mixture, was collected by filtration and washed with ether to give 9.5 g (63% yield) of a light yellow solid, mp 244–246°. Recrystallization from $CHCl_3$–MeOH yielded 8.5 g of analytically pure white crystals: mp 249–250°; ir (Nujol) 3190 (NH), 1695 cm^{-1} (C=O, γ-lactam); uv (EtOH) λ_{max} 230 nm (log ε 4.00), 285 (3.76); nmr ($CDCl_3$–TMS) δ 7.24 (5 P, s, Ar H), 6.66 (1 P, s, Ar H), 6.52 (1 P, s, Ar H), 6.11 (1 P, NH), 3.86 (3 P, s, Ar OCH_3), 3.82 (3 P, s, Ar OCH_3), 3.80–2.00 (7 P, m, methine and methylene hydrogens); mass spectrum *m/e* 324 (M^+ + 1, 20.3%), 323 (M^+, 81.3%), 279 (24.2%), 266 (20.3%), 232 (46.0%), 193 (34.0%), 192 (24.2%), 189 (25.0%), 176 (34.4%), 161 (40.5%), 131 (81.3%).

Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.36; H, 6.34; N, 4.42.

7,8-Dimethoxy-4-(3,4,5-trimethoxyphenyl)-3a,4,5,9b-tetrahydrobenz[*e*]isoindolin-3-one (IVb, R = CH_3).—A solution of 4.25 g of IIIb in 250 ml of toluene was heated at 210–225° for 48 hr. The product was collected in a similar manner as described for IVa (R = CH_3) and dried at 120° *in vacuo* to give 2.19 g of white crystals, mp 223–225°. An analytical sample was prepared by recrystallization from toluene: mp 225–227°; ir (Nujol) 3220, 1695, 1590, 1130 cm^{-1}; uv (EtOH) λ_{max} 282 nm (log ε 3.83); mass spectrum *m/e* 413 (M^+).

Anal. Calcd for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.58; N, 3.39. Found: C, 66.79; H, 6.45; N, 3.31.

7,8-Dimethoxy-4-phenyl-3a,4,5,9b-tetrahydrobenz[*e*]isoindoline Hydrochloride (I HCl, R = CH_3; R′ = H; R″ = H).—A boiling solution of 8.1 g of IVa (R = CH_3) in 350 ml of dry benzene was rapidly cooled and the resulting fine suspension was treated with 25 ml of Red-Al. The mixture was refluxed for 2.5 hr, cooled, and to it was cautiously added 200 g of 10% aqueous NaOH. The separated aqueous layer was extracted with 100 ml of benzene. The combined benzene extracts were washed with saturated aqueous NaCl solution, filtered, and distilled to remove most of the benzene. Anhydrous Et_2O (100 ml) was added. The mixture was stirred in an ice bath while 8 g of 21% ethanolic HCl in 100 ml of anhydrous Et_2O was added dropwise. The solid was collected by filtration, washed with Et_2O and dried to give 7.7 g (89% yield) of white powder. An analytical sample was obtained by precipitation from a methanolic solution with Et_2O: mp 285° dec; ir (Nujol) ν_{max} 2700, 2400 cm^{-1}; nmr ($CDCl_3$–TMS) δ 7.24 (5 P, s, Ar H), 6.62 (1 P, s, Ar H), 6.46 (1 P, s, Ar H), 3.83 (6 P, s, Ar OCH_3), 3.80–2.00 (9 P, m).

Anal. Calcd for $C_{20}H_{23}NO_2 \cdot HCl$: C, 69.45; H, 6.99; N, 4.05. Found: C, 69.28; H, 7.06; N, 3.83.

7,8-Dimethoxy-4-(3,4,5-trimethoxyphenyl)-3a,4,5,9b-tetrahydrobenz[*e*]isoindoline Hydrochloride (I HCl, R = CH_3; R′ = H; R″ = OCH_3).—This compound was prepared in a similar manner from 2.06 g of IVb and 170 ml of benzene. The product, 2.02 g (93% yield), was collected as a white powder, mp 261–262°. An analytical sample was prepared by precipitation from a methanolic solution with Et_2O: mp 261–262°; ir (Nujol) 3400, 2700, 2400, 1590, 1130 cm^{-1}; uv (EtOH) λ_{max} 282 nm (log ε 3.66); mass spectrum *m/e* 399 (M^+ − HCl).

