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Synthesis and Application of Imidazole Derivatives: Preparation of Various Diketones from 1,*n*-Bis(1-methyl-1*H*-imidazol-2-yl)alkane-1,*n*-diones[1]

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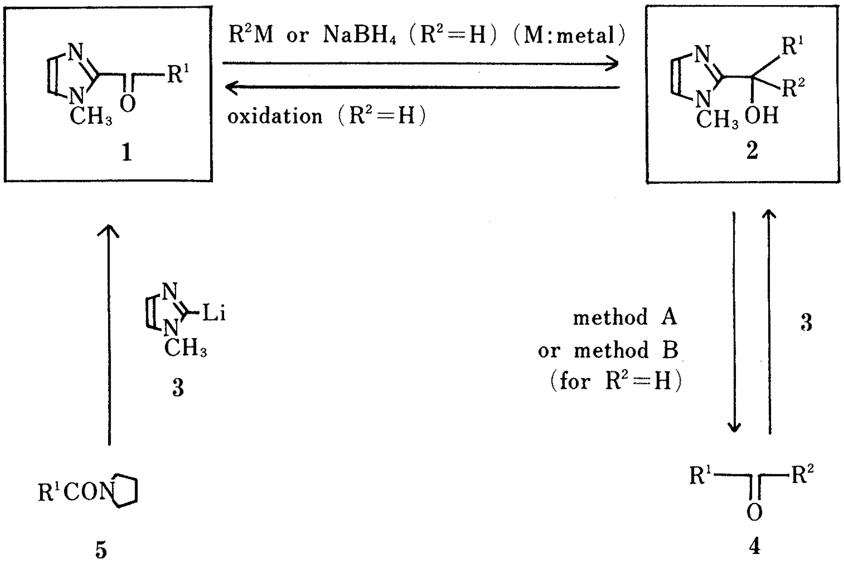
Reaction of 1,*n*-bis(1-methyl-1*H*-imidazol-2-yl)alkane-1,*n*-dione (**8**) with an excess of Grignard reagent was examined. In the cases of $n=4$ and 5, precursors (**14**) for synthesis of various asymmetric 1,4- and 1,5-diketones (**12**: $R^1 \neq R^2$), respectively, were obtained in good yields by treating **8** with an excess of methylmagnesium iodide in ether followed by trimethylsilylation. In the case of $n \geqq 8$, the two carbonyl groups of **8** were both attacked by the Grignard reagent, and the products (**11**: $R^1=R^2=CH_3$) were convertible to symmetrical diketones (**12**: $R^1=R^2=CH_3$) in good yields. In cases of $n=6$ and 7, the mode of the Grignard reaction was transitional between the two types.

Keywords——2-acyl-1*H*-imidazole; 1,*n*-bis(1-methyl-1*H*-imidazol-2-yl)-1,*n*-alkanedione; diketone synthesis; asymmetric diketone; symmetric diketone; Grignard reaction; dihydrojasmone; *cis*-jasmone; muscone; 2-(1-hydroxy-1-alkyl)-1-methyl-1*H*-imidazole

1-Acyl-1*H*-imidazole derivatives have been widely applied in organic synthesis as an important active acyl source.[2,3] On the other hand, 2-acyl-1-methyl-1*H*-imidazoles (**1**) have been little studied in regard to synthesis and their synthetic applications.[4] In the previous papers, we reported syntheses of the 2-acylimidazoles (**1**) and their conversion into various carbonyl compounds (**4**).[4,5] As illustrated in Chart 1, the previously reported methodology utilizes the superior leaving ability of the 2-imidazolium moiety.[4,5] Furthermore, the intermediary 2-(*n*-hydroxyalkyl-1-methyl-1*H*-imidazole (**2**) can be regarded as a protected form of the carbonyl group.[4,5]

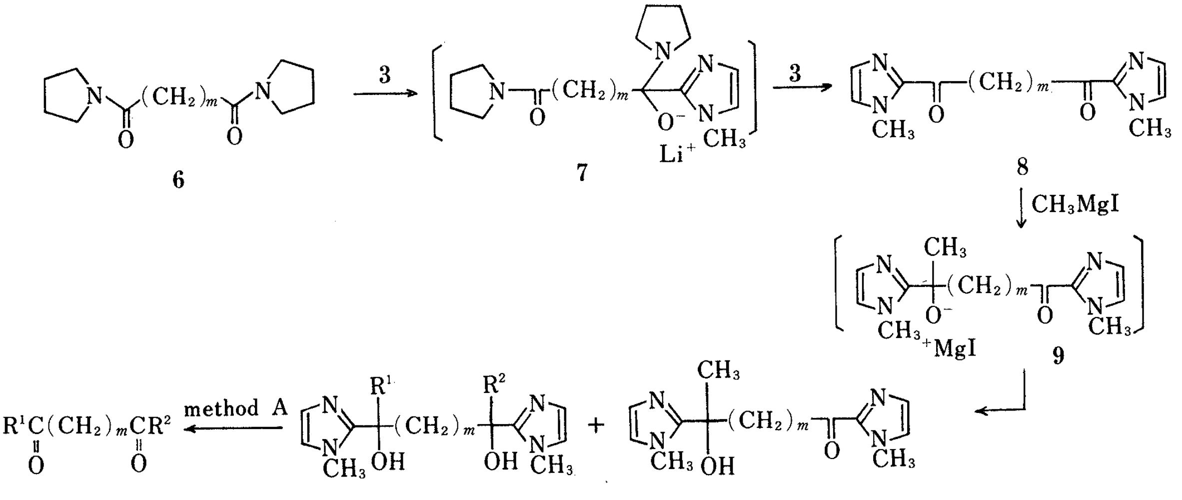
In the recent preliminary report,[1] we also briefly reported interesting syntheses of the natural perfume ingredients, dihydrojasmone (**15a**), *cis*-jasmone (**15b**) and *dl*-muscone (**16**) as further applications of the methodology starting from 1,*n*-bis(1-methyl-1*H*-imidazol-2-yl)alkane-1,*n*-diones (**8**: $m=2$—12). This paper presents details of the methodology including its scope and limitations for general application to the synthesis of 1,*n*-alkanediones (**12**) starting from diimidazolyldiketones (**8**).

Dipyrrolidine amides (**6**: $m=2$, 3, 4, 5, 6, 12) of various 1,*m*-dicarboxylic acids were prepared conveniently in good yields by treating the corresponding dimethyl esters with an excess of pyrrolidine in a sealed tube at 130—160 °C for more than 8 h. The dipyrrolidine amides (**6**) were converted to the corresponding 1,*n*-bis(1-methyl-1*H*-imidazol-2-yl)alkane-1,*n*-diones (**8**) in various yields (22.5—83.0%) according to the reported procedure.[4] In particular, the yield of 1,4-bis(1-methyl-1*H*-imidazol-2-yl)butane-1,4-dione (**8a**) was very low (22.5%) probably because the second attack of the 2-lithio-1-methyl-1*H*-imidazole (**3**) on the intermediate (**7**) was interfered with by the presence of the nearby negative charge in **7**. The results including cases of other different *m*-numbers are summarized in Table I.



method A: 1) CH_3I or $(CH_3)_2SO_4$/AcOEt/reflux
2) benzene/10% K_2CO_3/80 °C
method B: 1) CH_3I or $(CH_3)_2SO_4$/AcOEt/reflux
(for $R^2=H$) 2) benzene/1 N NaOH/6-aminocaproic acid/80 °C

Chart 1



12 : $R^1=R^2=CH_3$

11 : $R^1=R^2=CH_3$

10

Chart 2

We planned to examine the scope and limitations of the reaction of the 1,*n*-bis(1-methyl-1*H*-imidazol-2-yl)alkane-1,*n*-diones (**8**) with an excess amount (more than 2 eq) of an ethereal solution of methylmagnesium iodide by quantitative analyses of the products, which were presumed to be the halfway product (**10**), the doubly attacked product (**11**: $R^1=R^2=CH_3$) and the recovered substrate (**8**). The starting material (**8**) and the halfway product (**10**) have the 2-acylimidazole moiety, which has a strong ultraviolet (UV) absorption band near 278 nm.[4c)] Therefore, they were directly determined by analysis with high-performance liquid chromatography (HPLC). However, quantitative determinations of the diol (**11**: $R^1=R^2=CH_3$), which has no remarkable absorption band in the UV region, had to be performed indirectly by analysis with gas-liquid layer chromatography (GLC) after transformation to the corresponding diketone (**12**). The results, which were obtained by the procedure described

