The Thermal Transformation of Two Tetrahydroacridandionecarboxylic Acids

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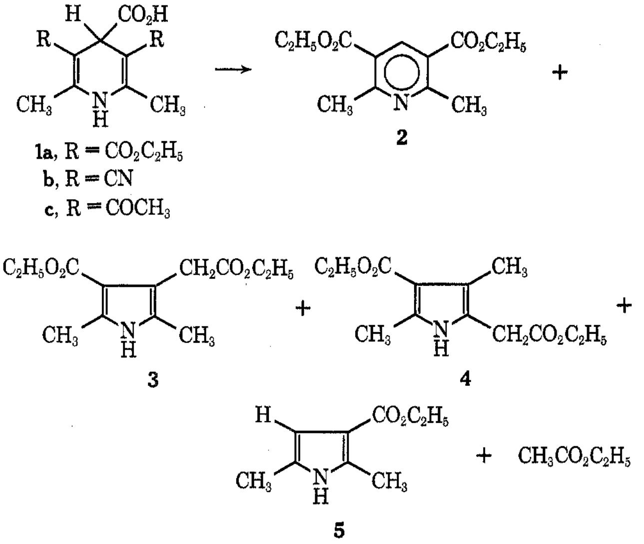
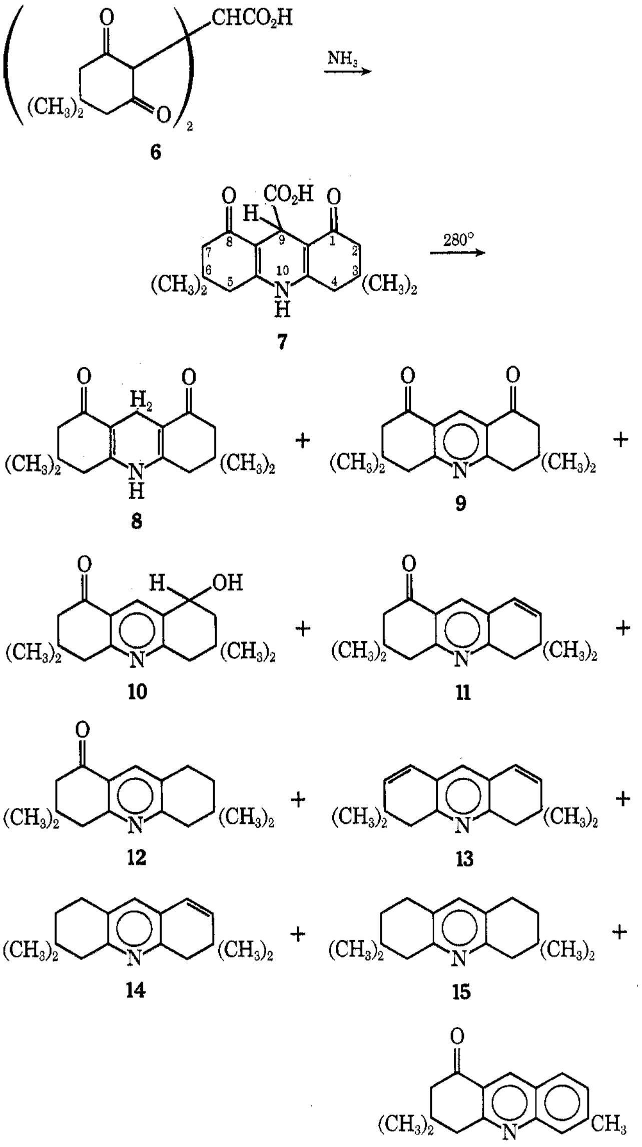
On melting, the tetrahydroacridandionecarboxylic acid **7** is converted into a complex series of products, **8** through **16**. It is shown that the primary products are the decarboxylation product **8** and the keto alcohol **10**, which interact by a novel intermolecular hydride transfer to produce the diketone **9** and the monoketone **12**; the keto olefin **11** arises from acid-catalyzed dehydration of **10**. The analogous acid **22** undergoes similar transformations.

Earlier studies have reported the thermal transformation of a series of 1,4-dihydropyridine-4-carboxylic acids, bearing such 3,5 substituents as carbethoxy (**1a**), cyano (**1b**), and acetyl (**1c**).[2] In particular, the diester **1a** has been shown to be converted by heating into the pyridine **2** and the pyrroles **3**, **4**, and **5**.[2b] Reasonable



mechanisms could be proposed for the formation of **2**, **3**, and **4** which were consistent with observations in related series, but the mode of the fragmentation which led to the pyrrole **5** and ethyl acetate remained obscure. The study of a tricyclic system in which the fragmentation products must remain part of a single molecule seemed a promising approach to these problems, and is described here. In the event, the reactions led to very different results.

The diketoacridancarboxylic acid **7** promised a suitable entry for this study, and proved to be readily available from the dimedone derivative of glyoxylic acid, **6**, *via* a Hantzsch condensation in ethanolic ammonia. The product has an ultraviolet absorption maximum characteristic of the desired structure.[2,3]



A pure sample of the acid **7** was stable when heated under nitrogen at 240°, the temperature which effected the decomposition of the monocyclic compounds **1a–c**; however, melting and ebulition occurred at 280°, transforming **7** into a mixture separable by chromatography on silicic acid. The most polar material was recognized as the product of simple decarboxylation **8**, for it retained the absorption at 388 nm, and proved to be identical with the known condensation product from the dimedone derivative of formaldehyde.[4]

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(1) Laboratoire associe au CNRS.

(2) (a) J. F. Biellmann and H. J. Callot, *Chem. Commun.*, 140 (1969); (b) J. F. Biellmann and H. J. Callot, *Tetrahedron*, **26**, 4799, 4809 (1970); (c) J. F. Biellmann, H. J. Callot, and M. P. Goeldner, *Chem. Commun.*, 141 (1969); (d) J. F. Biellmann, H. J. Callot, and M. P. Goeldner, *Tetrahedron*, **26**, 4655 (1970); (e) J. F. Biellmann, R. J. Highet, and M. P. Goeldner, *Chem. Commun.*, 295 (1970); (f) J. F. Biellmann and M. P. Goeldner, *Tetrahedron*, **27**, 1789 (1971).

(3) P. J. Brignell, U. Eisner, and P. G. Farrell, *J. Chem. Soc. B*, 1083 (1966).

(4) G. Y. Vanag and E. I. Stankevich, *Zh. Obshch. Khim.*, **30**, 3287 (1960).