Anal. Calcd for $C_{23}H_{29}NO_5 \cdot HCl$: C, 63.37; H, 6.94; N, 3.21. Found: C, 63.49; H, 7.05; N, 3.14.

2-Acetyl-7,8-dimethoxy-4-phenyl-3a,4,5,9b-tetrahydrobenz[*e*]-isoindoline (I, R = CH_3; R′ = $COCH_3$; R″ = H).—A mixture of 2.28 of I HCl (R = CH_3; R′ = H, R″ = H), 10 ml of Ac_2O, and 10 ml of pyridine was stirred at room temperature for 16 hr. After the usual work-up the residue was recrystallized from a mixture of EtOAc and heptane to give 1.8 g (78% yield) of product, mp 178–180°. An additional recrystallization from EtOAc yielded an analytically pure sample: mp 181–182°; ir (Nujol) ν_{max} 1630 cm^{-1} (C=O); mass spectrum *m/e* 352 (M^+ + 1, 24.9%), 351 (M^+, 100%), 292 (10.2%), 279 (55.0%), 265 (20.0%).

Anal. Calcd for $C_{22}H_{25}NO_3 \cdot {}^1/_4H_2O$: C, 74.23; H, 7.22; N, 3.94. Found: C, 74.40; H, 7.40; N, 3.96.

7,8-Dimethoxy-2-ethyl-4-phenyl-3a,4,5,9b-tetrahydrobenz[*e*]-isoindoline Hydrochloride (I HCl; R = CH_3; R′ = C_2H_5; R″ = H).—To a solution of 1.70 g of the aforementioned acetamide in 100 ml of dry benzene was added 4 ml of Red-Al. The mixture was refluxed for 1 hr and cooled. To the mixture was cautiously added, with stirring, 100 ml of 10% aqueous NaOH solution. The benzene layer was separated, washed with 100 ml of saturated aqueous NaCl solution, dried (Na_2SO_4), and filtered. The filtrate was evaporated *in vacuo* and the residual syrup diluted with 200 ml of anhydrous Et_2O. To this was added 5 ml of 20% ethanolic HCl and the precipitated white powder was collected by filtration to give 1.69 g (94% yield) of product, mp 278–280°. An analytically pure sample was prepared by dissolving the product in methanol and reprecipitation with ether, mp 279–280°, ir (Nujol) ν_{max} 2440 cm^{-1}.

Anal. Calcd for $C_{22}H_{27}NO_2 \cdot HCl$: C, 70.66; H, 7.55; N, 3.75. Found: C, 70.63; H, 7.62; N, 3.59.

Registry No.—I (R = CH_3; R′ = $COCH_3$; R″ = H), 35202-50-7; I HCl (R = CH_3; R′ = H; R″ = H), 35202-51-8; I HCl (R = CH_3; R′ = H; R″ = OCH_3), 35202-52-9; I HCl (R = CH_3; R′ = C_2H_5; R″ = H), 35202-53-0; IIa (R = CH_3), 35202-54-1; IIb (R = CH_3), 35202-55-2; IIIa (R = CH_3), 35202-56-3; IIIb (R = CH_3), 35202-57-4; IVa (R = CH_3), 35202-58-5; IVb (R = CH_3), 35202-59-6; 2-bromo-4,5-dimethoxyphenypropionitrile, 35249-62-8.

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Syntheses of the Dihydronepetalactones

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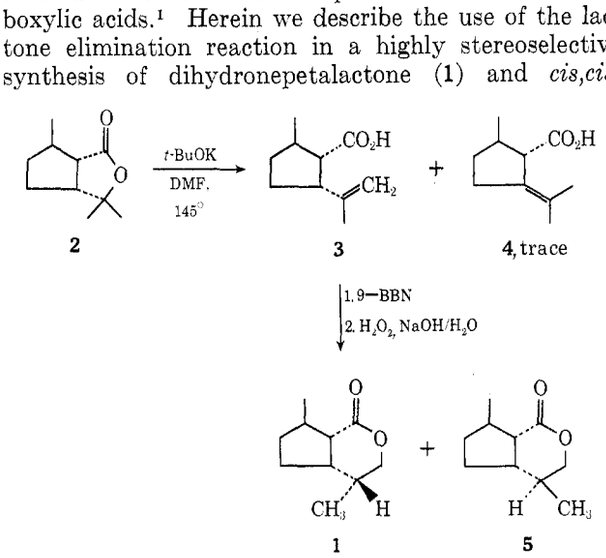
During a study of the base-catalyzed cyclization of methyl 6,7-epoxycitronellate it was discovered that alkoxides act on lactones to produce unsaturated carboxylic acids.[1] Herein we describe the use of the lactone elimination reaction in a highly stereoselective synthesis of dihydronepetalactone (**1**) and *cis,cis*-



dihydronepetalactone (**10**). Dihydronepetalactone (**1**), the enantiomer of a major constituent of matatabi-

