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The Formation of α-Acetoxy Ketones by Oxidation of Enamines with Thallium Triacetate

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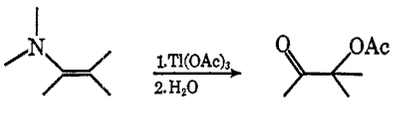
The morpholine enamine derivatives of cyclopentanone, cyclohexanone, cycloheptanone, 3-heptanone, 2-methyl- and 3- and 4-*t*-butylcyclohexanone, cholestanone, androstan-17-ol-3-one, *trans*-10-methyl-2-decalone, and cyclohexanecarboxaldehyde were oxidized with thallic acetate. The new reaction is of preparative value for formation of α-acetoxy ketones. The steric course of the reaction and factors affecting its rate were determined and possible reaction mechanisms are discussed.

While the reactions of enamines with electrophilic carbon, sulfur, halogen, and nitrogen species has been the subject of more than 500 separate investigations,[1] little attention has been given to their oxidation. The only preparative use of enamines as intermediates for the α oxygenation of aldehydes or ketones was found in the reaction of morpholinocyclohexene with benzoyl peroxide,[2,3] which furnished 2-benzoyloxycyclohexanone. Other oxidations are cleavages of the enamine double bond with ozone[4] or chromic acid,[5-7] an overoxidation observed in the reaction of a tertiary amine with mercuric acetate,[8] and the addition of hydrogen peroxide[9,10] to enamines in analogy to the formation of carbinolamines. The present report shows the formation of a number of α-acetoxy ketones from enamines and thallic acetate.



Results

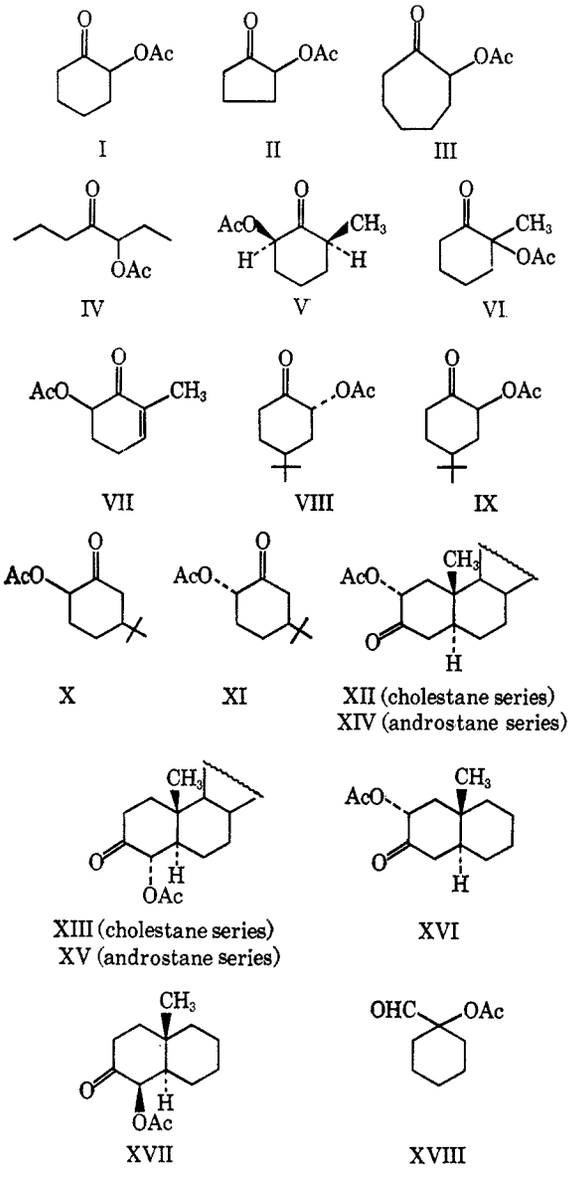
The new reaction is of preparative value. Yields of α-acetoxy ketones were mostly superior to the yields obtained on direct oxidation of the parent ketones with thallic acetate or lead tetraacetate. Also, the oxidations could be carried out under milder conditions than those required for the oxidations of ketones. Thus morpholinocyclohexene was oxidized rapidly at room temperature with 1 equiv of thallium triacetate in anhydrous acetic acid or in chloroform to give, after hydrolysis, 2-acetoxycyclohexanone (I) in at least 73 and 70% yields, respectively. From a combination of cyclohexanone, morpholine, and acetic acid, followed by thallium triacetate in chloroform, 2-acetoxycyclohexanone was obtained in 77% yield, showing the possibility of *in situ* generation of the enamine. In contrast, we found the oxidation of cyclohexanone with thallic acetate to give the same product in only 6% yield after 48 hr at room temperature and in 21% yield at reflux in acetic acid. An oxidation of cyclohexanone with thallic ions in aqueous acid led to cyclopentanecarboxylic acid in 75% yield.[11]

The oxidation of cyclohexanone with lead tetraacetate in refluxing benzene was reported to furnish a 61% yield of 2-acetoxycyclohexanone.[12]

In the oxidation of morpholinocyclohexene, lower yields were obtained in nonpolar solvents than in polar solvents. Exceptions were reactions in dimethyl sulfoxide and hexamethylphosphoramide, where yields were reduced owing to losses of the product in an extractive work-up with water. Oxidation with lead tetraacetate in anhydrous acetic acid gave only a 23% yield of 2-acetoxycyclohexanone. A lower yield was also found when the pyrrolidine enamine was used in place of the morpholine enamine in acetic acid. Oxidations of various enamines with thallic acetate led to the products I–XVIII (Chart I), yields of which are

(1) "Enamines: Their Synthesis, Structure and Reactions," A. G. Cook, Ed., Marcel Dekker, Inc., New York, N. Y., 1968.
(2) R. L. Augustine, *J. Org. Chem.*, **28**, 581 (1963).
(3) S. O. Lawesson, H. J. Jakobsen, and E. H. Larsen, *Acta Chem. Scand.*, **17**, 1188 (1963).
(4) M. E. Herr and F. W. Heyl, *J. Amer. Chem. Soc.*, **74**, 3627 (1952).
(5) D. A. Shepherd, R. A. Donia, J. A. Campbell, B. A. Johnson, R. P. Holysz, G. Slomp, J. E. Stafford, R. L. Pederson, and A. C. Ott, *ibid.*, **77**, 1212 (1955).
(6) G. Slomp, Y. F. Shealy, J. L. Johnson, R. A. Donia, B. A. Johnson, R. P. Holysz, R. L. Pederson, A. O. Jensen, and A. C. Ott, *ibid.*, **77**, 1216 (1955).
(7) G. K. Trivedi, P. S. Kalsi, and K. Chakravarti, *Tetrahedron*, **20**, 2631 (1964).
(8) N. J. Leonard, L. A. Miller, and P. D. Thomas, *J. Amer. Chem. Soc.*, **78**, 3463 (1956).
(9) A. Rieche, E. Schmitz, and E. Beyer, *Chem. Ber.*, **92**, 1206 (1959).
(10) A. Rieche, E. Schmitz, and E. Beyer, *ibid.*, **92**, 1212 (1959).
(11) K. B. Wiberg and W. Koch, *Tetrahedron Lett.*, 1779 (1966).
(12) C. W. K. Cavill and D. H. Solomon, *J. Chem. Soc.*, 4426 (1955).

CHART I



shown in Table I. These examples require some comment.

The morpholine and pyrrolidine enamines of 2-methylcyclohexanone showed a preference for reaction at the carbon bearing the methyl substituent, a result contrary to all previous experience with these enamines. The formation of 6-acetoxy-2-methylcyclohex-2-enone (VII) can be assumed to be due to further oxidation of an initially formed cross-conjugated enamine, XIX, rather than to oxidation of the 2-acetoxy-6-methylcyclohexanone enamine derivative since acetoxycyclohexenone or 2,6-diacetoxycyclohexanone were not formed on oxidation of morpholinocyclohexene. Thus, the 6-acetoxy-2-methylcyclohex-2-enone (VII) is also a product of initial oxidation at the methyl-substituted position (Scheme I).

The oxidation of cyclohexenamines with thallic acetate was found to be highly stereospecific. In acetic acid, oxidation of the morpholine enamine of 4-*t*-butylcyclohexanone and hydrolysis gave only *trans*-2-acetoxy-4-*t*-butylcyclohexanone (VIII). This product could be isomerized with aqueous sodium bicarbonate to *cis*-2-acetoxy-4-*t*-butylcyclohexanone (IX).

Similarly, the morpholine enamine of 3-*t*-butylcyclohexanone was oxidized in acetic acid to give primarily the *cis*-2,5-disubstituted ketone, X, and the *trans*-2,5-diequatorial product, XI (69:31). A possible 2-acetoxy-3-*t*-butylcyclohexanone product could only be detected in trace amounts by vapor phase chromatography.

In contrast to the axial introduction of acetoxy substituents in the preceding examples, it was found that equatorial α-acetoxy ketones were obtained from the oxidation of morpholine enamines derived from 3-keto-5α steroids in acetic acid or chloroform. This result is consistent with the bromination of the analogous enol acetate and enolate systems[13] where the axial angular methyl group also prevents the usual axial approach of the electrophile. Moreover, the enamine oxidation led to formation of a 1:1 complex of 2α- and 4α-acetoxy steroids.

The same complex was formed from 2α-bromocholestanone and sodium acetate in refluxing acetic acid.[14] However, 2α- and 2β-acetoxycholestanone did not rearrange or epimerize under duplicated hydrolytic work-up conditions of the oxidation process and a 2,4-dinitrophenylhydrazone derivative of the 2α,4α-acetoxycholestanone complex was formed directly from the oxidation reaction mixture. This indicated that the complex was not just formed from a single acetoxycholestanone during the hydrolytic work-up of the reaction mixture but was generated during the reaction.

In contrast to the 2 and 4 acetoxylation, bromination of the cholestanone enamine in acetic acid led only to 2α-bromocholestanone in high yield.

Most remarkable was the formation of a mixture of 1β- and 3α-acetoxy ketones (XVI, XVII) (ratio 3:2) on oxidation of the morpholine enamine of *trans*-10-methyldecal-2-one in acetic acid. This result suggests less steric shielding of the 1 position in the decalone than at the analogous 4 carbon in the steroid skeleton.

Attempts to extend the oxidation reaction to enamines derived from aldehydes were only successful in the case of the morpholine enamine derivative of cyclohexanecarboxaldehyde. The corresponding butyraldehyde derivative led mostly to condensation products in acetic acid and to butyric acid and other unidentified products in chloroform.

The course of the oxidation reaction in acetic acid and its dependence on component concentrations were followed titrimetrically, by product assay, and with nuclear magnetic resonance and uv spectra (Figure 1). With morpholinocyclohexene the loss of oxidation potential, formation of acetoxycyclohexanone, and conversion of thallic into thallous ion followed about the same rates, which gave complete reaction in 1 hr at room temperature.

