1.8 g of pure IV: $[\alpha]D$ −66.3° (*c* 1.09, MeOH); ir (smear) 1740 cm^{-1}; 100-MHz nmr (CCl_4) δ 0.95 (CMe, t), 2.29 (H_4, d, J = 4 Hz), 2.80 (H_2, q, J = 16 Hz), 3.17 (C_3OMe, s), 3.70 (C_1 OMe, s).

Anal. Calcd for $C_{12}H_{22}O_5$: C, 58.51; H, 9.00. Found: C, 58.34; H, 8.80.

Fractions 17–28 from the silica gel column mentioned above gave, on concentration, 350 mg of white solid which was recrystallized from ether–hexane to give the analytical sample of V: mp 105–106°; $[\alpha]D$ −169° (*c* 0.72, MeOH); λ_{max}^{MeOH} 245 nm (ε 22,250); ir (KBr) 3450, 1720, and 1600 cm^{-1}; nmr δ 0.97 (CMe, t), 2.86 and 3.19 (H_{4a}, q, $J_{4,4}$ = 19, $J_{2,4a}$ = 2, $J_{4a,5}$ = 5 Hz), 3.45 (H_{4e}, 1 H, t, $J \cong$ 1.5 Hz), 4.25 (m, H_5 and H_6), 5.37 (H_2, m); mass spectrum *m/e* 214 ($C_{11}H_{18}O_4$).

Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 62.04; H, 8.45.

Conversion of I to III with Sodium Methoxide.—A solution of 1.07 g of I and 270 mg of sodium methoxide in 20 ml of methanol was gently warmed on a steam bath for 30 min. The solution was concentrated and the resultant oil was taken up in ethyl acetate and washed with 4 *N* hydrochloric acid. The ethyl acetate phase was dried and concentrated to an oil which was passed over 80 g of acid-washed silica gel and eluted with 10% ethyl acetate in hexane. This provided 550 mg of a colorless oil from which 150 mg was distilled[8] at 80° (100 μ) to give III. This material was identical in all respects with that obtained above.

Ozonolysis of V.—Ozone was passed through a solution of 400 mg of V in methanol at −70°. The reaction was worked up by the dimethyl sulfide procedure.[9] After removal of the solvent, the residual oil was distilled[8] at 135° (100 μ) to give 100 mg of colorless oil: $[\alpha]D$ −71.1 (*c* 0.73, MeOH); ir (smear) 1770 cm^{-1}; CD (2.44 mg/ml MeOH) $\Delta\epsilon_{216}$ −0.53.

Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.88; H, 8.79.

Application of Horeau's Method to I.—A solution of 59 mg of I and 215 mg of (±)-α-phenylbutyric anhydride in 3 ml of pyridine was allowed to stand over the weekend at ambient temperature. Then 1 ml of water was added with the consequent generation of heat. After 1 hr, 20 ml of water was added and the mixture was extracted three times with ether. The ether extracts were back-extracted twice with 10 ml of 10% sodium carbonate solution. The aqueous alkaline solution was washed with ether and then acidified and extracted once again with ether. This was dried over magnesium sulfate and evaporated to 154 mg of a colorless oil which solidified in the refrigerator. Tlc using benzene–dioxane–acetic acid (50:50:2) showed this material to be α-phenylbutyric acid as did the ir and nmr, $[\alpha]D$ −0.17 ± 0.07° (*c* 2.90, benzene).

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.26; H, 7.20.

Application of Horeau's Method to V.—To 3 ml of pyridine was added 65 mg of V and 218 mg of (±)-α-phenylbutyric anhydride. The solution was allowed to stand over the weekend at room temperature and then worked up as described above to give 145 mg of the acid, $[\alpha]D$ −2.27 ± 0.07° (*c* 2.9, benzene).

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.24; H, 7.46.

Registry No.—I, 34565-32-7; II, 34565-33-8; III, 34565-34-9; IV, 34565-35-0; V, 34565-36-1; VI, 34565-37-2; α-phenylbutyric acid, 938-79-4.

Acknowledgments.—We wish to thank our colleagues for their assistance in particular, Dr. H. Tresner and Miss Jean Hayes for culture isolation and identification, Mr. A. J. Shay for large-scale fermentations, Mr. M. Dann for large-scale work-ups, Mr. L. Brancone for microanalytical data, Mr. W. Fulmor for spectral data and optical rotations, and Miss Pat Mullen of Cyanamid Stamford Laboratories for the CD curves.

(9) J. J. Pappas, W. P. Keaveney, E. Gancher, and M. Berger, *Tetrahedron Lett.*, 4273 (1966).

