It has been shown earlier that internal cyclizations involving dicarbomethoxyacetone, R′ = CO_2CH_3 in Scheme I, do not involve enamine intermediates like **6**.[1a,g] Complex **5** (R′ = CO_2CH_3; R = C_6H_5) is thus most likely the precursor to **4d**. Detailed kinetics of similar cyclizations have been reported earlier.[1g] It appears that **5** (R′ = CO_2CH_3; R = C_6H_5) cyclizes by path a and not b in Scheme I.

It is well known that σ complexes prepared from acetone and *sym*-trinitrobenzene are quite stable in the presence of *tertiary* amines.[3,4] Addition of *secondary* amines causes rapid reaction to a variety of products through enamine intermediates.[4,5] In the case of the σ complex of acetone with *sym*-trinitrobenzene a bridged product analogous to **4** is rapidly formed with the negative charge delocalized on a nitropropene nitronate function.[1b,4,5] Since 3,5-dinitroacetophenone does not react with acetone in the presence of tertiary amines to give isolable products, it is thus quite likely that **6** (R = C_6H_5; R′ = H) is the precursor to **3c** and that attack on the ortho substituent occurs *via* path a as previously proposed[2] (Scheme I). An attempt was made to directly observe **6** in the pmr spectrum of the reaction solution. In the region without reactant or product absorption two overlapping triplets develop at δ ~5 (about 1% of the total absorption) and rapidly disappear as those for **3c** increase. These could result from protons on the tetrahedral ring carbons of **5** and **6** (R′ = H; R = C_6H_5).[6]

The reactivity differences causing **5** (R′ = CO_2CH_3; R = C_6H_5) to cyclize *via* path a and **6** (R′ = H; R = C_6H_5) *via* path b could result from increased flexibility in the side chain of the former relative to the latter. Such flexibility would allow the nucleophilic site in **5** (R′ = CO_2CH_3; R = C_6H_5) to more closely approach the meta ring position. Such ideas are supported by Drieding models of **5** and **6**. Alternately it may be that the initial product of intramolecular ortho substituent attack in **5** does not have a suitable route for aromatization to **3**.

Experimental Section

Melting points are uncorrected. Pmr spectra were obtained on a Jeol MH-100 spectrometer in $CDCl_3$ or DMSO-d_6 using tetramethylsilane as an internal standard. Uv spectra were obtained on a Perkin-Elmer 402 spectrometer in anhydrous methanol. Elemental analyses were performed by George I. Robertson Laboratories, Florham Park, N. J.

1-Phenyl-3-diethylamino-5,7-dinitronaphthalene (3c). To a solution of 0.5 g (0.0018 mol) of 3,5-dinitrobenzophenone[7] in the minimum of distilled dry acetone to effect dissolution was added 0.5 ml of diethylamine. The dark greenish-black solution which developed was kept at 25° for 12 hr and then cooled to about 8° for 2 days. Black needles deposited from the solution. These were filtered, washed with a small portion of cold ether, and dried at 0.5 mm and 50° for 8 hr. The resulting product (~0.25 g) melted at 167–168° and had uv-visible maxima in MeOH at 245, 320, 355, 420, and 468 nm. The pmr spectrum in DMSO-d_6 (saturated) had absorptions at δ 8.95 (d, 1 H, $J \simeq 2$ Hz), 8.75 (d, 1 H, $J \simeq 2$ Hz), 7.75 (d, 1 H, $J \simeq 2$ Hz), and 7.2 (d, 1 H, $J \simeq 2$ Hz) for the aromatic ring protons of **3c**. The phenyl group appeared as a complex multiplet centered at δ 7.5 (5 H) and the $N(CH_2CH_3)_2$ absorptions appeared as a coupled triplet (6 H) and doublet (4 H) at δ 1.25 and 3.6, respectively, J = 7.0 Hz. *Anal.* Calcd for $C_{20}H_{19}N_3O_4$: C, 65.74; H, 5.24; N, 11.50.Found: C, 65.71; H, 5.49; N, 11.28.