TABLE I
NMR CHARACTERISTICS[a]

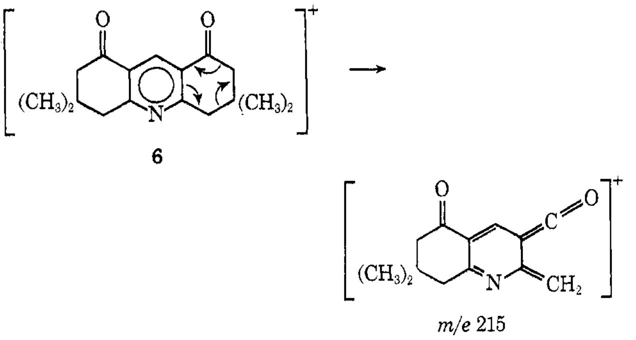
Compd	Solvent[b]	Proton position (in ppm, J in Hz): 1	2	3:C(CH$_3$)$_2$	4	5	6:C(CH$_3$)$_2$	7	9	Other
7	D		2.36 2.40[c]	1.03:1.05	2.17 2.20	2.17 2.20	1.03:1.05	2.36 2.40	4.50	CO$_2$H, 9.36 (br)
7 (CO$_2$CH$_3$)	D		2.32 2.39	0.98:1.02	2.14:2.17	2.14 2.17	0.98:1.02	2.32 2.39	4.56	OCH$_3$, 3.44
8	D		2.28	1.01	2.20	2.20	1.01	2.28	3.10	NH, 8.80 (br)
9	C		2.57	1.12	3.05	3.05	1.12	2.57	8.80	
10	C	4.90 (X) J_{AX} = 10.0, J_{AB} = −12.0, J_{BX} = 7.0	1.60 (A) 2.10 (B)	0.98 1.14	2.78	2.97	1.10	2.52	8.48	
10 (OCOCH$_3$ for OH) {H-1, 2.08} {H-1, 1.65}	C	6.04 J = 6.5 (H, d, 6.04), J = 6.0 (d), J = 14.0	2.08 1.65	0.98 1.07	2.76	2.95	1.05	2.48	8.13	OCOCH$_3$, 2.10
11	C	6.35 J = 10	5.88	1.08	2.98	2.90	1.08	2.50	7.85	
12	C	2.84 J = 6.0	1.60	1.03	2.72	2.96	1.12	2.50	7.97	
16	C	7.82 J_{12} = 8.5, J_{24} = 1.5	7.36	2.54	7.84	3.15	1.10	2.60	8.77	
17	C	4.62 (X) J_{AX} = 9.0, J_{AB} = −13.5, J_{BX} = 6.0	1.63 (A) 2.10 (B)	1.00 1.15	2.78	2.98	1.11	2.53	8.35	OH, ~2.3 OCH$_2$CH$_2$OH, 3.8 (m)
22	C		2.36 2.38	1.10	2.30	2.30	1.10	2.36 2.38	4.88	OAc, 2.17
23	F		2.62 (m)[d]	2.02 (m)[e]	2.38 (m)[d]	2.38 (m)[d]	2.02 (m)[e]	2.62 (m)[e]	4.77	NH, 9.70

[a] Peaks not shown with coupling constants were observed as singlets. Integrated areas corresponded to the required number of protons. In **9**, the peak at 2.57 is tentatively assigned to H-2 and H-7 because its position is less changed by structural modification than that at 3.05; assignments in the remaining compounds are made to correspond. [b] C, CDCl$_3$; D, (CD$_3$)$_2$SO; M, CD$_3$OD; F, (CD$_3$)$_2$NCO). [c] Outer limbs of anticipated AB quartet are obscured by neighboring peaks. [d] These assignments could be interchanged. [e] CH.

A product of intermediate polarity and melting point was recognized as the diketone **9** by its ir spectrum, absorption at 290 nm, and a peak in the nmr spectrum at low field, δ 8.98 ppm (Table I). It proved to be identical with known material prepared by the nitrous acid oxidation of **8**.[4] A material of similar polarity and uv absorption and mp 150° displayed a carbinol proton at δ 4.90 ppm and an aromatic proton at δ 8.48 ppm, appropriate to the keto alcohol **10**; it was readily converted to the known diketone by manganese dioxide oxidation.

The least polar components of the reaction mixture were isolated as a mixture, from which a pure component of mp 97° could be obtained by crystallization. Ultraviolet absorption at 320 nm and, in the nmr spectrum, an AB system of δ 6.28, 5.82 ppm (J = 10 Hz), implied an olefin conjugated with the aromatic ring, as in **11**. To demonstrate the structure, the same material was prepared by elimination of acetic acid at 260° from the acetyl derivative of **10**. The filtrates from the crystallization of the nonpolar column fractions were rechromatographed on thick layer, to provide a material of mp 95°, displaying a pair of triplets at δ 1.56 and 2.84 ppm. That this was the monoketone **12** could be shown by preparation of the same material by hydrogenation of the olefin, **11**.

Mass Spectral Characteristics.—The fragmentations observed in the mass spectra of these compounds followed familiar courses and provided useful structural information for trace products which could be studied only by the gas–liquid chromatography–mass spectra (glc–ms) pairing. The predominant process was the loss of 56 mu (Table II), corresponding to elimination of isobutene from the side rings by the familiar reverse Diels–Alder process.[5] This process produces the base peak of both the diketone **9** and the monoketone **12**. Since the loss occurs twice in the fragmentation of **12** (*m/e* 257 to 201 and 201 to 145) it is clear that both the unsubstituted alicyclic system and that bearing the keto group undergo this process. Losses of methyl and of carbonyl radicals provide less abundant fragments.



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m/e 215

The spectrum of the acid **7** shows no molecular ion peak, the heaviest ion observed resulting from the loss of car-

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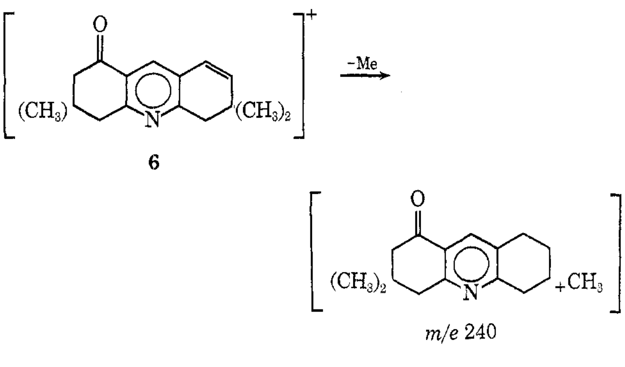
(5) K. Biemann, "Mass Spectrometry," McGraw-Hill, New York, N. Y., 1962, p 105.