TABLE I. Preparation of 1,*n*-Bis(1-methyl-1*H*-imidazol-2-yl)alkane-1,*n*-dione (**8**) from Alkane-1,*n*-dicarboxylic Acid Pyrrolidine Diamide (**6**)

Entry	*m*	mp or bp (°C) of **6** (Recryst. solvent)		mp of **8** (°C) (Recryst. solvent)		Isolated yield (%) of **8**
1	2	mp 77.0—78.5 (IPA–*n*-hexane) bp 205.0—210.0 (2 mmHg)	**6a**	176.0—177.5 (Dimethyl cellosolve)	**8a**	22.5
2	3	mp 38.0—39.0 (Ethyl acetate) bp 185.0—188.0 (0.01 mmHg)	**6b**	129.0—130.0 (IPA)	**8b**	45.3
3	4	mp 86.0—87.0 (Ethyl acetate)	**6c**	174.0—176.0 (Methanol)	**8c**	42.2
4	5	bp 218.0—220.0 (0.01 mmHg)	**6d**	94.0—95.5 (IPA)	**8d**	62.8
5	6	mp 74.5—75.0 (Ethyl acetate)	**6e**	119.5—120.5 (Ethyl acetate–CCl_4)	**8e**	83.0
6	12	mp 63.0—64.0 (*n*-Hexane)	**6f**	111.5—112.0 (Ethanol)	**8f**	45.1

TABLE II. Quantitative Analysis of the Reaction of Diimidazolyldiketones (**8**) with CH_3MgI

Entry	*m*	Product yield (%)					
		8[a]		**10**[a] ($R^1=CH_3$)		**11** ($R^1=R^2=CH_3$)	
1	2	**8a**	4.3	**10a**	96.3 (87.7)[e]	**11g**	nil[c]
2	3	**8b**	11.7	**10b**	75.0 (68.9)[e]	**11h**	trace[c]
3	4	**8c**	4.5	**10c**	37.6 (14.5)[e]	**11i**	33.3[c] (23.3)[d]
4	5	**8d**	nil	**10d**	32.4	**11j**	66.9[c] (60.5)[d]
5	6	**8e**	nil	**10e**	nil	**11k**	93.2[c] (87.6)[d]
6	12	**8f**	nil	**10f**	nil	**11l**	(94.9%)[b]

a) The yield was determined by HPLC analysis. *b*) Isolated yield of **11**. *c*) The yield was obtained after conversion of **11** into **12** (GLC analysis). *d*) The yield was obtained after conversion of **11** into **12** (isolated yield). *e*) Isolated yield of **10**.

in the experimental section, are summarized in Table II. As shown in the table, in the cases of $m=2$ and 3, the halfway products (**10a** and **10b**, respectively) were obtained predominantly while the corresponding doubly attacked product (**11**: $R^1=R^2=CH_3$, $m=2$ and 3) was minor. On the contrary, in the cases of $m=6$ and 12, the doubly attacked products (**11**: $R^1=R^2=CH_3$, $m=6$ and 12) were predominant. In the cases of $m=4$ and 5, the results were transitional between both types. These results clearly indicate that in the cases of $m=2$ and 3, the second attack of the Grignard reagent on the intermediate (**9**) is strongly interfered with by the nearby oxide anion [four ($m=2$) and five ($m=3$) linkages are present between the oxide-anion portion (O^-) and the carbonyl carbon atom in **9**], but such interference gradually ceases with increase of the *m*-number [$m \geqq 4$; more than six linkages are present between the oxide-anion portion ($-O^-$) and the carbonyl carbon atom in **9**].

Next, we tried to isolate the halfway product (**10**) from the reaction mixture after conversion into the corresponding silyl ethers (**14**) starting from the diimidazolyldiketones [**8a** ($m=2$), **8b** ($m=3$) and **8c** ($m=4$)] and various Grignard reagents. A halfway product, obtained from the reaction of **8a** with methylmagnesium iodide, was converted *in situ* (without isolation of **10a**: $m=2$) into the viscous oily trimethylsilyl ether (**14a**) in 81.2% yield by treatment with trimethylsilyl (TMS) chloride. The infrared spectrum (IR) of **14a** in chloroform showed the presence of a carbonyl group (1678 cm^{-1}) and the high-resolution mass spectrum (HRMS) showed an exact molecular ion peak at m/z 334.1850. The proton nuclear magnetic resonance spectrum (^{1}H-NMR) of the product (**14a**) showed signals of $(C\underline{H}_3)_3Si$– at -0.01 ppm, $C\underline{H}_3C(O\text{–}TMS)$– at 1.79 ppm, $-(C\underline{H}_2)_2-$ at 2.10—3.35 ppm and two $NC\underline{H}_3$ at 3.80 and 3.93 ppm. The results including other cases, are summarized in Table III. The corresponding halfway products (**14**) were obtained in good yields with the sole exception of entry 9 ($m=4$, 25.4%).

As an application of the present methodology, we planned to explore the synthesis of various asymmetric diketones (**12**: $R^1 \neq R^2$) on the basis of the result of the cases of $m=2$ and 3 (entries 1—8) listed in Table III. The synthetic scheme is shown in Chart 3.

For example, the silyl ether (**14**) was treated with an excess of an ethereal solution of methylmagnesium iodide and (Z)-hex-3-enylmagnesium bromide[6)] to give the dihydroxy products **11a** ($R^1=CH_3$, $R_2=n$-hexyl) and **11b** [$R^1=CH_3$, $R^2=(Z)$-hex-3-enyl], respectively. Although thin-layer chromatography (TLC) of these products showed only a single spot, the stereochemistry around the two hydroxy groups of these products was not determined (probably they were produced as diastereomeric mixtures). These products (**11a** an **11b**) were successfully converted without purification to the corresponding 1,4-diketones **12a** (76.9% from **14a**) and **12b** (60.5% from **14a**), respectively, according to the reported procedure.[5b)] These oily 1,4-diketones (**12a** and **12b**) are key intermediates for the total syntheses of the natural perfume ingredients, dihydrojasmone (**15a**)[6,7)] and *cis*-jasmone (**15b**),[8)] respectively.

The 2-thienyl derivative (**14b**) was treated with *tert*-butyl lithioacetate at -78 °C to give the corresponding dihydroxyester (**11c**) as a viscous material, which was presumed to be a diastereomeric mixture. The conversion of 2-(1-hydroxy-1-alkyl)-1-methyl-1*H*-imidazole (**2**) into the corresponding ketone was carried out according to the procedure of method A, reported in the previous paper.[5b)] The dihydroxy product (**11c**) was first converted to the corresponding quaternary salt by refluxing in ethyl acetate in the presence of a slight excess of dimethyl sulfate and then the formed quaternary salt was treated without purification with an excess of aqueous 10% K_2CO_3 at 80 °C for several hours to produce a crude viscous oil in 74.7% yield. The oily product was not the corresponding ketoester **12c** but was suggested to

TABLE III. Preparation of Trimethylsilyloxyimidazolylketone (**14**) from Diimidazolyldiketone (**8**)

Entry	Diketone (**8**)	m	R^1MgX	Product (**14**)[a)]	Isolated yield of **14** (%)
1	**8a**	2	CH_3MgI	**14a**	81.2
2	**8a**	2	2-Thienyl-MgBr	**14b**	62.0
3	**8a**	2	$C_6H_5CH_2MgBr$	**14c**	72.3
4	**8a**	2	n-Hexyl-MgBr	**14d**	43.7[b)]
5	**8b**	3	CH_3MgI	**14e**	73.3
6	**8b**	3	$C_6H_5CH_2MgBr$	**14f**	84.0
7	**8b**	3	C_6H_5MgBr	**14g**	67.5
8	**8b**	3	$C_6H_5CH_2CH_2MgBr$	**14h**	47.8[b)]
9	**8c**	4	CH_3MgI	**14i**	25.4

a) Viscous oily material. *b*) The low yield may be due to β-hydride reduction of the excess of R^1MgBr.