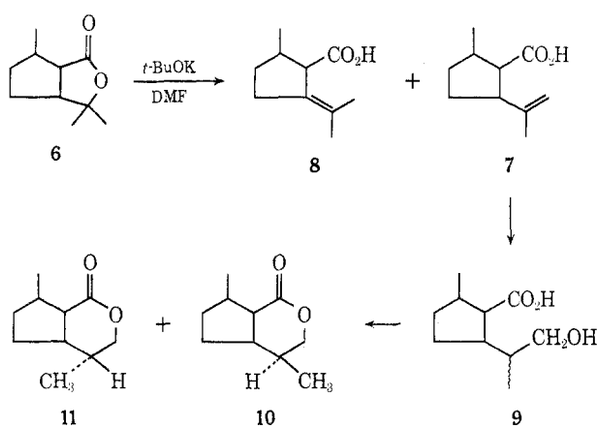
(1) J. Wolinsky, P. Hull, and E. J. Eustace, Abstracts, 161st National Meeting of the American Chemical Society, Los Angeles, Calif., spring, 1971. Details of this work will be described in a forthcoming publication.

lactone[2] and a trace ingredient in catnip oil,[2] is more attractive to cats[3] than nepetalactone or epinepetalactone.[4]

The reaction of potassium *tert*-butoxide with *cis,trans*-puleganolide (**2**)[5] in dry DMF to yield *cis,trans*-2-isopropenyl-5-methyl-1-cyclopentanecarboxylic acid (**3**) was best conducted at 145° for 4–5 hr using a 1.05:1.00 ratio of base to lactone. The presence of water seemed to increase the proportion of pulegenic acid (**4**) in the product. Unlike pulegenic acid (**4**), acid **3** readily converts to lactone **2** and care must be taken to avoid elevated temperature in the reaction work-up. The crude acid **3** was generally obtained in ~90% yield and was used immediately in the next step.

Hydroboration of acid **3** with 9-BBN[6] gave a 46% yield (based on lactone **2**) of a mixture of dihydronepetalactone (**1**) and isodihydronepetalactone (**5**) in a 7:1 ratio.

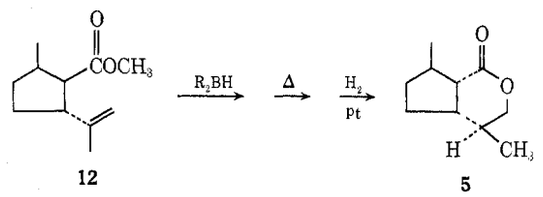
Heating *cis,cis*-puleganolide (**6**)[7] with potassium *tert*-butoxide in DMF gave a mixture of unsaturated acid **7** and *cis*-pulegenic acid (**8**) in a ratio of 2.6:1.0.



The crude acid was hydroborated with 9-BBN, but in this instance a mixture of hydroxy acids **9** was isolated. Heating **9** at 175° for 1 hr gave a mixture of *cis,cis*-dihydronepetalactone (**10**) and *cis,cis*-isodihydronepetalactone (**11**) in a 5:1 ratio.

The configurations of **10** and **11** were assigned on the basis of ir and nmr spectral comparison with **1** and **5**. The ir spectra of **1** and **10** were nearly identical, while the spectra of **5** and **11** were very similar. The nmr signals for the CH_2O protons in these compounds were characteristic of the AB portion of an ABX pattern. In the case of **1** and **10** coupling constants J_{AX} and J_{BX} were small while in lactones **5** and **11** J_{AX} and J_{BX} were large.[8]

It is of interest to point out that stereoselective routes to dihydronepetalactone (**1**) and isodihydronepetalactone (**5**) are now available. Hydroboration of **3** affords dihydronepetalactone (**1**), whereas hydroboration of **12**, followed by catalytic hydrogenation gives isodihydronepetalactone (**5**)[9] as the major product.



cis,cis-Isodihydronepetalactone (**11**) proved to be identical with a minor product isolated from the hydroboration of **12**.[9]

Experimental Section[10]

cis,trans-2-Isopropenyl-5-methyl-1-cyclopentanecarboxylic Acid (**3**).—To a stirred slurry of 3.5 g (31.2 mmol) of potassium *tert*-butoxide in 20 ml of anhydrous DMF at 120°, under a nitrogen atmosphere, was rapidly added 5.0 g (29.8 mmol) of *cis,trans*-puleganolide (**2**). The deep red solution was heated at 145° for 4 hr, cooled, and poured onto ice. The mixture was extracted with ether; the ether was dried and removed to leave 650 mg of lactone **2**.

