

has been observed in Ni(SacSac)(PEt<sub>3</sub>)Cl,<sup>9</sup> and the solid-state structure of Zn[S<sub>2</sub>CN(CH<sub>3</sub>)<sub>2</sub>]<sub>3</sub><sup>-</sup> exhibits four short and two long zinc-sulfur bonds with  $d(\text{Zn-S})_{\text{av}} = 2.31$  and 3.13 Å, respectively.<sup>10</sup> In the present case, fast F<sub>2</sub>acac exchange and rearrangement in **1** and **2** may be facilitated by the electron-withdrawing effect of the CF<sub>3</sub> groups.

We refer to the hexafluoroacetylacetonate bonding mode in **1**, which features one short and one long metal-oxygen separation, as semichelating and suggest that it is an attractive model for transition states in some substitution or isomerization reactions of metal chelates.

**Supplementary Material Available:** A listing of the positional and thermal parameters derived from the crystallographic analysis (3 pages). Ordering information is given on any current masthead page.

(9) J. P. Fackler and R. F. Masters, *Inorg. Chim. Acta*, **39**, 111 (1980). SacSac refers to pentane-2,4-dithionato(1-).

(10) C. C. Ashworth, N. A. Bailey, M. Johnson, J. A. McCleverty, N. Morrison, and B. Tabbiner, *J. Chem. Soc., Chem. Commun.* 743 (1976).

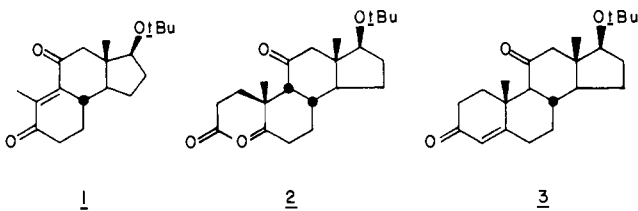
## A New Route to 11-Oxygenated Steroids

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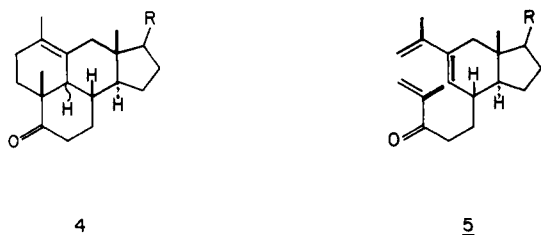
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The steroid structure is an extremely useful target in the development of new regio- and stereochemically controlled synthetic methods.<sup>1</sup> For that reason, and because of their continued importance, we have been particularly interested in 11-oxygenated steroids. We have recently described<sup>2</sup> the transformation **1** → **2** → **3** which served to demonstrate the feasibility and stereochemistry of the kinetic enolate trapping method<sup>3</sup> in the reductive alkylation of enediones of type **1**.



The usefulness of triones such as **2** as precursors to the Δ<sup>4</sup>-3, 11-diketo system raised the question whether the particular methylcyclohexene **4**, another potential precursor of the trione **2**, might not be readily accessible via the [4 + 2] cycloaddition of a trienone like **5**.



The [4 + 2] cycloaddition of **5** can formally generate four diastereoisomers (cf. **6**). Only two of these are likely, however, because the transition state for approach of the enone chain from the underneath (α) side of the indane system is clearly favored.

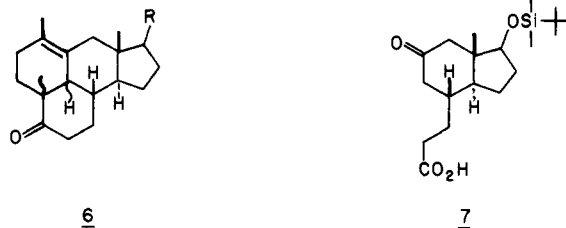
(1) For the most impressive illustration see: Johnson, W. S.; Brinkmeyer, R. S.; Kapoor, V. M.; Yarnell, T. M. *J. Am. Chem. Soc.* **1977**, *99*, 8341.

