

## Synthesis of 2-Alkylidene Ketones. Chemistry of Boron Difluoride Complexes of 2-Formyl Ketones<sup>1</sup>

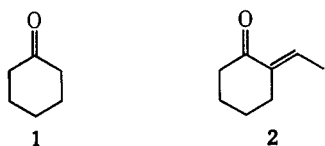
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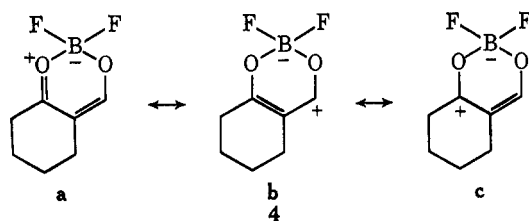
The chemistry of the long-known and readily prepared boron difluoride complexes of 1,3-dicarbonyl compounds had not been investigated except for hydrolysis. The reaction of such  $\text{BF}_2$  complexes of 2-formyl ketones (*e.g.*, 4) with organometallic reagents has been found to constitute an effective synthesis of 2-alkylidene ketones. For example, 4 reacts with 1 equiv of methyllithium to yield, after treatment with acid, 81% 2-ethylidenecyclohexanone. Other syntheses of 2-alkylidene ketones have been compared with this new procedure. In particular, reinvestigation of the reaction of 2-formyl ketones with Grignard reagents has shown this to be a comparably effective method of preparation of 2-alkylidene ketones.

Preparation of 2-alkylidene ketones by direct aldol condensation of an aldehyde with a ketone (as in **1**  $\rightarrow$  **2**) is usually not a practical synthetic method.<sup>2</sup> Less direct but more effective procedures devised for the synthesis of 2-alkylidene ketones have included the use



of enamine intermediates,<sup>3</sup> the reaction of 2-amino-methylene ketones with Grignard reagents,<sup>4</sup> and the reaction of enolates generated by zinc reduction of 2-bromo ketones with aldehydes.<sup>5</sup> Of particular relevance to the research described herein is the report by Dreiding and Nickel<sup>6</sup> of the preparation of **2** by direct reaction of the 2-formyl ketone<sup>7</sup> **3**, as well as its *O*-isopropyl derivative, with organometallic reagents.

The long-known<sup>8</sup> and readily prepared (see below) boron difluoride complexes of 1,3-dicarbonyl compounds (*e.g.*, 4) seemed to offer an attractive alternative method for the synthesis of 2-alkylidene ketones, if the electrophilicity at the exocyclic carbon implied in contributing structure **4b** could be manifested by its attachment to a carbanionic nucleophile. Accordingly, an investigation of the reactions of  $\text{BF}_2$  complexes of 2-formyl ketone, with organometallic reagents was undertaken.



(1) This research was presented at the 159th National Meeting of the American Chemical Society, Houston, Texas, Feb 22-27, 1970.

(2) A. T. Nielsen and W. J. Houlihan, *Org. React.*, **16** (1968), provide references to specific examples and on p 38 the conclusion that "yields are low" in this type of reaction.

(3) L. Birkofer, S. M. Kim, and H. E. Engels, *Ber.*, **95**, 1495 (1962).

(4) *E.g.*, (a) L. I. Zakharkin and V. V. Korneva, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2206 (1964); (b) P. N. Weintraub, *Chem. Ind. (London)*, 1497 (1966); (c) R. E. Ireland and P. W. Schiess, *J. Org. Chem.*, **28**, 6 (1963).

(5) T. A. Spencer, R. W. Britton, and D. S. Watt, *J. Amer. Chem. Soc.*, **89**, 5727 (1967).

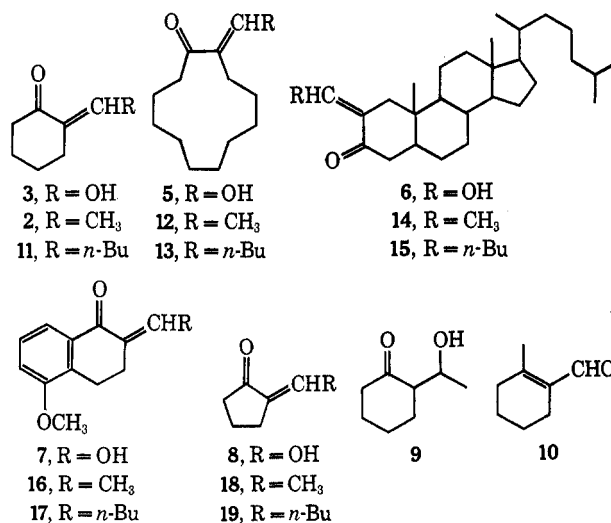
(6) A. S. Dreiding and S. N. Nickel, *ibid.*, **76**, 3965 (1954).