Photoreduction of Conjugated Cyclopropyl Ketones in Isopropyl Alcohol[1]

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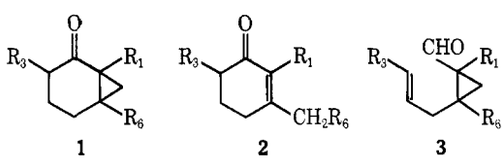
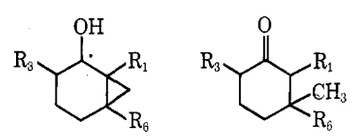
Previous photochemical studies of substituted bicyclo[4.1.0]heptan-2-ones (**1**) under photoisomerization conditions, *i.e.*, *tert*-butyl alcohol used as solvent, have established that the relative efficiencies of three possible reaction pathways from **1** in the triplet state are affected by the pattern of substitution on the ring system.[2] The general photoisomerization of such a conjugated system (**1**, R_3, R_6 = H) to a 3-substituted cyclohex-2-en-1-one (**2**, R_3, R_6 = H) is blocked when R_6 is an alkyl group; in such a case only efficient intersystem crossing from the excited triplet state to the singlet ground state of the starting material occurs. However, with substitution at R_3, the Norrish type I cleavage to an aldehyde **3** becomes the favored primary photoprocess.



1 **2** **3**

On the other hand, irradiation of **1** (R_1, R_3 = H, R_6 = H or CH_3) in isopropyl alcohol, *i.e.*, photoreduction conditions, has been shown to lead to a selective reductive opening of the outside bond of the cyclopropyl ring.[3] In this photoreduction, the intervention of the α-hydroxycyclopropylcarbinyl radical **4** (R_1, R_3 = H, R_6 = H or CH_3) has been established and it is its collapse which leads to a 3-substituted 3-methylcyclohexanone **5** (R_1, R_3 = H). The effect of the pattern of substitution of the ring system on this photoreduction process has now been investigated.



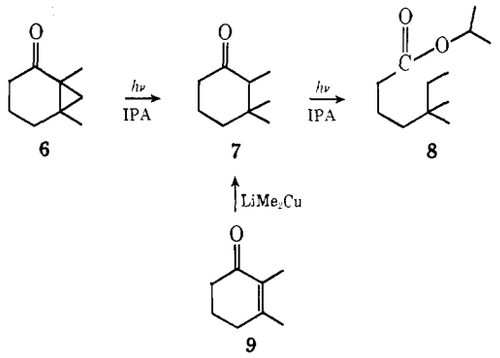
4 **5**

It was found that the disubstituted derivative 1,6-dimethylbicyclo[4.1.0]heptan-2-one (**6**) upon irradiation in isopropyl alcohol was rapidly transformed to isopropyl 5,5-dimethylheptanoate (**8**). When the irradiation was monitored using infrared spectroscopy, it was found that the expected 2,3,3-trimethylcyclohexanone (**7**) was the first photoproduct formed. This latter ketone **7**, prepared from 2,3-dimethylcyclohex-2-en-1-one (**9**) and lithium dimethylcopper, upon ir-

(1) This work was supported by Public Health Service Grant No. 00709, National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service.

(2) W. G. Dauben, G. W. Shaffer, and E. J. Deviny, *J. Amer. Chem. Soc.*, **92**, 6273 (1970).

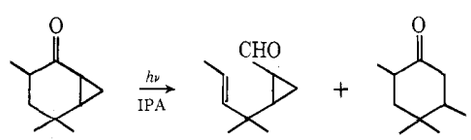
(3) W. G. Dauben, L. Schutte, R. E. Wolf, and E. J. Deviny, *J. Org. Chem.*, **34**, 2512 (1969).



6 7 8 9

radiation in isopropyl alcohol rapidly yielded ester **8**.[4] Thus, these experiments show that hydrogen abstraction by the triplet of ketone **6** is more efficient than intersystem crossing to the ground-state singlet. It also is of interest to note that, whereas the 2,3,3-trimethylcyclohexanone undergoes a rapid type I photolysis, the related cyclopropyl ketone **6** does not undergo α cleavage.

To evaluate the relative efficiencies of the type I cleavage and the hydrogen abstraction from solvent, 3,5,5-trimethylbicyclo[4.1.0]heptan-2-one (**10**) was studied, since it had been found earlier[2] that in *tert*-butyl alcohol type I cleavage was the sole reaction pathway. Irradiation of **10** in isopropyl alcohol was found to yield, in a ratio of 1.5:1, the unsaturated aldehyde **11** from the cleavage route and 2,4,4,5-tetra-



10 11 12

methylcyclohexanone (**12**) from the reduction route. Thus, the hydrogen abstraction process is more efficient than photoisomerization and the resulting α-hydroxycyclopropylcarbinyl radical still leads to the selective opening of the outside bond of the cyclopropane ring.