(2) Stork, G.; Logusch, W. E. *J. Am. Chem. Soc.* **1980**, *102*, 1219.

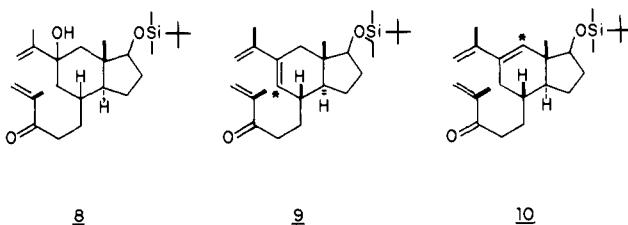
(3) Stork, G.; Rosen, P.; Goldman, N.; Coombs, R. V.; Tsuji, J. *J. Am. Chem. Soc.* **1965**, *87*, 275.

Of the resulting two possible cis B/C products the major one should have the correct β orientation of the pro-C-10 methyl group, as a result of what appears to be a very reasonable endo transition state. It is therefore an attractive possibility that the major product from the cyclization of **5** would have the desirable structure shown in **4**.

We now demonstrate the effectiveness of this approach starting with the keto acid **7**<sup>4</sup> which can thus be transformed into the desired 11-ketotestosterone derivative **15** in just five steps.



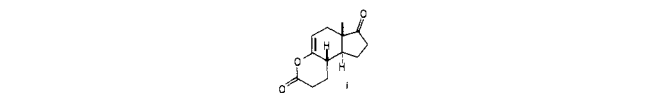
Addition of an excess of lithium isopropenyl<sup>5</sup> to **7** (4 equiv in ether, -78 → 25 °C, quenched with acetic acid in ethyl acetate) gave, after purification on silica, the enone alcohol **8** in >90% yield [NMR δ 1.0 (quaternary CH<sub>3</sub>), 1.77, 1.36 (allylic methyls), 4.8, 5.02 (CH<sub>3</sub>C=CH<sub>2</sub>), 5.75, 5.85 (H<sub>2</sub>C=C-C=O)]. Dehydration of **8** (Burgess' salt<sup>6</sup>, tetrahydrofuran, room temperature) gave largely the conjugated diene **9** (NMR δ 5.65 for the starred vinyl hydrogen) with the new double bond parallel to the ring junction, as expected. The minor isomer (**10**) from the dehydration was noticeable by the position of the starred vinyl hydrogen at δ 6.05. The small quantity of isomeric diene does not undergo the cycloaddition reaction, after which it is most easily removed.



Various conditions were tried for the [4 + 2] cycloaddition. It was possible to effect both dehydration and cycloaddition simultaneously by simple heating of the enone alcohol **8** with iodine (1 mg/mL) in dimethoxyethane to ~70 °C. Under these conditions, however, the ratio in favor of the desired endo isomer was only ~1.5:1. It was eventually found that the desired adduct **11** could be obtained as the major product by conducting the reaction at -78 °C in methylene chloride in the presence of 2 equiv of trifluoroacetic acid. Quenching with triethylamine after 4 h gave, after silica gel purification, the endo-exo mixture of cyclization products **11** and **12** in ~70% yield. The ratio of desired endo to exo isomer was 94:6, as determined by MPLC. The two quaternary methyl groups of **11** occur at δ 0.94 and 1.06, while resonances occur at δ 0.72 and 1.0 in **12**.

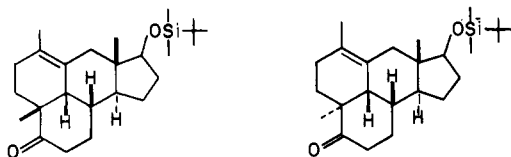
Ozonolysis of **12** (1:1 methanol-methylene chloride -78 °C, decomposition with triphenylphosphine) now led to the triketone

(4) Since the purpose at this stage was to examine the possibility of the **7** → **15** transformation, the hydrindanone **7** was simply made by moving the carbonyl of the steroid intermediate **i** which is readily available in optically active form. The transformation, while not a particularly satisfactory way to make indanones of type **7** proved of some interest and is detailed elsewhere.