The aqueous phase was acidified with dilute hydrochloric acid and extracted with ether. The ether solution was washed with water and dried ($MgSO_4$), and the ether was removed under diminished pressure to give 4.2 g of crude acid: ir 5.83, 6.05, and 11.13 μ; nmr (CCl_4) 1.09 (d, 3, CH_3), 1.76 (s, 3, $CH_3C{=}C$), 4.78 (s, 2, $C{=}CH_2$), and 11.20 ppm (s, 1, CO_2H). Nmr analysis indicated that acid **3** was contaminated with 2% lactone **2** and ~10% *trans*-pulegenic acid (**4**).

An ether solution of crude **3** was treated with an ether solution of diazomethane and a pure sample of methyl *cis,trans*-2-isopropenyl-5-methyl-1-cyclopentanecarboxylate (**13**) was isolated by glpc: ir (CCl_4) 5.74, 11.22 μ; nmr (CCl_4) 1.05 (d, 3, J = 6 Hz, CH_3), 1.72 (s, 3, $CH_3C{=}C$), 3.52 (s, 3, OCH_3), and 4.67 ppm (s, 2, $C{=}CH_2$).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.32; H, 10.00.

Dihydronepetalactone (**1**).—To 44 ml of 0.57 *M* solution (25 mmol) of 9-BBN in THF[6] at 0° was added 4.2 g (~25 mmol) of crude acid **3** in 10 ml of dry THF. A total of 24 mmol of hydrogen gas was evolved. An additional 44 ml of 9-BBN solution was then added and the solution was stirred at ambient temperature for 6 hr. The solution was cooled to 0° and 30 ml of 3 *N* potassium hydroxide solution was added rapidly, followed by the slow addition (30 min) of 30 ml of 30% hydrogen peroxide. The solution was allowed to warm to ambient temperature and was stirred for 18 hr. The reaction mixture was poured onto ice and extracted with ether. The aqueous solution was acidified with dilute hydrochloric acid and allowed to stir at ambient temperature for 1 hr before it was extracted with ether. The ether solution was washed with water, dried ($MgSO_4$), and distilled to give 2.27 g (45% based on **2**) of liquid, bp 107–110° (1 mm). Glpc analysis indicated the liquid was comprised of 82% dihydronepetalactone (**1**), 11% isodihydronepetalactone (**5**), and 7% lactone **2**. Pure samples of each lactone were isolated by preparative glpc and each showed ir, nmr, and vpc retention times identical with those of authentic samples.[2]

cis,cis-2-Isopropenyl-5-methyl-1-cyclopentanecarboxylic Acid (**7**).—A mixture of 2.4 g (21.4 mmol) of potassium *tert*-butoxide and 3.5 g (20.8 mmol) of *cis,cis*-puleganolide (**6**) in 25 ml of anhydrous DMF was heated at 145° for 4.5 hr. The usual work-up gave 420 mg of **6** in the neutral fraction and 2.70 g of oil in the acidic fraction: ir 5.86, 6.08, and 11.17 μ; nmr (CCl_4) 1.06 (d, 3, CH_3), 1.78 (s, 3, $CH_3C{=}C$), 4.77 (s, 2, $C{=}CH_2$), and 11.17 ppm (s, 1, CO_2H). Nmr analysis indicated that acid **7** was con-