(7) The term 2-formyl ketone is used [as it was by E. W. Garbisch, *ibid.*, **85**, 1696 (1963)] to designate the enolic mixtures often referred to, and shown structurally in this paper, as 2-hydroxymethylene ketones.

(8) G. T. Morgan and R. B. Tunstall, *J. Chem. Soc.*, **125**, 1963 (1924).

No examples of  $\text{BF}_2$  complexes derived from 2-formyl ketones had been reported at the outset of the study, but their preparation proved facile, as might have been anticipated on the basis of the isolation of such complexes from 1,3 diketones. These are most frequently encountered as intermediates in boron trifluoride catalyzed acylation of ketones with anhydrides.<sup>9</sup> Hydrolysis to the parent 1,3-dicarbonyl compound was the only chemistry of these species which had been studied.

The best procedure for preparation of the desired  $\text{BF}_2$  complexes consists in treatment of a methylene chloride solution of the 2-formyl ketone with 1.5-2.0 equiv of boron trifluoride etherate at room temperature. In this manner, nicely crystalline  $\text{BF}_2$  complexes were obtained in 70-86% yield from 2-formylcyclohexanone (**3**), 2-formylcyclohexanone (**5**), 2-formylcholestan-3-one (**6**), and 2-formyl-5-methoxy-1-tetralone (**7**). The complex from 2-formylcyclopentanone (**8**) was liquid and relatively unstable, and could not be purified, but it displayed the same spectral properties and chemistry as the others. These complexes have distinctive infrared and ultraviolet absorption; the complexes from 2-formyl derivatives of unconjugated ketones all show absorption at  $\sim 6.2$  and  $6.7 \mu$  and at  $310-311 \text{ m}\mu$  (in cyclohexane), with  $\epsilon \sim 14,000$ . They are stable in aprotic solvents, such as hexane, benzene, methylene



(9) C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. React.*, **8**, 98 (1954); R. D. Youssefeyeh, *J. Amer. Chem. Soc.*, **85**, 3901 (1963); H. Musso and K. Figge, *Justus Liebig's Ann. Chem.*, **668**, 1, 15 (1963); T. F. Crimmins and C. R. Hauser, *J. Org. Chem.*, **32**, 2615 (1967).

(10) No indication of consumption of organometallic reagent by reaction with the  $\text{BF}_2$  moiety to give alkylboron compounds [cf. E. Krause and R. Nitsche, *Ber.*, **54**, 2784 (1921)] was ever observed.

chloride, or carefully dried ether or tetrahydrofuran. Protic solvents such as ethanol effect rapid conversion to the original 2-formyl ketone and chromatography is not suitable for purification.

When the boron difluoride complex **4** in benzene solution was treated with 1 equiv<sup>10</sup> of methyllithium in ether, followed by hydrolysis with aqueous ammonium chloride, the major product was  $\beta$ -hydroxy ketone **9**, accompanied by some enone **2**. In order to facilitate isolation of product and determination of yields by vapor phase chromatography (vpc), the crude reaction products were subsequently routinely treated with *p*-toluenesulfonic acid in benzene to effect complete dehydration to enone. If the intermediate ketol were the desired product, however, it presumably could be obtained.

After this acid-catalyzed dehydration, the product from **4** was 2-ethylidenecyclohexanone (**2**) (81% by vpc analysis), containing only small amounts of other substances. The 2-ethylidenecyclohexanone obtained possessed exclusively the *trans* geometry (see Experimental Section) as shown in **2**, but at least some of the other 2-alkylidene ketones synthesized were obtained as mixtures of *cis* and *trans* isomers. No attempt was made to separate or, in most cases, determine ratios of geometrical isomers. No products, such as **10**, resulting from attack at the endocyclic electrophilic position (*cf.* **4c**) were isolated from **4** or any other BF<sub>2</sub> complex studied, although minor products were not identified. Use of more than 1 equiv of methyllithium did not affect the product composition.

The results from all the reactions of boron difluoride complexes with organometallic reagents are shown in Table I. Methyllithium was distinctly superior to methylmagnesium iodide in the two cases where comparison was made. The generality of the 2-alkylidene ketone synthesis was demonstrated by the preparation of comparable yields of 2-pentylidene ketones with 1 equiv of *n*-butyllithium, except in the case of the 2-formyl-5-methoxy-1-tetralone BF<sub>2</sub> complex, which gave an anomalous and unexplained low yield of **17**.

Clearly, the BF<sub>2</sub> complexes provide an effective pathway to 2-alkylidene ketones. It was not clear, however, that this pathway represented an improvement over the direct reaction of the 2-formyl ketone with an organometallic reagent. The previous brief study<sup>6</sup> of this direct route reported 61 and 25% of **2** from **3** using methylmagnesium iodide and methyllithium, but these somewhat lower yields were of distilled products and, since we had learned in the course of the present work that distillation of the 2-alkylidene ketones lowered the yields, a reinvestigation seemed imperative.