(5) Made by adding 2-bromopropene slowly to a suspension of lithium (2% sodium) dispersion in ether. See: Smith W. N. *J. Organomet. Chem.* **1974**, *82*, 7. The various products described here had unambiguous spectral characteristics. The structures are, in any event, made unequivocal by their further transformations.

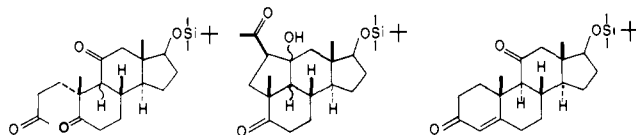
(6) Burgess, E. M.; Penton, H. R.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26.



11

12

13, 85% yield; NMR  $\delta$  0.76, 1.1 (quaternary  $\text{CH}_3$ 's), 2.09 ( $\text{C}-\text{H}_3\text{CO}$ ). It is clear that the triketone 13 can, in principle, cyclize to the acylcyclopentanol 14. The latter is indeed the kinetic product obtained, quantitatively [NMR  $\delta$  0.86, 1.30, 2.16 ( $\text{CH}_3\text{CO}$ )], upon treatment with 4% methanolic potassium hydroxide (room temperature, nitrogen, 5 min). The dehydration



13

14

15

of 14 is, fortunately, relatively slow, and the intermediate ketol 14, or the starting triketone 13, is converted by warming it to 40 °C (nitrogen, 30 min) in 85–90% yield to the 11-ketotestosterone 15 identical with the material made by silylation of authentic<sup>7</sup> 11-ketotestosterone.

The efficiency of this construction of an 11-ketosteroid system from the hydrindanone 7 has led us to seek novel and efficient processes for the synthesis of such hydrindanones. We will report shortly on this phase of our work.

**Acknowledgment.** We thank the National Institutes of Health and the National Science Foundation for their support of this work.

(7) Norymberski, J. K.; Woods, G. F. *J. Chem. Soc.* **1955**, 3426.

### Photosensitized Oxygenation of $\alpha$ -Diazoquinone

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The activation of molecular oxygen catalyzed by dioxygenases by which an oxygen molecule is incorporated into a substrate has received much attention in biological and chemical studies.<sup>1-5</sup>

Several reactions have been reported as nonenzymic models for the enzymatic hydroxylation<sup>6-9</sup> and cleavage of aromatic com-

(1) K. Block and O. Hayaishi, "Biological and Chemical Aspects of Oxygenases", Maruzene Co., Tokyo, 1966.

(2) Z. Yoshida and M. Kato, *Nippon Kagaku Kaishi*, **75**, 106, 109, 112 (1954).

(3) G. Jori, G. Galiazzo, and E. Scoffone, *Biochemistry*, **8**, 2868 (1969).

(4) J. E. Baldwin, H. H. Basson, and H. Krauss, Jr., *Chem. Commun.*, 984 (1968).

(5) T. Matsuura, H. Matsushita, and H. Sakamoto, *J. Am. Chem. Soc.*, **89**, 6370 (1967).

