Regioselectivity in the Reductive Acyloxylation of α,α′-Dibromo Ketones

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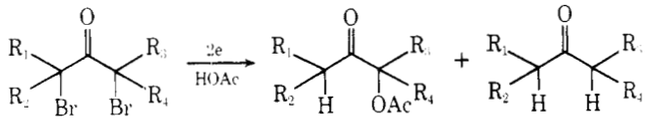
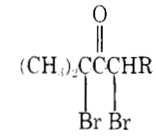
The reduction, either electrochemically or by ultrasonically-dispersed mercury, of a series of 2,4-dibromo-2-methyl-4-alkyl-3-butanones (alkyl = H, Me, Et, *i*-Pr, *t*-Bu, neopentyl) was carried out in a variety of solvent systems. It was possible to identify conditions under which either of the two possible isomeric α-acyloxy ketones could be made to predominate, and a number of examples of highly regioselective reactions were observed.

We have reported the fact that reduction of α,α′-dibromo ketones (**1**) in acetic acid, either electrochemically[2,3] or by ultrasonically-dispersed mercury,[4,5] affords primarily two types of products, α-acetoxy ketones (**2**) and the parent ketones (**3**). We have presented evidence[2,3] supporting the



1 **2** **3**

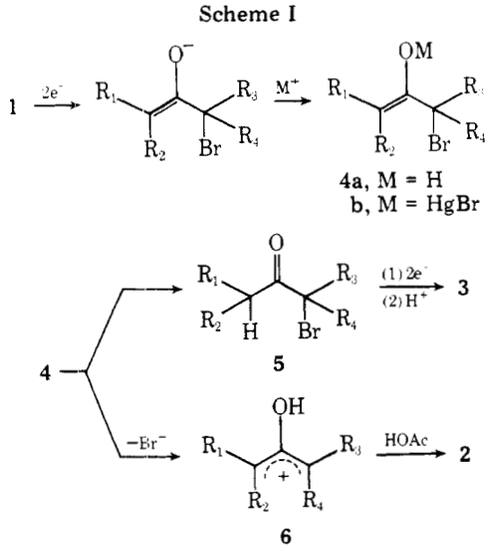
contention that in the electrochemical reaction **2** and **3** are formed from a common enol allylic bromide intermediate (**4a**) which may suffer either ionization to a 2-hydroxyallyl cation (**6**) or tautomerization to α-bromo ketone **5** and that **5** and **6** are the precursors of **3** and **2**, respectively (Scheme I). A related intermediate (**4b**) was suggested for the mercury reductions.[4,5] We have outlined[2,4] our reasons for believing the reductive substitution process embodied in the conversion **1** → **2** to be of synthetic value in the case where at least three of the R groups of **1** are alkyl. However, the fact that an unsymmetrical ketone may afford two isomeric α-substituted ketones is an obvious synthetic disadvantage, and we originally suggested[2] that for this reason the reaction would be of most interest with symmetrical ketones. We have now investigated this point further, however, and wish to report that the ratio of the two possible isomers from an unsymmetrical ketone is sufficiently sensitive to the experimental conditions employed so that the reaction can often be made highly regioselective, thus widening the range of synthetic utility of the reductive substitution process. The experiments to be described here involved reduction of a series of α,α′-dibromo ketones (**7a–f**) both electrochemically and by mercury. In order to test the effect of increasing the bulk of the carboxylic



7a, R = H
b, R = Me
c, R = Et
d, R = *i*-Pr
e, R = *t*-Bu
f, R = neopentyl

acid, some reductions were carried out in the presence of trimethylacetic acid, and reductions were also carried out in several solvent systems. The wide variety of conditions employed has permitted us to reach a number of conclusions concerning the effect of specific reaction variables and how these may be used to improve regioselectivity.