Table II
Mass Spectral Data

Compd	*m/e* (rel intensity)
7	Calcd 317; 274 (18), 273 (87), 272 (100), 271 (30), 258 (11), 256 (19), 243 (17), 215 (92), 203 (19), 45 (55); m* 151.0 (273 to 203)
8	Calcd 273; 274 (8), 273 (80), 272 (60), 271 (55), 270 (15), 258 (18), 256 (22), 243 (15), 216 (17), 215 (100), 203 (40), 189 (20); m* 151.0 (273–203)
9	Calcd 271; 272 (8), 271 (38), 257 (3), 256 (15), 243 (16), 216 (16), 215 (100), 159 (5), 131 (11); m* 171.0 (271–215), 138 (215–172)
10	Calcd 273; 274 (21), 273 (100), 272 (29), 271 (20), 259 (7), 258 (28), 256 (12), 255 (26), 240 (29), 217 (43), 215 (52), 190 (36), 189 (45), 161 (47), 83 (11); m* 226.0 (255–240), 119.5 (217–161), 132.5 (273–190)
11	Calcd 255; 256 (10), 255 (47), 254 (3), 241 (18), 240 (100), 158 (20), 156 (22), 83 (59); m* 226.0 (255–240), 132.0 (189–158)
12	Calcd 257; 258 (17), 257 (88), 256 (4), 242 (46), 229 (20), 202 (28), 201 (100), 173 (6), 158 (20), 145 (30); m* 204.0 (257–229), 149.0 (201–173), 124.5 (201–158), 104.7 (201–145)
13	Calcd for $C_{17}H_{21}N$, 239; 240 (8), 239 (38), 225 (19), 224 (100), 209 (6), 208 (16), 195 (5), 194 (16), 182 (20) 85 (38), 83 (60); m* 210.0 (239–224)
14	Calcd for $C_{17}H_{23}N$, 241; 242 (7), 241 (37), 227 (20), 226 (100), 85 (60), 83 (100); m* 212 (241–226)
15	Calcd for $C_{17}H_{25}N$, 243; 244 (19), 243 (93), 228 (34), 188 (36), 187 (100), 131 (21), 85 (60), 83 (100)
16	Calcd for $C_{16}H_{17}NO$, 239; 240 (18), 239 (89), 224 (22), 211 (38), 183 (100)
17	Calcd for 317; 318 (2), 317 (11), 273 (17), 272 (95), 258 (10), 257 (63), 256 (100), 255 (11), 240 (16), 215 (5), 214 (9); m* 233.8 (317–272)
22	Calcd 359; 274 (6), 273 (35), 272 (65), 271 (46), 256 (26), 243 (34), 216 (20), 215 (100), 177 (7), 159 (9); m* 214.5 (243–228), 171.0 (271–215)

bon dioxide; the spectrum thus produced closely resembles that of the decarboxylation product **8**. Both show a major fragmentation route *via* loss of a molecule of hydrogen to a fragment isomeric or identical with the molecular ion of the diketone **9**; peaks important in the spectrum of **9** also occur in those of **7** and **8**. A competing process involves the loss of isopentene from the intact ion of **8** (*m/e* 273 to 203). Surprisingly, the molecular ion of the keto alcohol **10** provides the base peak, the sequential loss of two isobutene moieties, supported by metastable peaks, leading to major fragment ions. Peaks resulting from the loss of methyl, carbonyl, and water moieties are present but less abundant. In the spectrum of the olefin **11**, the ion resulting from the loss of the methyl radical is stabilized by allyl resonance, and forms the base peak, twice as intense as the molecular ion. That the aromatic rings of these compounds remained intact was demonstrated by the spectra of the 9-deuterio derivatives, described below.[6] Thus the mass spectra provide an indication of the functional groups, the methyl substituents, and the styrene system of these series.



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m/e 240

Minor Products.—Examination of the total reaction mixture from the pyrolysis by gas–liquid chromatography confirmed that the materials isolated by chromatography on silicic acid formed the major reaction products, and revealed the presence of several trace products. The mass spectra of these materials could be obtained from glc–ms pairing and provided reasonable hypotheses for their structures. Thus, the material of least retention time showed a molecular ion of *m/e* 239 with prominent loss of 15 mu to give the base peak at *m/e* 224; the spectrum is devoid of prominent peaks arising from the loss of hydroxyl, carbonyl, or isobutenyl fragments. The diolefin **13** possesses an appropriate molecular weight, and accords well to the observed fragmentations.

The material next eluted from the column showed a molecular ion at *m/e* 241, again with a prominent loss of methyl to *m/e* 226, and sequential loss of 56 mu. Structure **14**, possessing a monostyrene system and saturated alicyclic system, satisfies these observations. The third material eluted (molecular ion at *m/e* 243) showed only minor loss of methyl, but loss of two isobutene moieties, and is presumably the symmetrical structure **15**.

A fourth minor product showed a molecular ion at *m/e* 239, with the loss of butene providing the base peak, while the loss of carbonyl and methyl fragments produced less abundant ions. Characterization of the material was facilitated by the observation that the same material was formed during the preparation of the olefin **11** by pyrolysis of the acetyl derivative of **10**. Chromatography provided material which could be shown by glc to be only slightly contaminated with **11**. The nmr spectrum of this material showed, in addition to the singlet at low field, an aromatic AA'B system with δ 7.82, 7.82, and 7.36 ppm and coupling constants of $J_{AB} = 8.5$, $J_{A'B} = 1.5$, and $J_{AA'} = 0$ Hz. Accurate mass measurement showed the molecular formula to be $C_{16}H_{17}NO$.[7] These observations suggested the structure **16**, which is supported by the ultraviolet spectrum, which resembled that of 3-acetylquinoline.

