2,8-diene-4,10-dione (14c). To a solution of 210 mg (1 mmol) of **8** in hexane (2 mL) was added 160 mg (1 mmol) of isopropylphenylcarbodiimide[22] (**12c**). After 2 h at room temperature the precipitated crystals were filtered and recrystallized from hexane to give 130 mg (45% based on **8**) of **14c**, mp 156–158 °C. Evaporation of the mother liquor and recrystallization of this material from small amounts of hexane gave 180 mg (50%) of **13c**: mp 124–125 °C; IR (KBr) 1710, 1690, 1660, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 and 1.29 (2 s, 9 H each, 2 *t*-Bu), 1.57 (d, J = 6 Hz, $CH(CH_3)_2$), 5.19 (hept, J = 6 Hz, $CH(CH_3)_2$), 6.92–7.36 (m, 5 H, Ar-H); ^{13}C NMR ($CDCl_3$) δ 18.3, 28.4, 37.4, 45.3, 47.8, 114.1 (s, C-5), 122.5, 123.1, 128.5 (all Ar-C), 140.6 (d, ^3J = 5.6 Hz, C-2), 145.2 (m, quart, Ar-C), 160.8 (d, ^3J = 5 Hz, C-4), 166.9 (m, C-6), 209.9 (m, pivaloyl CO) ppm. Anal. Calcd for $C_{22}H_{30}N_2O_3$: C, 71.32; H, 8.16; N, 7.56. Found: C, 71.49; H, 8.05; N, 7.33.

14c: IR (KBr) 1700, 1660, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) 0.51 and 1.42 (2 d, J = 6 Hz, 6 H, $CH(CH_3)_2$), 1.26–1.30 (m, 36 H, 4 *t*-Bu), 3.71 (hept, J = 6 Hz, 1 H, $CH(CH_3)_2$), 7.21–7.44 (m, 5 H, Ph) ppm. Anal. Calcd for $C_{37}H_{48}N_2O_6$: C, 70.32; H, 8.33; N, 4.82. Found: C, 70.49; H, 8.29; N, 4.81.

Treatment of a solution of **13c** in hexane with an equimolar amount of **8** afforded **14c** in 92% yield.

2-[1-Isopropyl-4-(isopropylimino)-2-oxo-3-pivaloylazetidin-3-yl]-2,6-di-*tert*-butyl-5-pivaloyl-1,3-dioxin-4(2*H*)-one (15a). A mixture of 420 mg (1 mmol) of ketene **7** and 200 mg (1.6 mmol) of diisopropylcarbodiimide (**12a**) was kept at 60 °C for 48 h and then 16 h at room temperature. The resulting solid was treated with hexane and filtered to yield 315 mg (58%) of **15a**, mp 150–152 °C (hexane). Evaporation of the hexane solution and sublimation of the resulting material at 80 °C (10^{-1} mbar) gave 130 mg (24% based on **12a**) of **13a**, identified by comparison of mp and IR with authentic material prepared from **8** and **12a**.

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15a: IR (KBr) 1820, 1730, 1705, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90–1.50 (complex m, 48 H, 4 *t*-Bu, 2 $CH(CH_3)_2$), 4.06 and 4.44 (2 m, 2 H, $CH(CH_3)_2$); ^{13}C NMR ($CDCl_3$) δ 19.5–50.0 (aliphatic C), 83.4/83.5 (C-3'), 105.1/105.9 (C-2), 111.4/111.8 (C-5), 140.3/140.4 (C-4'), 156.9/157.5 (C-2'), 163.4/164.6 (C-4), 174.2/174.3 (C-6), 202.9/203.1 and 210.1/210.2 (2 pivaloyl CO) ppm. Anal. Calcd for $C_{31}H_{50}N_2O_6$: C, 68.10; H, 9.22; H, 5.12. Found: C, 68.06; H, 9.16; N, 5.12.