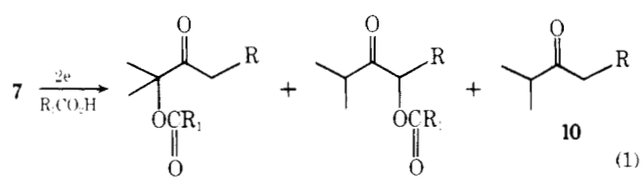
Scheme I



4a, M = H
b, M = HgBr

Results

Reduction of Dibromo Ketones. General Features. Electrochemical reductions were carried out at a mercury cathode at constant potential[6a] in one of three solvent systems: (a) acetic acid (HOAc) containing 1.0 M sodium acetate (NaOAc); (b) dimethylformamide (DMF) containing 10% (v/v) HOAc and 0.2 M NaOAc; or (c) DMF containing 10% (v/v) trimethylacetic acid (TMA) and 0.2 M sodium trimethylacetate (NaTMA). Chemical reductions were carried out by permitting the dibromide to react with ultrasonically-dispersed mercury at room temperature[6b] in one of three solvents: (a) HOAc; (b) TMA;[6] or (c) DMF containing 10% (v/v) HOAc and 0.2 M NaOAc. The crude reaction mixtures were analyzed by VPC and NMR spectroscopy. The major products were isolated by preparative VPC and identified by NMR and mass spectrometry. In general, two isomeric α-acyloxy ketones may be produced by reduction of each dibromide, i.e., **8** and **9**, or **11** and **12**. The pair of acyloxy ketones,



8, R_1 = Me
11, R_1 = *t*-Bu

9, R_1 = Me
12, R_1 = *t*-Bu

(1)

together with parent ketone **10**, generally constituted ≥90% of the crude product mixture; total yields were fair-to-good and were best in the larger molecular weight ketones (**7c–f**), where losses in workup due to solubility and/or volatility were minimal. The experimental results are summarized in Table I, along with experimental data obtained in this study for

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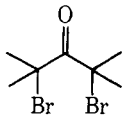
Table I. Reduction of Dibromo Ketones in the Presence of Carboxylic Acids

run no.	dibromo ketone	reduction method[a]	solvent[b]	yield,[c] % 2 (% III[c]/%) II°)[d]	10	other
1	**7a**	Hg	HOAc	26 (72:28)[e]	0	1
2	**7a**	Hg	DMF/HOAc/NaOAc	53 (20:80)[e]	0	2
3	**7a**	e⁻	DMF/HOAc/NaOAc	43 (11:89)[e]	0	0
4	**7a**	Hg	TMA	74 (87:13)[e]	0	0
5	**7a**	e⁻	DMF/TMA/NaTMA	65 (0:100)[e]	0	0
6	**7b**	Hg	HOAc	84 (80:20)[f]	0	0
7	**7b**	e⁻	HOAc/NaOAc	28 (87:13[f]	1	1
8	**7b**	Hg	DMF/HOAc/NaOAc	61 (77:23)[f]	0	6
9	**7b**	e⁻	DMF/HOAc/NaOAc	73 (33:67)[f]	0	4
10	**7b**	Hg	TMA	64 (98:2)[f]	0	1
11	**7b**	e⁻	DMF/TMA/NaTMA	71 (40:60)[f]	0	4
12	**7c**	Hg	HOAc	90 (85:15)[f]	4	1
13	**7c**	e⁻	HOAc/NaOAc	72 (86:14)[f]	23	2
14	**7c**	Hg	DMF/HOAc/NaOAc	82 (85:15)[f]	2	8
15	**7c**	e⁻	DMF/HOAc/NaOAc	74 (50:50)[f]	8	3
16	**7c**	Hg	TMA	72 (99:1)[f]	2	2
17	**7c**	e⁻	DMF/TMA/NaTMA	66 (30:70)[f]	4	0
18	**7d**	Hg	HOAc	89 (91:9)[f]	2	4
19	**7d**	e⁻	DMF/HOAc/NaOAc	74 (98:2)[f]	12	12
20	**7d**	Hg	TMA	68 (99:1)[f]	1	5
21	**7d**	e⁻	DMF/TMA/NaTMA	50 (99:1)[f]	6	8
22	**7e**	Hg	HOAc	58 (95:5)[f]	1	2
23	**7e**	e⁻	DMF/HOAc/NaOAc	48 (100:0)[f]	5	4
24	**7e**	Hg	TMA	50 (99:1)[f]	2	6
25	**7e**	e⁻	DMF/TMA/NaTMA	67 (100:0)[f]	7	1
26	**7f**	Hg	HOAc	85 (97:3)[e] (95:5)[f]	0	4
27	**7f**	e⁻	DMF/HOAc/NaOAc	37 (84:16)[e] (85:15)[f]	13	8
28	**7f**	Hg	TMA	85 (100:0)[e] (99:1)[f]	0	2
29	**7f**	e⁻	DMF/TMA/NaTMA	61 (39:61)[e] (40:60)[f]	20	3
30	**13**	Hg	HOAc	73	1	0
31	**13**	e⁻	DMF/HOAc/NaOAc	61	2	3
32	**13**	Hg	TMA	62	1	0
33	**13**	e⁻	DMF/TMA/NaTMA	57	0	0