The results of the reactions of the same set of 2-formyl ketones (**4**–**8**) directly with methyllithium or methylmagnesium iodide, followed by acid-catalyzed dehydration of intermediate ketols, are also shown in Table I. The yields with the Grignard reagent are in all instances comparable with those of the BF<sub>2</sub> complexes with methyllithium. As found by Dreiding,<sup>6</sup> methyllithium is relatively less effective in direct reaction with 2-formyl ketones.

The reaction of a Grignard reagent with a 2-formyl ketone thus should probably be the first method tried

for synthesis of a given 2-alkylidene ketone. However, this procedure requires at least 2 equiv of organometallic reagent, the first reacting with the acidic proton of the enolized 1,3-dicarbonyl system to yield the magnesium enolate which then reacts with the second equivalent. Use of a protecting group such as boron difluoride is advisable when conservation of organometallic reagent is desired.

One of the indirect routes may also provide the maximum yield in a particular case. As an example of the unpredictability of the best method for synthesis of a specific 2-alkylidene ketone, the low yields of 2-alkylidenecholestan-3-ones in all of the procedures involving 2-formyl ketones may be cited. In addition to the examples recorded in Table I, the reaction of 2-pyrrolidinomethylenecholestan-3-one with methylmagnesium iodide affords **14** in a comparably disappointing yield (30%).<sup>4b</sup> Preparation of 2-alkylidenecholestan-3-ones is best accomplished (*e.g.*, 90% yield of **14**) via the zinc enolate derived from 2-bromocholestan-3-one.<sup>5</sup> These contrasting results, for which there is no obvious explanation, emphasize the desirability of having a variety of methods available for the synthesis of 2-alkylidene ketones.

Further investigation of the chemistry of boron difluoride complexes of various 1,3-dicarbonyl compounds with organometallic and other reagents is in progress.

### Experimental Section<sup>11</sup>

**Preparation of 2-Formyl Ketones.**—Preparation of 2-formyl ketones was carried out by condensing the parent ketone with ethyl formate by reported procedures in the cases of 2-formylcyclohexanone (**3**),<sup>12</sup> 2-formylcyclododecanone (**5**),<sup>13</sup> 2-formylcholestan-3-one (**6**),<sup>14</sup> and 2-formylcyclopentanone (**8**).<sup>15</sup>

**2-Formyl-5-methoxy-1-tetralone (7).**—A 50% mineral oil dispersion of sodium hydride (1.90 g, 0.035 mol) was added to a stirred solution of 5-methoxy-1-tetralone<sup>16</sup> (3.26 g, 0.0185 mol) in freshly distilled ethyl formate (50 ml) held at 0°. Anhydrous methanol (0.75 ml) was then added and the mixture was stirred at room temperature under purified nitrogen for 18 hr. The resulting suspension was poured onto water (100 ml) and the organic layer was separated and extracted with two 100-ml portions of 2 *N* sodium hydroxide solution. Acidification of the combined aqueous extracts with cold 50% v/v aqueous hydrochloric acid and ether extraction afforded, after removal of the solvent at reduced pressure, 2-formyl-5-methoxy-1-tetralone (**7**) (3.78 g, 99.7%) as a yellow oil which crystallized on standing. Crystallization from hexane gave an analytical sample: mp

(11) Analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. Melting points were taken in an open capillary and are corrected. Ultraviolet (uv) spectra were determined on a Unicam SP800 spectrometer, using the solvents indicated. Infrared (ir) spectra were determined on a Perkin-Elmer Model 137 recording spectrophotometer. Nuclear magnetic resonance (nmr) spectra were determined on a Varian Associates DA-60-IL spectrometer. Vapor phase chromatography (vpc) was carried out on a Wilkens A-700 chromatograph using a 5 ft × 0.25 in. copper column packed with 60–80 mesh Chromosorb W coated with 7.5% Carbowax 20M. The column was operated at 150° at a helium gas flow rate of 60 ml/min. Vpc identification of compounds was performed by peak enhancement with authentic samples. Vpc yields were determined by triangulation of peak areas. Minor products were not identified, so response factors were not determined; neither were internal standard compounds used to determine yields. Analytical thin layer chromatography (tlc) was carried out on 250- $\mu$ -thick layers of Merck silica gel G. Preparative tlc was carried out on 1.25-mm-thick layers of Merck silica gel PF 234 + 386.

(12) C. Ainsworth, "Organic Syntheses," Coll. Vol. IV, Wiley, New York, N. Y., 1963, p 537.

(13) V. Prelog, L. Ruzicka, and O. Metzler, *Helv. Chim. Acta*, **30**, 1883 (1947).