Reaction Course and Mechanism.—Thus nine products were recognized from the decomposition on melting of **7**. Casual inspection of the accumulation of structures suggested that **8** must arise from simple decarboxylation of the acid **7**,[8] while the olefinic group of **11** could be produced by dehydration of the alcohol **10**. Experiment confirmed this suspicion that **8** and **10** are primary products. When **7** is refluxed under nitrogen in triglyme, **10** is formed in good yield, and may be

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[6] Although this observation is quite obvious in the mass spectra of the monodeuterated derivatives of compounds **9–12**, the spectrum of **8** is at first confusing, as important peaks arise from the loss of H or D from C-9. A less equivocal observation is that the base peak occurs as a doublet at *m/e* 216 and 215, consistent with the fragmentation postulated above through the dehydrogenation product, **9**.

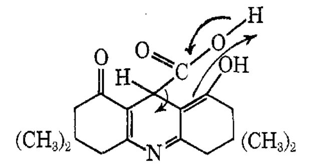
[7] We are indebted to Dr. David Rosenthal of Research Triangle Institute for the element map of this material. The formulae arising from accurate measurement of the fragment ions support the modes of fragmentation suggested above.

[8] *Cf.* B. R. Brown, *Quart. Rev., Chem. Soc.*, **5**, 131 (1951).

crystallized directly from the reaction products. A smaller quantity of **8** is produced concomitantly.

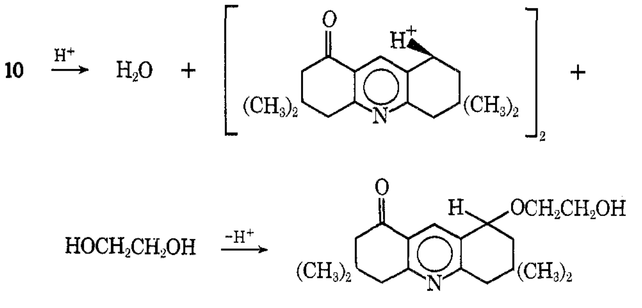
Although **10** might arise from the disproportionation of the isomeric **8**, in fact **8** is stable under conditions of the pyrolysis, and in the presence of dilute acetic acid. To gain further insight into the course of the reaction, the reactions of 9-deuterio-**7** were studied. Deuterioglyoxylic acid was prepared by the reduction of sodium oxalate by sodium amalgam in deuterium oxide[9] and led through the Hantzsch process as before. Refluxing 9-deuterio-**7** in triglyme provided 9-deuterio-**10**, essentially uncontaminated by the normal product.

This observation eliminates intermediates in the formation of **10** in which a double bond has shifted into conjugation with the carboxylic group, or in which the aromatic system is formed prior to decarboxylation. In view of the stability of the decarboxylation product **8**, the formation of **10** must involve concomittant reduction of the keto group and decarboxylation, as represented by the following mechanism.



The postulate that the keto olefin **11** arose from the keto alcohol **10** by dehydration could now be tested. Scrupulously purified, **10** proved to be stable at 280°. However, the presence of a carboxylic acid in the melt suggested that the dehydration might occur by acid catalysis. Indeed **11** was produced on heating **10** in 0.7 *N* acetic acid–triglyme.

The acid lability of **10** was further exemplified by an unexpected observation. Refluxing the carboxylic acid **7** in ethylene glycol produced a product readily recognized by composition and spectral characteristics as **17**, the ether of ethylene glycol and the alcohol **10**. Although mechanisms for its direct formation from **7** could be envisaged, it could be demonstrated that heating the keto alcohol **10** in ethylene glycol 0.7 *N* in acetic acid caused the formation of **17**, perhaps *via* the benzylic carbonium ion.



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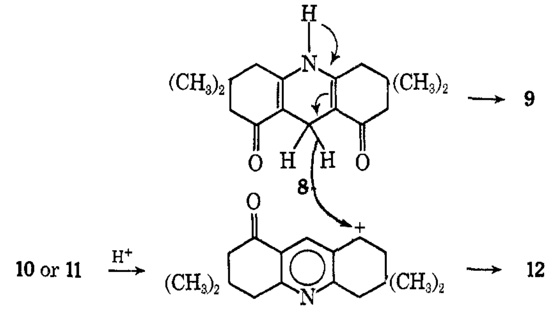
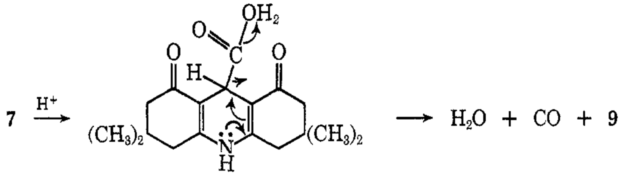
The keto alcohol **10** and the decarboxylation product **8** were individually stable at 280°; however, a mixture of **10** and **8** heated under nitrogen at 284° produced largely the diketone **9** and the monoketone **12**. In view of the lability to acid of the keto alcohol **10**, it is convenient to represent this interaction by such a process as



To test the hypothesis, dideuterio-**8** was prepared by leading dideuterioformaldehyde through the dimedone condensation and Hantszch reaction. A mixture of this material and normal **10** was heated at 280° with the following results. The sample of the diketone **9** produced bore a deuterium atom at the 9 position, as anticipated from its formation from **8**; most of the monoketone **12** formed was monodeuterated at C-1. A smaller portion was dideuterated, evidently 1,9-dideuterio-**12**, for the aromatic peak in the nmr was diminished in intensity. This portion may arise by disproportionation between **9** and **10**.

Other processes than those discussed here may be occurring in the melt. It could be shown, for instance, that the carboxylic acid **7** was converted cleanly to the diketone **9** by heating in the presence of dilute mineral acid. The procedure is evidently a decarbonylation favored by the formation of the aromatic system.[10]



Further indication of the complexity of the processes occurring could be seen in the pyrolysis of 9-deuterio-**7**. Mass spectra of the products formed showed clearly that they were primarily monodeuterio derivatives. However, an nmr spectrum of the benzene soluble products showed that an appreciable portion of **9**, **10**, and **12** possess aromatic protons. This is anticipated for **9**, and the protons of **10** and **12** may arise from minor reactions such as intermolecular hydride transfer reactions, not elucidated here.