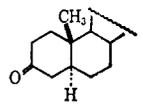
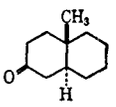
When lithium chloride, sodium acetate, or excess enamine (which is mainly converted into acetate and the imonium salt) were added to the oxidation mixture in acetic acid, the reaction rate was greatly decreased. Excess thallic acetate also decreased the reaction rate.

Oxidation of morpholinocyclohexene with thallic acetate in acetic acid containing a large amount of chloride ion gave only acetoxycyclohexanone and no chlorocyclohexanone. However, the addition of thallic

(13) C. Djerassi, N. Finch, R. C. Cookson, and C. W. Bird, *J. Amer. Chem. Soc.*, **82**, 5488 (1960).
(14) L. F. Fieser and M. A. Romero, *ibid.*, **75**, 4716 (1953).

TABLE I

OXIDATION OF MORPHOLINE ENAMINES WITH THALLIC ACETATE

Starting ketone or aldehyde	Products	Yield in acetic acid, %	Yield in chloroform, %	
			Morpholine enamine	Pyrrolidine enamine
Cyclohexanone	I	73,[a] 88[b]	70,[a] 84[b]	
Cyclopentanone	II	46[a]	81[c]	
Cycloheptanone	III	54[c]		
4-Heptanone	IV	56[c]		
2-Methylcyclohexanone	V	7[c]	24[c]	27
	VI	25[c]	35[c]	31
	VII	18[c]	0[c]	0[c]
4-*t*-Butylcyclohexanone	VIII	35[a]		
	IX		67[a]	
3-*t*-Butylcyclohexanone	X	36[a]		
	XI	16[a]	6[a]	
	XII (cholestane series)		38[a]	
	XIV (androstane series)	12[a]		
Cholestanone	XIII (cholestane series)		38[a]	
Androstan-17β-ol-3-one	XV (androstane series)	12[a]		
	XVI	19[a]	10[a]	
	XVII	29[a]		
Cyclohexylcarboxaldehyde	XVIII	12[d]		

[a] Minimum preparative value. [b] Value from DNP derivative. [c] Value from vpc. [d] Value from semicarbazone.

chloride to an acetic acid solution of the enamine gave primarily chlorocyclohexanone in a much slower reaction, but some acetoxycyclohexanone was also formed soon after an initial reaction period. The ratio of chlorocyclohexanone to acetoxycyclohexanone decreased somewhat with time after an initial rapid change at the beginning of the reaction and a value of 4:1 was found after 4 days, when half of the enamine was oxidized. The two products reflect a partial exchange of chloride for acetate ligands on thallium (also seen by nmr spectroscopy, below) prior to reaction with the enamine.

Further details of the enamine oxidation became evident by monitoring the reaction by nuclear magnetic resonance spectra. Thus, in acetic acid, morpholinocyclohexene and its 4-*t*-butyl derivative existed completely as the imonium salt XX. No vinyl proton was seen and the morpholine protons appeared at δ 3.7 and 3.8. On addition of thallic acetate a morpholine ammonium salt was immediately formed with the morpholine protons at δ 3.1 and 3.7. Again the vinyl hydrogen was absent. (In contrast, thallous acetate or sodium acetate did not alter the imonium spectrum and thallic chloride produced only a gradual change to the ammonium system. This change was also seen immediately when an aged solution of thallic chloride in acetic acid, in which at least partial exchange of acetate for chloride ligands had presumably taken place, was added to the enamine.) At this point (1 min) little of the oxidation equivalence of the reaction mixture had been lost ($Na_2S_2O_3$ titration), thallic ion was still present (uv absorbance at 244 mμ), and no α-acetoxycyclohexanone was produced on hydrolysis. The formation of an O-acylcarbinolamine complex with thallic acetate, XXI, is postulated for this stage. As the reaction proceeded to completion over 1 hr, a signal was generated at δ 4.8, which corresponded finally to one proton and was assigned to the hydrogen at the carbon undergoing substitution by acetate. This signal was better defined in the oxidation of the 4-*t*-butyl-substituted than the unsubstituted morpholinocyclohexene, owing to decreased conformational mobility.

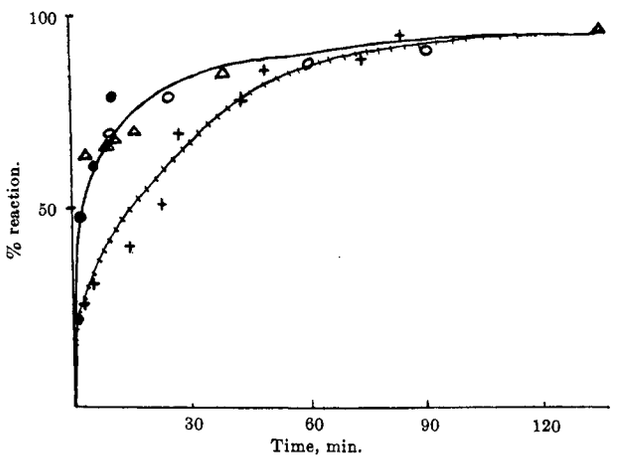
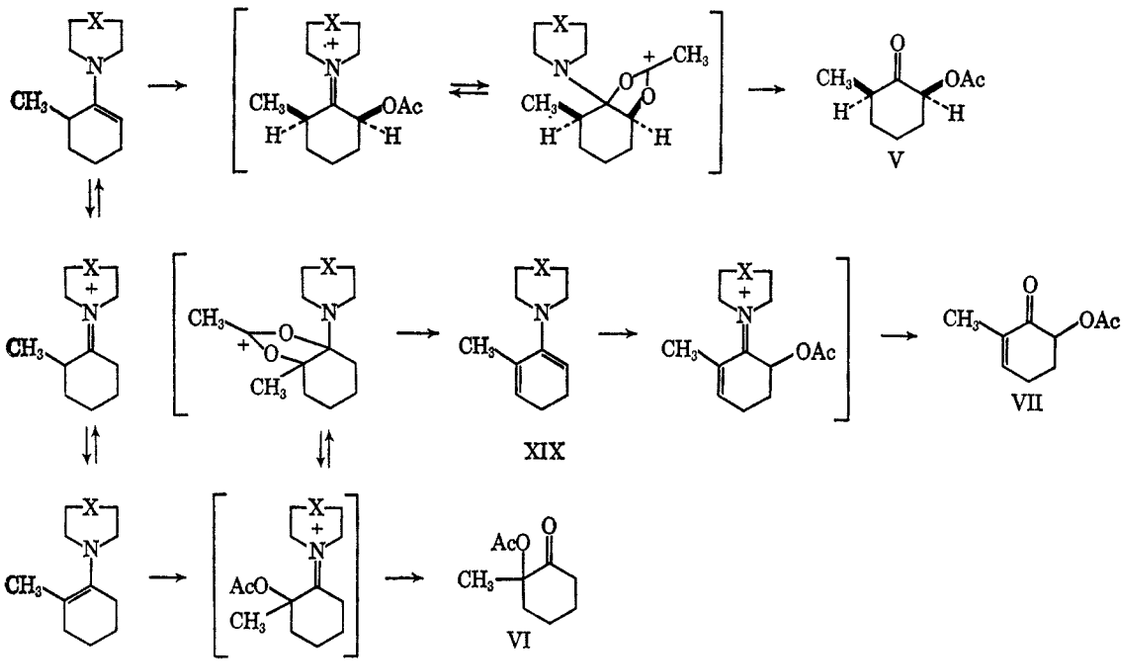


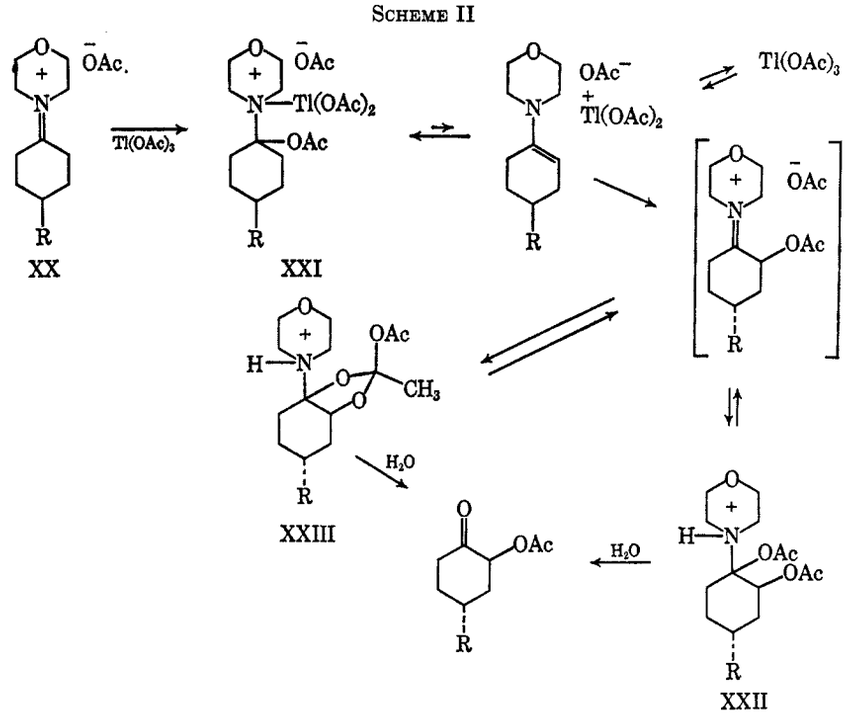
Figure 1.—Oxidation (++++++) of 4-*t*-butylmorpholinocyclohexene followed by proton nmr analysis at δ 4.8 (+); oxidation (———) of morpholinocyclohexene followed by titration of Ti^{3+} (△), uv spectroscopy of Ti^{3+} at 245 mμ (○), and vpc of ketone and acetoxy ketone (●).

A signal at δ 3.4 grew at a slower rate to a final maximum of two proton equivalents. No imonium salt became evident. The protons at δ 4.8 and 3.4 were found to be nonexchangeable in deuterioacetic acid. Thus the diacetate XXII and the 2-acetoxy-2-methyl-1,3-dioxolane XXIII were postulated as concurrent products, with the methyl group of the dioxolane responsible for the signal at δ 3.4 (see Scheme II).