Further information with regard to the nature of this type of radical intermediate has been obtained by study of the two isomeric 4,5-methanocholestan-3-ones **13** and **15**.[5] It was found that when the 4β,5β isomer **13** was irradiated in isopropyl alcohol the sole product of the reaction was the 5β-methyl derivative **14** (eq 1). Irradiation of the isomeric 4α,5α-methano compound **15**, however, yielded a mixture of products which was shown to contain only 15% of the expected 5α-methyl isomer **16** and quite surprisingly 85% of the 5β isomer **14**. Such a result can be visualized as involving the symmetrical homoallylic radical **17**, which can collapse to either **14** or **16**. That previous isomerization of **15** to **13** had not occurred was shown by the stability of the material upon irradiation in benzene.

Experimental Section

Unless otherwise noted, the following general conditions were used in all reactions. Infrared spectra were recorded in carbon tetrachloride using either a Perkin-Elmer 137 Infracord or a 237 grating spectrometer. Nmr spectra were obtained with a Varian T-60 spectrometer using carbon tetrachloride as the solvent and tetramethylsilane as an external reference. Mass spectral analyses and elementary analyses were obtained from the Analytical Laboratory, College of Chemistry, University of California, Berkeley, Calif.

Irradiation Procedure.—Irradiations were conducted in deaerated 0.2–0.5% solutions in 125 ml of isopropyl alcohol, using a Corex filter with a 450 W Hanovia lamp. The reactions were monitored by vpc (10% Carbowax). After termination of the irradiation, the solvent was rotary evaporated and the products were collected by chromatography.

Irradiation of 1,6-Dimethyl[4.1.0]heptan-2-one (6).—The solution of 6[6] was irradiated for 8 hr, at which time 50% of the starting material had disappeared. The photoproduct (~80% based upon recovered starting material) was isolated by preparative vpc and identified as isopropyl 5,5-dimethylheptanoate (**8**) by comparison with an authentic sample (see below). The material spectral properties were: ir (CCl_4) 1724, 1258, and 1110 cm^{-1}; mass spectrum (70 eV) *m/e* 185 (M − CH_3), 171 (M − C_2H_5), 141 (M − C_3H_7O), and 129 (M − C_5H_{11}).

When the reaction was monitored by infrared spectrometry, the carbonyl absorption at 1705 cm^{-1} of 2,3,3-trimethylcyclohexanone (**7**) was present at the early stages of the irradiation and then remained at a low concentration, steady-state intensity.

2,3,3-Trimethylcyclohexanone (7).—A solution of lithium dimethylcopper was prepared by the addition of 80 ml of a 2 *M* ethereal solution of methyl lithium to 11.6 g of cuprous bromide.[7] To the ice-cooled mixture there was added 2.0 g of 2,3-dimethyl-2-cyclohexenone (**9**) in 20 ml of ether. The reaction was stirred for 2 hr at ice temperature, and refluxed for 2 hr. The mixture was processed in the standard fashion[6] to yield 2 g of a 2:8 mixture of two compounds. The materials were separated by alumina chromatography (Woelm neutral, activity III), pentane eluting the minor product, tentatively identified as 1,2,3-trimethyl-1,3-cyclohexadiene. The ketone **7** was eluted with chloroform: yield 1.5 g (67%); ir (CCl_4) 1705, 1445, 1080, and 935 cm^{-1}; nmr (CCl_4) δ 2.50–1.45 (m, 7), 1.03 (s, 3), 0.87 (d, 3, J = 7 Hz), and 0.73 (s, 3); mol wt, 140 (mass spectrum).

Irradiation of the ketone **7** under the standard conditions gave ester **8**, whose properties are reported above.

Irradiation of 3,5,5-Trimethylbicyclo[4.1.0]heptan-2-one (10).—The solution of **10**[2] was irradiated for 2 hr, at which time 50% of the starting material had disappeared and two major products, **11** and **12**, appeared in a ratio of 1.5:1; the total yield by vpc was 80%, based upon reacted starting material. The photoproducts were separated by vpc and identified by comparison with authentic samples.

2,3-Methano-4,4-dimethyl-*trans*-Δ^5-heptanal (11).—The material was prepared as previously described[2] by irradiation of 3,5,5-trimethylbicyclo[4.1.0]heptan-2-one in *tert*-butyl alcohol and purified by vpc on two columns (10% Carbowax and 5% XF 1150 Cyanosilicone).