[a] Hg = reduction by mercury; e⁻ = controlled-potential reduction at ca. −1.2 V/SCE at a mercury cathode. [b] For solvent composition, see Results. [c] Yields were obtained by VPC analysis; accuracy is estimated as ±3%. [d] The value in parentheses is the ratio of **8/9** or **11/12**. [e] VPC analysis. [f] NMR analysis.

2,4-dibromo-2,4-dimethyl-3-pentanone (**13**), which has previously been investigated in this laboratory.[2,4]

The only pairs of isomeric α-acyloxy ketones which proved separable by VPC were those from **7a** and **7f**. The ratio of isomers in these cases, and the relative yield of **10**, were determined by VPC area integration. For all other dibromo ketones, the mixture of α-acyloxy ketones was collected by preparative VPC and the ratio of **8/9** was determined by integration of appropriate peaks in the NMR spectrum. While for each mixture several features of the spectrum were available for determining the ratio of isomers, this value was most reliably obtained for acetoxy ketones by integration of the two acetoxy methyl singlets, which generally appear at ca. δ 1.95 and 2.05 for **8** and **9**, respectively. The ratio of **11/12** could not be so determined, and analysis employed other areas of the spectrum, e.g., the α-methyne resonance of **12** at ca. δ 5.0.



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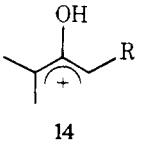
Discussion

The results embodied in Table I, while generally consistent with previous work in this area, demonstrate that the course of reaction is dependent to a considerable degree upon both the experimental conditions employed and the structure of the dibromo ketone. A number of interesting and useful conclusions may be reached.

Yields of α-acyloxy ketones are generally highest when the dibromo ketone bears three or four α-alkyl substituents. As we have argued,[2] this is consistent with a mechanism (Scheme I) involving as its key feature the ionization of an enol allylic bromide (**4**) to a 2-hydroxyallyl cation (**6**). Furthermore, and again as previously observed,[4] the ratio of acyloxy ketone(s)/parent ketone is greater in the mercury-promoted reduction than in the electrochemical reduction in almost every case for a given reactant–solvent combination.