Comparison of 1 and 7.—Thus, it is abundantly clear that the behavior of the acridan systems discussed here is quite different from that observed in the earlier studies of **1a–c**. The behavior of **1c** provides a particularly striking contrast of chemical properties. The two acids, **1c** and **7**, possess identical functional groups identically situated around the 1,4-dihydropyridine system. Their electronic characteristics are shown by their very similar spectra to be essentially identical, but, on melting, **1c** is converted into the lactone **19**, with the expulsion of an acetyl group, *via* an intermediate

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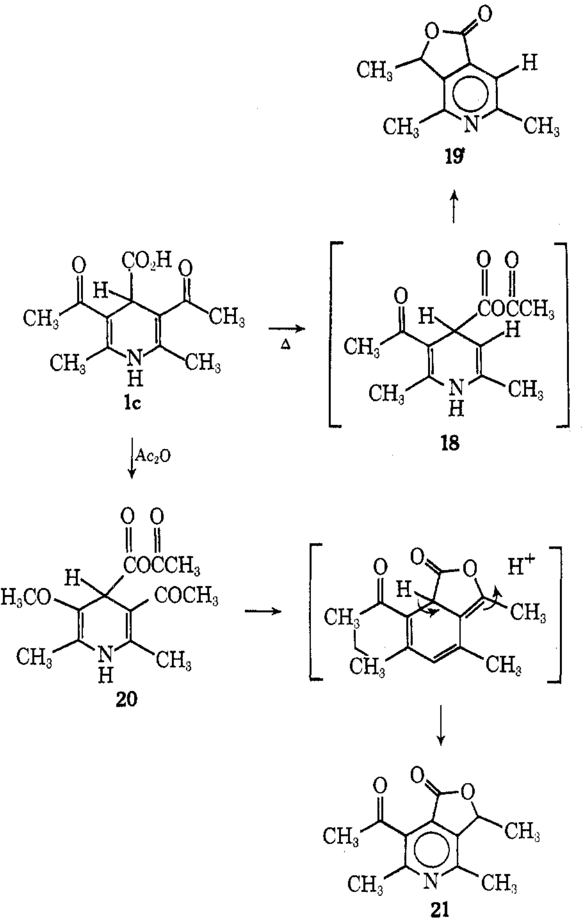
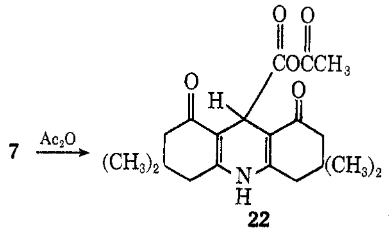
[9] A. Murray, C. W. Bills, and A. R. Ronzio, *J. Amer. Chem. Soc.*, **74**, 2405 (1952).

[10] Acid-catalyzed decarbonylation has previously been observed when the carbonium ion produced is stabilized by suitable substitution. *Cf.* J. Meinwald, H. C. Hwang, D. Christmar, and A. P. Wolf, *ibid.*, **82**, 483 (1960), and A. H. Blatt, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 5.

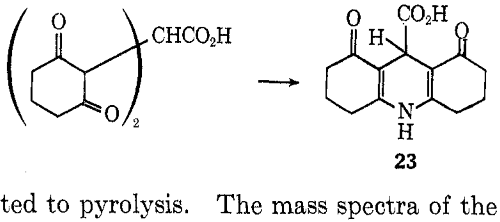
thought to be the anhydride **18**. In accord with this supposition, the mixed anhydride **20** can be prepared from **1c**, and is readily transformed to the keto lactone **21**.



To extend the comparison, the mixed anhydride **22** was prepared from **7** by stirring with acetic anhydride. It is perfectly stable at moderate temperatures, and, on melting, is converted to the diketone **9**, apparently with the expulsion of acetic acid and carbon monoxide.



It seemed worthwhile to eliminate the possibility that the *gem*-dimethyl groups of **7** were responsible for the different reaction course. Accordingly, a preliminary examination of the behavior of **23** was carried out. Dihydroresorcinol was led through the same reaction sequence as that leading to **7** to provide **23**, which was subjected to pyrolysis. The mass spectra of the products showed fragmentation corresponding closely to those of the earlier products, and the characteristic nmr peaks appeared at very similar chemical shifts. It is clear that the reaction followed a very similar course, and the difference in behavior in **7** and **1c** must be found in the effect of the tricyclic character of **7** upon the reaction mechanism. It must be presumed that tetracyclic systems corresponding to those leading to **18** and **21** are sufficiently strained in the reactions of **7** to prevent the reaction taking the same course as **1c** and its anhydride.



Experimental Section[11]

3,4,6,7-Tetrahydro-3,3,6,6-tetramethylacridan-1,8(2*H*,5*H*)-dione-9-carboxylic Acid (7).—The dimedone adduct of glyoxylic acid,[12] 5 g, was treated with 50 ml of ethanol which had been saturated with ammonia at 4°. The suspension was sealed in a glass tube, and heated cautiously with shaking until dissolution was complete. The solution was now heated overnight in a steam bath, gradually depositing yellow crystals. It was chilled, opened, and filtered. The product was washed with scanty portions of chilled ethanol, dissolved in ~50 ml of water, and added to excess chilled 1 *N* hydrochloric acid with stirring, precipitating a light yellow powder. This was filtered, dried by pressing on porous pot, and crystallized from ~70 ml of ethanol. The product was 1.4 g of handsome yellow crystals: mp 280° dec; uv max 247 nm (ε 23,500), 373 (7600); ir (Nujol film) 3200–2500 (br), 1720, 1640, 1570 cm^{-1}. *Anal.* Calcd for $C_{18}H_{23}O_4N$: C, 68.12; H, 7.31; N, 4.40. Found: C, 68.01; H, 7.42; N, 4.51.

Pyrolysis of 7.—A 1.2-g sample of **7** was heated under N_2 at 280° for 15 min until ebullition ceased. A 93-mg sample of the crude product, which amounted to 1.0 g, was removed and the remainder was chromatographed on 30 g of silicic acid. Elution by 20% ethyl ether in petroleum ether removed 143 mg of a mixture of **11** and **12**; 33% ether eluted 180 mg of **9**; 50% ether eluted 530 mg of **10**; methanol eluted 100 mg (10%) of **8**. The following yields were based on glc analysis on 3% OV-1 on Gas-Chrom P at 180° (retention times): **13**, trace (3.3 min); **14**, trace (3.7 min); **15**, trace (4.2 min); **11**, 17% (6.1 min); **12**, 15% (7.1 min); **16**, trace (9.7 min); **9**, 20% (12.1 min); **10**, 28% (13.9 min); **8** not observed.

3,4,5,6-Tetrahydro-3,3,6,6-tetramethyl-1(2*H*)-acridinone (11).—Recrystallization of the first fraction eluted from the column from hexane provided 49 mg of **11**: mp 97°; uv max 234 nm (ε 27,000), 271 (12,100), 279 sh (10,100), 320 (3560), (OH^-) no change, (H^+) 242 sh (12,100), 279 (9700), 330 (4200); ir ($CHCl_3$) 1680, 1592, 1320 cm^{-1}. *Anal.* Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29. Found: C, 79.81; H, 8.55.