SCHEME I



SCHEME II



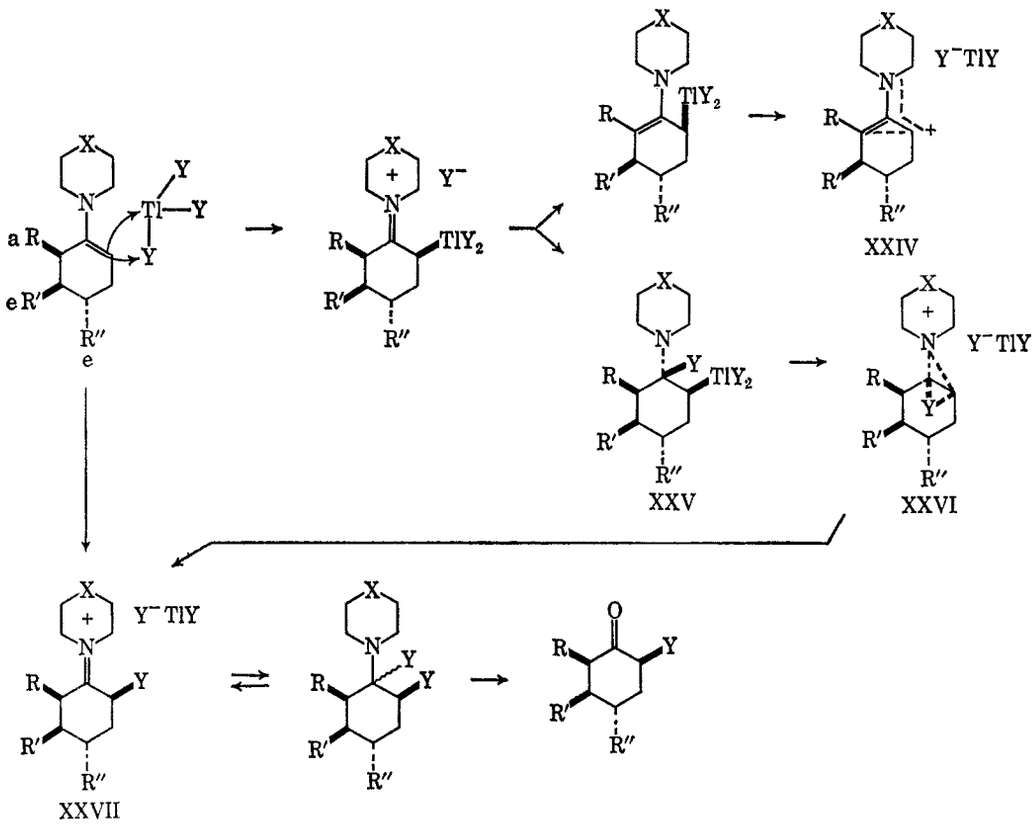
The addition of thallic acetate to morpholinocyclohexene in chloroform led to the immediate formation of an imonium salt and no ammonium complex was seen. This result could be ascribed to the reaction of some acetic acid, introduced with the thallic acetate, and a less favorable ionization of thallic acetate and consequent small tendency for complex formation. It could also be due to a difference in reaction mechanisms for the oxidation in chloroform compared with that in acetic acid.

Discussion

In acetic acid, the imonium salt XX of morpholinocyclohexene is converted instantaneously by thallic acetate into the O-acylcarbinolamine complex XXI, which then slowly undergoes oxidation through an initial dissociation to free enamine and thallic cation. The rate of oxidation is decreased on adding acetate or chloride ions because of a diminishing concentration of thallic ion. Excess thallic acetate retards the reaction because more enamine is trapped as the complex XXI. *Thus the use of equivalent amounts of the reaction components is demanded in practical applications of this oxidation.*

The critical generation of free enamine from an O-acylcarbinolamine complex is also reflected in the relative rates of oxidation of compounds in Table I. Thus, the morpholine enamine derivatives of cyclo-

SCHEME III



R = H, CH_3
R′,R″ = H, *t*-butyl, $-CH_2{\sim\sim}CH_2-$

hexanone and cyclopentanone were oxidized at comparable rates, while the cycloheptanone and heptanone derivatives, which were generated very slowly from the parent ketones,[15] also reacted very slowly.

For the critical oxidation step, one can postulate the initial formation of a carbon–thallium bond, followed by intramolecular displacement of thallium by a thallium ligand or direct introduction of the ligand. An intermolecular displacement is ruled out by the difference in products obtained with thallic chloride in acetic acid and thallic acetate in acetic acid with added chloride ions. A displacement reaction must, furthermore, proceed with retention of configuration in order to account for the specific formation of axial acetoxycyclohexanones and the α-acetoxy products obtained from enamine derivatives of 3-keto steroids. In addition, the intermediate carbon–thallium species would have to have exceptional reactivity, since no characteristic carbon–thallium intermediate became evident in nmr spectra[16] taken during the course of the reaction. In contrast, α-diacetoxythallium-β-methoxy-β-phenylethane[17] was relatively stable in acetic acid. The compound could be recovered unchanged from an acetic acid solution after 2 hr.

An allylic cation XXIV, which reacts with a proximate thallium ligand ion, would satisfy the given displacement requirements. It could account for the preferred reaction of the α-methylcyclohexanone-derived enamines at the substituted carbon and the 1:1 ratio of 2α- and 4α-acetoxy steroid products. However, it would not be consistent with the formation of *cis*-2-acetoxy-6-methylcyclohexanone (V), the formation of 4α- and 1β-acetoxy-10-methyl-2-decalones (XVI and XVII), or the reaction of an aldehyde-derived enamine.[18,19]

Thus the authors suggest that, if a carbon–thallium intermediate is formed, then the reaction proceeds by addition of thallium to the β carbon and by one of its ligands to the α carbon of the enamine. This is followed by rapid intramolecular displacement of thallium by the neighboring nitrogen in XXV–XXVI and subsequent rearrangement to an α-substituted imonium salt XXVII. The same stage would be reached more directly by nucleophilic abstraction of a thallium ligand by the enamine. In either mechanism, the oxidation products of α-methylcyclohexanone, 3-keto steroid, and *trans*-10-methyl-2-decalone could be accommodated by an allylic rearrangement (or displacement) of subsequent acetoxyenamines. Alternatively, it is possible that the isomeric product formation is governed by the relative reactivities of the enamine double-bond iso-

(15) G. Stork, A. Brizzolara, H. Landesman, J. Szmuskovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

(16) For nmr spectra of organothallium compounds see, for instance, F. Anet, *Tetrahedron Lett.*, 3399 (1964).

(17) H. J. Kabbe, *Ann. Chem.*, **656**, 204 (1962).

(18) Also, Favorskii-type products might be expected from a cyclopropyl imonium salt,[11,19] but were not isolated.

(19) J. Szmuszkovics, E. Cerda, M. F. Grostic, and J. F. Zieserl, Jr., *Tetrahedron Lett.*, 3969 (1967).

mers, rather than their kinetically or thermodynamically determined ratio.[20-24] (See Scheme III.)

Experimental Section

General.—Petroleum ether refers to the petroleum distillate boiling between 30 and 60°. Chloroform was dried by distillation from phosphorus pentoxide. Acetic acid was dried by distilling from boron triacetyl. Melting points are corrected. Combustion analyses were provided by Mr. George I. Robinson of Florham Park, N. J.

Thallium Triacetate.—Thallic oxide, 26.7 g (City Chemical), was mixed with 150 ml of glacial acetic acid and heated to 70° for 1 hr. The dark brown solution was filtered through a sintered-glass funnel of medium porosity. Portions of hot acetic acid (25 ml) were poured on the thallic oxide which remained in the funnel, and the mixture was stirred for several minutes before the acetic acid solution was drawn into the filter flask by reduced pressure. This was repeated five times. One liter of ether was added to the filtrate (275 ml), and the white, crystalline thallium triacetate was filtered and dried in a vacuum desiccator with phosphorus pentoxide for 18 hr. The yield of thallium triacetate was 28.3 g.

The thallium triacetate was standardized by dissolution of 200–500 mg in 25 ml of 50% aqueous acetic acid, addition of 5 ml of saturated potassium iodide solution, and several milliliters of starch solution and titration with standardized (0.04 *N*) sodium thiosulfate solution.[25] A brilliant yellow thallium(I) iodide, which did not show a color change by the addition of more thiosulfate solution, was taken as the end point for this titration. The thallium triacetate prepared by the above procedure and standardized in this manner was usually 70–80% pure with respect to thallium(III).

The thallium triacetate could be stored for long periods if kept in a well-sealed desiccator and away from light.

Thallium Triacetate Oxidation of Morpholinocyclohexene. 2-Acetoxycyclohexanone (I).—Thallium triacetate, 3.81 g (10 mmol), was added to a solution of freshly distilled cyclohexanone morpholine enamine,[15] 1.7 ml (10 mmol) in 75 ml of dry acetic acid. The reaction mixture was stirred for 2 days at room temperature under an atmosphere of nitrogen and most of the acetic acid removed *in vacuo* with gentle heating. After addition of 20 ml of water, the mixture was extracted with five 50-ml portions of ether. The combined ether extracts were washed with a saturated solution of sodium bicarbonate and with 10% hydrochloric acid, dried over sodium sulfate, and concentrated under vacuum. Alternatively, 200 ml of dichloromethane was added to the acetic acid concentrate, the solution cooled in ice and cold, and concentrated sodium hydroxide added until the aqueous layer was strongly basic. Enough magnesium sulfate was then added to absorb the water. The reaction mixture was filtered, the magnesium sulfate washed with fresh dichloromethane, the volume concentrated, and the product distilled at 130° (bath temperature) (0.2 mm) yielding 0.973 g of 2-acetoxycyclohexanone (62.3% yield). The product was analyzed as its 2,4-dinitrophenylhydrazone derivative, mp 171–172°.

Anal. Calcd for $C_{14}H_{16}O_6N_4$: C, 49.99; H, 4.80; N, 16.67. Found: C, 49.81; H, 4.80; N, 16.61.

Various Reaction Conditions.—The reaction was conducted as above except for substituting the following solvents and product yields: dichloromethane, 19.2%; dimethyl sulfoxide, 3.1%; hexamethylphosphoric triamide, 48%; dimethoxyethane, 14.3%; chloroform, 70%. When the reaction was allowed to stir for 11 days with dry acetic acid as the solvent, the yield of 2-acetoxycyclohexanone was 73.3%. In dry acetic acid at 75° for 1 hr, the yield was 62%. When the reaction was conducted in dry acetic acid saturated with anhydrous sodium acetate, the yield of 2-acetoxycyclohexanone was 56%.