Preparation of 4d. The procedure for the preparation of **3c** was followed exactly except that dicarbomethoxyacetone (Aldrich) was used instead of acetone. The reaction solution turned brilliant yellow and did not deposit crystals on cooling, however. It was extracted with five 100-ml portions of anhydrous ether, yielding a yellow oil. The oil was covered with 20 ml of ether and enough ethanol was added to effect dissolution with warming. After standing at 8° for 3 days bright yellow crystals were formed. These were filtered and dried at 0.5 mm and 50° for 8 hr. The resulting product (~0.5 g) melted at 110–113° and had uv-visible maxima in MeOH at 245, 252, and 411 nm. The pmr spectrum of a saturated solution in acetone-d_6 had absorptions at δ 7.5 (m, 6 H) for the C_6H_5 and $-CCHC{=}NO_2^-$ protons, δ 5.25 (br, 1 H) and 5.15 (br, 1 H) for the bridgehead protons, and δ 4.30 (br, 1 H) for the $CHNO_2$ bridge in **4d**. The $CHCO_2CH_3$ proton appears at δ 3.9 (s, br, 1 H). The two CO_2CH_3 methyls appear as sharp singlets at δ 3.8 and 3.7 (3 H each). The triplet and quartet of the $H_2N(CH_2CH_3)_2^+$ cation appear at δ 1.2 and 2.8 (6 H and 4 H, respectively). Although this spectrum is not particularly well resolved, comparison with similar spectra of other bicyclic adducts of 3,5-dinitro-X-substituted benzenes and dicarbomethoxyacetone[1a,f] supports the proposed structure. The visible maximum and elemental analysis further substantiate the compound as **4d**. *Anal.* Calcd for $C_{24}H_{29}N_3O_{10}$: C, 55.49; H, 5.63; N, 8.09. Found: C, 55.47; H, 5.87; N, 7.79.

Acknowledgment. The author thanks the U. S. Army Research Office at Durham for support of this work.

Registry No.—**1** (R = Ph), 51911-74-1; **3c**, 51911-76-3; **4d**, 51911-79-6; diethylamine, 109-89-7.

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A Convenient Stereospecific Synthesis of (+)-α-Cyperone[1]

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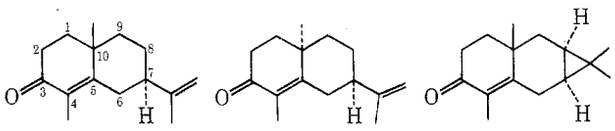
The eudesmane derivative (+)-α-cyperone (**1**)[2] has been rather widely used as a starting material for the synthesis of various other fused-ring sesquiterpenes.[3] However, convenient syntheses of **1** itself are rather limited. The original Howe and McQuillin synthesis of **1** which involves the Robinson annelation of (+)-dihydrocarvone with the methiodide of 1-diethylaminopentan-3-one allows the isolation of **1** in less than 5% yield.[2] This is because **1** is formed only as a minor product of the reaction and its separation from (−)-10-*epi*-α-cyperone (**2**) and the corresponding ketol which are the major reaction products is difficult. Piers and Cheng have found that (−)-α-santonin can be converted into **1** *via* an eight-step sequence.[4] Although lengthy, this synthesis represents a significant improvement over the method of Howe and McQuillin, since **1** was obtained in about 20% yield overall. Fringuelli, Taticchi, and Traverso have recently reported an apparently useful synthesis of α-cyperone.[5] These workers found that the tricyclic enone **3**, prepared by annelation of *cis*-4-caranone with 1-penten-3-one, undergoes preferential cleavage of the 8,11 bond of the cyclopropane ring with hydrogen bromide to form the 2-bromopropane derivative **4a** which could be converted into a mixture of α- and β-cyperone on dehydrohalogenation. An important feature of this synthesis is that annelation of the bicyclic ketone allows the establishment of the cis relationship of the angular methyl group and the dimethyl-substituted cyclopropane ring which ultimately becomes the three-carbon side chain in **1**. We wish to report a



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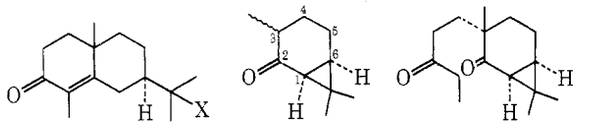

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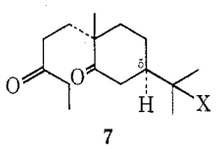

7

a, X = Br
b, X = Cl

convenient stereospecific synthesis of 1 which employs a similar concept and utilizes (−)-2-carone (**5**), which is readily available from (+)-dihydrocarvone,[6] as the starting material.

