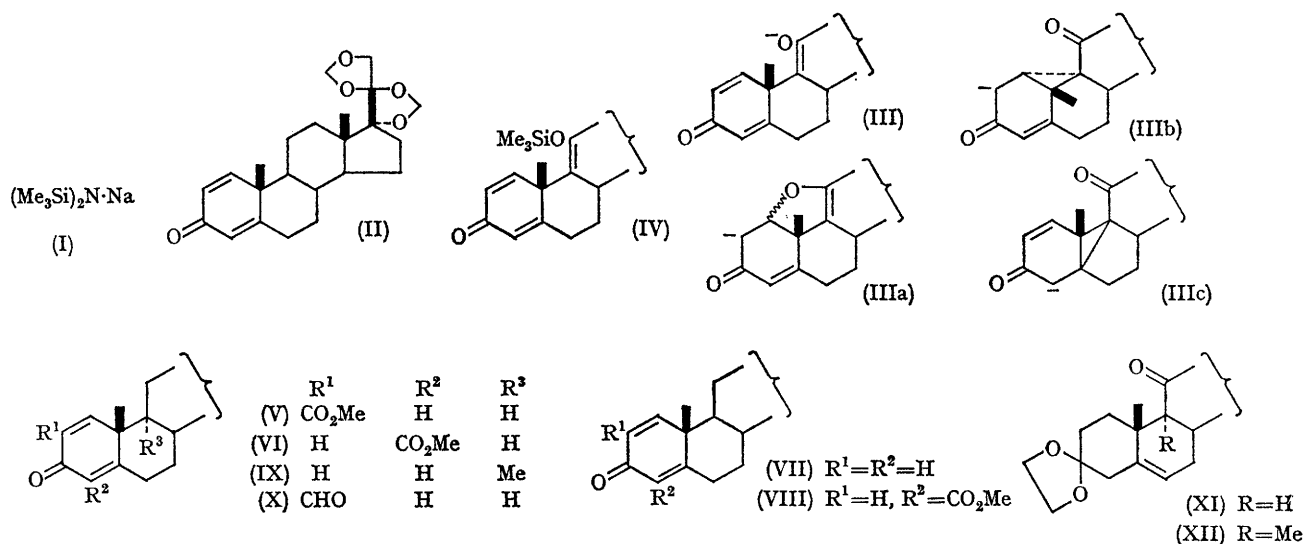
**Summary** Reaction of a steroidal 11-ketone with sodium bistrimethylsilylamide in tetrahydrofuran solution generates the 9(11)-enolate anion.

SODIUM BISTRIMETHYLSILYLAMIDE (I) is an extremely useful and effective base for the generation of sodium enolates from ketones. The base is soluble in most non-polar solvents, and this facilitates rapid and almost quantitative conversion into enolates.<sup>1</sup> Its utility in enolate ion formation is illustrated by the reaction of (I) with 17,20;20,21-bismethylenedioxypregna-1,4-diene-3,11-dione (II) in tetrahydrofuran solution at 20° to yield a deep red enolate (III). Quenching of (III) with chlorotrimethylsilane yields a hitherto undescribed class of compound, a 9(11)-enol ether of a 3-oxo-1,4-diene (IV), †  $M^+ m/e$  472;  $\lambda_{\max}$  (ether) 234 nm. ( $\epsilon$  15,000);  $\lambda_{\max}$  (Nujol) 6.0 (C=O), 6.15, 6.20 (C=C), 8.0, and 11.5–12  $\mu\text{m}$  (Si-C);  $\tau$  2.38 (1-H, d,  $J_{1,2}$  10 Hz), 3.9 (2-H, q,  $J_{2,1}$  10,  $J_{2,4}$  1.5 Hz), 3.92 (4-H), 8.58 (19-H<sub>3</sub>), 9.08 (18-H<sub>3</sub>), 9.9 [9H; (CH<sub>3</sub>)<sub>3</sub>Si].

Saturation of a solution of the enolate ion (III) with carbon dioxide, followed by isolation of the acids produced as the methyl esters, unexpectedly yields as the major product, 2-methoxycarbonyl-17,20;20,21-bismethylenedioxypregna-1,4-diene-3,11-dione (V) (40%). Carboxylation at C-2 of the anion (III) is clearly indicated by the absence of the C-2 proton in the n.m.r. spectrum and a shift to lower field of the singlet C-1 proton, also isolated along with (V) in lower yield (10%) is the corresponding 4-methoxycarbonyl derivative (VI), whose carboxylation at C-4 is indicated by the absence of the C-4 proton in the n.m.r. spectrum.

The formation of (V) can be visualized as arising from the carbonation of the 3-enolate anion (IIIa) formed by the internal Michael addition of the  $\Delta^9(11)$  enolate anion oxygen of (IIIa) to C-1. Subsequent  $\beta$ -elimination of the 1,11-oxide bridge regenerates the 11-oxo- $\Delta^1,4$ -dienone system. Several stable 1,11-epoxides are known and in the presence of a 3-ketone function ready  $\beta$ -elimination of the epoxide

† Satisfactory elemental analyses and spectra (mass, i.r., u.v., and n.m.r.) have been obtained for all new compounds. N.m.r. spectra were measured on a Varian A-60A spectrometer in CDCl<sub>3</sub> solutions using SiMe<sub>4</sub> as internal standard. Mass spectra were determined on a modified CEC 21-103C spectrometer with a direct heated inlet system at 125°. We thank Mr. Frank M. Church for these measurements.



bridge occurs.<sup>2</sup> Alternative structures for the 3-enolate, the  $1\alpha,9\alpha$ -cycloenolate ion (IIIb), and the  $5\alpha,9\alpha$ -cycloenolate ion (IIIc) derived from the 11-enolate ion (III) are considered less likely on steric grounds, although several well authenticated 5,9-cyclo-steroids are known.<sup>3</sup> Since carbonation of the sodium enolate of the 11-deoxo-derivative (VII) yields only the 4-methoxycarbonyl compound (VIII), formation of the small quantity of 4-methoxycarbonyl compound (VI) can come from competitive enolization of the 3-keto-group in (II).

This result with (VII) also eliminates the formal possibility of addition and elimination of bistrimethylsilylamide ion at C-1 to generate a 3-enolate ion to account for the formation of the 2-carboxylated product (V). Alkylation of the enolate ion (III) with methyl iodide yields the  $9\alpha$ -methyl derivative (IX). The  $9\alpha$ -stereochemistry follows from previous studies of the methylation of a 9(11)-enolate ion.<sup>4</sup> No evidence for the formation of a 2-methylated compound could be obtained by examination of the n.m.r. spectrum of the total reaction mixture.

These results appear to indicate that irreversible reactions

of the enolate ion (III) such as the methyl iodide alkylation occur at C-9, whereas the reversible carbonation reaction occurs at C-2. Support for this concept is derived from the reversible condensation reaction of the enolate ion (III) with ethyl formate which gives the known 2-formyl derivative (X),<sup>5</sup> whereas irreversible deuteration of the enolate ion (III) with deuterium oxide affords (II) with a minor quantity of deuterium incorporated into the 2-position as determined by n.m.r. spectroscopy.

The ready conversion of ketones into enolates with sodium bistrimethylsilylamide is further exemplified by the conversion of (XI) into the 9(11)-enolate ion in tetrahydrofuran, which with methyl iodide gives the known  $9\alpha$ -methyl compound (XII).<sup>4b</sup> This transformation is unsuccessful with either triphenylmethylsodium or sodium hydride.

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