Thallium Triacetate Oxidation of Morpholinocyclohexene Generated *in Situ*. 2-Acetoxycyclohexanone (I).—A solution of 0.985 g (10 mmol) of cyclohexanone, 5 drops of morpholine, 1 drop of glacial acetic acid, 100 ml of chloroform, and 7.37 g (15 mmol, 77.7% pure) of thallium triacetate was placed under a nitrogen atmosphere and stirred for 41 hr. On addition of thallium triacetate the reaction immediately turned black-brown, but returned to light amber when the reaction was terminated. The reaction was filtered, and the thallium salts were washed with chloroform. All chloroform washings were combined and extracted with half-saturated sodium sulfate solution that contained enough concentrated sulfuric acid (6 drops) to make the aqueous phase strongly acidic. The chloroform was removed by distillation at atmospheric pressure and the remainder distilled *in vacuo*, at 130° (bath temperature) (0.2 mm), to yield 1.69 g of distillate which was collected in a Dry Ice trap. Vapor phase chromatography (vpc) (column, 20% SE 30 on 60–80 mesh Chrom W, 10 ft × 0.375 in.) indicated that the distillate contained 1.238 g of 2-acetoxycyclohexanone (77% yield). When the distillate was triturated with ether–petroleum ether and placed in a Dry Ice bath, 710 mg of crystalline 2-acetoxycyclohexanone was obtained.

Thallium(III) Chloride Oxidation of Morpholinocyclohexene in Acetic Acid. 2-Chlorocyclohexanone, 2-Acetoxycyclohexanone.—A solution of 1.56 g (9.50 mmol) of morpholinocyclohexene[15] and 150 ml of dry acetic acid was placed under a nitrogen atmosphere. Thallium(III) chloride, 2.91 g (9.35 mmol) (City Chemical), was added to the solution under a positive pressure of nitrogen, and this solution was allowed to stir for 4 days. Though the oxidizing power of the solution had not been entirely consumed (starch–potassium iodide indicator paper), the reaction was halted by removal of the acetic acid *in vacuo* and stirring the residue with 10 ml of water for 3 hr. The aqueous mixture was extracted with ether. The combined ether extracts were dried over anhydrous sodium sulfate, and the volume was reduced *in vacuo*. The residue, 1.28 g, consisted of cyclohexanone (46%), 2-chlorocyclohexanone (42.3%), and 2-acetoxycyclohexanone (11.6%). The components of the mixture were established by enriching a portion of the mixture with authentic samples and examining the enriched mixture by vpc (column, 20% SE 30 on 60–80 mesh Chrom W, 10 ft × 0.375 in.).

The same reaction was repeated and aliquots were withdrawn periodically over 48 hr. The aliquots were examined by vapor phase chromatography. The initial product was 2-chlorocyclohexanone with the concentration of the 2-acetoxycyclohexanone increasing with time.

Thallium Triacetate Oxidation of Morpholinocyclohexene in Acetic Acid Saturated with Lithium Chloride. 2-Acetoxycyclohexanone (I).—A solution of 1.61 g (9.7 mmol) of morpholinocyclohexene,[15] 4.62 g (0.0097 mol, 79.8% pure) of thallium triacetate, 12.3 g (290 mmol) of lithium chloride, and 150 ml of dry acetic acid were placed under an atmosphere of nitrogen and stirred for 10 days. Though the reaction was tremendously retarded by the addition of the chloride ion (after 10 days it was still positive to potassium iodide–starch indicator paper), the reaction was worked up as in the preceding section and the resultant analyzed by vpc (column, 20% SE 30 on 60–80 mesh Chrom W, 10 ft × 0.375 in.). The major component of the solution was cyclohexanone (identified by enrichment) and a small amount of 2-acetoxycyclohexanone (identified by enrichment), but no 2-chlorocyclohexanone could be detected even when the amount of material injected into the chromatograph was increased tremendously.

Thallium Triacetate Oxidation of Morpholinocyclopentene in Acetic Acid. 2-Acetoxycyclopentanone (II).—Morpholinocyclopentene,[15] 1.53 g (10 mmol) dissolved in 200 ml of dry acetic acid, was oxidized according to the procedure for morpholinocyclohexene, the product was distilled at 100° (bath temperature) (0.06 mm), and 0.659 g (46%) of 2-acetoxycyclopentanone was col-

(20) Under equilibrating conditions, the morpholine enamine of 2-methylcyclohexanone has been shown to consist of a 52:48 mixture of unsubstituted to substituted double-bond isomers.[21] With the pyrrolidine enamines the unsubstituted isomer is favored 90:10. One can also expect the less-substituted enamines to be the favored kinetic products if their generation hinges on the transfer of an α proton from an imonium salt to the solvent. This would certainly be so in acetic acid. An axial proton, which is stereoelectronically favored for abstraction, is only available on an unsubstituted α position in the imonium salt since a methyl substituent is forced into an axial orientation by steric interaction with a methylene group of the enamine heterocycle.[22] While the equilibrium mixture of pyrrolidine enamines of 2-methylcyclohexanone has been found to give only 2,6-dimethylcyclohexanone on methylation, a 1:1 mixture of 2,2- and 2,6-substituted ketones was formed on reaction with methyl acrylate.[23] With cyanogen chloride 2-cyano-6-methylcyclohexanone was formed as the major product.[24]

(21) W. D. Gurowitz and M. A. Joseph, *J. Org. Chem.*, **32**, 3289 (1967).

(22) W. R. W. Williamson, *Tetrahedron*, **3**, 314 (1958).

(23) H. O. House and M. Schellenbaum, *J. Org. Chem.*, **28**, 34 (1963).

(24) M. E. Kuehne, *J. Amer. Chem. Soc.*, **81**, 5400 (1959).

(25) I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," 3rd ed, The Macmillan Co., New York, N. Y., 1952, pp 589, 592.

lected. The identity of the product was confirmed by its semicarbazone: ir 1740 cm^{-1} (ester); mp 195–196° (lit.[26] mp 192°).

Thallium Triacetate Oxidation of Morpholinocyclopentene in Chloroform. 2-Acetoxycyclopentanone (II).—A solution of 1.005 g (6.57 mmol) of freshly distilled morpholinocyclopentene[15] and 3.55 g (6.57 mmol, 70.5% pure) of thallium triacetate in 25 ml of dry chloroform was placed under an atmosphere of nitrogen and stirred overnight. The mixture was filtered, and the thallium salts were washed with chloroform. The chloroform washings were combined (60 ml) and washed with 20 ml of half-saturated sodium sulfate solution containing 1 ml of concentrated sulfuric acid. The chloroform was distilled *in vacuo*, bp 85° (0.07 mm). The distillate, 1.100 g, was shown by vpc to contain 0.755 g of 2-acetoxycyclopentanone (81%).

Thallium Triacetate Oxidation of Morpholinocycloheptene in Acetic Acid. 2-Acetoxycycloheptanone (III).—Morpholinocycloheptene,[15] 1.41 g (7.8 mmol), in 60 ml of anhydrous acetic acid was oxidized with 1 equiv of thallic acetate for 12 days at 44°, when the reaction mixture gave a negative potassium iodide–starch test. It was worked up as in the case of morpholinocyclohexene and distilled at 100° (bath temperature) (0.2 mm) to yield 1.53 g of distillate. The distillate was extracted with 10% hydrochloric acid and redistilled to give 1.03 g of distillate which was shown by vpc to contain 0.79 g (54.4%) of 2-acetoxycycloheptanone. The 2,4-dinitrophenylhydrazone of 2-acetoxycycloheptanone melted at 116–117° (from ethanol).

Anal. Calcd for $C_{15}H_{18}N_4O_6$: C, 51.42; H, 5.18; N, 15.99. Found: C, 51.71; H, 5.14; N, 16.22.

Thallium Triacetate Oxidation of 4-Morpholino-4-heptene in Acetic Acid. 3-Acetoxy-4-heptanone (IV).—A solution of 1.57 g (8.6 mmol) of the 4-heptanone morpholine enamine[15] and 4.33 g (8.6 mmol, 75.7% pure) of thallium triacetate in 60 ml of dry acetic acid gave a positive potassium iodide–starch test after 30 days at 43°, but no test after a further 3 days at 85°. The reaction mixture was worked up as above and the crude product distilled at 85° (bath temperature) (0.1 mm) to give 0.830 g of distillate. Vpc (column, 29% SE 30 on 60–80 mesh Chrom W, 10 ft × 0.375 in.) indicated that the distillate contained 0.827 g (55.8%) of 3-acetoxy-4-heptanone: ir 1730 and 1745 cm^{-1} (acetoxy ketone); nmr δ 4.85 [1 H, t, J = 6 Hz, –CHCO(OAc)–], 2.08 (3 H, s, $-COCH_3$).

Thallium Triacetate Oxidation of 2-Methylcyclohexanone Morpholine Enamine in Acetic Acid. 2-Methyl-2-acetoxycyclohexanone (VI), *cis*-2-Acetoxy-6-methylcyclohexanone (V), 2-Methyl-6-acetoxycyclohex-2-enone (VII).—A solution of 2-methylcyclohexanone morpholine enamine,[15,21] 1.483 g (8.2 mmol) [which was shown in its infrared and nuclear magnetic resonance spectra to exist as a mixture composed of 6-methyl-1-morpholinocyclohexene (60%) and 2-methyl-1-morpholinocyclohexene (40%)], and 3.91 g (8.3 mmol, 79.8% pure) of thallium triacetate in 150 ml of dry acetic acid was placed under a nitrogen atmosphere, and stirred for 26 days at room temperature and for 4 days at 40° ± 0.5°. The acetic acid was then removed from the reaction *in vacuo;* the residue was dissolved in 200 ml of dichloromethane and extracted with an aqueous solution of sodium bicarbonate until the aqueous phase was neutral to litmus paper. The dichloromethane solution was washed with 20 ml of 10% hydrochloric acid, dried with anhydrous sodium sulfate, concentrated *in vacuo*, and placed on a Florisil column (1.5 cm × 16 cm). The column was eluted with 10% benzene in ligroin (bp 60–90°), benzene, and, finally, dichloromethane. The benzene eluates (which contained the acetoxy compounds as determined by their infrared spectra) were separated into three components by preparative vpc (column, 20% SE 30 on 60–80 mesh Chrom W, 10 ft × 0.375 in., column temperature 130°, carrier gas, He, 40 psi). The fractions were collected by bubbling the carrier gas through carbon tetrachloride. The three components (listed in order of elution) were identified by their ir, uv, nmr, and mass spectra. (1) 2-Methyl-2-acetoxycyclohexanone had ir 1745 and 1730 cm^{-1} (acetoxy ketone); nmr δ 1.25 (3 H, s, methyl group at C-2); mass spectrum parent peak at m/e 170. (2) *cis*-2-Acetoxy-6-methylcyclohexanone had ir 1750 and 1735 cm^{-1} (acetoxy ketone); nmr δ 1.06 (3H, d, J = 6 Hz, methyl group on C-6), 5.0 (1 H, q, width at half-height 18 Hz and spacing between the lines 6 Hz, –COCHOAc–); mass spectrum parent peak, m/e 170; mp 50–52° (from petroleum ether). The nmr spectrum of this compound taken in dry benzene with tetramethylsilane as an internal standard showed a doublet (J = 6 Hz) for the methyl group on C-6. (3) 2-Methyl-6-acetoxycyclohex-2-enone had ir 1755 and 1695 cm^{-1} (acetoxy group, unsaturated ketone); uv λ_{max} 246 mμ (ethanol); nmr δ 1.73 (3 H, d, J = 2 Hz, methyl group on C_2), 5.17 (1 H, q with a spacing between the lines of 7–5–7 Hz), 6.58 (1 H, unresolved multiplet, vinyl proton); mass spectrum parent peak, m/e 168. The relative percentages of products 1, 2, and 3 were 50, 15, and 35%, respectively.