2-[1-Methyl-4-(methylimino)-2-oxo-3-pivaloylazetidin-3-yl]-2,6-di-*tert*-butyl-5-pivaloyl-1,3-dioxin-4(2*H*)-one (15b). Ketene **7** was dissolved in an excess of dimethylcarbodiimide[21] (**12b**) (molar ratio 1:5). After 8 h at 20 °C the oily residue was diluted with hexane, precipitating a colorless solid which was recrystallized from hexane to give 370 mg (76%) **15b**: mp 144–145 °C; IR (KBr) 1820, 1720, 1710, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10–1.30 (m, 36 H, 4 *t*-Bu), 2.92 and 3.21 (2 s, 3 H, C=NMe), 3.30 and 3.38 (2 s, 3 H, ring NMe) ppm, assignments based on a ^1H,^{13}C HMQC experiment. Anal. Calcd for $C_{27}H_{42}N_2O_6$: C, 66.10; H, 8.63; H, 5.71. Found: C, 65.91; H, 8.68; N, 5.77.

FVP of 15a. **15a** (100 mg, 0.2 mmol) was gently sublimed at 120 °C and pyrolyzed at 400 °C (10^{-3} mbar). After the pyrolysis was completed (ca. 2 h), the cold finger was allowed to warm to ca. −40 °C, and at this point the apparatus was pressurized to 1 atm with dry N_2. After the cold finger had reached ambient temperature, the crystalline product, **14a**, was collected in 84% yield (mp, IR).

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Supplementary Material Available: X-ray crystallographic data for **9** and **15a** (13 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

N-(8-Quinolyl)-*N'*-(2-pyridylmethyl)malonamide Derivatives as a Novel Cu(II) Carrier with High Efficiency and Selectivity for Proton-Driven Uphill Transport through Liquid Membranes

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Several N,N'-disubstituted malonamide derivatives have been designed as a carrier for ion transport. Their ability to transport transition-metal ions through liquid membranes has been investigated. It has been found that *N*-(8-quinolyl)-*N'*-(2-pyridylmethyl)malonamide derivatives can transport Cu(II) with high efficiency and selectivity against its concentration gradient from nearly a neutral aqueous phase (pH 6.2) to an acidic aqueous phase through a chloroform liquid membrane.

Introduction

Selective transport of transition-metal ions as well as alkali and alkaline earth metal ions through liquid membranes, i.e, carrier-mediated continuous solvent extraction, has become increasingly important and noteworthy as an attractive method for the separation, recovery, and condensation of available resources.[1] So far, a number of carriers for heavy metal ions have been reported, but few can transport them selectively and efficiently.[2-6] In the solvent extraction, transition-metal ions can be usually separated with extractants by varying the acidic pH range in the aqueous phase, but the ion-selectivity could not be expected near the neutral pH range. It might be important to realize the highly selective and efficient separation under the mild conditions.

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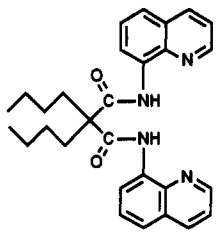
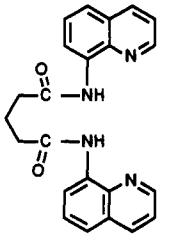
Recently, we have found that *N,N'*-di(8-quinolyl)-malonamide derivative **1** can selectively extract Cu(II) among transition-metal ions from an aqueous phase buffered at pH 6.2 into a chloroform phase, although its ability to transport Cu(II) through liquid membranes is low.[7] It should be noted that **1** can selectively extract Cu(II) at the nearly neutral pH range. On the other hand, *N,N'*-di(8-quinolyl)glutaramide (**2**) can hardly extract any metal ions under the same conditions as carried out in **1**, but can transport Cu(II) with high selectivity through liquid membranes as we reported previously.[8]



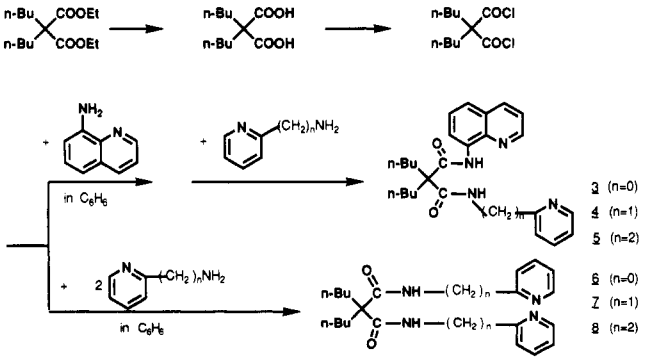
1



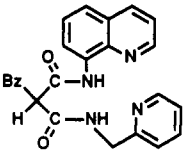
2

We have intended to design a better Cu(II) carrier based on the results as described above and planned to synthesize carriers which not only have a malonamide structure like **1**, to extract ions rapidly and selectively from the aqueous phase into the organic phase, but also have comparably small stability of the complex like glutaramide **2** at the same time so that they could release ions from a liquid-membrane phase into an aqueous phase easily and rapidly.