Michael reaction of **5** with 1-penten-3-one using alcoholic potassium hyroxide as the base gave a single product in 72% yield based upon recovered starting material. The subsequently described transformation demonstrated that this material should be assigned the structure **6** and its spectral properties were in agreement with this assignment.[7] Although carone (**5**) has been shown to be capable of undergoing base-catalyzed exchange of both the α hydrogens,[8] Michael reaction at the 3 position is expected, since the presence of the cyclopropane ring should cause the 1-enolate anion to be much less stable than the 2-enolate.[9,10] In addition, the top side of the 2-enolate is hindered by the endo methyl group on the cyclopropane ring so that nucleophilic attack on the Michael acceptor should take place exclusively from the bottom side of the molecule. No evidence was obtained for the formation of epimaalienone,[11] the possible product of base-catalyzed cyclization of the diketone **6**. Indeed, efforts to prepare this compound by treatment of **6** with a variety of basic catalysts were unsuccessful. This observation is in complete agreement with the previous report of Büchi and coworkers.[7]

By reaction of **6** with an anhydrous saturated ethanolic solution of hydrogen chloride the chloro enone **4b** was obtained in 78% yield. Opening of the three-membered ring of the conjugated cyclopropyl ketone system with acid should take place with exclusive cleavage of the 1,7 bond, leading to a tertiary carbonium ion which could be attacked by halide ion to produce a diketone intermediate, *i.e.*, **7**.[12,13] This species can then undergo rapid acid-catalyzed aldol cyclization to produce **4b**. Acid-catalyzed cyclizations of 1,5-diketones related to **7** often lead to partial or exclusive formation of bicyclo[3.3.1]nonanone derivatives.[14] However, the formation of such products requires the ketonic side chain to adopt a pseudo-axial orientation with respect to the enolized cyclohexanone ring. In the case of **7** this would require the six-membered ring to adopt a half-boat conformation or a half-chair conformation having the bulky 5 substituent axial. Both of these conformations would be of relatively high energy with respect to the species having the side-chain carbonyl group enolized and the cyclohexanone ring in a chair conformation with the 5 substituent equatorial. Cyclization of the latter would lead to **4** *via* the corresponding cis- and/or trans-fused ketols.

The synthesis of **1** was completed by dehydrohalogenation of **4b** with sodium acetate in acetic acid.[10] A crude product which was greater than 85% **1** by glc was obtained. The minor product of the reaction mixture showed identical glc behavior with an authentic sample of β-cyperone. Distillation of the oil obtained from dehydrohalogenation of **4b** afforded a fraction (82% yield) which was greater than 94% **1** by glc. This material showed identical spectral properties and glc behavior with an authentic sample of **1** prepared by the method of Howe and McQuillin.[2]

Experimental Section[15]

Synthesis of the Diketone 6. To a solution of 28.95 g (0.19 mol) of (−)-2-carone (**5**) in 290 ml of anhydrous ether was added a solution of 2.20 g (0.04 mol) of potassium hydroxide in 22.0 ml of anhydrous ethyl alcohol under nitrogen. The mixture was cooled to −5° and a solution of 15.85 g (0.19 mol) of ethyl vinyl ketone in 160 ml of anhydrous ether was added dropwise with stirring. After the addition was complete stirring was continued for 75 min while the mixture was allowed to warm to room temperature and the mixture was poured into 350 ml of an ice-cold solution of 10% hydrochloric acid. The aqueous layer was saturated with sodium chloride and extracted with three 100-ml portions of ether, and the combined organic extracts were washed with two 75-ml portions of a saturated aqueous solution of sodium bicarbonate followed by two 75-ml portions of a saturated sodium chloride solution. The organic phase was dried over anhydrous sodium sulfate and the solvent was removed *in vacuo* to give a pale yellow oil. Distillation yielded 17.0 g of (−)-2-carone, bp 45–55° (0.1 mm), and 14.35 g (72%) of **6**: bp 109–120° (0.1 mm); uv λ_{max} (95% EtOH) 216 nm (ϵ 2790);[16] ir (CCl_4) 1721 and 1692 cm^{-1};[16] nmr δ_{TMS} (CCl_4) 0.83 (s, 3 H), 1.02 (s, 3 H), 1.10 (s, 3 H), 0.98–1.24 (broad absorption, 5 H), 1.33–2.51 (broad absorption, 10 H): *m/e* (70 eV) 236.177 (calcd, 236.177); $[\alpha]^{25}D$ −149° (*c* 0.57, $CHCl_3$).

Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.17; H, 10.25.

Reaction of 6 with Ethanolic Hydrogen Chloride. The diketone **6** (6.04 g, 0.026 mol) was added dropwise with stirring to 60 ml of an anhydrous saturated solution of ethanolic hydrogen chloride at 5°. After the addition was complete the reaction mixture was allowed to warm to room temperature and stirring was continued for 30 min. The reaction mixture was then poured into 60 ml of ice water and extracted with four 60-ml portions of chloroform. The combined chloroform extracts were then washed with a saturated solution of sodium chloride until the washings were neutral. The organic layer was than dried over anhydrous magnesium sulfate and the solvent was removed *in vacuo* to give a yellow solid (6.0 g). Recrystallization of this material from pentane gave 5.09 g (78%) of **4b**: mp 86–87°; uv λ_{max} (EtOH) 248 nm (ϵ 20,100); ir (CCl_4) 1668 and 1612 cm^{-1}; nmr δ_{TMS} (CCl_4) 1.22 (s, 3 H, 10-CH_3), 1.62 (s, 6 H, 13 and 14-CH_3), 1.75 (s, 3 H, 4-CH_3), 1.80–3.20 ppm (broad absorption, 11 H): $[\alpha]^{25}D$ +165° (*c* 0.40, $CHCl_3$).

Anal. Calcd for $C_{15}H_{23}ClO$: C, 70.71; H, 9.10. Found: C, 70.57; H, 9.13.

(+)-α-Cyperone. A solution of 4.0 g (0.016 mol) of **4b** and 6.57 g (0.08 mol) of sodium acetate in 50 ml of glacial acetic acid was stirred rapidly and heated at 90–100° for 1 hr. The reaction mixture was then allowed to cool to room temperature and poured into 50 ml of water. The resulting mixture was extracted with four 50-ml portions of carbon tetrachloride and the combined organic extracts were washed with two 50-ml portions of 2% aqueous potassium hydroxide, one 50-ml portion of 2 *N* hydrochloric acid, one 50-ml portion of 5% aqueous sodium bicarbonate, and three 50-ml portions of a saturated aqueous solution of sodium chloride. The organic layer was then dried over anhydrous magnesium sulfate and the solvent was removed to give 3.65 g of a yellow oil. Glc analysis (column A) of the crude mixture revealed that it contained α- and β-cyperone in *ca.* 85:15 ratio. Distillation of the crude material gave 2.85 g (82%) of (+)-α-cyperone, bp 109–118° (0.05 mm), which was greater than 94% one component by glc (column A). The product showed identical optical properties (ir, nmr, optical rotation) and glc behavior (columns A and B) with an authentic sample of (+)-α-cyperone prepared by the method of Howe and McQuillin.[2]

Registry No.—**1**, 473-08-5; **4b**, 51911-68-3; **5**, 5561-14-8; **6**, 51911-69-4; ethyl vinyl ketone, 1629-58-9.

References and Notes

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(16) The uv and ir spectra of **6** were essentially identical with those reported by Büchi and coworkers (ref 7).