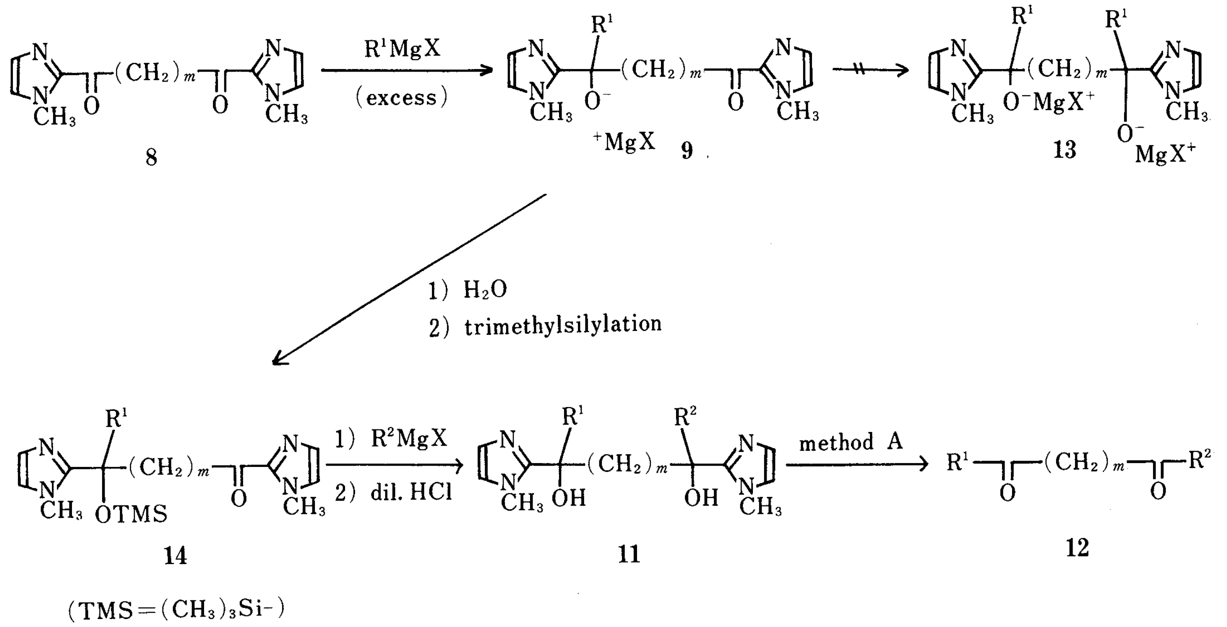


Chart 3

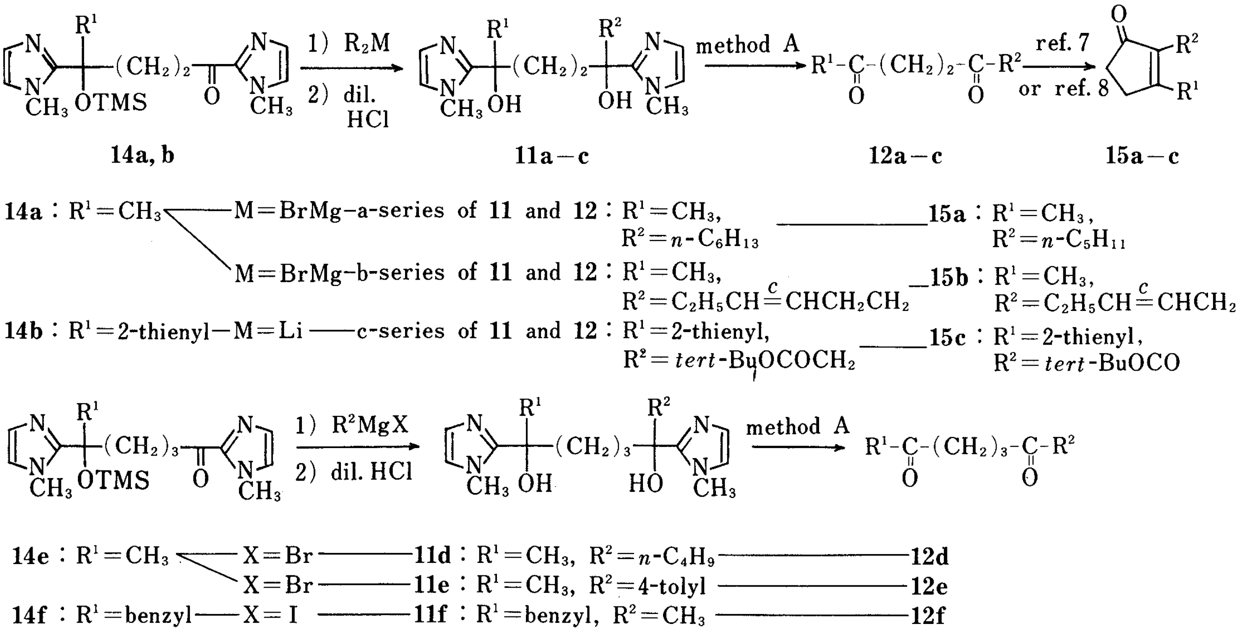


Chart 4

be the cyclized product **15c** because the product did not give any color reaction on addition of a methanolic ferric chloride solution.

Similar results were obtained with **14e** and **14f** when they were treated with *n*-butylmagnesium bromide, 4-tolylmagnesium bromide and methylmagnesium iodide, and the produced dihydroxy compounds (**11d**, **11e** and **11f**, respectively; used without purification) were successfully converted to the corresponding 1,5-diketones (**12d**, **12e** and **12f**, respectively) in good yields according to method A.

Only one example of the practical application of the preparation of the symmetrical diketone (**12**: $R^1=R^2$) in the case of $n \geqq 6$ was examined. Thus 1,14-bis(1-methyl-1*H*-imidazol-2-yl)tetradecane-1,14-dione (**8f**) was treated with an ethereal solution of an excess of

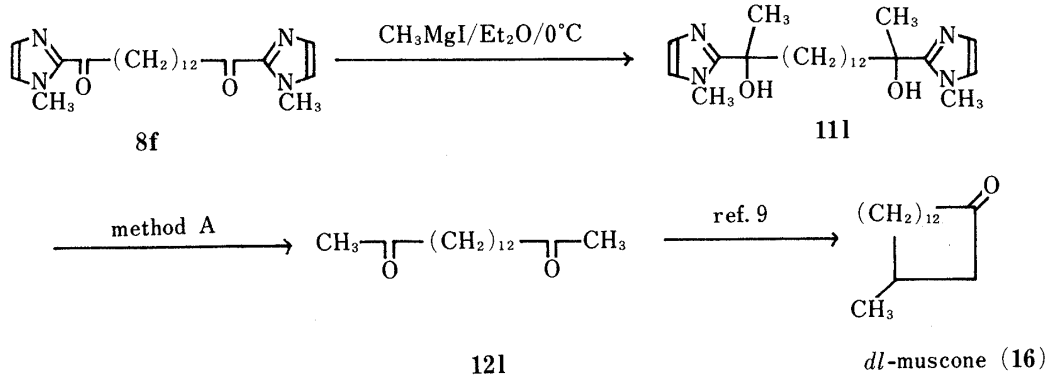
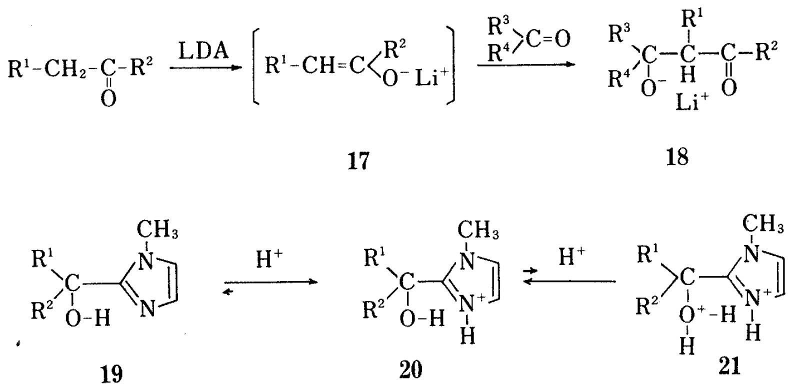


Chart 5



(LDA: lithium diisopropylamide)
Chart 6

methylmagnesium iodide to give directly the corresponding dihydroxy compound (**11l**: $R^1 = R^2 = CH_3$) as a crystalline product (mp 131—132 °C) in 94.9% yield. When methyllithium was used instead of the Grignard reagent, the reaction mixture gave a clearer TLC picture than that of the Grignard reaction mixture and the same product (**11l**) was obtained in a similarly excellent yield. The diol (**11l**) could be converted hexadecane-2,15-dione (**12l**) in a fair yield; this product is a key intermediate for the total synthesis of *dl*-muscone (**16**).[9)]

We have demonstrated here an example of the effect of mutual repulsion between negative charges. This principle also rationally explains several known reactions. For example, in the well-known aldol reaction, the carbonyl group of the intermediately formed oxide anion product (**18**) is not further attacked by enolate anion (**17**), and this phenomenon can be reasonably explained in terms of repulsion between the same electronic charges of **17** and **18**. On the other hand, we have observed an extraordinary stability of 2-(1-tertiary-hydroxy-1,1-dialkylmethyl)-1-methyl-1*H*-imidazole (**19**) in hot 20% sulfuric acid,[5b)] and this may be similarly explained by an intramolecular interference arising from the positive charge of the protonated imidazole ring in **20**, preventing further approach of a proton to the hydroxy group in **20**.