3,4,5,6,7,8-Hexahydro-3,3,6,6-tetramethyl-1(2*H*)-acridinone (12).—Filtrates from the above procedure were chromatographed on a 2-mm-thick plate of silicic acid developed three times with 20% ether in hexane. Elution of the lower portion of the band provided material substantially free of **11**; recrystallization from hexane provided material of mp 95–96°, identical with material prepared as follows.

A 21-mg sample of **11** was stirred in ethanol with 5 mg of 10% Pd/C under hydrogen; the solution absorbed 2.0 ml in 15 min. Filtration and evaporation of the solvent provided 21 mg of compound **12**: uv max 213 nm (ε 14,800), 241 (8300), 293 (6500),

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(11) Melting points were observed on a microscope hot stage. Uv spectra were obtained in absolute ethanol solution on recording spectropolarimeters; those designated "(OH^-)" were recorded after adding 1 drop of 1 *N* sodium hydroxide to the ethanolic solution; those designated "(H^+)" were obtained after adding 1 drop of 1 *N* hydrochloric acid to the ethanolic solution. Ir spectra were obtained on chloroform solution unless otherwise described. Nmr spectra were obtained on a Varian A-60 or HA-100 spectrometer using tetramethylsilane (δ 0.0) as an internal standard. Mass spectra were obtained on an LKB 9000 mass spectrometer at 70 eV; those of trace products were obtained as the material was eluted from an OV-1 (1%) column heated from 150 to 230° at 5°/min. The identities of materials from alternative preparations were established by nmr spectra and, in the case of **7** and **8**, by thin layer chromatography on silicic acid, eluting by 5% methanol in chloroform; in the case of **9–12**, by gas chromatography on a column of 3% OV-1 Gas-Chrom P at 180°.

(12) D. Vorlander, *Z. Anal. Chem.*, **77**, 244 (1929).

301 sh (6300), (H^+) 235 sh (6170), 292 (9400) [*cf.* 3-acetylpyridine: 228 (8500), 267 (2900), (H^+) 224 (5700), 267 (3900)[13]]. *Anal.* Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01. Found: C, 79.41; H, 9.06.

3,4,6,7-Tetrahydro-3,3,6,6-tetramethyl-1,8(2*H*,5*H*)-acridinedione (**9**).—Recrystallization of column fractions from ethyl acetate provided material of mp 147° (lit.[4] 146); uv max 248 nm (ϵ 10,650), 289 (6200), 299 (5720), (OH^-) no change, (H^+) 245 (10,300), 289 (8100), 298 (7500); ir ($CHCl_3$) 1690, 1580. *Anal.* Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.21; H, 8.01; N, 5.25.

1,2,3,4,6,7-Hexahydro-3,3,6,6-tetramethyl-8(5*H*)-acridinon-1-ol (**10**).—Repeated recrystallization of column eluates provided material of mp 153–153.5°; uv max 242 nm (ϵ 8900), 291 (7200), 296 sh (7100), (OH^-) no change, (H^+) 235 (6100), 291 (9700); ir ($CHCl_3$) 3580, 3400 (br), 1678, 1590, 1560 cm^{-1}. *Anal.* Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.64; H, 8.67; 8.43; N, 5.31.

Oxidation.—A solution of 30 mg of the above keto alcohol (**10**) was stirred 24 hr with 300 mg of Merck manganese dioxide; the suspension was filtered and concentrated to dryness. The product (24 mg) was identical in infrared spectrum and tlc with the diketone **9**.

This compound (**10**) was more conveniently prepared by the following procedure. A 0.25-g sample of **7** was refluxed under nitrogen for 90 min in 1 ml of triglyme, which was diluted with benzene and filtered to yield a small quantity of **8**. The solution was washed three times with water and concentrated to dryness. The residue was crystallized from benzene–hexane, to provide 112 mg (52%) of mp 145–150°.

1,2,3,4,6,7-Hexahydro-3,3,6,6-tetramethyl-8(5*H*)-acridinon-1-yl Acetate (**10, OCOCH$_3$ instead of OH**).—An 83-mg sample of the pure alcohol was dissolved in 1 ml of cold acetic anhydride–pyridine (1:1) and allowed to stand in a freezer overnight. The solution was diluted with benzene and stirred with 10 ml of 1 *N* potassium bicarbonate for 3 hr, then extracted twice with chloroform; the extract was washed with water and concentrated to dryness. The residue, 95 mg, mp 100–103°, was recrystallized from ether to provide material of mp 103–103.5°; ir ($CHCl_3$) 1735, 1692, 1602 cm^{-1}. *Anal.* Calcd for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99; N, 4.44; Found: C, 72.60; H, 7.96; N, 4.62.

3,4,6,7-Tetrahydro-3,3,6,6-tetramethyl-1,8(2*H*,5*H*)-acridandione (**8**).[4]—A 2.0-g sample of formaldehyde dimedone[14] was heated with 20 ml of concentrated ammonium hydroxide for 24 hr. The solution was chilled and the precipitate filtered, to provide 1.45 g of **8**: mp >310° dec; uv max 248 nm (ϵ 16,600), 263 sh (7500), 388 (6400); ir (Nujol) 1590 cm^{-1}.

Preparation of 11 by Dehydroacetoxylation.—The acetate of **10** prepared as described above from 106 mg of **10** was distilled at 120° (0.1 mm), then sealed in a test tube under nitrogen and heated 25 min at 260°. Chromatography over 10 g of silicic acid, eluting with 10% ether–hexane, produced 28 mg of pure olefin **11**, identical by glc and nmr with material obtained from the pyrolysis of **7**.

Continued elution provided 11 mg of **6,7-dihydro-3,6,6-trimethyl-8(5*H*)-acridinone** (**16**) as a glass: uv max 215 nm (ϵ 17,700), 253 (36,400), 312 (9000), (H^+) 212 (19,300), 257 (30,200), 336 (9700) [*cf.* 3-acetylquinoline: 243 (50,000), 287 (8000), 322 (1000)[15]]. On addition of $NaBH_4$ the solution of **16** showed uv max 210 (62,000), 236 (36,000), 239 (36,400), 298 (6200), 305 (6100), 311 (7400), 317 (6200), 350 (3800) [*cf.* quinoline: 235 (35,500), 278 (3500) 300 (2600), 314 (3030)[16]]; ir ($CHCl_3$) 1680, 1628, 1590, 1495, 880 cm^{-1}; mass spectrum[7] *m/e* 239.131 (calcd for $C_{16}H_{17}NO$, 239.131), 224.107 ($C_{15}H_{14}NO$, 224.105), 216.137 ($C_{15}H_{17}N$, 211.136), 183.067 ($C_{12}H_9NO$, 183.068), 155.072 ($C_{11}H_7N$, 155.073).