(2) T. Sakan, J. Wolinsky, *et al.*, *Tetrahedron Lett.*, 4097 (1965).
(3) J. Wolinsky and D. L. Nelson, unpublished results.
(4) R. B. Bates and C. W. Sigel, *Experientia*, **19**, 565 (1963).
(5) J. Wolinsky, H. Wolf, and T. Gibson, *J. Org. Chem.*, **28**, 274 (1963).
(6) H. C. Brown and E. F. Knight, *J. Amer. Chem. Soc.*, **90**, 5281 (1968).
(7) J. Wolinsky, T. Gibson, D. Chan, and H. Wolf, *Tetrahedron*, **21**, 1247 (1965).
(8) See K. Sisido, K. Inomata, T. Kageyema, and K. Utimoto, *J. Org. Chem.*, **33**, 3149 (1968), for a discussion of the nmr spectra of the iridolactones.
(9) J. Wolinsky and D. Nelson, *Tetrahedron*, **25**, 3767 (1969).
(10) All boiling and melting points are uncorrected. Infrared spectra were measured with a Perkin–Elmer Infracord. Nuclear magnetic resonance spectra were determined at 60 MHz with a Varian Associates A-60 spectrometer. Optical rotations were measured with a Zeiss polarimeter. Mass spectra were recorded on a Hitachi RMU-6A spectrometer employing an ionization energy of 70 eV, an inlet temperature of *ca.* 185°, and a source temperature of 160°. Microanalyses were performed by Dr. C. S. Yeh and associates.

taminated with ~28% *cis*-pulegenic acid. A pure sample of **7** proved difficult to obtain because of its conversion to lactone **6**.

Methyl *cis,cis*-2-isopropenyl-5-methyl-1-cyclopentanecarboxylate (**14**), prepared by treatment of acid **7** with diazomethane and purified by glpc, showed ir absorption at 5.75, 6.07, and 11.18 μ; nmr (CCl_4) 0.97 (d, 3, CH_3), 1.72 (s, 3, $CH_3C{=}C$), 2.85–3.05 (m, 1, $CHCO_2Me$), 3.48 (s, 3, OCH_3), and 4.71 (s, 2, $C{=}CH_2$).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.50; H, 10.22.

***cis,cis*-Dihydronepetalactone (10) and *cis cis*-Isodihydronepetalactone (11).**—A solution of crude **7** in THF was added to 28 ml of 0.57 *M* 9-BBN under a nitrogen atmosphere. A total of 0.90 equiv of hydrogen gas was evolved. An additional 24 ml of 9-BBN solution was added and the solution was stirred at ambient temperature for 13 hr. The reaction was worked up in the usual manner and the basic aqueous solution was acidified and allowed to stir overnight. Extraction with ether afforded 2.65 g of liquid whose ir spectrum showed the presence of a hydroxy acid and only a small amount of lactone. The liquid was heated at 175° for 1 hr, and some acidic material was removed by dissolving the oil in ether and washing with sodium bicarbonate solution. The ether was removed and glpc (20% Carbowax 20M column at 195°) indicated the presence of two major components and three minor components (2%) which were not investigated further. The major component were isolated by glpc.

cis,cis-Isodihydronepetalactone (**11**) (15–20% of the mixture) showed a retention time of 68 min; $[\alpha]^{28}D$ −92.4° (*c* 4.30, $CHCl_3$); ir (CCl_4) 5.70 μ; nmr 0.92 (d, 3, J = 6 Hz, CH_3), 1.12 (d, 3, J = 5.5 Hz, CH_3), 3.69 and 4.28 (m, 2, J_{AB} = 11.5 Hz, J_{AX} = 6.5 Hz, J_{BX} = 7.5 Hz, $CHCH_2O$); mass spectrum *m/e* (rel intensity) 168 (7), 113 (37), 110 (46), 95 (44), 82 (33), 81 (92), 69 (47), 67 (56), 55 (40), 41 (100), and 39 (74).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.62; H, 9.76.

cis,cis-Dihydronepetalactone (**10**) (75–80% of the mixture) showed a retention time of 82 min; $[\alpha]^{28}D$ −15.6° (*c* 11.0, $CHCl_3$); ir (CCl_4) 5.74 μ; nmr 0.90 (d, 3, J = 6.5 Hz, CH_3), 0.92 (d, 3, J = 7 Hz, CH_3), 3.0 (m, 1, J_{AX} = 10 Hz, J_{BX} = 8.5 Hz, CHCO), and 3.95 ppm (m, 2, J_{AB} = 7 Hz, J_{BX} = 8.5 Hz, CHCO), and 3.95 ppm (m, 2, J_{AB} = 7 Hz, J_{AX} = 1.5 Hz, J_{BX} = 0, $CHCH_2O$); mass spectrum *m/e* (rel intensity) 168 (5), 113 (55), 81 (38), 67 (45), 55 (30), 53 (28), 41 (100), and 39 (83).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.66; H, 9.69.

Registry No.—**1**, 35337-11-2; **3**, 35337-12-3; **7**, 35337-13-4; **10**, 35337-14-5; **11**, 35337-15-6; **13**, 35337-16-7; **14**, 35337-17-8.

