

tritium. Conversely, the 2 α -tritiated substrate IX suffered only a 7% loss. These figures establish that the hydrogen loss at C-2 in the aromatization process is highly stereoselective and is β , and hence the overall C-1,2 dehydrogenation is *cis*. The starting material recovered from both incubations exhibited an increase in tritium content, indicating the presence of primary and secondary isotope effects. More importantly, however, the retention of tritium confirms that the hydrogen removal from C-2 is not a reversible process under the conditions employed.

Present concepts⁹ of the mechanism of enzymatic aromatization imply that the hydrogen loss from C-2 proceeds *via* enolization as one step in the biotransformation sequence. The removal of the axial 2 β hydrogen may be considered in accord with the enolization mechanism since such is the preferred stereochemistry of enolization. However, the irreversibility of the hydrogen loss suggests that the enolization, if such it is, takes place concurrently or subsequently to the expulsion of the C-19 methyl group since then the driving force of the aromatization would prevent reversal of the enol formation. Alternatively, enolization need not be involved in the hydrogen loss at C-2 which may instead be linked to that at C-1 by a dehydrogenation sequence. The demonstrated *cis* nature of this process is in agreement with the stereochemistry of dehydrogenation at other sites of the steroid molecule.¹⁰ It is hoped that further clarification of this and other aspects of the aromatization mechanism will result from work now in progress.

Acknowledgment. This investigation was supported by a grant from the American Cancer Society and Grant CA-07304 from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

(9) J. D. Townsley and H. J. Brodie, *Biochemistry*, **7**, 33 (1968).

(10) A. M. Paliokas and G. J. Schropfer, *J. Biol. Chem.*, **243**, 453 (1968).

Jack Fishman, Henry Guzik

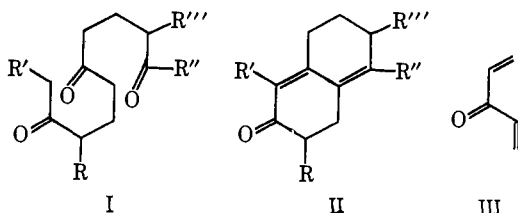
Institute for Steroid Research, Montefiore Hospital and Medical Center, New York, New York 10467

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β -Chloroethyl Vinyl Ketone, a Useful Reagent for the Facile Construction of Fused Ring Systems

Sir:

Multiple intramolecular aldol condensations, where the consecutive carbonyl groups are arrayed in a 1,5 pattern, provide an interesting potential for the facile construction of fused six-membered rings. If this concept, generalized as I \rightarrow II, could be reduced to



practice, it could find extensive application in the synthesis of natural products. We now report (i) an

effective method for generating a 2,6,10-triketo system and (ii) its utility in the production of a tricyclic system in high yield.

In principle, a system such as I could be assembled *via* successive Michael additions of appropriate carbonyl systems to divinyl ketone (III, DVK). In practice, mono Michael addition has never been successfully conducted with DVK.¹ Fragmentary evidence obtained in our laboratory suggests that the reason lies in the greater electrophilicity of an alkyl vinyl ketone relative to DVK itself. Hence bisalkylation of DVK is, at minimum, competitive with monoalkylation—a situation which adversely affects the smooth production of an unsymmetrical 2,6,10-trione such as I.

We now report that β -chloroethyl vinyl ketone² (IV, CVK) is an effective synthetic equivalent of DVK (III). The compound,³ bp 25° (0.08 mm), is prepared in 37% yield by a two-step sequence involving acylation of ethylene with β -chloropropionyl chloride followed by controlled monodehydrohalogenation of the crude 1,5-dichloro-3-pentanone so produced.⁴ Its nmr (neat) spectrum [τ 3.58–4.33 (3 H), nine-line multiplet; 6.28 (2 H), t, $J = 7$ Hz; 7.00 (2 H), t, $J = 7$ Hz] is in accord with the assigned structure.

We have studied the reaction of the sodium salt of V with CVK under a variety of conditions. Preliminary evidence strongly suggests that Michael addition occurs at a substantially faster rate than either alkylation by the primary chloride or dehydrohalogenation (formation of DVK). Thus, in an ether–water mixture, the initial product obtained is compound VI.⁵ Its structure follows from its ir [$\lambda_{\max}^{\text{CHCl}_3}$ 5.69, 5.80, and 5.85 μ], nmr [τ 6.48 (2 H), t, $J = 7$ Hz (CH₂Cl)], and mass [m/e 230 (P), 232 (P + 2)] spectra. In monoglyme the Michael adduct suffers dehydrohalogenation resulting in the formation of VII^{6,7} (bp 100° (0.03 mm); mp ca. 17°; $\lambda_{\max}^{\text{EtOH}}$ 211 m μ (ϵ 9000)) in crude yield⁸ of 85%. Its ir spectrum (CCl₄) exhibits maxima at 5.65, 5.80, 5.92, and 6.19 μ and its nmr (CCl₄) contains a 3H nine-line multiplet from τ 3.67 to 4.38 (vinylic protons).