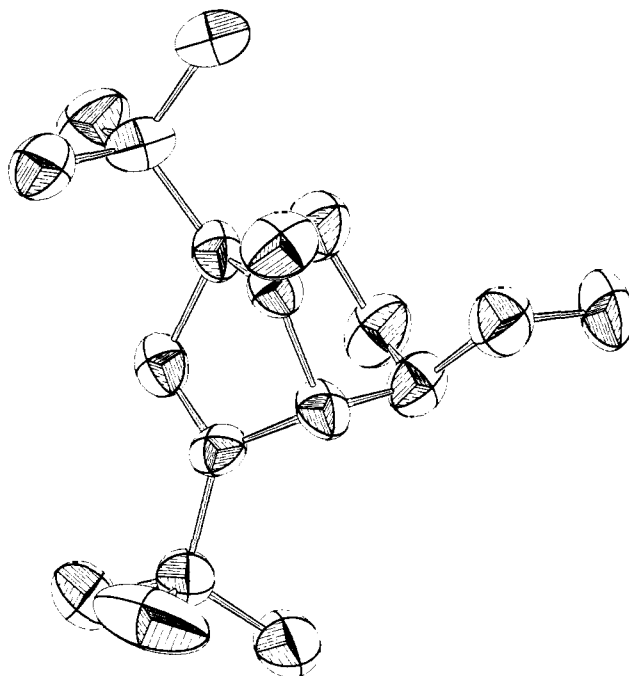
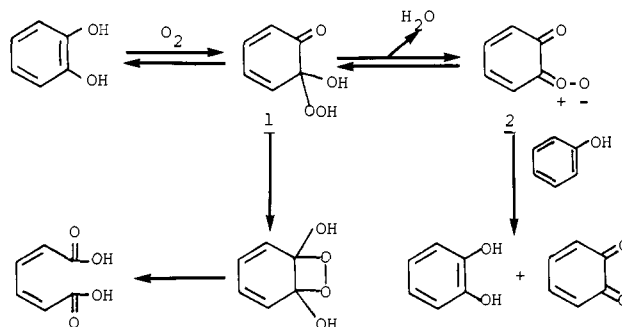
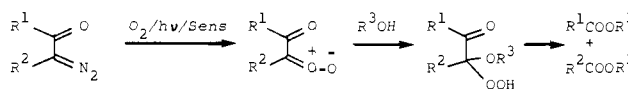


Figure 1. Perspective view of the cyclic peroxide 5.

pounds by oxygenases.<sup>10,11</sup> Catechol is oxidized to muconic acid derivatives by singlet oxygen,<sup>12</sup> superoxide,<sup>13</sup> and molecular oxygen activated with cuprous chloride.<sup>14</sup> Some of these cleavage reactions are rationalized by assuming hydroperoxy hemiketal 1 or  $\alpha$ -carbonyl carbonyl oxide 2 as a possible intermediate of enzymic model oxidations.<sup>15</sup>



Recently, we observed that the reaction of singlet oxygen with  $\alpha$ -diazo ketone gave the products derived from  $\alpha$ -keto hydroperoxide and 1,2-dioxetane via  $\alpha$ -carbonyl carbonyl oxide.<sup>16-18</sup>



(6) R. E. Keay and G. A. Hamilton, *J. Am. Chem. Soc.*, **97**, 6877 (1975).

(7) G. A. Hamilton and J. R. Giacini, *J. Am. Chem. Soc.*, **88**, 1584 (1966).

(8) S. K. Chaudhary, R. A. Hoyt and R. W. Murray, *Tetrahedron Lett.*, 4235 (1976).

(9) I. Saito, Y. Chujo, H. Shimazu, M. Yamane, T. Matsuura, and H. J. Cahnmann, *J. Am. Chem. Soc.*, **97**, 5272 (1975).

(10) O. Hayaishi, "Molecular Mechanism of Oxygen Activation", O. Hayaishi, Ed., Academic Press, New York, 1974, Chapter 1; P. Feigelson and F. O. Brady, *ibid.*, Chapter 3.

(11) M. Nozaki, ref 10, Chapter 4.

(12) T. Matsuura, H. Matsushima, S. Kato, and I. Saito, *Tetrahedron*, **28**, 5119 (1972).

(13) Y. Moro-oka and C. S. Foote, *J. Am. Chem. Soc.*, **98**, 1510 (1976).

(14) (a) J. Tsuji, H. Takayanagi, and I. Saiki, *Tetrahedron Lett.*, 1245 (1975); (b) J. Tsuji and H. Takayanagi, *ibid.*, 1365 (1976); (c) M. M. Rogic and T. R. Demmin, *J. Am. Chem. Soc.*, **100**, 5472 (1978).

(15) G. A. Hamilton, ref 10, Chapter 10.

(16) W. Ando, H. Miyazaki and S. Kohmoto, *Tetrahedron Lett.*, 1317 (1979).