2,4,9-Trioxaadamantanes from Isobutylene and Pivaloyl Halides

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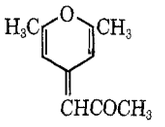
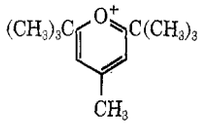
The Friedel–Crafts acylation of olefins has been one of the more thoroughly studied reactions.[1] Monoacylation is known to give chloro ketones and α,β- and β,γ-unsaturated ketones, whereas diacylation forms pyrilium salts. One type of triacylation is known in which formation of the pyrane **1** from 3 mol of acetyl chloride and 1 mol of isobutylene in the presence of aluminum chloride involves each of the terminal carbon atoms of isobutylene.[2] However, acylation of isobutylene with pivaloyl chloride in the presence of aluminum chloride has only been reported to give $(CH_3)_3CCOCH{=}C(CH_3)_2$[3] and a pyrilium salt (**2**) when stannic chloride is used.[4]



1



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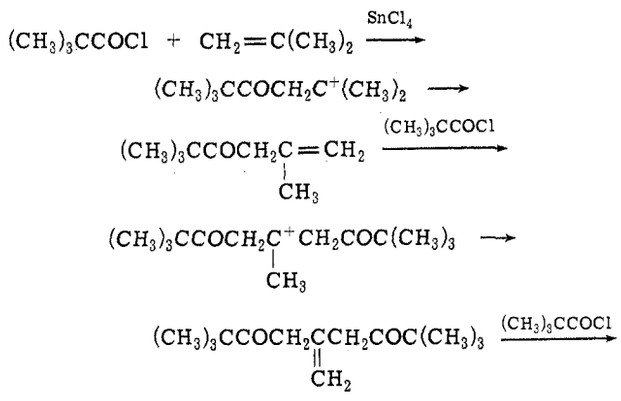
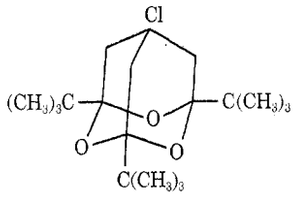
A new type of triacylation product has now been found in the reaction of pivaloyl halides with isobutylene. Simply by adding less than 0.1 molar equiv of stannic chloride to a liquid mixture of isobutylene and pivaloyl chloride at −15°, a 32–35% yield of 7-chloro-1,3,5-tri-*tert*-butyl-2,4,9-trioxaadamantane (**4**) can be filtered off. Another 6% can be obtained from the filtrate. The compound presumably arises through the intermediate formation of triketone **3** by a reaction sequence of the following type.



3



4

That a tricarbonyl compound of the structure $R'C(CH_2COR)_3$ will cyclize to a 2,4,9-trioxaadamantane was established by Stetter and Dohr,[5] who ozonized trimethallylcarbinol. The triketone was not isolated but spontaneously formed the 7-hydroxytrioxaadamantane, which they converted to 7-chloro-1,3,5-trimethyl-2,4,9-trioxaadamantane. Only one other synthesis for 2,4,9-trioxaadamantanes, that of Stetter and Stark,[6] has been reported. This route involved the preparation of $HC(CH_2COCHN_2)_3$ and conversion with hydrogen chloride or bromide to $HC(CH_2COCH_2X)_3$, which cyclized.

The ir spectrum of 7-chloro-1,3,5-tri-*tert*-butyl-2,4,9-trioxaadamantane (**4**) was taken at 155, 165, and 183° but gave no indication of reversion to the carbonyl form. The chlorine atom, as in the Stetter and Dohr compound, was unaffected by refluxing al-

(1) C. D. Nenitzescu and A. T. Balaban in "Friedel-Crafts and Related Reactions," Vol. III, Part 2, G. A. Olah, Ed., Interscience, New York, N. Y., 1964, pp 1033–1152.

(2) A. T. Balaban, P. T. Frangopol, A. R. Katritzky, and C. D. Nenitzescu, *J. Chem. Soc.*, 3889 (1962).

(3) M. E. Grundy, W. H. Hsü, and E. Rothstein, *ibid.*, 4136 (1952).

(4) A. T. Balaban and C. D. Nenitzescu, *Justus Liebigs Ann. Chem.*, **625**, 74 (1959).

(5) H. Stetter and M. Dohr, *Chem. Ber.*, **86**, 589 (1953).

(6) H. Stetter and H. Stark, *ibid.*, **92**, 732 (1959).