2,4,4,5-Tetramethylcyclohexanone (12).—The material was prepared from 4,4,6-trimethyl-2-cyclohexenone and lithium dimethylcopper following the procedure described for **7**: yield 90%; ir (CCl_4) 1690, 1450, 1375, 1365, 1135, and 1065 cm^{-1}; nmr (CCl_4) δ 1.8–2.8 (m, 3), 1.2 (br s, 3), 0.95 (s, 6), and 0.81 (d, 3, J = 4 Hz); mol wt, 154 (mass spectrum).

Irradiation of 4β,5β-Methanocholestan-3-one (13).—A solution of 0.5 g of **13**[5] in 125 ml of isopropyl alcohol was irradiated with a 200-W Hanovia lamp (Vycor filter) for 90 min, at which time 65% of the starting material had been consumed. The reaction mixture was chromatographed on 500 g of silica gel (Brinkmann 7734) according to the procedure of Duncan[8] using the solvent system benzene–acetone (9:1). In the early eluates there was obtained the photoproduct, which was recrystallized from methanol–acetone, yield 225 mg, mp 87–88°. The material was identical in all respects with the known 5β-methylcholestan-3-one (**14**).[9] In the later fraction there was obtained 155 mg of starting ketone.

Irradiation of 4α,5α-Methanocholestan-3-one (15).—A solution of 0.5 g of **15**[5] in 125 ml of isopropyl alcohol was irradiated for

(4) The ketone **7** and the ester **8** were not separable on the vpc columns used in this research.

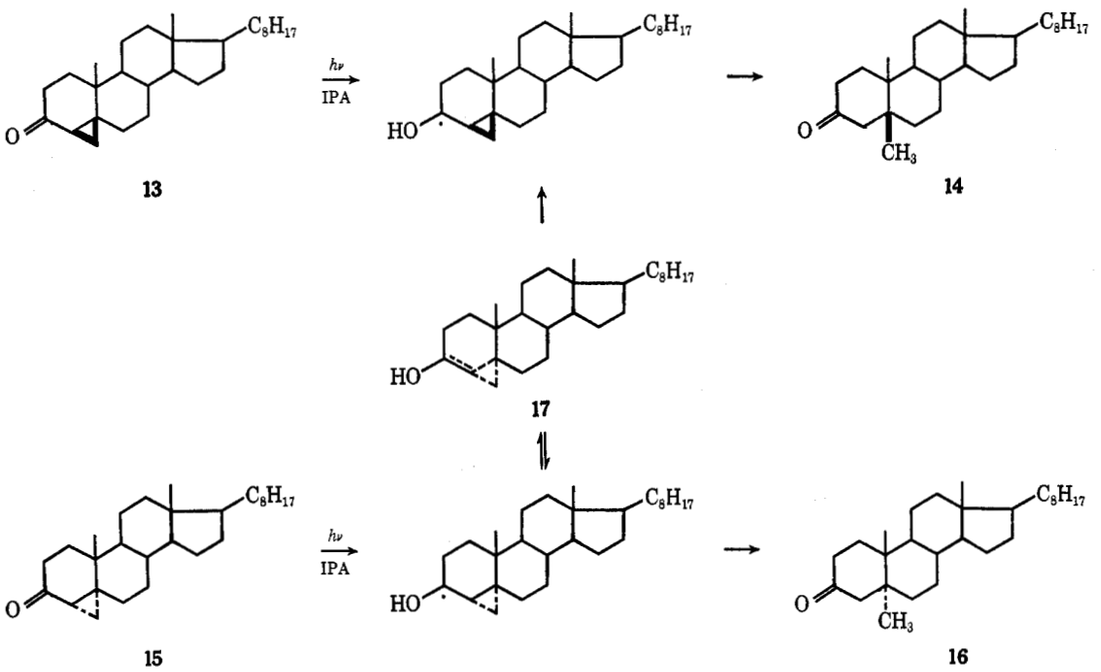
(5) W. G. Dauben, P. Laug, and G. H. Berezin, *J. Org. Chem.*, **31**, 3869 (1966).

(6) W. G. Dauben and G. H. Berezin, *J. Amer. Chem. Soc.*, **89**, 3449 (1967).

(7) H. O. House and W. F. Fisher, *J. Org. Chem.*, **33**, 949 (1968).

(8) G. R. Duncan, *J. Chromatogr.*, **8**, 37 (1962).

(9) W. G. Dauben and E. J. Deviny, *J. Org. Chem.*, **31**, 3794 (1966); W. Nagata, H. Hirai, H. Itazaki, and K. Takeda, *Justus Liebigs Ann. Chem.*, **641**, 196 (1961).