The dibromides reduced in this study were designed to provide information on possible effects upon regioselectivity of introduction of the α-acyloxy substituent. The *gem*-dimethyl group adjacent to the carbonyl in all ketones provides a site of constant size as the size of the group on the opposite flank of the carbonyl is increased in size across the series **7a–f.** This, together with the use of both acetic and trimethylacetic acids, which differ considerably in bulk, was expected to provide information on the role of steric effects in directing introduction of the α substituent. Furthermore, in all cases we are balancing a tertiary against a secondary site (in the case of **7a,** primary), and hence a rather constant electronic effect ought to be operating throughout the series. Unequal charge distribution in the corresponding allylic carbonium ion (**14**) ought to exert an electronic effect on regioselectivity of attack, but it was anticipated that increasing bulk at the secondary site in cations **14b–f** would permit separation of the electronic



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and steric effects. The use of solvent systems containing either the neat acid or DMF containing the acid was designed to assess the effect of solvent dielectric constant on the regioselectivity of attack.[7]

Electronic effects should be most pronounced with **14a,** which balances a tertiary against a primary site. Reduction in acetic acid gives mostly tertiary acetate, but the primary acetate predominates in DMF/HOAc. Presumably, the tertiary site is tightly solvated in the less polar solvent, acetic acid, thus leading to preferred reaction at this site. In DMF/HOAc, the ion ought to be less tightly solvated, and formation of the primary acetate (runs 2 and 3) may be a steric phenomenon, solvation at the two sites being comparable in

this solvent. These conclusions are reinforced by the results of run 4, in which reaction in neat (and presumably quite nonpolar)[8] trimethylacetic acid afforded roughly the same isomer ratio as in neat acetic acid, and of run 5, in which the primary isomer was formed exclusively in DMF/TMA. Similar behavior can be noted by comparing runs 7 and 9 or 13 and 15. Thus, solvent polarity clearly plays a role in determining product ratios. At the same time, a steric effect can be detected by comparing, for example, the reduction of **7b–e** in the polar medium DMF/HOAc/NaOAc. As R increases in size (runs 9, 15, 19, 23), the relative amount of secondary acetate (**9**) decreases in the sequence 67, 50, 2, and 0%. When R is neopentyl (**7f**), 16% secondary acetate is formed since the secondary site of **14f** is neohexyl and presumably less hindered than the neopentyl-type site of **14e**. With trimethylacetate as nucleophile (runs 11, 17, 21, 25), the ratios of **11/12** are surprisingly similar (60, 70, 1, and 0% **12**) to those in acetic acid, suggesting that the bulk of the carboxylic acid is not as important in attack upon **14b–e** as with **14a**. Inspection of runs 6, 12, 18, 22, and 26 and runs 10, 16, 20, 24, and 28 shows that the mercury reactions in acetic and trimethylacetic acids exhibit similar trends to the electrochemical reductions, supporting our contention[3-5] that the two types of reduction are mechanistically similar.

Another interesting correlation is apparent by comparing runs 2 and 3, 8 and 9, or 14 and 15. In the same solvent, the mercury reduction always favors formation of tertiary product when compared with the electrochemical reaction. The origin of this phenomenon is not obvious; it may be a steric effect associated with complexation of mercury (with its associated ligands) with the oxygen atom of **14**. Finally, we note that the mercury reaction is not as sensitive to solvent polarity as the electrochemical reduction (cf. runs 6 and 8 vs. 7 and 9).

Synthetic Applications. The data presented in this paper indicate that orientation in the reductive substitution process is a sensitive function of solvent, mode of reduction (electrochemical or chemical), and the structure of the dibromide, but less sensitive to the bulk of the carboxylic acid used. We may summarize some generalizations which may be used to control regioselectivity for synthetic purposes. Tertiary isomer **8** or **11** can be maximized by mercury reduction in the carboxylic acid as solvent; when the secondary site is sterically hindered, the tertiary isomer can be expected to form highly regiospecifically relatively independent of the conditions chosen for reduction. Formation of the primary isomer from the dibromide derived from a methyl ketone, e.g., **7a**, is favored by electrochemical reduction in a polar solvent (DMF) containing a sterically hindered carboxylate (TMA/NaTMA). When steric hindrance is not great at a secondary site (**7b** and **7c**), these conditions can be used to maximize the yield of secondary isomer.