In this study we report some novel carriers which can exhibit highly selective and efficient Cu(II) transport through liquid membranes and discuss their structural features in detail. Thus, we synthesized several malonamide derivatives with different N-substituted groups, characterized them, and investigated the influence of their substituents and chain length either on the Cu(II) transport ability or on the extractability. On the basis of the hypothesis that the potential carrier could be designed by weakening the coordination ability of nitrogen atoms on malonamide **1**, the new compounds **3–5**, in which 2-pyridyl,



2-pyridylmethyl, and 2-pyridyl-2-ethyl groups are substituted for the 8-quinolyl group of **1**, respectively, have been synthesized stepwise starting from ethyl malonate. We preliminarily reported that 2,2-dibutyl-*N*-(8-quinolyl)-*N'*-(2-pyridylmethyl)malonamide (**4**) could transport Cu(II) with high selectivity and efficiency through liquid membranes.[9] For comparison, 2,2-dibutyl-*N,N'*-di(2-pyridyl)malonamide (**6**), 2,2-dibutyl-*N,N'*-di(2-(2-pyridylmethyl)malonamide (**7**), and 2,2-dibutyl-*N,N'*-di(2-(2-pyridyl)ethyl)malonamide (**8**) were also prepared. To investigate the effect of the substituent at the 2 position of malonamide on the transport ability, 2-benzyl-*N*-(8-quinolyl)-*N'*-(2-pyridylmethyl)malonamide (**9**) was also prepared. A commercially available 7-undecyl-8-quinolinol (commercial name: Kelex 100) was also used for comparison of transport ability because it is well-known as one of prominent extractants for practical use.



9

Table I. Amount of Cu(II) Transported through the $CHCl_3$ Phase after 2 days[a]

carrier	Cu(II) transported into the receiving phase, % (μmol)	Cu(II) remaining in the source phase, % (μmol)
1	0.2 (0.3)	94 (141)
2[b]	63 (94.5)	35 (52.5)
3	25 (37.5)	74 (111)
4	93 (139.5)	4 (6)
5	15 (22.5)	85 (127.5)
6	45 (67.5)	55 (82.5)
7	56 (84)	43 (64.5)
8	0 (0)	100 (150)

[a] Initial transport conditions (25 °C): (source phase) 10 mM $Cu(OAc)_2$, pH 6.2, 15 mL; (liquid membrane) 0.3 mmol of carrier in 30 mL of chloroform; (receiving phase) 0.05 M sulfuric acid, 15 mL. [b] Reference 8.

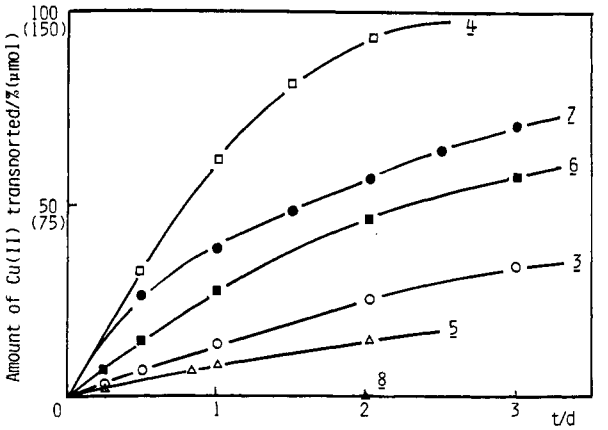


Figure 1. Plots of amount of Cu(II) transported into the receiving phase vs time: **3**, ○; **4**, □; **5**, △; **6**, ■; **7**, ●; and **8**, ▲. Initial transport conditions: see Table I.