Synthesis of Furano Steroids and Analogs *via* Claisen Rearrangement

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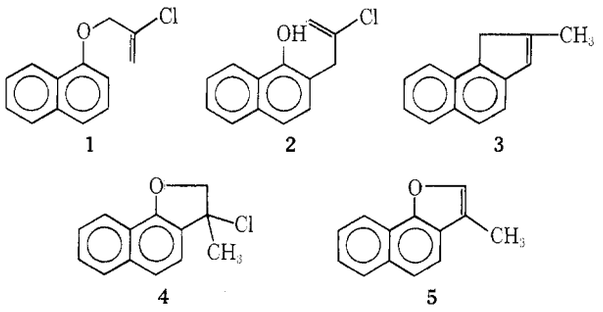
Interest in fused oxa steroids and related systems is evidenced by the variety of synthetic approaches[1] described in the recent literature. We report here the preparation of such compounds through a convenient route based on the work of Hurd and Webb.[2]

Commercially available 2,3-dichropropene-1 was used to alkylate an appropriate phenol and the resulting ether was rearranged by heating in *N,N*-dimethylaniline. Of the two compounds formed the major product was a chlorine-containing phenol derivative which could be cyclized in good yield to the minor product under the influence of a strong acid. The structure of the various compounds could be easily deduced from their pmr spectra.

Thus, the α-naphthol ether **1** produced a phenol **2** and a furanonaphthalene which could be separated on a neutral-alumina column. Two alternative structures **3** and **5** appeared reasonable for the furanonaphthalene, the former arising from the Claisen rearrangement product **2** and the latter *via* a possible intermediate such as **4**.

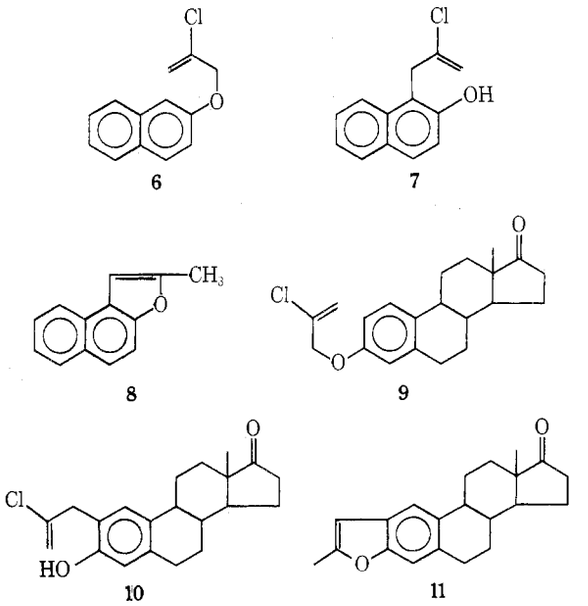


1 2 3 4 5

Extensive studies[3] on the pmr spectra of furan compounds have shown that α protons resonate at about τ 2.5 and β protons at about τ 3.5. A one-proton singlet at τ 3.6 in the pmr spectrum of the minor product from the rearrangement of **1** clearly indicated **3** to be the correct structure. The picrate of this compound had the same melting point as that recorded by Wilds and Johnson[4] for the picrate of **3** prepared by a different method. The intermediacy of a propynyl naphthyl ether in this rearrangement is excluded because such an ether cyclizes to a naphthopyran.[5]

The formation of the minor product **3** in good yield when **2** was treated with polyphosphoric acid is in accord with the assigned structure because the acid hydrolysis of the vinyl chloride would generate an acetyl function. It was observed that heating of the phenolic product **2** (or **7**) for a long period (10–14 hr) at a higher temperature (250°) failed to produce any significant amount of **3** (or **8**).

The allyl ether **6** from β-naphthol gave the rearrangement products **7** and **8**. The structure of the furano compound was again based on pmr spectra and identity of melting point of the picrate with that recorded for the picrate of **8** in the literature.[6]



6 7 8 9 10 11

The β-chloro allyl ether **9** from estrone gave a phenol **10** on rearrangement. The pmr spectrum of this compound showed the presence of two p protons; therefore, the allyl group had migrated to C-2 rather than to C-4. Treatment of the phenol **10** with polyphosphoric acid led to the furano steroid **11** in poor yield; cold sulfuric acid (90%), which proved to be a better cyclizing agent, produced **11** in 15% yield. The single-proton signal at τ 3.6 in the pmr of **11** is in