(14) C. Djerassi, N. Finch, R. C. Cookson, and C. W. Bird, *J. Amer. Chem. Soc.*, **82**, 5488 (1960).

(15) W. S. Johnson and W. E. Shelberg, *ibid.*, **67**, 1752 (1945).

(16) Aldrich Chemical Co., Milwaukee, Wis.

TABLE I  
FORMATION OF 2-ALKYLIDENE KETONES BY REACTION OF 2-FORMYL KETONES AND THEIR BORON DIFLUORIDE COMPLEXES  
WITH ORGANOMETALLIC REAGENTS

2-Formyl ketone	Reactions of BF <sub>2</sub> complexes of 2-formyl ketones, % yield <sup>a</sup> (product)			Reactions of 2-formyl ketones, % yield (product)		
	CH <sub>3</sub> Li	CH <sub>3</sub> MgI	<i>n</i> -BuLi	CH <sub>3</sub> Li	CH <sub>3</sub> MgI	<i>n</i> -BuLi
2-Formylcyclohexanone (3)	81 <sup>b</sup> (2)	45 <sup>b</sup> (2)	85 <sup>b</sup> (11)	44 <sup>b</sup> (2)	85 <sup>b</sup> (2)	49 <sup>b</sup> (11)
2-Formylcyclododecanone (5)	61 (12)	35 (12)	53 (13)	33 (12)	58 (12)	35 (13)
2-Formylcholestan-3-one (6)	37 (14)		32 (15)	25 (14)	41 (14)	17 (15)
2-Formyl-5-methoxy-1-tetralone (7)	87 (16)		38 (17)	89 (16)	81 (16)	20 (17)
2-Formylcyclopentanone (8)	62 <sup>b</sup> (18)		60 <sup>b</sup> (19)	56 <sup>b</sup> (18)	75 <sup>b</sup> (18)	48 <sup>b</sup> (19)

<sup>a</sup> Yields are of isolated purified material unless indicated otherwise. <sup>b</sup> Yield based on vpc analysis.

67–68°; uv max (95% EtOH) 311 m $\mu$  ( $\epsilon$  10,700), 262 (5700), and 230 (10,900); uv max (95% EtOH–NaOH) 354 m $\mu$  ( $\epsilon$  14,790), 318 shoulder (6120), and 248 (15,000); ir (KBr) 6.3–6.4 (broad)  $\mu$ ; nmr (CDCl<sub>3</sub>)  $\delta$  2.3–3.0 (m, 4), 3.78 (s, 3, H<sub>3</sub>C–O–), 6.83–7.66 (AMX system, 3, H<sub>A</sub> 7.58, H<sub>B</sub> 7.20, H<sub>X</sub> 6.92,  $J_{AX}$  = 1.5 Hz,  $J_{AM}$  =  $J_{MX}$  = 8.0 Hz, aromatic ring protons), 8.17 [s, broad, 1, HC(OH)=], and 13.67–14.83 ppm (m, 1, H–O–).

Anal. Calcd for C<sub>12</sub>H<sub>12</sub>O<sub>3</sub>: C, 70.58; H, 5.92. Found: C, 70.49; H, 5.97.

**Preparation of Boron Difluoride Complexes of 2-Formyl Ketones.**—The boron difluoride (BF<sub>2</sub>) complexes were prepared by adding 1.5–2 equiv of freshly distilled boron trifluoride etherate to a stirred (~10% w/v) solution of the appropriate 2-formyl ketone in methylene chloride at room temperature under nitrogen. After 1 hr the methylene chloride solution was washed with water until free of excess boron trifluoride and the solvents were removed under reduced pressure. The crystalline products (all cases except 2-formylcyclopentanone) were then recrystallized from hexane or methylene chloride–hexane until constant melting points were obtained. The individual yields and properties of the BF<sub>2</sub> complexes follow.

**BF<sub>2</sub> complex of 2-formylcyclohexanone (4)**<sup>17</sup> was formed in 72% yield: mp 44–45°; uv max (cyclohexane) 311 m $\mu$  ( $\epsilon$  14,750); ir (KBr) 6.20 and 6.68  $\mu$ ; nmr (CDCl<sub>3</sub>)  $\delta$  1.8 (m, 4), 2.5 (m, 4), and 7.9 ppm [s, 1, HC(OBF<sub>2</sub>)=]; mass spectrum M<sup>+</sup> at *m/e* 174.

Anal. Calcd for C<sub>7</sub>H<sub>9</sub>O<sub>2</sub>BF<sub>2</sub>: C, 48.28; H, 5.17; F, 21.84. Found: C, 48.28; H, 5.22; F, 21.75.