Reaction of VII with *t*-butyl acetoacetate in *t*-butyl alcohol containing catalytic amounts of potassium *t*-butoxide afforded a gummy product which, upon treatment with TsOH–HOAc at 78° for 3 hr, gave a

(1) Bisalkylation of DVK was reported in its base-catalyzed reaction with 2-methyldihydroresorcinol: I. Nazarov and S. I. Zavyalov, *Zh. Obsch. Khim.*, **23**, 1703 (1953). Bisalkylation where the second step is intramolecular has been employed by Wynberg and coworkers as an interesting route to spiro systems: H. A. P. DeJongh and H. Wynberg, *Rec. Trav. Chim.*, **82**, 202 (1963).

(2) CVK is mentioned in the literature as an impurity in various preparations of DVK and 1,5-dichloro-3-pentanone: J. R. Miller and E. M. Wilkinson, British Patent 789,128 (1958), *Chem. Abstr.*, **52**, P9669b (1958); G. Baddeley, H. T. Taylor, and W. Pickles, *J. Chem. Soc.*, 124 (1953).

(3) Combustion analyses within 0.3% of theory were obtained for this compound.

(4) The method of acylation was developed by N. Jones and H. T. Taylor, *J. Chem. Soc.*, 1345 (1961). The modification came at the dehydrohalogenation step. We employed a 1.1:1 ratio of sodium carbonate:dichloropentanone and milder distillation conditions than the British workers.

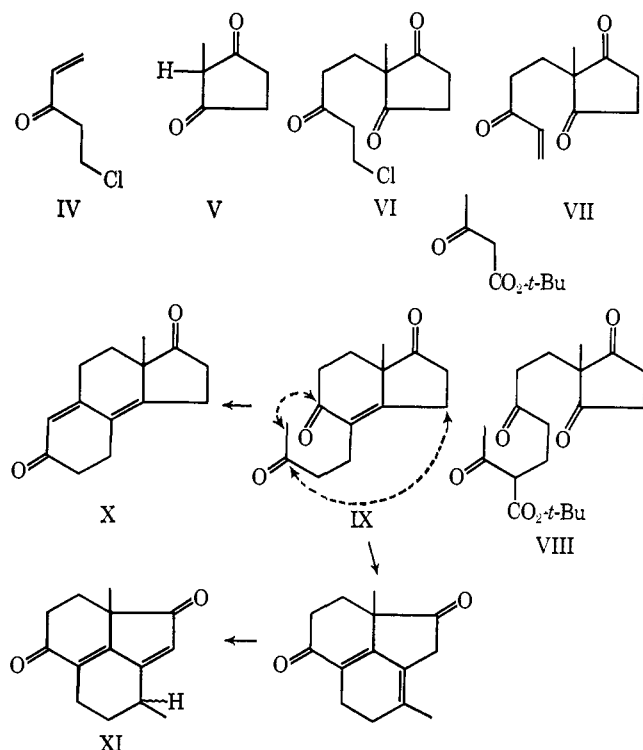
(5) This compound was obtained as an oil which could not be purified for analysis by distillation. The presence of VII as an impurity was suggested by its nmr spectrum.

(6) That VII did not arise from alkylation by the primary halide is suggested from the studies of Rosenthal,⁷ who observed predominantly *ortho* alkylation in the reaction of V with alkyl halides.

(7) D. Rosenthal and K. H. Davis, Jr., *J. Chem. Soc.*, 1973 (1966).

(8) Examination of the nmr spectrum of the crude material suggests the presence of small amounts of compound VI. Compound VII can be purified by vacuum distillation. This reduces its yield to 60%.

52 ± 2% yield (from VII) of the tricyclic ketone, X, ^{3,9,10} mp 56–58°; $\lambda_{\text{max}}^{\text{EtOH}}$ 296 m μ (ϵ 17,500); $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.75, 6.01, 6.10, 6.30 μ ; τ (CDCl₃) 4.22 (1 H), s; 8.80 (3 H), s. The genesis of X clearly entails the formation of the desired 2,6,10-triketeto system, VIII, which undergoes some, as yet undefined, sequence of twofold cyclo-dehydration, *t*-butyl ester cleavage, and β -keto acid decarboxylation.