Experimental Section

General. Mass and NMR spectra were measured as previously described.[2] Analytical VPC separations were carried out using a Varian Model 1720 dual column thermal conductivity instrument on a 3 m × 6 mm column packed with 15% Reoplex 400 on Chromosorb P (column A). Preparative VPC separations were made using a Varian A-90P thermal conductivity instrument on a 3 m × 6 mm column packed with 10% SE-30 on Chromosorb P (column B). Electrochemical experiments were carried out using a Princeton Applied Research Electrochemistry System and a previously described electrochemical cell.[2,9] Elemental analyses were performed by Chemalytics, Inc., Tempe, Ariz.

Synthesis of Ketones. 3-Methyl-2-butanone (**10a**), 2-methyl-3-hexanone (**10c**), and 2,4-dimethyl-3-pentanone were commercial samples (Aldrich Chemical Co.). 2-Methyl-3-pentanone (**10b**), 2,5-dimethyl-3-hexanone (**10d**), 2,5,5-trimethyl-3-hexanone (**10e**) and 2,6,6-trimethyl-3-heptanone (**10f**) were prepared by reaction of the appropriate Grignard reagent with isobutyraldehyde, followed by oxidation of the crude alcohol by the method of Brown and Garg.[10] The alkyl halides were commercial samples (Aldrich) except for 3,3-dimethyl-1-bromobutane, which was prepared by reacting the corresponding alcohol (Aldrich) with tri-*n*-butylphosphine and bromine according to the method of Wiley.[11] NMR spectra of the distilled ketones agreed with expected and, where available, literature values.

Synthesis of Dibromo Ketones. The dibromination of the above ketones was carried out in carbon tetrachloride at 0 °C. Microanalyses were not obtained for new dibromo ketones (**7c,e,f**), which were found to undergo slow decomposition with time, but their NMR and mass spectra were consistent with the assigned structures. Only the largest mass spectral lines are listed.

1,3-Dibromo-3-methyl-2-butanone (7a): bp 54 °C (0.4 mm) [lit.[12] bp 87 °C (10 mm)]; NMR δ 1.97 (s, 6 H), 4.5 (s, 2 H); mass spectrum, *m/e* (intensity) 246 (21), 244 (40), 242 (22), 165 (25), 163 (27), 151 (50), 149 (50), 123 (94), 121 (100), 70 (52), 56 (74).

2,4-Dibromo-2-methyl-3-pentanone (7b):[13] bp 40 °C (0.15 mm); NMR δ 1.85 (d, 3 H), 1.98 (s, 3 H), 2.08 (s, 3 H), 5.15 (q, 1 H); mass spectrum, *m/e* 260 (3), 258 (6), 256 (3), 151 (16), 149 (22), 123 (51), 121 (58), 119 (23), 117 (24), 70 (47), 69 (38), 56 (100).

2,4-Dibromo-2-methyl-3-hexanone (7c): bp 42 °C (0.15 mm); NMR δ 1.1 (t, 3 H), 1.98 (s, 3 H), 2.08 (s, 3 H), 2.05 (q, 2 H), 5.1 (t, 1 H); mass spectrum, *m/e* 274 (1.5), 272 (3), 270 (1.5), 149 (15), 123 (36), 70 (89), 55 (22), 41 (100).

2,4-Dibromo-2,5-dimethyl-3-hexanone (7d):[2] bp 51 °C (0.1 mm) [lit. bp 45 °C (0.3 mm)].

2,4-Dibromo-2,5,5-trimethyl-3-hexanone (7e). This material contained a small amount (~5%) of monobromide, and reaction yields were corrected accordingly: NMR δ 1.25 (s, 9 H), 1.87 (s, 3 H), 2.10 (s, 2 H), 4.75 (s, 1 H); mass spectrum *m/e* 302 (0.2), 300 (0.4), 298 (0.2), 179 (22), 177 (22), 151 (33), 149 (35), 123 (35), 121 (35), 98 (41), 83 (65), 69 (57), 57 (100).