Results and Discussion

Table I shows the amounts of Cu(II) transported after 2 days, along with the transport conditions. These results show that **4** has the greatest ability of Cu(II) transport among these carriers. In the carriers, **1–8**, the Cu(II) transport ability largely depends on the kind of N-substituents; that is, their abilities are as follows: **4** > **2** > **7** > **6** > **3** > **5** ≫ **1** = **8**. As previously reported,[8] glutaramide **2** has considerable transport ability toward Cu(II), but **4** is distinctly superior to **2**. Noticeably, **4** can efficiently transport Cu(II) against its concentration gradient under the mild conditions where the source phase is arranged to pH 6.2 and 0.05 M sulfuric acid is initially contained in the receiving phase (pH 1.4). Thus, most of the Cu(II)

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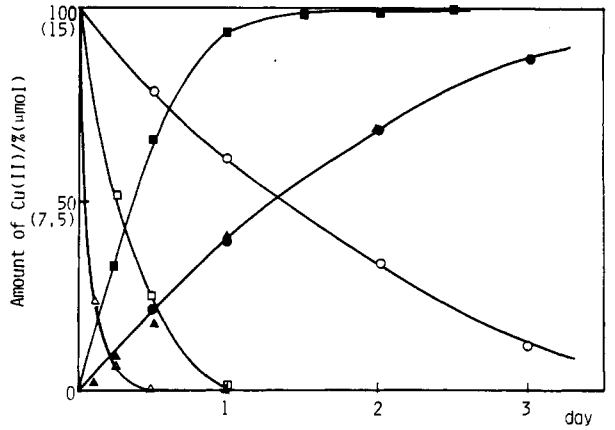

Figure 2. Time-dependence of the amount of Cu(II) in both source and receiving phases. Initial transport conditions (25 °C): (source phase) 1 mM $Cu(OAc)_2$, pH 6.2, 15 mL; (liquid membrane) carrier (0.1 mmol for **2** and **4**, 0.2 mmol for Kelex 100) in 30 mL of chloroform; (receiving phase) 0.05 M sulfuric acid, 15 mL. **2**: ○ and ●. **4**: □ and ■. Kelex 100: △ and ▲.

which was initially in the source phase is transported by **4** to the receiving phase after 2 days.

Figure 1 shows the time-dependence of the Cu(II) transport by **3**–**8**. Under the same conditions, **4** apparently transports Cu(II) at an appreciable rate compared with **3** and **5**–**8**. It should be noticed that **4** exhibits the most excellent Cu(II) transport ability among **3**–**5**. Similarly, **7** exhibits the best ability among **6**–**8**. Inspecting the CPK model building, when the methylene group between the amide-N atom and the pyridyl group is not introduced, the coordinated structure with Cu(II), which is favorably coordinated in square planar, might be distorted presumably to make the complex unstable. On the other hand, the ethylene chain between the amide-N atom and the pyridyl group makes rotational freedom larger than the methylene group. This might cause carriers with an ethylene chain to catch the metal ion less favorably. Here, **4** is considered to be superior to **7** because the former has a rigid quinolyl group which bears a large binding ability to heavy metal ions. In these cases, the curves of decreasing amount with time in the source phase, which are not depicted in Figure 1 (cf. Figure 2), are almost symmetrical about the lines corresponding to the increasing amount with time in the receiving phase where the proton plays an important role in the enforced ion release due to protonation of the nitrogen atoms.[5,6] It is presumed that the releasing rate is very rapid and the rate-determining step is the uptake process. When the transport conditions are changed as described in the caption of Figure 2, the resulting time-dependence of the Cu(II) transport by **2**, **4**, and commercially available Kelex 100 is shown in Figure 2. In this experiment, twice the molar quantity of bidentate ligand Kelex 100 was used in respect to tetradentates **2** and **4**. Among them, **4** exhibits the most excellent transport ability. With **4**, hardly any Cu(II) remains in the source phase after 1 day. As shown in Figure 2, the curves of decreasing amounts of **2** and **4** with time in the source phase are approximately symmetrical about the lines corresponding to the increasing amount with time in the receiving phase, whereas in the case of Kelex 100 the uptake of Cu(II) from the source phase to chloroform one is very fast but the release rate is moderate. Consequently, **4** can not only smoothly remove Cu(II) from the source phase to the chloroform phase but also rapidly release it from the chloroform phase to the receiving phase.