The 2-methyl-6-acetoxycyclohex-2-enone was shown to be a true reaction product and not an artifact of isolation. An aliquot withdrawn from the reaction, hydrolyzed with water, concentrated *in vacuo* at room temperature, and triturated with 95% ethanol showed the same ultraviolet maximum at 246 mμ.

Thallium Triacetate Oxidation of 2-Methylcyclohexanone Morpholine Enamine in Chloroform. *cis*-2-Acetoxy-6-methylcyclohexanone (V), 2-Acetoxy-2-methylcyclohexanone (VI).—A solution of freshly distilled [bp 112° (5.5 mm)] 2-methylcyclohexanone morpholine enamine, 1.783 g (9.85 mmol), and 5.14 g (9.85 mmol, 73% pure) of thallium triacetate in 125 ml of dry chloroform was placed under an atmosphere of nitrogen and stirred for 13 days at room temperature and for 6 days at 40°. The reaction was filtered; the thallium salts were washed thoroughly with chloroform. The filtrates were combined and washed with 30 ml of half-saturated sodium sulfate solution containing 10 drops of concentrated sulfuric acid; the aqueous portion was extracted with chloroform. Concentration and separation into two components by preparative vpc (column, 20% SE 30 on 60–80 mesh Chrom W, 10 ft × 0.375 in.) gave two components, which were identified as *cis*-2-acetoxy-6-methylcyclohexanone (40%) and 2-acetoxy-2-methylcyclohexanone (60%) by comparison with the compounds isolated from the reaction in acetic acid (*vide supra*).

Thallium Triacetate Oxidation of 2-Methylcyclohexanone Pyrrolidine Enamine in Chloroform. *cis*-2-Acetoxy-6-methylcyclohexanone (V), 2-Acetoxy-2-methylcyclohexanone (VI).—A mixture of 2-methylcyclohexanone pyrrolidine enamine,[15,21] 1.53 g (9.3 mmol), 60 ml of dry chloroform, and 4.58 g (9.3 mmol, 77% pure) of thallium triacetate, under nitrogen at 42°, became negative to potassium iodide–starch indicator paper after 3 days. The crude product mixture was isolated as above and distilled at 130° (bath temperature) (0.2 mm), to yield 1.0 g of distillate which was shown by vpc to contain 0.93 g of acetoxy products (59% yield). *cis*-2-Acetoxy-6-methylcyclohexanone (46.5%) and 2-acetoxy-2-methylcyclohexanone (53.5%) were separated by preparative vpc.

4-*t*-Butylmorpholinocyclohexene.—A solution of 20.5 g (0.132 mol) of 4-*t*-butylcyclohexanone (Aldrich), 35 ml (0.40 mol) of morpholine, and a crystal of *p*-toluenesulfonic acid monohydrate in 75 ml of benzene was refluxed for 18 hr under a nitrogen atmosphere with a water separator. The benzene was distilled at atmospheric pressure and the enamine distilled at 98–99° (0.15 mm), to yield 29.0 g (98%) of 4-*t*-butylcyclohexanone morpholine enamine. The enamine solidified on standing: mp 59–61° (in an evacuated melting point capillary); ir 1655 cm^{-1} (vinylamine).

Thallium Triacetate Oxidation of 4-*t*-Butylmorpholinocyclohexene in Acetic Acid. *trans*-2-Acetoxy-4-*t*-butylcyclohexanone (VIII), *cis*-2-Acetoxy-4-*t*-butylcyclohexanone (IX).—A mixture of 2.25 g (10.1 mmol) of 4-*t*-butylcyclohexanone morpholine enamine and 4.82 g (10.1 mmol, 79.8% pure) of thallium triacetate in 25 ml of acetic acid was stirred overnight (negative to starch–potassium iodide indicator). The acetic acid was removed *in vacuo* and the residual oil triturated with 50 ml of water and extracted five times with 50-ml portions of ether. The ether extracts were combined and washed with a saturated sodium bicarbonate solution until no carbon dioxide was evolved. Dry sodium bicarbonate was added periodically to the aqueous phase during the neutralization process, which took approximately 1 hr. The ethereal layer was washed with 50 ml of 10% hydrochloric acid, dried over sodium sulfate, and concentrated *in vacuo*. Addition of petroleum ether gave 0.75 g (35% yield) of *cis*-2-acetoxy-4-*t*-butylcyclohexanone, which crystallized in a Dry Ice bath. This acetoxy ketone was further purified by sublimation (bath temperature, 100°; pressure, 0.03 mm): mp 64–65°; ir 1748 and 1730 cm^{-1} (acetoxy ketone); nmr δ 5.25 (1 H, q with apparent J = 6 Hz, width at half-height of the quartet 20 Hz, –COCHOAc–).

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.90; H, 9.49. Found: 67.62; H, 9.44.

(26) H. W. Wanzlick, G. Gollmer, and H. Milz, *Chem. Ber.*, **88**, 69 (1955).

The 2,4-dinitrophenylhydrazone of *cis*-2-acetoxy-4-*t*-butylcyclohexanone melted at 174–176° (ethanol): nmr δ 5.38 [1 H, unresolved multiplet, width at half-height 28 Hz, –CH(OAc)–].

If the initial ether extracts were not neutralized with sodium bicarbonate, but concentrated *in vacuo* and treated with 2,4-dinitrophenylhydrazine reagent, the 2,4-dinitrophenylhydrazone of *trans*-2-acetoxy-4-*t*-butycyclohexanone was obtained: mp 219–220°. The melting point was depressed in a sample mixed with the 2,4-dinitrophenylhydrazone of *cis*-2-acetoxy-4-*t*-butylcyclohexanone. An nmr spectrum was markedly different from that of the *cis* isomer, δ 5.67 [1 H, unresolved multiplet, width at half-height 8 Hz, –CH(OAc)–].

Anal. Calcd for $C_{18}H_{24}N_4O_6$: C, 55.08; H, 6.17; N, 14.28. Found: C, 54.79; H, 6.09; N, 14.02.

If the initial ether extracts were not neutralized with aqueous sodium bicarbonate, but purified by preparative vpc (column, 20% SE 30 on 60–80 mesh Chrom W, 10 ft × 0.375 in., 145°, helium pressure 40 psi), the *trans*-2-acetoxy-4-*t*-butylcyclohexanone was obtained as an oil which failed to crystallize: ir 1750 and 1730 cm^{-1} (acetoxy ketone); nmr δ 4.97 [1 H, multiplet, width at half-height 9 Hz, –CH(OAc)–]; retention time on vpc was 52.5 min in contrast to 67.5 min for *cis*-2-acetoxy-4-*t*-butylcyclohexanone.

Thallium Triacetate Oxidation of 4-*t*-Butylmorpholinocyclohexene in Chloroform. *cis*-2-Acetoxy-4-*t*-butylcyclohexanone (IX).—A mixture of 1.126 g (5.1 mmol) of 4-*t*-butylcyclohexanone morpholine enamine and 2.7 g (5.1 mmol, 72% pure) of thallium triacetate in 50 ml of chloroform was stirred under nitrogen until the reaction mixture was negative to potassium iodide–starch indicator paper (about 48 hr). The reaction mixture was filtered and the filtrate washed with 20 ml of half-saturated sodium sulfate solution containing enough concentrated sulfuric acid to make the aqeuous layer acidic (about 10 drops). The chloroform was then shaken with a saturated solution of sodium bicarbonate for 30 min and dried with sodium sulfate, and the volume was reduced *in vacuo*. The residue was distilled (bath temperature 120°) (6.0 mm), and 0.73 g (67%) of distillate crystallized. It was identical with *cis*-2-acetoxy-4-*t*-butylcyclohexanone (*vide supra*).

Thallium Triacetate Oxidation of 3-*t*-Butylcyclohexanone Morpholine Enamine in Chloroform. *trans*-2-Acetoxy-5-*t*-butylcyclohexanone (XI).—A solution of 1.501 g (7.57 mmol) of 3-*t*-butylcyclohexanone (Aldrich), 4 ml (46 mmol) of morpholine, and a crystal of *p*-toluenesulfonic acid in 50 ml of benzene was refluxed for 18 hr with a water separator under an atmosphere of nitrogen. Periodically, 2–3 ml of benzene was withdrawn. The reaction mixture was concentrated by distillation at atmospheric pressure and *in vacuo* at room temperature. An ir spectrum of the ehamine[27] showed a strong maximum at 1640 cm^{-1} (vinylamine).

The enamine was not purified but dissolved in 75 ml of dry chloroform and thallium triacetate, 5.16 g (9.57 mmol, 72% pure), was added under nitrogen. After 3 days the reaction was extracted as described in the preceding example, and the extracts were concentrated and chromatographed on a Florisil column (3 cm × 15 cm). The column was eluted with 250 ml of petroleum ether followed by 200 ml of 10% ether in petroleum ether. In the latter eluates, 125 mg (6%) of *trans*-2-acetoxy-5-*t*-butylcyclohexanone was obtained: mp 48–50° [after sublimation, bath temperature 90° (0.1 mm)].

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.88; H, 9.50. Found: C, 68.02; H, 9.56.

A mixture of *trans*-2-acetoxy-5-*t*-butylcyclohexanone and *cis*-2-acetoxy-4-*t*-butylcyclohexanone melted below room temperature: ir 1755 and 1735 cm^{-1} (acetoxy ketone); nmr δ 5.02 (1 H, q, apparent spacing of 7–4–7 Hz, –COCHOAc–), 2.05 (3 H, s, $-OCOCH_3$); 2,4-dinitrophenylhydrazone mp 158–159°.

Anal. Calcd for $C_{18}H_{24}N_4O_6$: C, 55.08; H, 6.17; N, 14.28. Found: C, 55.31; H, 6.15; N, 14.35.