2,4-Dibromo-2,6,6-trimethyl-3-heptanone (7f): NMR δ 1.1 (s, 9 H), 1.93 (s, 3 H), 2.17 (s, 3 H), 2.20 (m, 2 H), 5.4 (t, 1 H); mass spectrum, *m/e* 316 (0.2), 314 (0.4), 312 (0.2), 193 (33), 191 (33), 123 (29), 121 (30), 112 (53), 98 (18), 83 (20), 70 (33), 57 (100).

Reductions by Mercury. The dibromo ketone to be reduced was added to a 25-mL Erlenmeyer flask, together with 10–15 mL of solvent. The amount of dibromide used was calculated to yield 2.0 g (theoretical) of α-substituted ketone. A 7-mL amount of mercury was added to the flask, which was then sealed with a rubber serum cap and placed in a Varian 9661-00 ultrasonic cleaner maintained at 14 ± 2 °C for 72 h. At the end of this time, the flask was allowed to stand for some time to permit suspended solids to settle. The clear supernatant liquid was removed, and the mercury–solids sludge was washed with carbon tetrachloride by decantation.[14] The combined organic extracts were washed with water, saturated sodium bicarbonate, and water and dried over $MgSO_4$. The solvent was removed at the rotary evaporator to afford the crude product.

Electrochemical reductions were carried out as previously described.[2] Spectral measurements on α-acetoxy ketones and parent ketones were made on samples isolated by preparative VPC (column B). Microanalytical samples were prepared by a second pass through column B.

Analysis of mixtures was made by measuring relative areas of VPC peaks (column A) and then collecting the acetoxy ketone fraction (column B) and measuring the ratio of **8/9** (or **11/12**) by NMR (see Results). When the two isomeric acetoxy ketones were separable by VPC, this ratio could be measured by both NMR and VPC; results generally agreed to within ±2% between the two procedures (Table I). Relative intensities of absorptions in NMR spectra of mixtures of α-acyloxy ketones were consistent with the assignments given. Some regions of some NMR spectra exhibited overlapping peaks from both isomers; data listed below include only unequivocal assignments.

Properties of New Acyloxy Ketones. Physical properties of new acyloxy ketones are listed below. Acetoxy ketones from the reduction of **7a, 7b,** and **7d** (and one of the isomers from **7e**)[15c] are known substances[2,15] and are not listed. Data are listed for pairs of isomers where the individual isomers were inseparable by preparative VPC.[16]

2-(Trimethylacetoxy)-2-methyl-3-butanone (11a): NMR δ 1.13 (d, 6 H), 1.23 (s, 9 H), 2.60 (m, 1 H), 4.62 (s, 2 H); mass spectrum, *m/e* 186 (0.9), 143 (26), 119 (11), 85 (37), 71 (56), 69 (9), 57 (100), 43 (56).

4-(Trimethylacetoxy)-2-methyl-2-butanone (12a): NMR δ 1.18 (s, 9 H), 1.38 (s, 6 H), 1.97 (s, 3 H); mass spectrum, *m/e* 186 (1), 143 (29), 85 (36), 69 (6), 59 (65), 58 (14), 57 (100), 43 (33).

2-(Trimethylacetoxy)-2-methyl-3-pentanone (11b) and 4-(Trimethylacetoxy)-2-methyl-3-pentanone (12b):[16] NMR δ 0.98 (t), 1.07 (dd),* 1.20 (s), 1.25,* 1.42 (s), 2.35 (q), 2.75 (m),* 5.10 (q);* mass spectrum, *m/e* 200 (0.8), 143 (14), 142 (6), 99 (5), 85 (50), 71 (6),* 59 (36), 58 (9), 57 (10). Peaks attributable to **12b** are marked with an asterisk.