**BF<sub>2</sub> complex of 2-formylcyclododecanone** was formed in 70% yield: mp 66–67°; uv max (cyclohexane) 311 m $\mu$  ( $\epsilon$  14,100); ir (KBr) 6.25 and 6.78  $\mu$ ; nmr (CDCl<sub>3</sub>)  $\delta$  1.1–2.1 (m, 16), 2.2–2.8 (m, 4), and 7.9 ppm [s, broad, 1, HC(OBF<sub>2</sub>)=].

Anal. Calcd for C<sub>13</sub>H<sub>21</sub>O<sub>2</sub>BF<sub>2</sub>: C, 60.49; H, 8.20. Found: C, 60.53; H, 8.25.

**BF<sub>2</sub> complex of 2-formylcholestan-3-one** was formed in 86% yield: mp 133–134°; uv max (cyclohexane) 311 m $\mu$  ( $\epsilon$  14,100); ir (KBr) 6.18 and 6.69  $\mu$ .

Anal. Calcd for C<sub>28</sub>H<sub>46</sub>O<sub>2</sub>BF<sub>2</sub>: C, 72.72; H, 9.81. Found: C, 72.84; H, 9.76.

**BF<sub>2</sub> complex of 2-formyl-5-methoxy-1-tetralone** was formed in 80% yield: mp 167–167.5°; uv max (cyclohexane) 353 m $\mu$  ( $\epsilon$  19,800); ir (KBr) 6.53 and 6.70  $\mu$ ; nmr (CDCl<sub>3</sub>)  $\delta$  2.4–3.2 (m, 4), 3.82 (s, 3, H<sub>3</sub>CO–), 7.0–7.85 (AMX system, 3, H<sub>A</sub> 7.75, H<sub>M</sub> 7.33, H<sub>X</sub> 7.10,  $J_{AX}$  = 2.0 Hz,  $J_{AM}$  =  $J_{MX}$  = 8.0 Hz, aromatic protons), and 8.10 ppm [s, 1, HC(OBF<sub>2</sub>)=].

Anal. Calcd for C<sub>12</sub>H<sub>11</sub>O<sub>3</sub>BF<sub>2</sub>: C, 57.19; H, 4.40. Found: 57.08; H, 4.36.

**BF<sub>2</sub> complex of 2-Formylcyclopentanone.**—The general procedure outlined above produced a dark oil (65% yield) which could not be solidified or purified by distillation or chromatography. The crude product showed uv max (cyclohexane) 310 m $\mu$  and ir (film) 6.18 and 6.65  $\mu$  indicating that the BF<sub>2</sub> complex was indeed present and subsequent reactions were carried out with this crude product.

**Preparation of 2-Alkylidene Ketones. A. General Method for the Reactions of the BF<sub>2</sub> Complexes of 2-Formyl Ketones with Organometallic Reagents.**—Methylolithium (CH<sub>3</sub>Li) and *n*-butyllithium (*n*-BuLi), obtained<sup>18</sup> in ether and hexane solutions respectively, were analyzed by the method of Gilman, *et al.*<sup>19</sup> Methylmagnesium iodide (CH<sub>3</sub>MgI) was prepared from magne-

sium and methyl iodide in approximately 1 *M* ethereal solutions and filtered under nitrogen prior to use. To a stirred 10% w/v solution of the BF<sub>2</sub> complex in anhydrous benzene at room temperature under nitrogen was added 1 equiv of the organometallic reagent solution. The reaction was essentially instantaneous and after 15 min the benzene solution was washed with 10% w/v aqueous ammonium chloride and dried (MgSO<sub>4</sub>). To the resulting mixture was added 15–20 mg of *p*-toluenesulfonic acid and it was then heated under reflux with azeotropic removal of water utilizing a Dean–Stark apparatus. After 2 hr the benzene solution was cooled, washed with water until free of acid, and dried (MgSO<sub>4</sub>), and the solvents were removed under reduced pressure. Purification of each product is described under its respective heading.

2,4-Dinitrophenylhydrazones (2,4-DNP) derivatives were prepared by adding 1 equiv of a solution of 0.30 g of 2,4-dinitrophenylhydrazine in a mixture of 95% ethanol (10 ml), water (3 ml), and concentrated sulfuric acid (2 ml) to a solution of the 2-alkylidene ketone in 95% ethanol. The mixture was stored overnight at 0° and the precipitate was collected and crystallized to constant melting point from methylene chloride–ethanol mixtures.

**B. General Method for the Reactions of 2-Formyl Ketones with Organometallic Reagents.**—To a stirred 10% w/v solution of the 2-formyl ketone in anhydrous ether at 0° under nitrogen was added 2–2.2 equiv of the same organometallic reagent solutions used with the BF<sub>2</sub> complexes. After 15 min the ethereal solution was washed with 10% w/v aqueous ammonium chloride and dried (MgSO<sub>4</sub>), and the solvents were removed under reduced pressure. The residue was then treated with acid in the same manner as the products from the BF<sub>2</sub> complexes. Purification of each product is described under its respective heading and 2,4-DNP's were prepared as outlined above.