Experimental

All melting points are uncorrected. IR spectra were taken with a Shimadzu IR-410 spectrometer. ^{1}H-NMR spectra were obtained at 80 MHz on a Varian CFT-20 spectrometer in δ-values (ppm) with tetramethylsilane as an internal standard. Abbreviations of ^{1}H-NMR signal patterns are as follows: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); br (broad). HPLC were performed on a Shimadzu LC-3A with a UV detector. MS were obtained by using a Hitachi RMU-6E spectrometer. GLC were performed on a Shimazu GC-9A apparatus equipped with FID. All solvents in the organic layer containing the desired product were removed under reduced pressure by using a rotary evaporater in the work-up procedure. Anhydrous sodium sulfate was used as a drying agent. A Kugel–Rohr distillation apparatus was used in the vacuum distillations of the crude oily or low-melting-point products.

General Procedure for Conversions of Dimethyl Ester of Alkanedioic Acid into Corresponding Dipyrrolidine Amide (6)——A mixture of commercially available dimethyl ester of alkanedioic acid (20 ml) and pyrrolidine (30 ml) was heated at 130—160 °C for more than 8 h in a sealed tube. Excess of pyrrolidine and formed methanol were evaporated off under reduced pressure, and the residual crystalline material was purified by recrystallization or vacuum distillation.

1,1′-Succinyldipyrrolidine (**6a**): Yield, quantitative. Recrystallized from *n*-hexane–isopropyl alcohol. Colorless leaflets. mp 77.0—78.5 °C. bp 205.0—210.0 °C (2 mmHg). IR ($CHCl_3$): 1630 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.60—2.20 (m, 8H, $-(C\underline{H}_2)_2CH_2N- \times 2$), 2.63 (s, 4H, $-CO(C\underline{H}_2)_2$), 3.20—3.70 (m, 8H, $-C\underline{H}_2NC\underline{H}_2- \times 2$), *Anal.* Calcd for $C_{12}H_{20}N_2O_2$: C, 64.26; H, 8.99; N, 12.49. Found: C, 64.09; H, 9.12; N, 12.26.

1,1′-Glutaryldipyrrolidine (**6b**): Yield, quantitative. Recrystallized from ethyl acetate. Colorless needles. mp 38.0—39.0 °C. bp 185.0—188.0 °C (0.01 mmHg). IR ($CHCl_3$): 1619 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.75—2.15 (m, 10H, $-(C\underline{H}_2)_2CH_2N- \times 2$ and $-C\underline{H}_2CH_2CO-$), 2.38 (t, 4H, $-C\underline{H}_2CH_2C\underline{H}_2CO-$, $J=6$ Hz), 3.30—3.60 (m, 8H, $-C\underline{H}_2NC\underline{H}_2- \times 2$). *Anal.* Calcd for $C_{13}H_{22}N_2O_2$: C, 65.51; H, 9.31; N, 11.76. Found: C, 65.11; H, 9.65; N, 11.50.

1,1′-Adipoyldipyrrolidine (**6c**): Yield, quantitative. Recrystallized from ethyl acetate. Colorless needles. mp 86.0—87.0°C. IR ($CHCl_3$): 1625 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.50—2.60 (m, 16H, $-(C\underline{H}_2)_2CH_2N- \times 2$ and $-CO(C\underline{H}_2)_4-$), 3.20—3.70 (m, 8H, $-C\underline{H}_2NC\underline{H}_2- \times 2$). *Anal.* Calcd for $C_{14}H_{24}N_2O_2$: C, 66.63; H, 9.59; N, 11.10. Found: C, 66.58; H, 9.29; N, 11.32.

1,1′-Pimeloyldipyrrolidine (**6d**): Yield, quantitative. Colorless oil. bp 218.0—220.0 °C (0.01 mmHg). IR ($CHCl_3$): 1622 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.10—2.50 (m, 18H, $-(C\underline{H}_2)_2CH_2N- \times 2$ and $-(C\underline{H}_2)_5CO-$), 3.20—3.70 (m, 8H, $-C\underline{H}_2NC\underline{H}_2- \times 2$). HRMS *m/z*: Calcd for $C_{15}H_{26}N_2O_2 = 266.1992$. Found $= 266.1951$ (M^+).

1,1′-Suberoyldipyrrolidine (**6e**): Yield, quantitative. Recrystallized from ethyl acetate. Colorless needles. mp 74.5—75.0 °C. IR ($CHCl_3$): 1630 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$): 1.10—2.10 (m, 16H, $-NCH_2(C\underline{H}_2)_2- \times 2$, and $-COCH_2(C\underline{H}_2)_4-$), 2.26 (t, 4H, $-COC\underline{H}_2- \times 2$, $J=7$ Hz), 3.15—3.60 (m, 8H, $-C\underline{H}_2NC\underline{H}_2- \times 2$). High-resolution MS *m/z*: Calcd for $C_{16}H_{28}N_2O_2 = 280.2148$. Found $= 280.2138$.

1,1′-Tetradecanedioyldipyrrolidine (**6f**): Yield, quantitative. Recrystallized from *n*-hexane. Colorless needles. mp 63.0—64.0 °C. IR ($CHCl_3$): 1622 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.10—1.80 (m, 20H, $-(C\underline{H}_2)_{10}CH_2CO-$), 1.80—2.10 (m, 8H, $-(C\underline{H}_2)_2CH_2N- \times 2$), 2.26 (t, 4H, $-C\underline{H}_2CO- \times 2$, $J=7$ Hz), 3.30—3.60 (m, 8H, $-C\underline{H}_2NC\underline{H}_2- \times 2$). *Anal.* Calcd for $C_{22}H_{40}N_2O_2$: C, 72.48; H, 11.06; N, 7.68. Found: C, 71.91; H, 11.06; N, 7.79.

General Procedure for Synthesis of 1,*n*-Bis(1-methyl-1*H*-imidazol-2-yl)alkane-1,*n*-dione (8) Starting from Pyrrolidine Amide (6)——A THF solution (100 ml) of 1-methyl-1*H*-imidazole (3.28 g, 40 mmol) was cooled to −78 °C, and 1.6 M *n*-butyllithium solution in hexane (25 ml, 40 mmol) was added. The mixture was stirred for 15 min at −78 °C, then dipyrrolidine amide (**6**) (15 mmol) was added, and the whole was stirred for 30 min with removal of the cooling bath. Ether and 10% HCl were added to the mixture. The aqueous layer was washed with ether, then basified by addition of solid K_2CO_3 to precipitate a crystalline material, which was filtered off and washed with water. The crude product was purified by recrystallization.

1,4-Bis(1-methyl-1*H*-imidazol-2-yl)butane-1,4-dione (**8a**): Yield, 22.5%. Recrystallized from dimethyl cellosolve. Colorless prisms. mp 176.0—177.5 °C. IR ($CHCl_3$): 1660 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 3.55 (s, 4H, $-(C\underline{H}_2)_2CO-$), 3.97 (s, 6H, $C\underline{H}_3N- \times 2$), 7.02, 7.14 (d each, 2H each, imidazole H, $J=1$ Hz each). *Anal.* Calcd for $C_{12}H_{14}N_4O_2$: C, 58.53; H, 5.73; N, 22.75. Found: C, 58.71; H, 5.83; N, 22.46.