Thallium Triacetate Oxidation of 3-*t*-Butylcyclohexanone Morpholine Enamine in Acetic Acid. *cis*-2-Acetoxy-5-*t*-butylcyclohexanone (X), *trans*-2-Acetoxy-5-*t*-butylcyclohexanone (XI).—A mixture of 1.93 g (8.7 mmol) of 3-*t*-butylcyclohexanone morpholine enamine,[27] 150 ml of dry acetic acid, and 4.30 g (8.7 mmol, 77% pure) of thallic acetate was stirred under nitrogen at 42° for 8 days after which time the reaction mixture was negative to potassium iodide–starch indicator. The acetic acid was removed *in vacuo* at 42°; the residue was triturated with ether and filtered. The filtrate (116 ml) was extracted with half-saturated sodium sulfate solution, which contained enough concentrated sulfuric acid (about 6 drops) to keep the aqueous phase acidic. The ethereal solution was dried with sodium sulfate and distilled at 150° (bath temperature) (0.2 mm) to yield 2.05 g of distillate which was collected in a Dry Ice–acetone trap. Vpc (column, 20% SE 30 on 60–80 mesh Chrom W, 10 ft × 0.375 in., 130°, helium pressure 50 psi) indicated that the distillate was composed of 0.613 g of *cis*-2-acetoxy-5-*t*-butylcyclohexanone, 0.273 g of *trans*-2-acetoxy-5-*t*-butylcyclohexanone, and a trace of a compound tentatively identified as 2-acetoxy-3-*t*-butylcyclohexanone. The total yield of acetoxy products was 52.3%. The two major products were purified by preparative vpc (same conditions as above). *trans*-2-Acetoxy-5-*t*-butylcyclohexanone (retention time 65.5 min) was identified by vpc, ir, and nmr comparison with the product of the preceding section. *cis*-2-Acetoxy-5-*t*-butylcyclohexanone (retention time 53.0 min) had ir 1750 and 1735 cm^{-1} (acetoxy ketone); nmr δ 4.88 [1 H, multiplet (unresolved), width at half-height 6 Hz, –CH–(OAc)–]; 2,4-dinitrophenylhydrazone mp 139–142° (ethanol–water).

5α-Cholestan-3-one Morpholine Enamine.—A solution of 1.5104 g (3.92 mmol) of 5α-cholestan-3-one (Steraloids Inc.), 5 ml (57 mmol) of morpholine, and a crystal of *p*-toluenesulfonic acid monohydrate in 50 ml of benzene was refluxed under nitrogen for 24 hr with a water separator. Occasionally several milliliters of the benzene in the water separator were drawn off. The benzene was removed by distillation, and the last traces of benzene and morpholine were removed by a vacuum pump. The ir spectrum showed a strong absorption maximum at 1645 cm^{-1} (vinylamine). This enamine was not purified but used at once for the thallium triacetate oxidation.

Thallium Triacetate Oxidation of 5α-Cholestan-3-one Morpholine Enamine in Chloroform. 2α-Acetoxy-5-α-cholestan-3-one (XII)–4α-Acetoxy-5α-cholestan-3-one (XIII) Complex.—Dry chloroform (75 ml) was distilled into a flask containing 5α-cholestan-3-one morpholine enamine from 1.51 g (3.92 mmol) of cholestanone. This solution was placed under an atmosphere of nitrogen, and 2.075 g (3.92 mmol, 72% pure) of thallium triacetate was added. The reaction was stirred for 18 hr and then filtered. The thallium salts were washed with fresh chloroform and all of the chloroform solutions combined and washed with 10 ml of half-saturated sodium sulfate solution. During this washing, concentrated sulfuric acid was added dropwise to the aqueous phase until it was acidic. The volume was reduced *in vacuo*, and the residue was triturated with methanol to give 1.333 g (76%) which, after several recrystallizations from methanol, had mp 145–147°; $[\alpha]^{24}D$ 27.1 (*c* 1.86, $CHCl_3$); ir 1755 and 1725 cm^{-1} (acetoxy ketone); nmr δ 5.33 (1 H, six-line multiplet, width at half-height 30 Hz, –COCHOAc–). This substance was identical (mixture melting point, ir, nmr, and optical rotation) with the 2α-acetoxy-5α-cholestan-3-one–4α-acetoxy-5α-cholestan-3-one complex prepared from 2α-bromo-5α-cholestan-3-one[28] by reaction with sodium acetate according to the procedure of Fieser and Romero.[14]

Two other work-up procedures were used in this reaction to establish that the complex was a reaction product rather than an artifact of isolation. First, when the reaction was negative to potassium iodide–starch indicator, the chloroform was removed *in vacuo*, acetic acid (25 ml) containing 2 drops of concentrated hydrobromic acid was added, and the mixture was stirred for 30 hr (the conditions used[29] to isomerize 2β-acetoxy-5α-cholestan-3-one to 2α-acetoxy-5α-cholestan-3-one). Isolation again gave the same complex.

Second, the 2,4-dinitrophenylhydrazone was made of the reaction mixture before it was washed with the half-saturated sodium sulfate solution and sulfuric acid. The 2,4-dinitrophenylhydrazone was made of the reaction mixture after this washing procedure. The two 2,4-dinitrophenylhydrazones were identical when examined by thin layer chromatography (Eastman silica sheets eluted with benzene).

Lastly, 2α-acetoxy-5α-cholestan-3-one and 2β-acetoxy-5α-cholestan-3-one were subjected to simulated reaction conditions and were recovered unchanged (*vide infra*).

Bromination of 5α-Cholestan-3-one Morpholine Enamine in Acetic Acid.—To a solution of 1.18 g (2.6 mmol) of the 5α-

(27) G. Descotes and Y. Querou, *C. R. Acad. Sci., Paris, Ser. C*, 1231 (1966).

(28) A. Butenandt and A. Wolff, *Chem. Ber.*, **68**, 2091 (1935).

(29) K. L. Williamson and W. S. Johnson, *J. Org. Chem.*, **26**, 4563 (1961).

cholestan-3-one morpholine enamine in 12 ml of dry acetic acid 0.13 ml (2.6 mmol) of bromine was added under nitrogen. The bromine color was discharged immediately. The reaction was stirred for 30 min, then poured into 50 ml of water, and stirred for several minutes. The product was filtered and dried *in vacuo* to give 1.15 g (96%) of 2α-bromo-5α-cholestan-3-one. After one recrystallization from chloroform–acetic acid, the product did not depress the melting point of an authentic sample of 2α-bromo-5α-cholestan-3-one.[28] Thin layer chromatography of the crude, unrecrystallized product on silica gel (Eastman sheets eluted with benzene) gave only one spot which corresponded to an authentic sample of the bromo compound.

2α- and 2β-Acetoxy-5α-cholestan-3-one Subjected to Simulated Reaction Conditions for the Thallium Triacetate Oxidation of 5α-Cholestan-3-one Morpholine Enamine.—A solution of 53 mg (0.118 mmol) of 2β-acetoxy-5α-cholestan-3-one (synthesized by the thermal rearrangement of the epoxide formed from the *m*-chloroperbenzoic acid oxidation of 3-cholestenol acetate[29]), 2 drops of N-ethylmorpholine, and 30 mg of thallous(I) acetate in 1 ml of chloroform was allowed to stir for several minutes. This solution was then washed with 0.5 ml of half-saturated sodium sulfate solution containing enough concentrated sulfuric acid (2 drops) to make the aqueous layer acidic. The aqueous layer was extracted with chloroform, and the combined chloroform washings were extracted with 0.5 ml of water, dried over sodium sulfate, and filtered. The filtrate was reduced to dryness *in vacuo* and the residue crystallized from ethanol. The recrystallized material was identical in mixture melting point and ir and nmr spectra with 2β-acetoxy-5α-cholestan-3-one.

A solution of 56 mg of 2α-acetoxy-5α-cholestan-3-one (synthesized by the lead tetraacetate oxidation of 5α-cholestan-3-one[30]) was treated as the 2-β-acetoxy compound and similarly recovered unchanged.

Thallium Triacetate Oxidation of 5α-Androstan-3-one Morpholine Enamine in Acetic Acid. 2α,17β-Diacetoxy-5α-androstan-3-one (XIV)–4α,17β-Diacetoxy-5α-androstan-3-one (XV) Complex.—To a solution of 5α-androstan-17-β-ol-3-one morpholine enamine[31] from 5.0 g (17.2 mmol) of 5α-androstan-17-β-ol-3-one, dissolved in 60 ml of dry acetic acid, 6.57 g (17.2 mmol) of thallium triacetate was added under an atmosphere of nitrogen. After stirring for 24 hr at room temperature, the reaction was negative to potassium iodide–starch indicator. Most of the acetic acid was removed *in vacuo* while heating gently on a water bath. Then 200 ml of dichloromethane and 50 ml of water were added, the residual acetic acid was neutralized with sodium bicarbonate, the organic and aqueous layers separated, and the aqueous phase was extracted with dichloromethane. The combined dichloromethane solutions were dried over sodium sulfate, concentrated *in vacuo*, and chromatographed on a Florisil column (3 cm × 30 cm). The acetoxy product, 1.547 g (24.4% based on ketone), was eluted with 10% methanol in dichloromethane and was crystallized from ether–dichloromethane. Difficulty was encountered in trying to purify this product by recrystallization. The nmr spectrum showed two methyl groups adjacent to an ester carbonyl function. It was therefore assumed that the hydroxyl group at C-17 was partially esterified by the acetic acid. A solution of 315 mg (0.856 mmol) of the crude acetoxyandrostanolone in 30 ml of acetyl chloride was allowed to stand at room temperature overnight. The excess acetyl chloride was removed and the 2α,17β-diacetoxy-5α-androstan-3-one–4α,17β-diacetoxy-5α-androstan-3-one complex was recrystallized several times from ligroin: mp 205–206°; ir 1750 and 1730 cm^{-1} (acetoxy ketone and ester); nmr δ 5.25 [1 H, six-line multiplet, width at half-height 32 Hz, superimposable with the splitting pattern for the 2α- and 4α-acetoxycholestanone complex (*vide supra*), –COCHOAc–].

Anal. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.42; H, 8.78.

***trans*-10-Methyldecal-2-one Morpholine Enamine.**—A solution of 17.9 g (0.108 mol) of *trans*-10-methyldecal-2-one,[32,33] 30 ml (0.34 mol) of morpholine, and a crystal of *p*-toluenesulfonic acid monohydrate in 50 ml of benzene was refluxed under an atmosphere of nitrogen with a water separator for 6 hr. The water formed during the reaction was removed from the water separator, and it was then filled with molecular sieve. The reaction was refluxed for an additional 18 hr. The solution was concentrated at atmospheric pressure and distilled *in vacuo*, bp 134–136° (0.3 mm), to give 21.61 g (85.7%) of the enamine. The enamine solidified when placed in a freezer, mp 45–49.5°. The ir spectrum showed a strong absorption maximum for the vinylamine chromophore at 1645 cm^{-1}. The nmr spectrum showed an ill-defined triplet at δ 4.4 (vinyl proton), and a singlet at δ 0.8 corresponding to the hydrogens on the methyl group at C-10. The oxidation of *trans*-10-methyl-decal-2-ol with chromic acid did not result in satisfactory yields of the ketone as described by Gaspert, *et al.*,[33] unless 1 ml of concentrated sulfuric acid was used for each gram of chromic anhydride.

