

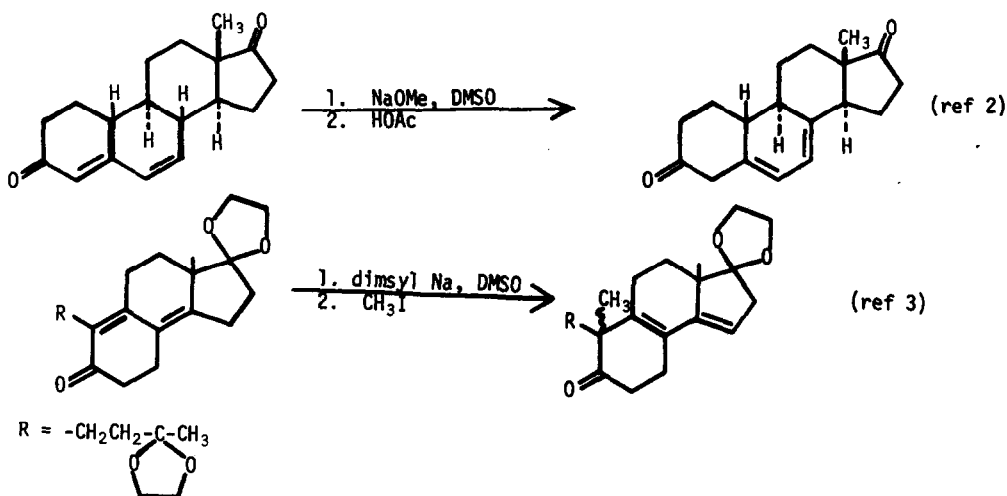
ALKYLATION VIA A CROSS- RATHER THAN A FULLY-CONJUGATED ENOLATE ANION

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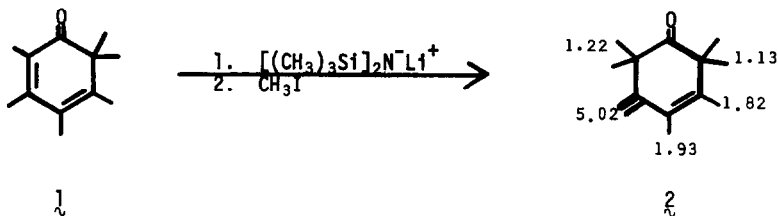
Enolization of  $\alpha,\beta,\gamma,\delta$ -dienones usually occurs by removal of a proton from the  $\epsilon$ -position; either protonation or alkylation then occurs most commonly at the  $\alpha$ -position, as the following examples illustrate.<sup>1</sup> In each of these cases, an available  $\gamma'$ -proton goes unused in the



ionization process, the preferred anion being fully rather than cross conjugated. We wish to describe here our observation that homocyclic conjugated cyclohexadienones with enolizable hydrogens at the  $\gamma'$  and  $\epsilon$  positions alkylate via the cross conjugated anion produced by removal of a  $\gamma'$  proton.

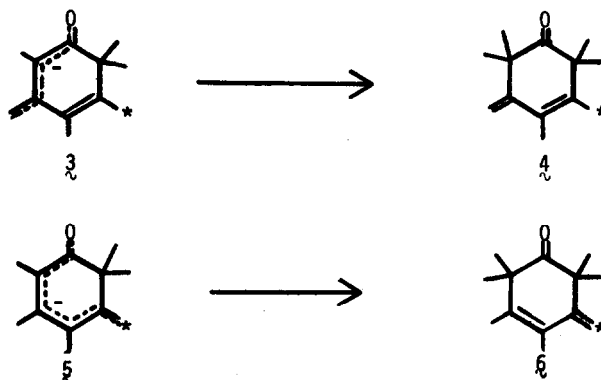
A tetrahydrofuran (THF) solution of hexamethyl-2,4-cyclohexadienone  $1^4$  (25 g, 0.14 mol) was added at 0° to base prepared by adding hexamethyldisilazane (50 ml) to a solution of  $n$ -butyllithium (100 ml of 1.6M in hexane + 50 ml of THF). After 1 hr, excess methyl iodide (25

ml) was added, and the mixture was stirred for 12 hr at room temperature, then worked up to give a 90-95% yield of **2** (colorless liquid, bp 46° at 0.5 Torr). The product showed a nonconjugated