1,5-Bis(1-methyl-1*H*-imidazole-2-yl)pentane-1,5-dione (**8b**): Yield, 45.3%. Recrystallized from isopropyl alcohol. Colorless needles. mp 129.0—130.0 °C. IR ($CHCl_3$): 1680 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$ in 80 MHz) δ: 1.85—2.30 (m, 2H, $-C\underline{H}_2CH_2CO-$), 3.14 (t, 4H, $-C\underline{H}_2CH_2C\underline{H}_2CO-$, $J=7$ Hz), 3.99 (s, 6H, $C\underline{H}_3N- \times 2$), 7.00, 7.10 (d each, 2H each, imidazole H, $J=1$ Hz each). *Anal.* Calcd for $C_{13}H_{16}N_4O_2$: C, 59.98; H, 6.20; N, 21.53. Found: C, 60.25; H, 6.22; N, 21.31.

1,6-Bis(1-methyl-1*H*-imidazol-2-yl)hexane-1,6-dione (**8c**): Yield, 42.2%. Recrystallized from methanol. Colorless needles. mp 174.0—176.0 °C. IR ($CHCl_3$): 1682 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.60—1.90 (m, 4H, $-(C\underline{H}_2)_2CH_2CO-$), 2.90—3.30 (m, 4H, $-C\underline{H}_2CO- \times 2$), 3.98 (s, 6H, $C\underline{H}_3N- \times 2$), 7.00, 7.11 (d each, 2H each, imidazole H, $J=1$ Hz each). *Anal.* Calcd for $C_{14}H_{18}N_4O_2$: C, 61.30; H, 6.61; N, 20.42. Found: C, 61.59; H, 6.70; N, 20.12.

1,7-Bis(1-methyl-1*H*-imidazol-2-yl)heptane-1,7-dione (**8d**): Yield, 62.8%. Recrystallized from isopropyl alcohol. Colorless needles. mp 94.0—95.5 °C. IR ($CHCl_3$): 1678 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.10—2.10 (m, 6H, $-(C\underline{H}_2)_3CH_2CO-$), 3.12 (t, 4H, $-C\underline{H}_2CO- \times 2$, $J=7$ Hz), 3.99 (s, 6H, $C\underline{H}_3N- \times 2$), 7.00, 7.11 (d each, 2H each, imidazole H, $J=1$ Hz each). *Anal.* Calcd for $C_{15}H_{20}N_4O_2$: C, 62.48; H, 6.99; N, 19.43. Found: C, 62.76; H, 7.12; N, 19.22.

1,8-Bis(1-methyl-1*H*-imidazol-2-yl)octane-1,8-dione (**8e**): Yield, 83.0%. Recrystallized from ethyl acetate–carbon tetrachloride. Colorless needles. mp 119.5—120.5 °C. IR ($CHCl_3$): 1680 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.20—2.00 (m, 8H, $-COCH_2(C\underline{H}_2)_4-$), 3.11 (t, 4H, $-COC\underline{H}_2- \times 2$, $J=7$ Hz), 3.99 (s, 6H, $NC\underline{H}_3$), 7.01, 7.12 (d each, 2H each, imidazole H, $J=1$ Hz each). *Anal.* Calcd for $C_{16}H_{22}N_4O_2$: C, 63.55; H, 7.33; N, 18.53. Found: C, 63.08; H, 7.33; N, 18.23.

1,14-Bis(1-methyl-1*H*-imidazol-2-yl)tetradecane-1,14-dione (**8f**): Yield, 45.1%. Recrystallized from ethanol. Colorless needles. mp 111.5—112.0 °C. IR ($CHCl_3$): 1680 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.10—1.90 (m, 20H, $-(C\underline{H}_2)_{10}CH_2CO-$), 3.11 (t, 4H, $2\times -C\underline{H}_2CO-$, $J=7$ Hz), 3.99 (s, 6H, $2\times NC\underline{H}_3$), 7.01, 7.12 (d each, 2H each, imidazole H, $J=1$ Hz each). *Anal.* Calcd for $C_{22}H_{34}N_4O_2$: C, 68.36; H, 8.89; N, 14.50. Found: C, 68.12; H, 9.06; N, 14.26.

General Procedure for Quantitative Analyses of Grignard Reaction of 8 with an Excess of Methylmagnesium Iodide——An ethereal Grignard reagent solution, prepared from iodomethane (355 mg, 2.5 mmol), magnesium metal (122 mg, 5 mgatom) and ether (2.5 ml), was added dropwise at 0 °C under nitrogen atmosphere over 30 min to a stirred solution of **8** (0.25 mmol) in THF (6.25 ml). After being stirred for 1 h, the reaction mixture was diluted exactly to 20 ml with the eluting solvent of HPLC (described later), and quantities of **8** and **10** were analyzed by HPLC in the usual manner.[12] Conditions of HPLC: column, Zorbax-ODS (4.6 mm i.d. × 150 mm); column temperature, 40 °C; flow rate, 2 ml/min; detector, UV at 278 nm.

Analysis of the reaction of **8a** ($m=2$): Eluting solvent, pH 2.6 phosphate buffer containing 1% $HClO_4$ in 70% methanol. Quantity: **8a** (2.57 mg, 4.3%); **10a** (63.06 mg, 96.3%).

Analysis of the reaction of **8b** ($m=3$): Eluting solvent, pH 2.6 phosphate buffer in 70% methanol containing 0.01% $HClO_4$. Quantity: **8b** (7.60 mg, 11.7%); **10b** (51.75 mg, 75.0%).

Analysis of the reaction of **8c** ($m=4$): Eluting solvent, pH 2.6 phosphate buffer containing 0.005% $HClO_4$ in 70% methanol. Quantity of **8c**, 3.06 mg (4.47%); **10c**, 27.34 mg (37.6%).

Analysis of the reaction of **8d** ($m=5$): Eluting solvent, pH 2.6 phosphate buffer in 70% methanol. **8d** was not detected at all. Quantity of **10d** (25.63 mg, 32.4%).

Analysis of the reactions of **8e** ($m=6$) and **8f** ($m=12$): **8** and **10** were not detected in the reaction mixture.

General Procedure for the Quantitative Analysis of the Doubly Attacked Product (11: $R^1=R^2=CH_3$) in the Reaction of 8 and CH_3MgI——The Grignard reaction mixture of **8** with methylmagnesium iodide described above was concentrated by evaporation. 20% K_2CO_3 was added to the residue and separated viscous material was extracted five times with ethyl acetate. After evaporation of the solution, dimethyl sulfate (82 mg, 0.65 mmol) and ethyl acetate (1.25 ml) were added to the residue, and the mixture was refluxed for 3 h. After removal of ethyl acetate by evaporation, the residue was stirred at 80 °C for 2 h in the presence of 10% K_2CO_3 (1.25 ml) and benzene (1 ml). The benzene layer was diluted exactly to 20 ml and the produced alkane-1,*n*-dione (**12**: $R^1=R^2=CH_3$) was determined by GLC. Conditions of GLC: column, 5% SE-30 (3 mm i.d. × 2 m); N_2 flow rate, 50 ml/min; detector, FID; injection temperature, 200 °C; column temperature, 100—200 °C.

11g ($R^1=R^2=CH_3$; $m=2$): Yield, nil.

11h ($R^1=R^2=CH_3$; $m=3$): Yield, nil.

11i ($R^1=R^2=CH_3$; $m=4$): Yield, 11.83 mg (33.3%)

11j ($R^1=R^2=CH_3$; $m=5$): Yield, 26.09 mg (66.9%)

11k ($R^1=R^2=CH_3$; $m=6$): Yield, 39.58 mg (93.2%)