Thallium Triacetate Oxidation of *trans*-5-methyldecal-2-one Morpholine Enamine in Chloroform. 3α-Acetoxy-*trans*-5-methyldecal-2-one (XVI).—Thallium triacetate, 4.76 g (9.0 mmol, 72% pure), was added to 9.0 mmol of the enamine in about 60 ml of dry chloroform under a positive pressure of nitrogen. After stirring for 2 days, the reaction was filtered and the thallium salts were washed with chloroform. The combined chloroform washings were extracted with half-saturated sodium sulfate solution and enough concentrated sulfuric acid so that the aqueous phase remained acidic during the extraction. The chloroform was removed *in vacuo* and the residue distilled at 110–115° (bath temperature) (0.3 mm). The distillate was dissolved in ether and twice extracted with small portions of 10% hydrochloric acid solution (this discharged most of the yellow color from the ether layer). The volume was reduced *in vacuo* and the residue was triturated with methanol. The methanolic solution, when placed in a Dry Ice bath, yielded 200 mg of 3α-acetoxy-*trans*-5-methyldecalone-2: mp 71–72° [after sublimation at 100° (0.4 mm)]; ir 1755 and 1730 cm^{-1} (acetoxy ketone); nmr δ 5.2 (1 H, q with apparent J = 6 Hz, identical with that of 2α-acetoxy-5α-cholestan-3-one,[29] –COCHOAc–), 2.06 (3 H, s, $-OCOCH_3$).

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.75; H, 8.92.

Thallium Triacetate Oxidation of *trans*-10-Methyldecal-2-one Morpholine Enamine in Acetic Acid. 3α-Acetoxy-*trans*-10-methyldecal-2-one (XVI), 1β-Acetoxy-*trans*-10-methyldecal-2-one (XVII).—To a solution of 2.08 g (8.87 mmol) of *trans*-10-methyldecal-2-one morpholine enamine in 50 ml of dry acetic acid, 4.375 g (8.87 mmol, 77% pure) of thallium triacetate was added under a positive pressure of nitrogen. The reaction was stirred at 42° for 18 hr, after which it was negative to potassium iodide–starch indicator. The acetic acid was removed *in vacuo*, and the residual oil was triturated with ether and filtered. The filtrate was washed with 10 ml of half-saturated sodium sulfate solution, which contained 4 drops of concentrated sulfuric acid, and dried over sodium sulfate. It was concentrated *in vacuo* and distilled at 150° (bath temperature) (0.2 mm), to yield 1.494 g which was shown by vpc (column, 20% SE 30 on 60–80 mesh Chrom W, 140°, helium pressure 45 psi) to contain 0.94 g (48% yield) of two acetoxy products (in a ratio of about 3:2). These products were partially separated using these conditions for the vpc and collected by bubbling the carrier gas (helium) through carbon tetrachloride. The second of the two acetoxylated products was identified as 3α-acetoxy-*trans*-10-methyldecal-2-one (*vide supra*). The first acetoxylated product, which did not crystallize, was identified as 1β-acetoxy-*trans*-10-methyldecal-2-one (because of the similarity of its nmr spectrum with that of 4β-acetoxy-5α-cholestan-3-one[29]): nmr δ 4.9 (1 H, unresolved signal, –COCHOAc–); ir 1725 and 1750 cm^{-1} (acetoxy ketone).

The structure of this first acetoxy product, 1β-acetoxy-*trans*-10-methyldecal-2-one, was further substantiated when 150 mg of a mixture of the two acetoxy isomers was dissolved in 1 ml of *t*-butyl alcohol–potassium *t*-butoxide (made by reaction of 22 mg of potassium metal with 1 ml of dry *t*-butyl alcohol). The solution was allowed to stand for 30 min, and the *t*-butyl alcohol was removed *in vacuo*. The residue was triturated with ether, extracted with 10% hydrochloric acid, dried over sodium sulfate, and distilled at 120° (bath temperature) (0.1 mm): nmr δ 5.17 (1 H, six-line multiplet, nearly identical with the 2α-acetoxy-5α-cholestan-3-one–4α-acetoxy-5α-cholestan-3-one complex, *vide supra*); mp 143–148°.

Cyclohexylmethanal Morpholine Enamine.—Cyclohexylmethanal (Baker), 10 g (89.4 mmol), was cooled in an ice bath under an atmosphere of nitrogen. A crystal of *p*-toluenesulfonic acid monohydrate was added, and 25 ml (290 mmol) of morpholine was

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added slowly while the solution was being stirred. The solution was allowed to come to room temperature and stir for 1 hr and was distilled to give 12.95 g (80%) of the enamine: bp 65° (1.5 mm); ir 1640 cm^{-1} (vinylamine).

Thallium Triacetate Oxidation of Cyclohexylmethanal Morpholine Enamine in Dichloromethane–Acetic Acid (1:1). 1-Acetoxycyclohexylmethanal (XVIII).—A solution of 1.325 g (7.33 mmol) of cyclohexylmethanal morpholine enamine was dissolved in 75 ml of dry dichloromethane (from P_2O_5) and 75 ml of dry acetic acid was added. The solution was put under an atmosphere of nitrogen and cooled in an ice bath. Then 3.91 g (7.3 mmol, 71.5% pure) of thallium triacetate was added and the mixture allowed to stir for 13 days. Semicarbazide hydrochloride, 815 mg (7.3 mmol), dissolved in 2 ml of water, was added to the reaction mixture. This was stirred overnight, the solvent removed *in vacuo*, the residue triturated with methanol, and 0.26 g (12%) of 1-acetoxycyclohexylmethanal semicarbazone isolated, when water was added to the methanol solution. This semicarbazone showed strong maxima in the ir at 1730 and 1700 and a shoulder at 1650 cm^{-1} corresponding to the acetoxy and semicarbazone chromophores, respectively. It was recrystallized from methanol–water, mp 191–192°.

Anal. Calcd for $C_{10}H_{17}N_3O_3$: C, 52.85; H, 7.54; N, 18.49. Found: C, 53.11; H, 7.84; N, 18.19.

Thallium Triacetate Oxidation of Morpholinocyclohexene in Acetic Acid Followed Titrimetrically.—A solution of 1.7 ml (0.010 mol) of cyclohexanone morpholine enamine and 100 ml of dry acetic acid was placed under an atmosphere of nitrogen and thallium triacetate, 5.34 g (0.010 mol, 71.5% pure), was added. Periodially 10-ml aliquots were withdrawn under a positive pressure of nitrogen and immediately quenched with 10 ml of water, and 2 ml of saturated potassium iodide solution and 1 ml of starch solution[25] added to the aliquot. The liberated iodine was titrated with 0.41 *N* sodium thiosulfate solution.[25] A blank of 10 ml of water and 2 ml of saturated potassium iodide solution was colorless. Time (min), *t*, volume of $Na_2S_2O_3$, *v*, and % Tl(III) present were found as follows: *t*, 3.25 (*v*, 17.4, 34.7%); *t*, 7.95 (*v*, 15.85, 32.5%); *t*, 12.3 (*v*. 15.05, 30.8%); *t*, 16.73 (*v*, 13.9, 27.5%); *t*, 39.2 (v, 10.9, 22.3%); *t*, 135 (*v*, 2.4, 4.9%).

Thallium Triacetate Oxidation of Morpholinocyclohexene in Acetic Acid Saturated with Sodium Acetate Followed Titrimetrically.—The procedure and amounts of reactants used were identical with those of the previously described experiment except 10.1 g of anhydrous sodium acetate was added to the dry acetic acid: *t*, 0.64 (*v*, 40.3, 82.7%); *t*, 2.58 (*v*, 32.1, 65.8%); *t*, 12.40 (*v*, 25.1, 51.5%); *t*, 16.48 (*v*, 22.1, 45.4%); *t*, 21.68 (*v*, 18.8, 38.4%); *t*, 36.80 (*v*, 13.3, 27.3%).

Thallium Triacetate Oxidation of 2 Equiv of Morpholinocyclohexene in Acetic Acid Followed Titrimetrically.—To a solution of 3.4 ml (0.020 mol) of the cyclohexanone morpholine enamine in 100 ml of dry acetic acid 5.03 g (0.010 mol, 75.7% pure) of thallium triacetate was added under a positive nitrogen pressure. The procedure used was identical with that of the preceding experiments, except that 0.0425 *N* $Na_2S_2O_3$ was used: *t*, 2.2 (*v*, 29.8, 63.4%); *t*, 9.6 (*v*, 21.7, 46.3%); *t*, 197 (*v*, 15.7, 33.4%); *t*, 408 (*v*, 7.0, 14.9%); *t*, 537 (*v*, 3.3, 7.03%); *t*, 660 (*v*, 1.7, 3.62%); *t*, 803 (*v*, 0, 0%).

Thallium Triacetate Oxidation of Morpholinocyclopentene in Acetic Acid Followed Titrimetrically.—The previous procedure was repeated with 1.61 g (0.0105 mol) of morpholinocyclopentene and 5.29 g (0.0105 mol) of thallium triacetate in 100 ml of acetic acid: *t*, 0 (*v*, 0, 100%); *t*, 2.75 (*v*, 50.9, 85%); *t*, 5.25 (*v*, 31.4, 63.7%); *t*, 10 (*v*, 8.3, 16.8%); *t*, 50 (*v*, 6.3, 12.7%); *t*, 97 (*v*, 1.2, 2.43%).

Thallium Triacetate Oxidation of Morpholinocyclohexene Followed by Vpc.—To a mixture of 4.83 g (0.01 mol, 79% pure) of thallium triacetate in 30 ml of dry acetic acid, 1.7 ml (0.01 mol) of cylohexanone morpholine enamine was added under a stream of nitrogen. The entire reaction became homogeneous as soon as the enamine was added. Aliquots, 10 ml, were withdrawn periodically and placed in 50 ml of water. The water was extracted four times with 50-ml portions of ether. The ether extracts were combined and washed with a saturated solution of sodium bicarbonate followed by a washing with 10% hydrochloric acid solution. The ethereal solution was dried over sodium sulfate and the volume concentrated *in vacuo*. Portions of this concentrated solution were injected into a vapor phase chromatograph (column, 20% SE 30 on 60–80 mesh Chrom W, 10 ft × 0.375 in). The ratio *a* of the areas of the peak due to the 2-acetoxycyclohexanone to the area of the peak due to cyclohexanone was established for each aliquot with the time (*t*) in min: *t*, 0 (*a*, 0.0); *t*, 2 (*a*, 0.319); *t*, 6 (*a*, 1.61); *t*, 10 (*a*, 3.89).