Two minor products each isolated in 3% yield bear on the sequence in the transformation of VIII → X. One of these is assigned as compound IX³ by the correspondence of its melting point (95–96°) and spectral properties with those previously reported.¹⁰ The other is assigned as a diastereomeric mixture corresponding to gross structure XI.³ Its broad melting range (76–96°) and nmr (CDCl₃) spectrum [τ 8.67 and 8.72 (sum = 3 H), two doublets, $J = 7$ Hz for each] attest to its being a mixture of two components, each bearing a secondary methyl group. Its infrared [$\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.88 (conjugated cyclopentenone), 6.01, and 6.08 μ], nmr [τ 3.98 (1 H), s (vinylic hydrogen); 8.72 (3 H), s (angular methyl)], and mass [m/e 216 (P), 182 (base peak)] spectra support the assigned gross structure. A sequence which embodies these results is VIII → IX → X + XI.¹¹

The CVK method has been applied to other cases and has led to the total synthesis of steroids. The results of these studies will be reported soon.

(9) This compound was previously reported¹⁰ as an oil. We obtained it in crystalline form by chromatography on silicic acid and crystallization from ether–hexane. The yield was obtained through gas chromatographic analysis and was reproducible in three runs under varying work-up conditions.

(10) O. I. Fedorova, G. S. Grinenko, and V. I. Maksimov, *Zh. Org. Khim.*, 4, 611 (1968); *Chem. Abstr.*, 69, 3061 (1968).

(11) While this sequence seems to be occurring, it is probably not the sole source of compound X. Thus, when a pure sample of compound IX was subjected to the simulated reaction conditions of TsOH–HOAc, the ratio of X:XI produced was 7:1. Since the reaction by way of VII produces these products in a ratio of ca. 17:1, a concurrent route to X which does not involve IX is suggested.

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S. Danishefsky, Bruce H. Migdalof

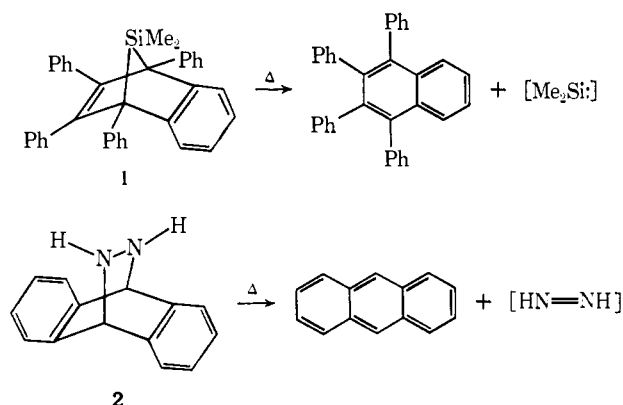
Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15213

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7,8-Disilabicyclo[2.2.2]-2,5-octadienes. An Approach to Tetramethyldisilene

Sir:

The thermal dissociation of bicyclo[2.2.1]heptadienes and of bicyclo[2.2.2]octadienes has been used to prepare a variety of unstable intermediates. Thus Gilman, Cottis, and Atwell¹ prepared dimethylsilene by the pyrolysis of 1 and Corey and Mock prepared diimide by the pyrolysis of 2.² We wish to report the results



of a systematic attempt to prepare tetramethyldisilene *via* the retrodiene reaction³ of a 7,8-disilabicyclo[2.2.2]-octadiene.

The addition of a dilute solution of 1,2-dichlorotetramethyldisilane (0.4 mol) in THF (375 ml) to the dianion of anthracene (0.4 mol) in THF (450 ml) gave a mixture of products from which 3, mp 162–164°⁴ (2%), was isolated by recrystallization from ethanol. Similarly, the dianion of naphthalene gave 4, mp 64–66°.⁵

At temperatures below 450°, 3 was stable. However, when heated for 12 hr at 500° it dissociated to give anthracene and a mixture of high molecular weight silicon compounds. By analogy with the proposals

(1) H. Gilman, S. G. Cottis, and W. H. Atwell, *J. Amer. Chem. Soc.*, 86, 1596 (1964).

(2) E. J. Corey and W. L. Mock, *ibid.*, 84, 685 (1962).

(3) H. Kwart and K. King, *Chem. Rev.*, 68, 415 (1968).

(4) The nmr spectrum (CCl₄) of 3 had singlets at τ 3.01, 6.29, and 10.13 with relative areas of 4:1:6, respectively. Satisfactory carbon-hydrogen analyses were obtained for all compounds reported.

(5) The nmr spectrum of 4 had singlets at τ 2.95, 9.81, and 10.18 and multiplets at τ 3.97 and 6.61, with relative areas of 2:3:3:1:1, respectively.