General Procedure for Preparation of 1,*n*-Bis(1-methyl-1*H*-imidazol-2-yl)-*n*-(trimethylsilyloxy)alkan-1-one (14) from Diketone (8) [Synthesis of 1,4-Bis(1-methyl-1*H*-imidazol-2-yl)-4-(trimethylsilyloxy)pentan-1-one (14a) as an Example]——A Grignard reagent solution, which was prepared from iodomethane (1.42 g, 10 mmol), magnesium metal (486 mg, 20 mgatom) and ether (10 ml), was added dropwise at 0 °C under a nitrogen atmosphere over 30 min to a stirred solution of **8a** (896 mg, 4 mmol) in THF (100 ml). The mixture was stirred for 15 min, then ether and 10% HCl were added. The aqueous layer was basified with solid K_2CO_3 after washing the acidic layer with ether several times. The separated organic material was extracted with ethyl acetate. The organic layer was evaporated after drying with anhydrous Na_2SO_4 to give a viscous material, 1,4-bis(1-methyl-1*H*-imidazol-2-yl)-4-hydroxypentan-1-one (**10a**). Yield, 87.7%. IR ($CHCl_3$): 3310 (OH), 1678 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.61 (s, 3H, $C\underline{H}_3C-OH$), 2.10—3.30 (m, 4H, $CO(C\underline{H}_2)_2-$), 3.30—3.60 (br, 1H, $O\underline{H}$), 3.82, 3.93 (s each, 3H each, $NC\underline{H}_3\times 2$), 6.70, 6.79, 6.96, 7.05 (d each, 1H each, imidazole H, $J=1$ Hz each). High-resolution MS *m/z*: Calcd for $C_{13}H_{18}N_4O_2=262.1428$. Found $=262.1431$ (M^+). The intermediate was converted to the corresponding trimethylsilyloxy ether in a usual manner (imidazole/trimethylsilyl chloride method). The crude product was purified by silica gel column chromatography (solvent: ethyl acetate/hexane/methanol = 9/10/1) to give **14a** as a viscous oil. Yield, 1.08 g (81.2%). IR ($CHCl_3$): 1678 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: −0.01 (s, 9H, $(C\underline{H}_3)_3Si-$), 1.79 (s, 3H, $C\underline{H}_3C-OTMS$), 2.10—3.35 (m, 4H, $-(C\underline{H}_2)_2-$), 3.80, 3.93 (s each, 3H each, $NC\underline{H}_3\times 2$), 6.73, 6.82, 6.79, 7.09 (d each, 1H each, imidazole H, $J=1$ Hz each). High-resolution MS *m/z*: Calcd for $C_{16}H_{26}N_4O_2Si=334.1823$. Found $=334.1850$ (M^+).

1,4-Bis(1-methyl-1*H*-imidazol-2-yl)-4-(2-thienyl)-4-(trimethylsilyloxy)butan-1-one (**14b**): Viscous oil. Yield, 62.0%. IR ($CHCl_3$): 1678 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.15 (s, 9H, $(C\underline{H}_3)_3Si-$), 2.80—3.60 (m, 4H, $-(C\underline{H}_2)_2-$), 3.45, 4.06 (s each, 3H each, $NC\underline{H}_3\times 2$), 6.50—7.30 (m, 7H, imidazole H and thiophene H). High-resolution MS *m/z*: Calcd for $C_{19}H_{26}N_4O_2SSi=402.1545$. Found $=402.1546$ (M^+).

1,4-Bis(1-methyl-1*H*-imidazol-2-yl)-4-(trimethylsilyloxy)-5-phenylpentan-1-one (**14c**): Viscous oil. Yield, 72.3%. IR ($CHCl_3$): 1680 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.18 (s, 9H, $(C\underline{H}_3)_3Si-$), 2.00—3.00 (m, 4H, $-(C\underline{H}_2)_2-$), 3.27 (s, 2H, $-C\underline{H}_2C_6H_5$), 3.34, 3.97 (s each, 3H each, $NC\underline{H}_3$), 6.50—7.30 (m, 9H, imidazole H and benzene H). High-resolution MS *m/z*: Calcd for $C_{22}H_{30}N_4O_2Si=410.2136$. Found $=410.2141$ (M^+).

1,4-Bis(1-methyl-1*H*-imidazol-2-yl)-4-trimethylsilyloxy)decan-1-one (**14d**): Viscous oil. Yield, 43.7%. IR ($CHCl_3$): 1680 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.10 (s, 9H, $(C\underline{H}_3)_3Si-$), 0.60—1.40 (m, 11H, $C\underline{H}_3(C\underline{H}_2)_4-$), 1.80—2.10 (m, 2H, $(CH_2)_4C\underline{H}_2-$), 2.10—2.65 (m, 2H, $-C(OTMS)C\underline{H}_2$), 3.09 (t, 2H, $-C\underline{H}_2CO-$, $J=7$ Hz), 3.80, 3.94 (s each, 3H each, $NC\underline{H}_3\times 2$), 6.55—7.00 (m, 4H, imidazole H). High-resolution MS *m/z*: Calcd for $C_{21}H_{37}N_4O_2Si=405.2686$. Found $=405.2675$ (M^++1).

1,5-Bis(1-methyl-1*H*-imidazol-2-yl)-5-(trimethylsilyloxy)hexan-1-one (**14e**): Viscous oil. Yield, 73.3%. IR ($CHCl_3$): 1678 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: -0.01 (s, 9H, $(C\underline{H}_3)_3Si-$), 1.75 (s, 3H, $C\underline{H}_3C-OTMS$), 1.30—2.10 (m, 4H, $-C(OTMS)(C\underline{H}_2)_2-$), 3.05 (t, 2H, $-C\underline{H}_2CO-$, $J=7$ Hz), 3.72, 3.94 (s each, 3H each, $NC\underline{H}_3\times 2$), 6.73, 6.83, 6.97, 7.07 (m, 1H each, imidazole H, $J=1$ Hz each). High-resolution MS *m/z*: Calcd for $C_{17}H_{28}N_4O_2Si=348.1979$. Found $=348.1970$ (M^+).

1,5-Bis(1-methyl-1*H*-imidazol-2-yl)-5-hydroxyhexan-1-one (**10b**): Colorless leaflets (recrystallization from $CHCl_3$), mp 177.5—178.5 °C. Yield, 68.9%. IR (KBr): 3000—3500 cm^{-1} (OH), 1672 cm^{-1} (C=O). ^{1}H-NMR (d_6-DMSO) δ: 1.49 (s, 3H, $C\underline{H}_3C-OH$), 1.30—2.00 (m, 4H, $-(C\underline{H}_2)_2C-OH$), 2.95 (t, 2H, $-C\underline{H}_2CO$, $J=7$ Hz), 3.77, 3.89 (s each, 3H each, $NC\underline{H}_3\times 2$), 5.18 (s, 1H, $-O\underline{H}$), 6.69, 6.98, 7.07, 7.45 (d each, 1H each, imidazole H, $J=1$ Hz each). *Anal.* Calcd for $C_{14}H_{20}N_4O_2$: C, 60.85; H, 7.30; N, 20.28. Found: C, 61.02; H, 7.23; N, 20.16.

1,5-Bis(1-methyl-1*H*-imidazol-2-yl)-6-phenyl-5-(trimethylsilyloxy)hexan-1-one (**14f**): Viscous oil. Yield, 84.0%. IR ($CHCl_3$): 1658 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.12 (s, 9H, $(C\underline{H}_3)_3Si-$), 1.50—2.50 (m, 4H, $-C(OTMS)(C\underline{H}_2)_2-$), 3.12 (t, 2H, $COCH_2$, $J=7$ Hz), 3.25 (s, 2H, $-C\underline{H}_2C_6H_5$), 3.43, 3.96 (s each, 3H each, $NC\underline{H}_3\times 2$), 6.50—7.30 (m, 9H, imidazole H and benzene H). High-resolution MS *m/z*: Calcd for $C_{23}H_{32}N_4O_2Si=424.2292$. Found $=424.2305$ (M^+).

1,5-Bis(1-methyl-1*H*-imidazol-2-yl)-5-phenyl-5-(trimethylsilyloxy)pentan-1-one (**14g**): Viscous oil. Yield, 67.5%. IR ($CHCl_3$): 1680 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.15 (s, 9H, $(C\underline{H}_3)_3Si-$), 1.00—2.00 (m, 2H, $-COCH_2C\underline{H}_2-$), 2.70 (t, 2H, $-C(OTMS)CH_2-$, $J=6$ Hz), 3.22 (t, 2H, $COC\underline{H}_2$, $J=6$ Hz), 3.22, 4.09 (s each, 3H each, $NC\underline{H}_3\times 2$), 6.60—7.40 (m, 9H, imidazole H and benzene H). High-resolution MS *m/z*: Calcd for $C_{22}H_{30}N_4O_2Si=410.2136$. Found $=410.2143$ (M^+).

1,5-Bis(1-methyl-1*H*-imidazol-2-yl)-7-phenyl-5-(trimethylsilyloxy)heptan-1-one (**14h**): Viscous oil. Yield, 47.8%. IR ($CHCl_3$): 1678 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.10 (s, 9H, $(C\underline{H}_3)_3Si-$), 1.50—2.80 (m, 8H, $C_6H_5(C\underline{H}_2)_2C(C\underline{H}_2)_2-$), 3.11 (t, 2H, $COC\underline{H}_2$, $J=7$ Hz), 3.81, 3.97 (s each, 3H each, $NC\underline{H}_3\times 2$), 6.65—7.35 (m, 9H, imidazole H and benzene H). High-resolution MS *m/z*: Calcd for $C_{24}H_{34}N_4O_2Si=438.2449$. Found $=438.2454$ (M^+).