Figure 3 shows the pH-dependence of the Cu(II) amount(%) extracted by these carriers. The extractability

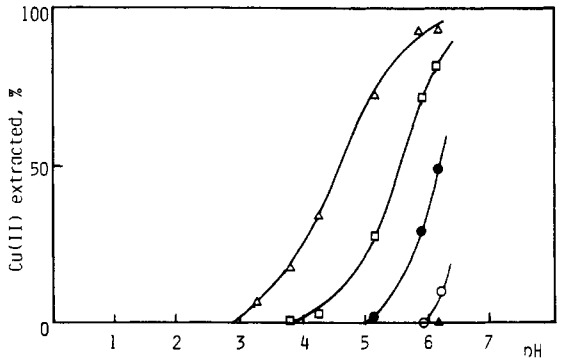

Figure 3. pH-Dependent of Cu(II) extraction with carriers: **1**, △; **2**, ○; **4**, □; **7**, ●; and **8**, ▲. Shaking time 1 day, 25 °C.

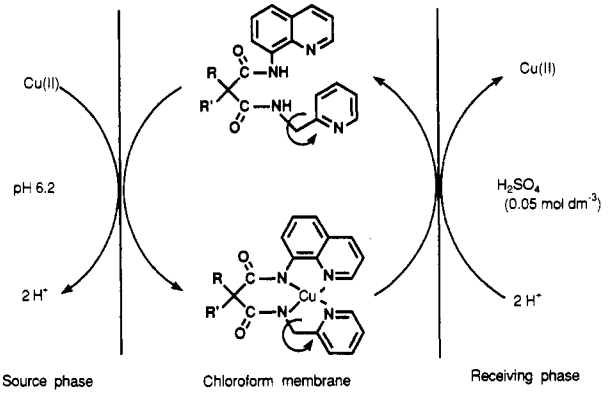

Figure 4. Schematic carrier-mediated uphill transport of Cu(II) by **4** through chloroform liquid membrane.

of carrier **4** is inferior to that of **1**, although its transport ability is greater than **1**. This fact implies that the balance between uptake and release of Cu(II) is of substantial importance for transport. The reason why malonamide **7** can exhibit the second best transport ability among these malonamide derivatives is presumed to be due to it having the second highest appropriate extractability following **4** as shown in Figure 3. Malonamide **8**, which can hardly transport any metal ions, does not extract Cu(II), even from the pH 6.2 aqueous phase, at all. Although Cu(II) extractability of glutaramide **2** is rather low, **2** can extract a small amount of Cu(II) at pH 6.2. The appreciable transport ability of **2** could be attributed to very rapid release of Cu(II) from the **2**–Cu(II) complex. 2-Benzyl-*N*-(8-quinolyl)-*N'*-(2-pyridylmethyl)malonamide (**9**) has been prepared as an analogue of **4**. When the transport ability of **9** was investigated under the same conditions as those in Table I, the amount of Cu(II) transported reached 86%. This means that the ability of **9** is comparable to that of **4**. Introduction of both 8-quinolyl and 2-pyridylmethyl groups seems to be significant for realizing the prominent transport ability among such malonamide derivatives.

The single-ion transport of Ni(II), Co(II), and Zn(II) by **4** was attempted under the same conditions, but none of them could be transported at all even after 2 days. In the competitive transport of transition-metal ions by **4** and **7**, only Cu(II) was transported with high efficiency against its concentration gradient through liquid membranes. The amount of Cu(II) transported after 2 days decreased to some extent compared with the results of the single-ion transport experiment of Cu(II); **4** and **7** transported 68% and 47% of Cu(II), respectively, after 2 days. The presumed transport process is dipicted in Figure 4. One of the important factors for the excellent transport ability of **4** and **9** may be the presence of a methylene chain be-

tween NH and pyridyl, which allows the pyridine moiety to rotate easily to release captured Cu(II) from the complex. Additionally, the pyridine-N atom is more basic and protonated more easily than the quinolyl-N atom to promote the release of Cu(II). Thus, it is elucidated that asymmetric malonamide derivatives having two different N-substituents (8-quinolyl and 2-pyridylmethyl groups) would be an excellent carrier for ion transport and could be a potential candidate for the practical use of Cu(II) separation.