Thallium Triacetate Oxidation of Morpholinocyclohexene in Acetic Acid Followed in the Ultraviolet Spectrum at 245 mμ.—To a solution of 2.52 g (5.0 mmol, 75.7% pure) of thallium triacetate in 70 ml of dry acetic acid was added 0.85 g (5.0 mmol) of freshly distilled cyclohexanone morpholine enamine. Aliquots, withdrawn periodically under a positive pressure of nitrogen, were put into 50 ml of 0.5 *M* sodium chloride solution in 10% hydrochloric acid. The absorbance *A* of the samples was measured on a Perkin-Elmer 202 ultraviolet spectrometer at 245 mμ at time intervals *t* given in min. A solution of 50 μl of acetic acid in 50 ml of 0.5 *M* sodium chloride solution in 10% hydrochloric acid was used in the reference cell. The results were *t*, 0 (*A*, 1.49); *t*, 2.5 (*A*, 1.18); *t*, 9 (*A*, 1.04); *t*, 25 (*A*, 0.99); *t*, 62 (*A*, 0.93); *t*, 92 (*A*, 0.90); *t*, 184 (*A*, 0.85); *t*, 1131 (*A*, 0.63).

Thallium Triacetate Oxidation of the 4-*t*-Butylmorpholinocyclohexene in Acetic Acid Followed by Nuclear Magnetic Resonance Spectroscopy.—Of a solution of 3.2404 g (14.5 mmol) of 4-*t*-butylcyclohexanone morpholine enamine in 25 ml of dry acetic acid 5 ml (2.9 mmol) was added to 1.56 g (2.9 mmol, 70.5% pure) of thallium triacetate. A small portion of this solution was quickly transferred to an nmr sample tube and the signal at δ 4.8 (the proton on the carbon bearing the recently introduced acetoxy group) was integrated and is given as a fraction *f* of one proton at various intervals *t*, in min (integration of the signal at δ 3.7 for four of the protons on the morpholine moiety was used as an internal standard): *t*, 3 (*f*, 0.26); *t*, 6 (*f*, 0.32); *t*, 15 (*f*, 0.41); *t*, 24 (*f*, 0.52); *t*, 30 (*f*, 0.68); *t*, 44 (*f*, 0.78); *t*, 52 (*f*, 0.87); *t*, 75 (*f*, 0.88); *t*, 85 (*f*, 0.94).

The nmr spectrum of 4-*t*-butylcyclohexanone morpholine enamine in dry acetic acid showed a large bell-shaped peak for the protons adjacent to the imonium nitrogen at δ 3.75, with a sharp cleft in the center. This spectrum showed no evidence of a vinyl proton even at high amplification. When the thallium triacetate was added to the imonium salt solution, the bell-shaped peak immediately diverged to two multiplets centered at δ 3.70 and 3.10—identical with the nmr spectra of morpholine and N-ethylmorpholine in acetic acid.

After the reaction of the enamine and thallium triacetate was complete (about 90 min), the acetic acid was removed *in vacuo* and deuterioacetic acid (previously distilled from phosphorus pentoxide) was added. The proton on the carbon bearing the recently introduced acetoxy group was again monitored at δ 4.8. This signal continued to integrated for one proton after more than 2 days.

A second 5-ml portion of the enamine solution (2.9 mmol) was added to 3.13 g (5.8 mmol, 70.5% pure) of thallium triacetate. The time was recorded. A small portion of this solution was quickly transferred to an nmr sample tube, and the signal at δ 4.8 (the proton on the carbon bearing the recently introduced acetoxy group) was integrated at various intervals. Not all of the thallium triacetate dissolved; hence the solution did not contain exactly 2 equiv of thallium triacetate. Time (min) and the fraction (*f*) of proton at δ 4.8 were found: *t*, 2 (*f*, 0.0); *t*, 4 (*f*, 0.0); *t*, 13 (*f*, 0.17); *t*, 20 (*f*, 0.28); *t*, 32 (*f*, 0.30); *t*, 74 (*f*, 0.33); *t*, 4560 (76 hr) (*f*, 0.39).

Thallium Triacetate Oxidation of Morpholinocyclopentene in Acetic Acid Quenched after 5-Min Reaction Time.—To a solution of 1.58 g (10.3 mmol) of cyclopentanone morpholine enamine in 50 ml of dry acetic acid was added 5.22 g (10.3 mmol, 75.7% pure) of thallium triacetate under a stream of dry nitrogen. The reaction was stirred for 5 min and poured into an aqueous solution of sodium thiosulfate. This solution was extracted four times with 100-ml portions of ether. The ether was washed with a saturated solution of sodium bicarbonate until carbon dioxide evolution ceased, then washed with 10% hydrochloric acid solution, dried over sodium sulfate, and distilled at 100° (bath temperature, 0.5 mm), to give 0.6 g of distillate which was collected in a Dry Ice–acetone trap. Vpc (column, 5 ft × 0.25 in. Apiezon L on 60–80 mesh Chrom W) indicated that the distillate was composed of 42.3% cyclopentanone and 57.5% 2-acetoxycyclopentanone.

Thallium Triacetate Oxidation of Cyclohexanone in Acetic Acid.—A solution of 0.50 ml (5.0 mmol) of cyclohexanone and 10 ml of dry acetic acid was combined with 1.9 g (5.0 mmol) of thallium triacetate under nitrogen. After stirring for 2 days at room temperature, the reaction mixture was diluted with ether and the precipitated salts were filtered. The filtrate was concen-

trated *in vacuo* and distilled at 80° (bath temperature) (0.2 mm). The distillate, 0.442 g, was collected in a Dry Ice trap. Vapor phase chromatographic analysis of the distillate showed it to be a mixture of which 10% was 2-acetoxycyclohexanone (6.2% yield). Repeating the reaction except for substitution of 2 hr at reflux for the 2 days at room temperature gave a 20.5% yield (lit.[17] 25%).

Registry No.—Thallium triacetate, 2570-63-0; I dinitrophenylhydrazone, 16963-08-9; III dinitrophenylhydrazone, 16963-09-0; IV, 2983-04-2; V, 16963-11-4; VI, 16963-12-5; VII, 16963-13-6; VIII, 16963-14-7; VIII dinitrophenylhydrazone, 16976-43-5; IX, 16963-15-8; IX dinitrophenylhydrazone, 16963-16-9; X, 16963-17-0; X dinitrophenylhydrazone, 16963-18-1; XI, 16963-19-2; XI dinitrophenylhydrazone, 16963-20-5; XII, 14161-45-6; XIII, 16963-22-7; XIV, 14026-24-5; XV, 16963-24-9; XVI, 16963-25-0; XVII, 16963-26-1; XVIII, 16963-27-2; 4-*t*-butylcyclohexanone morpholine enamine, 16963-28-3; cyclohexylmethanol morpholine, enamine, 16963-29-4.

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Pyrolytic Ring Contraction of 2-Acetoxy-2-methylcyclohexane-1,3-diones[1]

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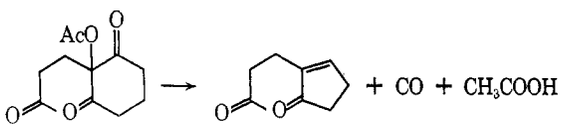
The pyrolytic ring contraction of 2-acetoxy-2-alkylcyclohexane-1,3-diones to 2-alkyl-Δ^2-cyclopentenones, previously observed only in the case of 2-acetoxy-2-(3-oxobutyl)cyclohexane-1,3-dione (**1**), has been shown to be a general reaction which proceeds in high yields (60–80%) at temperatures as low as 220°. Acetoxydiones **3** and **4** were prepared in low yield by the reaction of the corresponding 2-methylcyclohexane-1,3-diones with lead tetraacetate. 2-Acetoxy-2-methylcyclopentanone (**5**) was also prepared and was found to pyrolyze to 2-methyl-Δ^2-cyclopentenone under the same conditions as **3**. In ancillary experiments, 2,2-dimethylcycloalkane-1,3-diones **16**, **17**, and **18** were stable at 350°, and 2-acetoxy-2-methylindan-1,3-dione (**19**) evolved only acetic acid at 300–320°.

The remarkably efficient thermal ring contraction observed[3] when 2-acetoxy-2-(3-oxobutyl)cyclohexane-1,3-dione (**1**) was pyrolyzed at 350° to afford 2-(3-oxobutyl)-Δ^2-cyclopentenone (**2**) in 70% yield led us



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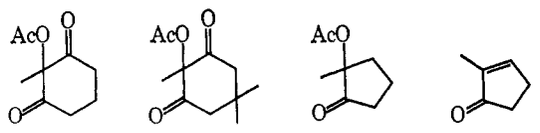
to investigate the generality and potential usefulness of this reaction. In this paper the preparation and pyrolytic behavior of two 2-acetoxy-2-alkylcyclohexane-1,3-diones (**3** and **4**) are described. These substances undergo an analogous loss of carbon monoxide and acetic acid to afford cyclopentenones in good yield at temperatures as low as 220°. The preparation and pyrolysis of 2-acetoxy-2-methylcyclopentanone (**5**),



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(1) Portions of this work were presented in the symposium on "The Chemistry of Tall Oil and Turpentine" at the 153rd National Meeting of the American Chemical Society in Miami Beach, Fla., April 1967.

(2) (a) Alfred P. Sloan Foundation Research Fellow. (b) Goodyear Foundation Fellow, 1965–1966.

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an intermediate in one of the possible pathways (discussed below) for the conversion of **3** into 2-methyl-Δ^2-cyclopentenone (**6**), are also described.

Preparation of Compounds 3, 4, and 5 for Pyrolysis.—Synthesis of the simplest suitably substituted cyclohexane-1,3-dione, the 2-acetoxy-2-methyl derivative **3**, was first attempted by methylation of 2-acetoxycyclohexane-1,3-dione (**7**).[4] Treatment of **7** in benzene with sodium hydride followed by methyl iodide afforded only a small and variable yield (maximum, 21%) of the desired **3**, mp 103–104°. Accordingly, attention was turned to introduction of the acetoxyl group into the more readily available starting material, 2-methylcyclohexane-1,3-dione (**8**).

Acetoxylation of carbonyl compounds by their reaction with lead tetraacetate has been accomplished in a variety of systems,[5] including β diketones.[6] When **8** was treated with lead tetraacetate in benzene at room temperature for 2 hr, **3** was indeed obtained, but again in a disappointing yield (16%). The predominant product, mp 145–146°, isolated in 27% yield, was assigned structure **9**, mainly on the basis of its elemental analysis and spectral properties, which included ultraviolet absorption consistent with an enol ether of a 1,3-dione and no nmr peaks other than those ascribable to the two methyl groups and the methylene groups of **9**. Mild treatment of the 145–146° substance with aqueous acid afforded **8**, consonant with its structural assignment as **9**.

Compound **9** presumably arises from an unsymmetrical coupling of radical **10**. Symmetrical carbon-

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