1,6-Bis(1-methyl-1*H*-imidazol-2-yl)-6-(trimethylsilyloxy)heptan-1-one (**14i**): Viscous oil. Yield, 25.4%. IR ($CHCl_3$): 1680 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 9H, $(C\underline{H}_3)_3Si-$), 0.90—2.05 (m, 6H, $-C(OTMS)(C\underline{H}_2)_3-$), 1.73 (s, 3H, $C\underline{H}_3C-OTMS$), 3.07 (t, 2H, $-C\underline{H}_2CO-$, $J=7$ Hz), 3.77, 3.96 (s each, 3H each, $NCH_3\times 2$), 6.73, 6.85, 6.99, 7.10 (m, 1H each, imidazole H, $J=1$ Hz each). High-resolution MS *m/z*: Calcd for $C_{18}H_{30}N_4O_2Si=362.2136$. Found $=362.2132$ (M^+).

1,6-Bis(1-methyl-1*H*-imidazol-2-yl)-6-hydroxyheptan-1-one (**10c**): Viscous material. Yield, 14.5%. IR ($CHCl_3$): 3050—3600 (OH), 1678 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.00—2.15 (m, 6H, $-(C\underline{H}_2)_3C-OH$), 1.61 (s, 3H, $C\underline{H}_3C-OH$), 2.70 (br, 1H, $-O\underline{H}$), 3.07 (t, 2H, $-C\underline{H}_2CO$, $J=7$ Hz), 3.78, 3.97 (s each, 3H each, $NC\underline{H}_3\times 2$), 6.77, 6.85, 6.99, 7.09 (d each, 1H each, imidazole H, $J=1$ Hz each). High-resolution MS *m/z*: Calcd for $C_{15}H_{22}N_4O_2$: 290.1742. Found 290.1744 (M^+).

2,15-Bis(1-methyl-1*H*-imidazol-2-yl)hexadecane-2,15-diol (**11l**): A Grignard reagent solution, prepared from iodomethane (1.42 g, 10 mmol), magnesium metal (486 mg, 20 mgatom) and ether (10 ml), was added dropwise at 0 °C under a nitrogen atmosphere over 30 min to a stirred solution of **8f** (1.54 g, 4 mmol) in THF (100 ml). The mixture was stirred for 15 min, then ether and 10% HCl were added, and the aqueous layer was basified with solid K_2CO_3 after washing the acidic layer with ether. The separated organic material was extracted with AcOEt. The organic layer was evaporated after drying with anhydrous Na_2SO_4 to give a crystalline material, which was purified by recrystallization from CCl_4. Colorless needles. Yield, 1.66 g (94.9%). IR ($CHCl_3$): 3000—3500 cm^{-1} (OH). ^{1}H-NMR ($CDCl_3$) δ: 1.00—1.45 (m, 20H, $-C(OH)CH_2(C\underline{H}_2)_{10}$), 1.61 (s, 6H, $C\underline{H}_3C(OH)\times 2$), 1.65—2.10 (m, 4H, $-C(OH)C\underline{H}_2\times 2$), 3.00 (br, 2H, $-O\underline{H}\times 2$), 3.78 (s, 6H, $NC\underline{H}_3\times 2$), 6.78, 6.84 (d each, 4H, imidazole H, $J=1$ Hz each).

2,7-Bis(1-methyl-1*H*-imidazol-2-yl)octane-2,7-diol (**11i**): This product was purified by silica gel PTLC (solvent: AcOEt/MeOH=3/1). Viscous material. IR ($CHCl_3$): 3100—3700 cm^{-1} (OH). ^{1}H-NMR ($CDCl_3$) δ: 1.58 (s, 6H, $C\underline{H}_3C(OH)\times 2$), 0.62—2.20 (m, 8H, $-(C\underline{H}_2)_4-$), 3.74 (s, 6H, $NC\underline{H}_3\times 2$), 4.15 (br, 2H, $-O\underline{H}\times 2$), 6.76, 6.83 (d each, 4H, imidazole H, $J=1$ Hz each).

2,8-Bis(1-methyl-1*H*-imidazol-2-yl)nonane-2,8-diol (**11j**): This product was purified by silica gel PTLC (solvent: AcOEt/MeOH=3/1). Viscous material. IR ($CHCl_3$): 3350 cm^{-1} (OH). ^{1}H-NMR ($CDCl_3$) δ: 1.00—1.40 (m, 6H, $-C(OH)CH_2(C\underline{H}_2)_3-$), 1.57 (s, 6H, $C\underline{H}_3C(OH)\times 2$), 1.65—2.15 (m, 4H, $-C(OH)C\underline{H}_2-\times 2$), 3.15 (br, 2H, $-O\underline{H}\times 2$), 3.76 (s, 6H, $NC\underline{H}_3\times 2$), 6.76, 6.83 (d each, 4H, imidazole H, $J=1$ Hz each).

2,9-Bis(1-methyl-1*H*-imidazol-2-yl)decane-2,9-diol (**11k**): This product was purified by silica gel PTLC (solvent: AcOEt/MeOH=3/1). Viscous material. IR ($CHCl_3$): 3120 cm^{-1} (OH). ^{1}H-NMR (d_6-DMSO) δ: 0.80—1.30 (m, 8H,

$-C(OH)CH_2(C\underline{H}_2)_4-$), 1.45 (s, 6H, $C\underline{H}_3C(OH) \times 2$), 1.50—1.90 (m, 4H, $-C(OH)C\underline{H}_2- \times 2$), 3.76 (s, 6H, $NC\underline{H}_3 \times 2$), 5.13 (br, 2H, $-OH \times 2$), 6.71, 6.98 (d each, 4H, imidazole H, $J = 1$ Hz each).

General Procedure for Reaction of the Trimethylsilyloxyketone (14) with Grignard Reagent [Preparation of 2,5-Undecadione (12a: *m* = 2; $R^1 = CH_3$, $R^2 = C_6H_{13}$) as an Example]——A Grignard reagent solution, prepared from *n*-hexyl bromide (495 mg, 3 mmol), magnesium metal (6 mgatom, 146 mg) and ether (3 ml), was added dropwise at 0 °C under nitrogen atmosphere to a stirred solution of **14a** (668 mg, 2 mmol) in ether (4 ml). The mixture was stirred for 15 min, then ether and 10% HCl were added. The organic phase was extracted again with 10% HCl. The combined aqueous layer was basified with solid K_2CO_3 after washing the ether. The separated material was extracted with AcOEt followed by evaporation of the solvent after drying with Na_2SO_4. A solution of the obtained viscous residue [IR ($CHCl_3$): no strong absorption near 1700 cm^{-1}] in AcOEt was refluxed for 4 h in the presence of dimethyl sulfate (630 mg, 5 mmol). The solvent was evaporated off, then 10% K_2CO_3 and benzene (2 ml) were added to the mixture, which was stirred overnight at room temperature. Water and AcOEt were added to the resulting mixture followed by a further extraction of the aqueous layer with AcOEt. The combined organic layer was washed with water and 10% HCl, and dried over anhydrous Na_2SO_4. The oil, which was obtained by evaporation of the solvent, was distilled *in vacuo*. bp 95—105 °C (1 mmHg). [lit. bp 70 °C (0.2 mmHg)].$^{7)}$ Yield, 283 mg (76.9%). IR ($CHCl_3$): 1715 cm^{-1} (C=O) [lit. 1715 cm^{-1}].$^{7)}$ ^1H-NMR ($CDCl_3$) δ: 0.87 (t, 3H, $C\underline{H}_3CH_2-$, $J = 8$ Hz), 1.10—1.85 (m, 8H, $CH_3(C\underline{H}_2)_4-$), 2.10 (s, 3H, $C\underline{H}_3CO-$), 2.44 (t, 2H, $-COC\underline{H}_2(CH_2)_4-$), 2.68 (s, 4H, $-CO(C\underline{H}_2)_2CO-$). Low-resolution MS *m*/*z*: 184 (M^+). The product was identified by comparison of the IR spectrum with that of an authentic sample.$^{5b)}$