2-Acetoxy-2-methyl-3-hexanone (8c) and 4-Acetoxy-2-methyl-3-hexanone (9c):[16] NMR δ 0.83 (t),* 0.87 (t), 1.03 (dd),* 1.40 (s), 1.50 (m), 1.97 (s), 2.04 (s),* 2.35 (t), 2.75 (m),* 5.02 (dd);* mass spectrum, *m/e* 172 (2), 129 (9), 101 (15), 71 (32),* 59 (28), 43 (100). Peaks due to **9c** are marked by asterisks.

2-(Trimethylacetoxy)-2-methyl-3-hexanone (11c) and 4-(Trimethylacetoxy)-2-methyl-3-hexanone (12c):[16] NMR δ 0.87 (t), 0.98 (dd),* 1.17 (s), 1.38 (s), 1.50 (m), 1.75 (m),* 2.30 (t), 2.75 (m),* 4.96 (dd);* mass spectrum, *m/e* 214 (0.3), 143 (6), 85 (39), 71 (12),* 59 (22), 58 (5), 57 (100). Peaks attributable to **12c** are marked with an asterisk.

2-(Trimethylacetoxy)-2,5-dimethyl-3-hexanone (11d) and 4-(Trimethylacetoxy)-2,5-dimethyl-3-hexanone (12d):[16] NMR δ 0.88 (m), 1.17 (s), 1.40 (s), 2.22 (broad d), 2.75 (m),* 4.97 (d);* mass spectrum, *m/e* 228 (0.4), 170 (7), 143 (8), 85 (71), 59 (23), 57 (100). Peaks attributable to **12d** are marked with an asterisk.

2-Acetoxy-2,5,5-trimethyl-3-hexanone (8e)[15c] **and 4-Acetoxy-2,5,5-trimethyl-3-hexanone (9e):**[16] NMR δ 1.00 (s), 1.20 (d), 1.40 (s), 1.98 (s), 2.05 (s),* 2.30 (s), 4.83 (s);* mass spectrum, *m/e* 200 (2), 157 (71), 101 (24), 99 (45), 84 (s), 71 (12),* 69 (6), 59 (32), 57 (65), 43 (100). Peaks attributable to **9c** are marked with an asterisk.

2-(Trimethylacetoxy)-2,5,5-trimethyl-3-hexanone (11e) and 4-(Trimethylacetoxy)-2,5,5-trimethyl-3-hexanone (12e): NMR δ 1.00 (s), 1.18 (s), 1.40 (s), 2.27 (s), 4.78 (s);* mass spectrum, *m/e* 242 (0.2), 99 (15), 85 (32), 59 (15), 57 (100). Peaks in the spectra attributable only to **12e** are marked with an asterisk.

2-Acetoxy-2,6,6-trimethyl-3-heptanone (8f) and 4-Acetoxy-2,6,6-trimethyl-3-heptanone (9f):[16] NMR δ 0.87 (s), 0.97 (s),* 1.40 (s), 1.45 (m), 2.00 (s), 2.04 (s),* 2.30 (m), 2.75 (m),* 5.13 (t);* mass spectrum, *m/e* 214 (0.8), 171 (7), 139 (13), 113 (46), 101 (18), 85 (12), 71 (6),* 69 (12), 59 (27), 57 (36), 55 (7), 43 (100). Peaks in the spectra attributable only to **9f** are marked with an asterisk.

2-(Trimethylacetoxy)-2,6,6-trimethyl-3-heptanone (11f) and 4-(Trimethylacetoxy)-2,6,6-trimethyl-3-heptanone (12f):[16] NMR δ 0.07 (s), 0.95 (s),* 1.15 (d),* 1.20 (s), 1.40 (s), 1.45 (m), 2.30 (m), 2.66 (m),* 5.08 (t);* mass spectrum, *m/e* 256 (0.7), 198 (10), 143 (9), 139 (20), 113 (36), 85 (80), 71 (7),* 70 (6), 69 (9), 59 (26), 58 (7), 57 (100). Peaks attributable only to **12f** are marked with an asterisk.