**2-Ethylidenecyclohexanone (2).**—Reaction of 4 with CH<sub>3</sub>Li afforded a product which was 81% 2 by vpc analysis, and from which 78% vpc-pure 2 was isolated by preparative tlc as a light yellow oil which darkened on exposure to light and air. This 2 showed the following: uv max (95% EtOH) 245 m $\mu$  ( $\epsilon$  6900); ir (film) 5.94 and 6.19  $\mu$ ; nmr (CDCl<sub>3</sub>)  $\delta$  1.73 (d of t, 3,  $J$  = 7, 1.5 Hz, H<sub>3</sub>CCH=), 1.5–2.00 (m, 4), 2.20–2.65 (m, 2), and 6.73 ppm [m, 1, HC(CH<sub>2</sub>)=]. These nmr data indicate that 2 was essentially pure *trans*-2-ethylidenecyclohexanone by comparison with literature<sup>20</sup> values for the *trans* olefinic proton of  $\delta$  6.62 and the *cis* olefinic proton of  $\delta$  5.60 ppm. The 2,4-DNP derived from 2 had mp 222–223°, uv max (CHCl<sub>3</sub>) 385 m $\mu$  ( $\epsilon$  22,100) [lit.<sup>21</sup> mp 222°, uv max (CHCl<sub>3</sub>) 388 m $\mu$  ( $\epsilon$  24,000)].

Reaction of 4 with CH<sub>3</sub>MgI afforded 2 as the major product in 45% yield (by vpc analysis), 2,4-DNP mp 221–222°. Reaction of 3 with CH<sub>3</sub>Li afforded 44% 2 by vpc analysis and 30% 2 isolated by column chromatography and preparative tlc, 2,4-DNP mp 220–221°. Reaction of 3 with CH<sub>3</sub>MgI afforded 85% 2 by vpc analysis, 2,4-DNP mp 219–220°.

**2-Pentylidenecyclohexanone (11).**—Reaction of 4 with *n*-BuLi produced 85% of 11 (by vpc analysis). Pure 11 was obtained by preparative tlc (using 1:3 ether–hexane) and showed uv max (95% EtOH) 247 m $\mu$  ( $\epsilon$  4500) and ir (film) 5.95 and 6.20  $\mu$ ; the 2,4-DNP had mp 102–104°.

Anal. Calcd for C<sub>17</sub>H<sub>22</sub>N<sub>4</sub>O<sub>4</sub>: C, 58.95; H, 6.40; N, 16.17. Found: C, 58.95; H, 6.26; N, 16.24.

Reaction of 3 with *n*-BuLi afforded 49% 11 (2,4-DNP mp 101–102°) by vpc analysis which also indicated the presence of at least nine minor products.

(17) We wish to thank Mr. James G. Magyar who isolated and characterized this compound.

(18) Alfa Inorganics, Beverly, Mass.

(19) H. Gilman and A. H. Haubein, *J. Amer. Chem. Soc.*, **66**, 1515 (1944).

(20) J. E. Dubois and M. Dubois, *C.R. Acad. Sci., Ser. C*, **256**, 715 (1963).

(21) R. Jacquier and G. Maury, *Bull. Soc. Chim. Fr.*, 308 (1967).

**2-Ethylidenecyclododecanone (12).**—Reaction of the  $\text{BF}_2$  complex of **5** with  $\text{CH}_3\text{Li}$  afforded, after preparative tlc, 61% **12** as an oil: uv max (95% EtOH) 235  $m\mu$  ( $\epsilon$  10,000); ir (film) 6.01 and 6.11  $\mu$ ; nmr ( $\text{CDCl}_3$ )  $\delta$  1.24 (s, broad, 16), 1.84 [d, 3,  $J = 7$  Hz,  $\text{H}_3\text{CC}(\text{H})=$ ], 2.2–2.8 (m, 4), and 6.65 ppm [q, 1,  $J = 7$  Hz,  $\text{HC}(\text{CH}_3)=$ ]; 2,4-DNP mp 156–157° (lit.<sup>3a</sup> mp 153.5–154°).

Reaction of the  $\text{BF}_2$  complex of **5** with  $\text{CH}_3\text{MgI}$  gave a brown oil which was adsorbed from hexane onto alumina. Elution with hexane gave a mixture (12%), whose ir displayed neither hydroxyl nor carbonyl absorption, and elution with 1:19 ether–hexane gave **12** (35%). Elution with ether gave a complex mixture (40–50%) which showed strong hydroxyl and carbonyl absorption in the infrared. Reaction of **5** with  $\text{CH}_3\text{Li}$  yielded 33% **12**, similarly isolated, which solidified, mp 28–29° (lit.<sup>3a</sup> mp 29–30°), 2,4-DNP mp 155–156°. Reaction of **5** with  $\text{CH}_3\text{MgI}$  yielded 58% **12**, similarly isolated, with mp 31–32°.