Undec-8(*Z*)-ene-2,5-dione (**12b**) from **14a** and 3(*Z*)-Hexenylmagnesium Bromide: bp 112—120 °C (11 mmHg). Yield, 220 mg (60.5%). IR ($CHCl_3$): 1715 cm^{-1} (C=O) [lit. 1715 cm^{-1}].$^{8)}$ ^1H-NMR (300 MHz in $CDCl_3$) δ: 0.95 (t, 3H, $C\underline{H}_3CH_2-$, $J = 7$ Hz), 1.95—2.10, 2.31 (m each, 2H each, allylic protons), 2.19 (s, 3H, $C\underline{H}_3CO-$), 2.51, 2.60—2.75 [t ($J = 7$ Hz) and m, 2H and 4H, methylene protons adjacent to C=O], 5.02, 5.45 (m, 2H, $-C\underline{H}=C\underline{H}-$). [lit. ^1H-NMR ($CDCl_3$): 0.95 (t, 3H), 2.17 (s, 3H), 2.68 (s, 4H), 5.35 (m, 2H)].$^{8)}$ Low-resolution MS *m*/*z*: 182 (M^+). The *cis* configuration was confirmed on the basis of the *J* value (10.75 Hz) between the two vinylic protons. The NMR data are consistent with the reported data.$^{8)}$

tert-Butyl 6-(2-Thienyl)-3,6-dioxohexanoate (**12c**) from **14b** and *tert*-Butyl Lithioacetate: *tert*-Butyl lithioacetate solution was prepared at −78 °C by treating *tert*-butyl acetate with lithium diisopropylamide (LDA). The substrate (**14b**) was added at −78 °C to the solution of the lithium enolate and the mixture was stirred at −78 °C for 30 min followed by a usual work-up. When decomposition of the corresponding imidazolium salt with 10% K_2CO_3 was carried out at room temperature, an oily viscous poroduct (**12c**) was obtained. IR ($CHCl_3$): 1718, 1672 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$) δ: 1.48 (s, 9H, $-C(C\underline{H}_3)_3$), 2.80—3.35 (m, 4H, $-CO(C\underline{H}_2)_2-$), 3.45 (s, 2H, $-C\underline{H}_2COO$), 6.95—7.25 and 7.45—7.75 (m each, 1H and 2H, thiophene protons). High-resolution MS *m*/*z* Calcd for $C_{14}H_{18}O_4S = 282.0925$. Found = 282.0927 ($M^+$).

2-(*tert*-Butoxycarbonyl)-3-(2-thienyl)cyclopent-2-en-1-one (**15c**): The reaction was carried out as described for the reaction of **14b** with *tert*-butyl lithioacetate. When decomposition of the corresponding imidazolium salt was carried out at 80 °C for 2 h, a crystalline product was obtained in 74.7% yield. Recrystallization from CCl_4 gave colorless needles, mp 141.0—142.0 °C. IR ($CHCl_3$): 1725, 1710, 1698 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$) δ: 1.60 (s, 9H, $-C(CH_3)_3$), 2.45—2.70 (m, 2H, $-C\underline{H}_2C=C-$), 2.95—3.20 (m, 2H, $-C\underline{H}_2CO-$), 7.00—7.25 and 7.50—7.70 (m each, 1H and 2H, thiophene). *Anal.* Calcd for $C_{14}H_{16}O_3S$: C, 63.60; H, 6.10. Found: C, 63.07; H, 6.28.

2,6-Decanedione (**12d**) from **14e** and *n*-Butylmagnesium Bromide: Colorless oil. Yield, 70.6%. bp 85.0—90.0 °C (2 mmHg). IR ($CHCl_3$): 1715 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$) δ: 0.97 (t, 3H, $C\underline{H}_3CH_2-$, $J = 6$ Hz), 1.05—2.05 (m, 6H, $COCH_2C\underline{H}_2CH_2COCH_2(C\underline{H}_2)_2-$), 2.12 (s, 3H, $C\underline{H}_3CO-$), 2.25—2.60 (m, 6H, $-COC\underline{H}_2CH_2C\underline{H}_2COC\underline{H}_2-$). High-resolution MS *m*/*z*: Calcd for $C_{10}H_{18}O_2 = 170.1305$. Found = 170.1300 ($M^+$).

1-(4-Methylphenyl)hexane-1,5-dione (**12e**) from **14e** and 4-Tolylmagnesium Bromide: Viscous material. Yield, 76.9%. IR ($CHCl_3$): 1718 cm^{-1}, 1682 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$) δ: 1.80—2.25 (m, 2H, $-COCH_2C\underline{H}_2-$), 2.14 (s, 3H, CH_3CO-), 2.40 (s, 3H, $C\underline{H}_3C_6H_4-$), 2.56 (t, 2H, $CH_3COC\underline{H}_2-$, $J = 7$ Hz), 2.98 (t, 2H, $C_6H_5COC\underline{H}_2-$, $J = 7$ Hz), 7.10—7.30, 7.15, 7.90 (m each, 2H, each, benzene H). High-resolution MS *m*/*z*: Calcd for $C_{13}H_{16}O_2 = 204.1150$. Found = 204.1148.

1-Phenyl-2,6-heptanedione (**12f**) from **14f** and Methylmagnesium Iodide: Viscous material. Yield, 87.5%. IR ($CHCl_3$): 1718 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$) δ: 1.65—2.00 (m, 2H, $-COCH_2C\underline{H}_2-$), 2.07 (s, 3H, CH_3CO-), 2.15—2.60 (m, 4H, $-COC\underline{H}_2CH_2C\underline{H}_2-$), 3.66 (s, 2H, $C_6H_5C\underline{H}_2-$), 7.40 (m, 5H, benzene H). High-resolution MS *m*/*z*: Calcd for $C_{13}H_{16}O_2 = 204.1150$. Found = 204.1154.

Preparation of 2,7-Octanedione (**12i**) starting from **8c** with Methylmagnesium Iodide: A Grignard reaction similar to that described in the preparation of **11l** was carried out starting from **8c** instead of **8f**. The corresponding dihydroxyimidazole (**11i**: *m* = 4; $R^1 = R^2 = CH_3$) was isolated and the crude product was converted into the diketone (**12i**) by method A.$^{5)}$ Oily material. Yield, 23.3%. bp 63.0—67.0 °C (1 mmHg). IR ($CHCl_3$): 1718 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$) δ: 1.20—1.70 (m, 4H, $-COCH_2(C\underline{H}_2)_2-$), 2.13 (s, 6H, $CH_3 \times 2$), 2.46 (t, 4H, $-COC\underline{H}_2- \times 2$, $J = 7$ Hz) [lit. 1.45 (m, 4H), 2.10 (s, 6H), 2.38 (t, 4H, $J = 7$ Hz)].$^{10)}$

2,8-Nonanedione (**12j**) from the Dihydroxydiimidazole (**11j**) by Method A: Oil. Yield, 60.5%. bp 108.0—112.0 °C (1 mmHg). IR ($CHCl_3$): 1718 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$) δ: 1.00—1.95 (m, 6H, $-COCH_2(C\underline{H}_2)_3-$), 2.13 (s, 6H, $C\underline{H}_3=2$), 2.43 (t, 4H, $-COC\underline{H}_2-\times 2$, $J=7$ Hz) [lit.: 1.00—1.70 (m, 6H), 2.08 (s, 6H), 2.38 (t, 4H, $J=7$ Hz)].[11]

2,9-Decanedione (**12k**) from the Dihydroxyimidazole (**11k**) by Method A[5]: Oil. Yield, 87.6%. bp 112.0—114.0 °C (0.5 mmHg). IR ($CHCl_3$): 1716 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.00—1.90 (m, 8H, $-COCH_2(C\underline{H}_2)_4-$), 2.12 (s, 6H, $C\underline{H}_3\times 2$), 2.41 (t, 4H, $-COC\underline{H}_2-\times 2$, $J=7$ Hz) [lit. δ: 1.00—1.70 (m, 8H), 2.06 (s, 6H), 2.36 (t, 4H, $J=7$ Hz)].[11]

2,15-Hexadecanedione (**12l**)[9] from the Dihydroxydiimidazole (**11l**) by Method A[5]: Crystalline product. Yield, 66.9%. Recrystallized from *n*-hexane. Colorless needles. mp 77.0—79.0 °C (lit. mp 83—84 °C).[11] IR ($CHCl_3$): 1710 cm^{-1} (C=O). ^{1}H-NMR (80 MHz) δ: 0.95—1.80 (m, 20H, $-COCH_2(C\underline{H}_2)_{10}-$), 2.12 (s, 6H, $C\underline{H}_3\times 2$), 2.41 (t, 4H, $-COC\underline{H}_2-\times 2$, $J=7$ Hz).

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References and Notes

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