(1)

2.5 hr as described for the 4β,5β isomer **13**, at which time 80% of the starting material had been consumed. The reaction mixture was chromatographed by the Duncan procedure[8] to yield 290 mg of reaction product and 80 mg of starting ketone. The reaction product was recrystallized from absolute ethanol to yield a granular solid, mp 76–132°, mol wt, 400 (mass spectrum).

Anal. Calcd for $C_{28}H_{48}O$: C, 83.93; H, 12.08. Found: C, 83.99; H, 11.91.

The product was analyzed by vpc and found to be composed of 85% of 5β-methylcholestan-3-one (**14**) and 15% of 5α-methylcholestan-3-one (**16**) by coinjection with authentic samples.[9]

Registry No.—**6**, 14845-43-3; **7**, 34562-14-6; **10**, 29750-24-1; **12**, 34562-16-8; **13**, 2429-48-3; **15**, 2602-40-6; isopropyl alcohol, 67-63-0.

Cycloaddition Reactions with *anhydro*-1,3-Dimethyl-4-hydroxy-1,2,3-triazolium Hydroxide[1]

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In a previous communication,[2] *anhydro*-3-aryl-4-hydroxy-1-methyl-1,2,3-triazolium hydroxides (**1**, R = aryl) were reported to undergo cycloaddition reactions with dimethyl acetylenedicarboxylate to the corresponding pyrazole. Reactive olefinic-type dipolarophiles such as ethyl azodicarboxylate also gave 1:1 adducts with the ring system and tetracyanoethylene formed "ene" type substitution products. Particularly noteworthy, however, was the lack of reaction with phenyl isocyanate and phenyl isothiocyanate, even over extended reaction periods.

The 3-aryl substituent would be expected to have considerable effect on the electron density associated with the nucleus of **1**. The inability of **1** (R = aryl) to form the corresponding methyl ether with methyl iodide whereas the 3-methyl compound **1** (R = CH_3) underwent ready methylation with methyl iodide[3] may be attributed to substituent effect. We have now found that replacement of the 3-aryl substituent with a methyl group facilitates cycloaddition reactions with this ring system and greatly extends the scope of the reaction.

anhydro-1,3-Dimethyl-4-hydroxy-1,2,3-triazolium hydroxide (**1**, R = CH_3) underwent reaction with dimethyl acetylenedicarboxylate in refluxing benzene (1 hr), giving dimethyl 1-methylpyrazole-3,4-dicarboxylate (**3**) in 60% yield, presumably *via* the intermediate **2** which lost methyl isocyanate under the reaction conditions. An equally facile reaction of **1** (R = CH_3) with ethyl azodicarboxylate also occurred, giving ethyl 6,7-dimethyl-5-oxo-1,2,3,6,7-pentaazabicyclo[2.2.1]heptane-2,3-dicarboxylate (**4**) in 95% yield. The assignment of this structure to the cycloadduct is based on analytical and spectral data (see Experimental Section) and is analogous to the structure of the product from **1** (R = aryl) and the ester.

Both phenyl isocyanate and phenyl isothiocyanate gave 1:1 cycloadducts with **1** (R = CH_3). In the former case, structure **5**, 2,7-dimethyl-3,5-dioxo-6-phenyl-1,2,6,7-tetraazabicyclo[2.2.1]heptane, was assigned to the product. The bridgehead proton at C-4 resonated at τ −0.23, broadened slightly by coupling with the bridge NCH_3 group,[2,4] and is at extremely low field consistent with it being deshielded by the carbonyl groups in the 3 and 4 positions. This would appear to exclude from consideration the isomeric 2,7-dimethyl-3,6-dioxo-5-phenyl-1,2,5,7-tetraazabicyclo[2.2.1]heptane formed by reverse addition of the phenyl isocyanate to **1**. Such a reverse addition has been observed with sydnone.[5] The adduct with phenyl isothiocyanate was assigned the analogous structure **6**.

(1) (a) Support of this work by U. S. Public Health Service Research Grant CA 08495, National Cancer Institute, is gratefully acknowledged. (b) Part XVII in the series, Mesoionic Compounds.

(2) K. T. Potts and S. Husain, *J. Org. Chem.*, **35**, 3451 (1970).

(3) M. Begtrup and C. Pedersen, *Acta Chem. Scand.*, **20**, 1555 (1966); M. Begtrup and P. A. Kristensen, *ibid.*, **23**, 2733 (1969).

(4) D. E. Ames and B. Novitt, *J. Chem. Soc. C*, 2355 (1969).

(5) H. Kato, S. Sato, and M. Ohta, *Tetrahedron Lett.*, 4261 (1967).