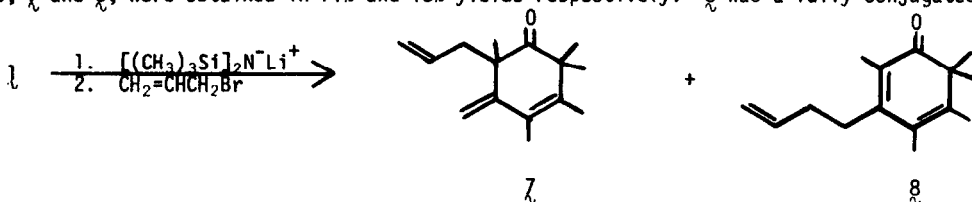
carbonyl group ( $1705 \text{ cm}^{-1}$ ), a conjugated diene moiety ( $\lambda_{\text{max}}^{\text{EtOH}} 232 \text{ nm}$ ), and an nmr spectrum consistent with the assigned structure, as shown (chemical shifts as  $\delta$ ).<sup>5</sup>

Structure **2** would of course be expected for the  $\alpha$ -methylation product regardless of whether the anion was derived from the methyl group at the  $\beta$  ( $\gamma'$ ) or  $\delta$  ( $\epsilon$ ) positions. These

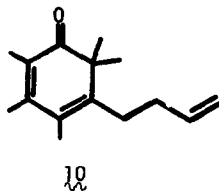
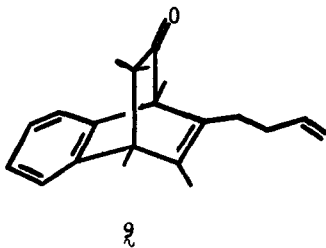


alternatives were distinguished by methylating **1** in which the methyl at C-5 was replaced by a  $\text{CD}_3$  group (asterisk in formulas **3-6**).<sup>6</sup> The nmr spectrum of the product lacked the allylic methyl signal at  $\delta 1.82$  but still had the 2-proton vinyl signal at  $\delta 5.02$ , showing the product to be **4**, not **6**.

Alkylation of **1** via the  $\gamma'$  anion **3** was supported by results with allyl bromide. Two products, **7** and **8**, were obtained in 71% and 18% yields respectively. **8** was a fully conjugated



dienone ( $\nu_{C=O}$  1650  $\text{cm}^{-1}$ ) which with benzyne<sup>14</sup> gave an adduct **9** which had only one allylic methyl group ( $\delta$  1.83),<sup>8</sup> thus eliminating structure **10** (the product of  $\epsilon$ -alkylation) for the conjugated



dienone.<sup>10</sup> The structure of **7** follows from its spectra<sup>11</sup> and its conversion to a 1:8 mixture of **7/8** on heating in  $\text{CCl}_4$  at 130° for 3 hr.

The alkylation of cyclohexadienones, not extensively studied previously,<sup>12</sup> provides a useful synthetic entry to otherwise difficultly accessible unsaturated ketones.<sup>13</sup>

ACKNOWLEDGEMENT. We are indebted to the National Institutes of Health for their generous financial support.

#### REFERENCES

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5. Elemental analyses and a mass spectrum are consistent with the assigned structure, as are the acid-catalyzed and photoinduced rearrangements to be described separately.
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7. With this fact established, methylation of **7** with  $\text{CD}_3\text{I}$ , which resulted in **2** with the nmr peak at  $\delta$  1.22 reduced in area to 3 protons, permitted the assignment of the gem-dimethyl signals as shown in the structure.
8. The five methyl signals in the nmr spectrum of **9** were sharp singlets and that assigned to the allylic methyl had the same chemical shift ( $\pm \delta$  0.01) as that of an analogous methyl group in a known compound (ref. 9, compound **4**). If structure **10** were correct, one would easily have observed homoallylic coupling (ca. 1 Hz) between two allylic methyl groups.
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10. Nmr of **8**:  $\delta$  1.19 (6H, s, gem dimethyls), 1.93 (9H, br s, allylic methyls), 2.05-2.80 (4H, m, methylenes), 4.87-5.32 (2H, m, terminal vinyls), 5.61-6.20 (1H, m, vinyl). Since allylic methyl groups at C-3 in conjugated cyclohexadienones occur at lower field than those at C-2, 4 or 5,<sup>4</sup> the absence of such a signal supports structure **8** over **10**: **8** only exchanged 2 methylene protons rapidly, on treatment with NaOCH<sub>3</sub>/CH<sub>3</sub>OD, further supporting structure **8**.<sup>4</sup>
11. Ir 1705 cm<sup>-1</sup>; nmr  $\delta$  1.09 (3H, s, methyl at C-2), 1.22 (6H, s, gem-dimethyls), 1.80 (3H, m, allylic methyl at C-5), 1.93 (3H, m, allylic methyl at C-4), 2.05-2.69 (4H, m, methylenes), 4.98-5.18 (4H, m, terminal vinyls), 5.29-5.83 (1H, m, vinyl).
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