Bis(1,3-dioxocyclohexyl-2)acetic Acid.—A 17-g portion of dihydroresorcinol and 6.5 g of glyoxylic acid were dissolved by warming in 50 ml of water and treated with 10 drops of concentrated HCl. On cooling, a white precipitate formed, which, when separated by filtration and washed, amounted to 16.0 g, mp 88–90°. *Anal.* Calcd for $C_{14}H_{16}O_6$: C, 59.99; H, 5.75. Found: C, 60.33; H, 6.08.

3,4,6,7-Tetrahydro-1,8(2*H*,5*H*)-acridandione-9-carboxylic Acid (**23**).—A 2.0-g portion of the above adduct was heated in 10 ml of concentrated ammonia for 16 hr, then acidified with HCl. The suspension was filtered and the precipitate was washed with water and dried, to provide 1.7 g, >250° dec pt. This was crystallized by dissolution in 350 ml of ethanol and concentrated to 75 ml, yielding, on scratching and chilling, 1.1 g of fine yellow crystals mp >250°. In a preliminary run, crystallization was allowed to proceed slowly, producing a mixture of crystalline forms, prisms, and needles. Solid-phase ir spectra of these different forms were very similar, but not identical and uv spectra had identical λ_{max}, but ϵ values were not closely reproducible: uv max 369 nm (ϵ 6600), (OH^-) 249 (45,600), 379 (6250); ir (Nujol) 3250–2000, 1700, 1610, 1565. *Anal.* Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.31; H, 6.06, 5.92; N, 5.53, 5.49.

A sample of this material was heated under nitrogen at 284° for 5 min. It was chromatographed on a silicic acid plate by repeated development with chloroform, providing sufficient separation of the products to allow the recognition of their salient spectrometric characteristics. An nmr spectrum of the benzene-soluble portion of the product showed the approximate composition **9a**,[16] 20%, **10a**, 35%, **11a**, 20%, **12a**, 25%. **9a**: nmr 880 ppm (s); mass spectrum 216 (9), 215 (60), 214 (10), 188 (6), 187 (100). **10a**: nmr 8.35 (s), 4.85 (br); mass spectrum 218 (13), 217 (92), 216 (60), 215 (29), 200 (15), 199 (38), 189 (54), 188 (33), 187 (46), m* 165 (217 → 189). **11a**: nmr 7.83 (s), 6.4 (m) 6.17 (m); mass spectrum 200 (29), 199 (100), 198 (36), 197 (35), 184 (33), 171 (40), 169 (35). **12a**: nmr 8.0 (s); mass spectrum 202 (12), 201 (70), 200 (24), 173 (100), 145 (29), m* 122.0 (173 → 145).

1-(2-Hydroxyethoxy)-1,2,3,4,6,7-hexahydro-3,3,6,6-tetramethyl-8(5*H*)-acridinone (**17**).—**7** (0.25 g) and 1 ml of ethylene glycol were refluxed under N_2 for 2 hr, cooled, and diluted with chloroform to precipitate 24 mg of **8**. The filtrates were chromatographed on a thick layer of silicic acid with 1:1 hexane–ether. Extraction of the band 0.1 cm from the base line provided 120 mg of **17**. Recrystallization from benzene–hexane provided material of mp 137–139°; uv max 239 nm (ϵ 9500), 293 (6700). *Anal.* Calcd for $C_{19}H_{27}O_3N$: C, 71.89; H, 8.57; Found: C, 71.90; H, 8.48.

Acid Treatment of 7.—An 102-mg sample of **7** was heated with 0.25 ml of 0.1 *N* sulfuric acid in triglyme in a sealed tube under nitrogen at 225° for 40 min. The solution was cooled, diluted with water, and filtered. The precipitate was washed repeatedly with water, and dried to provide 70 mg of **9**, mp 149–151°.

9-Deuterio Derivative of 7.—A solution of 670 mg of sodium oxalate in 20 ml of deuterium oxide was adjusted to pD 1 with concentrated deuteriosulfuric acid, and a total of 75 g of 1% sodium amalgam was added in five portions over a period of 1 hr together with the further addition of deuteriosulfuric acid as required to maintain the pD at ~1. To this solution was added 1.0 g of dimedone reagent. On standing overnight the solution precipitated 0.9 g of the adduct which was crystallized from aqueous ethanol.

A 0.416-g sample of this material was treated as above with ethanolic ammonia to produce material identical with previous preparations of **7** but lacking an nmr peak at δ 4.50 ppm.

Pyrolysis of this material was carried out as before. The product was taken up in benzene and filtered. The precipitate was chromatographed on thin layer, developing with 5% methanol in chloroform to provide a sample of **8b**:[17] *m/e* 275 (35), 274 (100), 273 (60), 272 (30), 259 (27), 216 (39), 215 (23), 204 (49), m* 152 (274 → 204). The benzene solution was examined by glc–ms to provide the following spectra: **9b**, 272 (35), 257 (15), 244 (17), 216 (100), 215 (26); **10b**, 275 (25), 274 (100), 273 (32), 259 (33), 256 (20), 241 (20), 218 (53), 191 (45), 190 (65), 189 (12); **11b**, 256 (42), 241 (100), 240 (12), 83 (70); **12b**, 258 (100), 257 (20), 243 (43), 202 (89), 201 (24).

Mixed Anhydride of 7 and Acetic Acid (**22**).—A 5.0-g sample of recrystallized **7** was stirred in the dark with 25 ml of acetic anhydride for 4 days. The suspension was diluted with ether and filtered to provide 5.3 g of the mixed anhydride, mp 184–187°. Crystallization from chloroform–ethanol provided material of mp 183–184°; uv max 363 nm (ϵ 6900); ir 3240, 3070, 1810, 1730, 1640, 1610, 1562. *Anal.* Calcd for $C_{20}H_{25}O_5N$: C, 66.83; H, 7.01; N, 3.90. Found: C, 66.44; H, 7.48; N, 3.79.