Experimental Section

General. The IR and UV spectra were recorded with a JASCO A-3 infrared and a Hitachi 330 spectrophotometer, respectively. The ^{1}H-NMR spectra were recorded with a Bruker MSL-300 NMR spectrometer. The chemical shifts for $CDCl_3$ solution were reported relative to tetramethylsilane (TMS) as an internal standard. The high-resolution mass spectra (precise mass spectra) were measured with a Hitachi M-80B instrument.

Extra pure grade benzene was dried by using molecular sieves (4 Å) which were purchased from Merck. Extra pure grade triethylamine was dried over potassium hydroxide. All other solvents and reagents were of extra pure grade quality and were used without further purification.

2,2-Dibutyl-*N,N'*-bis(8-quinolyl)malonamide (**1**)[10] and *N,N'*-bis(8-quinolyl)glutaramide (**2**)[8] were prepared as previously reported.

Preparation of 2,2-Dibutyl-*N*-(8-quinolyl)-*N'*-(2-pyridyl)malonamide (3). A mixture of dibutylmalonic acid (10 mmol) and 5 mL of thionyl chloride was heated at 60 °C for 5 h. Then, thionyl chloride was removed by evaporation in vacuo. The residual oil was dissolved in 30 mL of benzene, and 8-aminoquinoline (10 mmol) was added to the solution at below 5 °C. The mixture was then stirred at room temperature for 5 h. Next, 2-aminopyridine (10 mmol) and triethylamine (20 mmol) were added to the mixture. The mixture was stirred overnight at 80 °C. After being cooled to room temperature, the reaction mixture was poured into 50 mL of water and extracted with benzene. The benzene layer was washed with water three times and dried over anhydrous magnesium sulfate. After the solvent was removed under reduced pressure, the residue was subjected to column chromatography on silica gel (300 mesh) with chloroform as eluent to give 1.5 g of **1** as the first eluate and 0.85 g of **3** as the second eluate. Yield of **3**: 20%; colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$) 0.86 (6 H, t, J = 7 Hz, CH_3), 1.37 (8 H, m, $CH_2CH_2CH_2CH_3$), 2.08 (2 H, m, $CH_2CH_2CH_2CH_3$), 2.30 (2 H, m, $CH_2CH_2CH_2CH_3$), 7.05 (1 H, dd, J = 5 and 7 Hz, Py-H^5), 7.48 (1 H, dd, J = 4 and 8 Hz, Q-H^3), 7.56 (2 H, m, Q-H^5 and H^6), 7.72 (1 H, t, J = 8 Hz, Py-H^4), 8.19 (1 H, d, J = 8 Hz, Q-H^4), 8.30 (1 H, d, J = 8 Hz, Py-H^3), 8.34 (1 H, d, J = 5 Hz, Py-H^6), 8.84 (2 H, m, Q-H^2 and H^7), 10.77 (1 H, s, NH), and 10.81 (1 H, s, NH) ppm (Py = 2-pyridyl group, Q = 8-quinolyl group); precise mass found 418.216, calcd for $C_{25}H_{30}N_4O_2$ 418.237; IR (neat) 3330 and 3200 (NH), 1685 and 1650 (C=O) cm^{-1}; UV ($CHCl_3$) λ_{max} = 318 nm, $\epsilon \times 10^{-3}$ = 7.1. Anal. Calcd for $C_{25}H_{30}N_4O_2$: C, 71.74; H, 7.23; N, 13.39. Found: C, 71.49; H, 7.47; N, 13.19.