2-(Trimethylacetoxy)-2,4-dimethyl-3-pentanone (15):[16] NMR δ 1.02 (d, 6 H), 1.16 (s, 9 H), 1.47 (s, 6 H), 2.80 (m, 1 H); mass spectrum, *m/e* 214 (0.8), 156 (27), 143 (32), 113 (8), 86 (10), 85 (20), 71 (38), 70 (15), 69 (11), 59 (100), 58 (24), 57 (93), 56 (9), 55 (8), 43 (100).

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Registry No.—**7a,** 1518-06-5; **7b,** 37010-00-7; **7c,** 69204-79-1; **7d,** 56829-66-4; **7e,** 69204-80-4; **7f,** 69204-81-5; **8a,** 10235-71-9; **8c,** 69204-82-6; **8e,** 21503-00-4; **8f,** 69204-83-7; **9a,** 36960-07-3; **9c,** 69204-84-8; **9e,** 69204-85-9; **9f,** 69204-86-0; **10a,** 563-80-4; **10b,** 565-69-5; **10c,** 7379-12-6; **10d,** 1888-57-9; **10e,** 40239-50-7; **10f,** 40238-56-0; **11a,** 69204-87-1; **11b,** 69204-88-2; **11c,** 69204-89-3; **11d,** 69204-90-6; **11e,** 69204-91-7; **11f,** 69204-92-8; **12a,** 69204-93-9; **12b,** 69204-94-0; **12c,** 69204-95-1; **12d,** 69204-96-2; **12e,** 69204-97-3; **12f,** 69204-98-4; **13,** 17346-16-6; **15,** 67889-09-2; 2,4-dimethyl-3-pentanone, 565-80-0; 2-acetoxy-2,4-dimethyl-3-pentanone, 21980-75-6.

References and Notes

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Mechanistic Studies on the Photochemical Conversion of Enaminonitriles to Imidazoles

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Imidazoles are not formed by photolysis of the N,N-disubstituted enaminonitriles, 2-(dimethylamino)-1-cyclohexene-1-carbonitrile (**7**) and 3-(dimethylamino)acrylonitrile (**5**). These results show that the enaminonitrile must contain an NH group for the photochemical formation of the imidazole to proceed. *N*-Isopropyldiaminomaleonitrile (**11**) did not photodissociate to yield aminocyanocarbene (**4**) as shown by the absence of diaminomaleonitrile (DAMN) (**1**) as a photoproduct. Direct irradiation of *N*-isopropyliminoacetonitrile (**18A**) at −196 °C did not give the absorption spectrum attributed to aminocyanocarbene. Polymer formation was observed when the photolysis of **18A** was performed at room temperature. Benzophenone-sensitized photolysis of **18A** gave *N,N'*-diisopropyldiaminosuccinonitrile (**19A**). The reaction does not proceed by the dimerization of *N*-isopropylaminocyanocarbene to diisopropyldiaminomaleonitrile (**15**) followed by the reduction of **15,** since it was observed that **19A** is not formed by the benzophenone-sensitized photolysis of **15.** The significance of these results to the mechanism of the photochemical rearrangement of enaminonitriles to imidazoles and the postulated role of aminocyanocarbene as an intermediate in a number of thermal and photochemical reactions are discussed.

The photochemical conversion of the HCN oligomer, diaminomaleonitrile (DAMN) (**1**), to 4-aminoimidazole-5-carbonitrile (AICN) (**3**) is a key step in one of the pathways proposed for purine synthesis on the primitive earth (Scheme I).[1] This reaction has also been shown to be an efficient route for the synthesis of substituted imidazoles starting from the corresponding enaminonitrile.[2,3] The reaction is a monophotonic process in which the enaminonitrile with the cis orientation of the amino and cyano groups cyclizes to the imidazole.[3,4] The mechanism of the reaction has not been established with certainty. The route shown in path A of Scheme II finds support in the observation of IR bands at 2000 cm^{-1},

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