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[16] The suffix "a" denotes structures modified by the substitution of CH_2 for $C(CH_3)_2$.

[17] The suffix "b" denotes structures modified by substitution of D for H at C-9.

Acid Dehydration of 10.—A 10-mg sample of **10** was heated with 0.2 ml of 4 *M* acetic acid in triglyme. The solution was diluted with benzene and washed repeatedly with water. The organic layers were concentrated to dryness under reduced pressure to yield an 11-mg residue, which was shown by glc and nmr to be a mixture of **10** and **11**, approximately 1:1, slightly contaminated by triglyme.

Conversion of 9-Deuterio-7 to 9-Deuterio-10.—An 11-mg sample of 9-deuterio-**7** was heated under nitrogen with 0.1 ml of triglyme at 240° for 30 min. The solution was diluted with benzene and hexane and chilled. The precipitate amounted to 3.3 mg. The filtrates were washed repeatedly with water and concentrated to dryness under reduced pressure. The residue was crystallized from benzene to provide 4.3 mg of 9-deuterio-**10**, mp 148–151°. The nmr spectrum was identical to that of **10**, but lacked the aromatic proton absorption. Collection of 420 spectra and integration by cut and weigh showed that ~5% of this possessed an aromatic proton, δ 8.5 ppm; mass spectrum *m/e* 276 (3), 275 (22), 274 (100), 273 (32), 272 (19), 259 (30), 256 (22), 241 (19), 218 (48), 216 (38), 162 (60).

Interaction of 8 and 10.—A mixture of 73 mg of **8** and 76 mg of **10** was heated under nitrogen at 280° for 5 min. The product was taken up in benzene and filtered to recover 45 mg of **8**. The benzene solution was concentrated to dryness to leave 103 mg. Analysis by nmr and glc showed the following composition: **9**, 29%; **10**, 54%; **12**, 12%. When heating was continued 70 min, recovery of **8** amounted to 17%; the composition of the benzene soluble portion was **9**, 46%; **10**, 15%; **11**, 6%; **12**, 34%.

Interaction of 9,9-Deuterio-8 and 10.—A sample of dideuterioparaformaldehyde (0.32 g) was converted to the dimedone derivative[14] (2.5 g), of which 0.5 g was heated with 5 ml of ammonia in a steam bath overnight to provide 0.38 g of dideuterio-**8**. This material was recrystallized from ethanol. A recrystallized sample (20 mg) was mixed with an equal weight of **10** and heated in a sealed tube under nitrogen at 284° for 75 min. The material was suspended in benzene, filtered, and the filtrate concentrated to dryness (32 mg). Glc showed **9**, 43%; **10**, 13%; **11**, 17%; **12**, 28%. Mass spectra: 9-deuterio-**9**, *m/e* 273 (8), 272 (31), 271 (5), 216 (100), 215 (12); **10**, identical with that of pure material; **11**, identical with pure material, except for *m/e* 256 (19) and 241 (38); 1-deuterio-**12** and 1,9-dideuterio-**12**, 260 (24), 259 (72), 258 (72), 244 (45), 243 (45), 204 (42), 203 (100), 202 (95).

This material was chromatographed on a thick plate eluting by 1:1 hexane–ether. The slowest moving band provided **10**, with nmr identical with that of known material; the next band provided 9-deuterio-**9** with nmr identical with known material, but lacking the aromatic proton; the fastest moving band provided a 1:1 mixture of **11** and 9-deuterio-**12** with the nmr δ 7.88 ppm (relative strength 0.6), 7.76 (0.9), 6.25 (d, 1.0), and 5.75 (d, 1.0). Intensities were determined by cut and weigh of the spectrum obtained by accumulating 225 spectra.

Interaction of 8 and 11.—A mixture of 1.2 mg of **11** and 1.5 mg of **8** was heated under nitrogen at 280° for 18 min. Glc analysis of the volatile components of the mixture showed **9**:**11**:**12** in the approximate ratio 8:4:3.

Registry No.—**7**, 27448-28-8; **7** methyl ester, 35619-79-5; **8**, 2645-77-4; **9**, 27361-25-7; **10**, 35619-82-0; **10** acetate, 35619-83-1; **11**, 27447-99-0; **12**, 27361-27-9; **16**, 35619-86-4; **17**, 35619-87-5; **22**, 35619-88-6; **23**, 35619-89-7; bis(1,3-dioxocyclohexyl-2)acetic acid, 35619-90-0.

Asymmetric Induction in the Thermal Reactions of Allylic Alcohols with *N*,*N*-Dimethylacetamide Dimethyl Acetal and Triethyl Orthoacetate[1]

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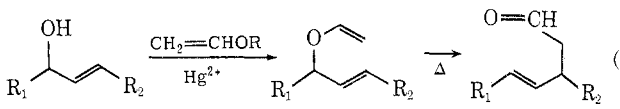
Optically active *trans*-3-penten-2-ol was used as the substrate for Claisen-type reactions with *N*,*N*-dimethylacetamide dimethyl acetal and triethyl orthoacetate. The products, the *N*,*N*-dimethyl amide and ethyl ester, respectively, of 3-methyl-4-hexenoic acid, were formed in greater than 90% optical purity and with inversion of configuration. The magnitude of asymmetric induction observed makes these reactions particularly useful for the stereospecific introduction of a carbon–carbon bond at an asymmetric center.

Stimulated by recent practical modifications,[2] the Claisen rearrangement of allyl vinyl ethers (eq 1) has seen increasing use in synthesis. A characteristic feature of the reaction, responsible in large measure for its success, is the high degree of stereospecificity which extends to the creation of asymmetric centers in high optical yield as well as to the production of predominantly trans double bonds.[3]



(1)

Of a number of variants of the Claisen rearrangement, two have proven particularly valuable for practical synthetic application in attaching a two-carbon chain because, in contrast to the original procedure, they can be carried out directly on an allylic alcohol without the need to isolate a vinyl ether intermediate. They are (a) the reaction of an allylic alcohol with *N*,*N*-dimethylacetamide dimethyl acetal (I) or its equivalent, 1-methoxy-1-dimethylaminoethylene (II), a reaction discovered by Meerwein[4] and systematized by Eschenmoser and coworkers[5] and which provides a one-step route to unsaturated amides (eq 2); and (b) the acid-catalyzed thermal reaction of allylic alcohols with triethyl orthoacetate (III), recently reported by

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