**2-Pentylidenecyclododecanone (13).**—Reaction of the  $\text{BF}_2$  complex of **5** with  $n\text{-BuLi}$  afforded, after preparative tlc, 53% **13**: uv max (95% EtOH) 237  $m\mu$  ( $\epsilon$  10,000); ir (film) 6.0 and 6.1  $\mu$ ; 2,4-DNP mp 110–111° (lit.<sup>3a</sup> mp 108–110°). Reaction of **5** with  $n\text{-BuLi}$  afforded a yellow-brown oil which was adsorbed from hexane onto alumina. Elution with hexane gave a non-polar mixture (17%), whose ir spectrum displayed neither hydroxyl nor carbonyl absorption, and elution with 1:19 ether–hexane gave impure **13** (43%). Elution with ether gave a complex mixture (25–35%). Purification by preparative tlc gave pure **13** in 35% yield, 2,4-DNP mp 110–111°.

**2-Ethylidenecholestan-3-one (14).**—Reaction of the  $\text{BF}_2$  complex of **6** with  $\text{CH}_3\text{Li}$  afforded, after preparative tlc, 37% **14**, which had mp 86–88° after several recrystallizations from ethanol; uv max (95% EtOH) 246  $m\mu$  ( $\epsilon$  6900); ir (KBr) 5.95 and 6.22  $\mu$  (lit.<sup>3b</sup> mp 93–94°; uv max (95% EtOH) 246  $m\mu$  ( $\epsilon$  7110)). Reaction of **6** with  $\text{CH}_3\text{Li}$  afforded, after preparative tlc, 25% **14**, mp 87–89°. Reaction of **6** with  $\text{CH}_3\text{MgI}$  afforded, after preparative tlc, 41% **14**, mp 88–90°.

**2-Pentylidenecholestan-3-one (15).**—Reaction of the  $\text{BF}_2$  complex of **6** with  $n\text{-BuLi}$  afforded a yellow oil which was adsorbed from benzene onto alumina. Elution with benzene and 1:19 ether–benzene afforded impure **15** (42%) while elution with ether afforded a complex mixture (35–40%) whose ir showed strong hydroxyl and carbonyl absorption. Purification by preparative tlc gave pure **15** in 32% yield as a light yellow oil: uv max (95% EtOH) 249  $m\mu$  ( $\epsilon$  7000); ir (film) 5.94 and 6.20  $\mu$ . The derived 2,4-DNP had mp 168–170°. Reaction of **6** with  $n\text{-BuLi}$  afforded, after similar purification, 17% **15**, 2,4-DNP mp 167–170°.

*Anal.* Calcd for  $\text{C}_{38}\text{H}_{58}\text{N}_4\text{O}_4$ : C, 71.89; H, 9.21; N, 8.82. Found: 71.95; H, 9.25; N, 8.79.

**2-Ethylidene-5-methoxy-1-tetralone (16).**—Reaction of the  $\text{BF}_2$  complex of **7** with  $\text{CH}_3\text{Li}$  afforded, after preparative tlc, 87% **16** as a yellow oil which nmr indicated was a 2:5 mixture of *cis* and *trans* isomers: uv max (95% EtOH) 329  $m\mu$  ( $\epsilon$  3600), 275 (14,600) and 232 (11,400); ir (film) 5.94, 6.13, 6.27 (sh), and 6.30  $\mu$ ; nmr ( $\text{CDCl}_3$ )  $\delta$  1.83 [d of t, 2.1,  $J = 7$ , 1 Hz,  $\text{H}_3\text{C}-\text{C}(\text{H})=$ ], 2.08 [d of t, 0.9,  $J = 7$ , 1.3 Hz,  $\text{H}_3\text{CC}(\text{H})=$ ], 2.5–3.1 (m, 4), 3.82 (s, 3,  $\text{H}_3\text{CO}-$ ), 6.07 [m, 0.3,  $\text{HC}(\text{CH}_3)=$ ], 7.07 [m, 0.7,  $\text{HC}(\text{CH}_3)=$ ], and 6.8–7.8 ppm (AMX system, 3,  $H_A$  7.71,  $H_M$  7.24,  $H_X$  6.94,  $J_{AX} = 1.5$  Hz,  $J_{AM} = J_{MX} = 7.5$  Hz, aromatic protons); 2,4-DNP mp 201–203°. A sample worked up prior to the acid dehydration step gave 2-(1-hydroxyethyl)-5-methoxy-1-tetralone which had a lower tlc  $R_f$  than **16**:

ir (film) 2.95 (br), 5.97 and 6.31  $\mu$ ; nmr ( $\text{CDCl}_3$ )  $\delta$  1.25 [d, 3,  $J = 7.5$  Hz,  $\text{H}_3\text{CC}(\text{H})\text{OH}-$ ], 1.6–3.5 (m, 5), 3.81 (s, 3,  $\text{H}_3\text{CO}-$ ), 4.25 [m, 1,  $\text{HC}(\text{OH})\text{CH}_2-$ ], and 6.82–7.7 (AMX system, 3,  $H_A$  7.60,  $H_M$  7.23,  $H_X$  6.95,  $J_{AX} = 2.0$  Hz,  $J_{AM} = J_{MX} = 7.5$  Hz, aromatic protons). Treatment of this compound with *p*-toluenesulfonic acid in benzene as outlined in the general method A gave **16** in 89% yield, 2,4-DNP mp 200–201°. Reaction of **7** with  $\text{CH}_3\text{Li}$  afforded, after elution from a Florisil column with benzene, 89% **16**, 2,4-DNP mp 200–202°. Reaction of **7** with  $\text{CH}_3\text{MgI}$  afforded, after similar purification, 81% **16**, 2,4-DNP mp 201–202°.

*Anal.* Calcd for  $\text{C}_{16}\text{H}_{18}\text{N}_4\text{O}_5$ : C, 59.68; H, 4.74; N, 14.65. Found: C, 59.71; H, 4.81; N, 14.79.

**2-Pentylidene-5-methoxy-1-tetralone (17).**—Reaction of the  $\text{BF}_2$  complex of **7** with  $n\text{-BuLi}$  afforded, after elution from a Florisil column with benzene, 38% **17** as a yellow oil: uv max (95% EtOH) 278  $m\mu$  ( $\epsilon$  12,500) and 233 (10,500); ir (film) 5.97, 6.17, 6.29 (sh), and 6.31  $\mu$ ; 2,4-DNP mp 213–214°. Reaction of **7** with  $n\text{-BuLi}$  afforded, after preparative tlc, 20% **17**, 2,4-DNP mp 208–210°.

*Anal.* Calcd for  $\text{C}_{22}\text{H}_{24}\text{N}_4\text{O}_5$ : C, 62.25; H, 5.70; N, 13.20. Found: C, 62.12; H, 5.75; N, 13.07.

**2-Ethylidenecyclopentanone (18).**—Reaction of the  $\text{BF}_2$  complex of **8** with  $\text{CH}_3\text{Li}$  afforded, after filtration in benzene through a grade II alumina column, 62% vpc-pure **18**: ir (film) 5.88 and 6.05  $\mu$ ; 2,4-DNP mp 211–213° (lit.<sup>21</sup> mp 216°). Reaction of **8** with  $\text{CH}_3\text{Li}$  afforded 56% **18** by vpc analysis, 2,4-DNP mp 213–215°. Reaction of **8** with  $\text{CH}_3\text{MgI}$  afforded 75% **18** by vpc analysis, 2,4-DNP mp 212–214°.

**2-Pentylidenecyclopentanone (19).**—Reaction of the  $\text{BF}_2$  complex of **8** with  $n\text{-BuLi}$  afforded 60% by vpc analysis of what was assumed to be **19** on the basis of the spectral properties of the crude reaction mixture: ir (film) 5.85 and 6.05  $\mu$ . The 2,4-DNP formed from the crude product had mp 115–117° (lit.<sup>22</sup> mp 120.7–121.4°). Reaction of **8** with  $n\text{-BuLi}$  afforded 48% **19** by vpc analysis, 2,4-DNP mp 117–118°.

**Registry No.**—**2**, 1122-25-4; **4**, 25726-01-6; **7**, 25677-39-8; **11**, 25677-40-1; **11** (2,4-dinitrophenylhydrazone), 25677-41-2; **12**, 1138-01-8; **13** (2,4-dinitrophenylhydrazone), 1178-47-8; **14**, 14026-01-8; **15**, 25677-44-5; **15** (2,4-dinitrophenylhydrazone), 25677-45-6; **16**, 25677-46-7; **16** (2,4-dinitrophenylhydrazone), 25677-47-8; **17**, 25677-48-9; **17** (2,4-dinitrophenylhydrazone), 25677-49-0; **18**, 14845-53-5; **19**, 16424-35-4;  $\text{BF}_2$  complex of 2-formylcyclododecanone, 25677-00-3;  $\text{BF}_2$  complex of 2-formylcholestan-3-one, 25677-01-4;  $\text{BF}_2$  complex of 2-formyl-5-methoxy-1-tetralone, 25677-02-5.

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