2,2-Dibutyl-*N*-(8-quinolyl)-*N'*-(2-pyridylmethyl)malonamide (4). In a similar manner as described above for **3**, malonamide **4** was obtained when 2-(aminomethyl)pyridine was substituted for 2-aminopyridine; yield 27%; sticky colorless liquid; ^{1}H-NMR (300 MHz, $CDCl_3$) 0.94 (6 H, t, J = 6 Hz, CH_3), 1.33 (8 H, m, $CH_2CH_2CH_2CH_3$), 2.13 (4 H, m, $CH_2CH_2CH_2CH_3$), 4.68 (2 H, d, J = 5 Hz, pyridyl-CH_2), 7.16 (1 H, dd, J = 5 and 7 Hz, Py-H^5), 7.30 (1 H, d, J = 5 Hz, Py-H^3), 7.46 (1 H, dd, J = 4 and 8 Hz, Q-H^3), 7.51–7.55 (2 H, m, Q-H^5 and H^6), 7.61 (1 H, dt, J = 2 and 8 Hz, Py-H^4), 8.16 (1 H, dd, J = 2 and 8 Hz, Q-H^4), 8.53 (2 H, broad, NH and Py-H^6), 8.79 (1 H, dd, J = 3 and 6 Hz, Q-H^7), 8.87 (1 H, dd, J = 2 and 4 Hz, Q-H^2), and 11.20 (1 H, s, NH) ppm; precise mass found 432.254, calcd for $C_{26}H_{32}N_4O_2$ 432.252; IR (neat) 3350 (NH, broad), 1660 (C=O, broad) cm^{-1}; UV ($CHCl_3$) λ_{max} = 319 nm, $\epsilon \times 10^{-3}$ = 7.3. Anal. Calcd for $C_{26}H_{32}N_4O_2$: C, 72.19; H, 7.46; N, 12.95. Found: C, 71.75; H, 7.62; N, 12.83.

2,2-Dibutyl-*N*-(8-quinolyl)-*N'*-(2-(2-pyridyl)ethyl)malonamide (5). In a similar manner as described above for **3**, malonamide **5** was obtained when 2-(2-aminoethyl)pyridine was substituted for 2-aminopyridine; yield 29%; sticky colorless liquid; ^{1}H-NMR (300 MHz, $CDCl_3$) 0.83 (6 H, t, J = 7 Hz, CH_3), 1.26 (8 H, m, $CH_2CH_2CH_2CH_3$), 2.03 (4 H, m, $CH_2CH_2CH_2CH_3$), 3.04 (2 H, t, J = 6 Hz, pyridyl-CH_2), 3.78 (2 H, m, pyridyl-CH_2CH_2), 7.08 (1 H, dd, J = 4 and 7 Hz, Py-H^5), 7.12 (1 H, d, J = 8 Hz, Py-H^3), 7.45 (1 H, dd, J = 4 and 8 Hz, Q-H^3), 7.52 (3 H, m, Py-H^4, Q-H^5, and H^6), 8.03 (1 H, broad, NH), 8.15 (1 H, dd, J = 1 and 8 Hz, Q-H^4), 8.50 (1 H, d, J = 4 Hz, Py-H^6), 8.75 (1 H, dd, J = 3 and 6 Hz, Q-H^7), 8.88 (1 H, dd, J = 1 and 4 Hz, Q-H^2), and 11.34 (1 H, s, NH) ppm; precise mass found 446.264, calcd for $C_{27}H_{34}N_4O_2$ 446.268; IR (neat) 3350 (NH), 1680 (C=O) cm^{-1}; UV ($CHCl_3$) λ_{max} = 320 nm, $\epsilon \times 10^{-3}$ = 6.3. Anal. Calcd for $C_{27}H_{34}N_4O_2$: C, 72.62; H, 7.67; N, 12.55. Found: C, 72.31; H, 7.84; N, 12.45.

General Procedure for the Preparation of 2,2-Dibutyl *N,N'*-Substituted Malonamide Derivatives 6–8. A mixture of dibutylmalonic acid (10 mmol) and 5 mL of thionyl chloride was heated at 60 °C for 5 h. Then, unreacted thionyl chloride was removed in vacuo. The residual oil was dissolved in 30 mL of benzene, and an amino compound (20 mmol) such as 2-aminopyridine, 2-(aminomethyl)pyridine, 2-(2-aminoethyl)-pyridine, or triethylamine (20 mmol) was added to the solution. The mixture was then stirred overnight at 80 °C. After being cooled to room temperature, the reaction mixture was poured into 50 mL of water and extracted with benzene. The benzene layer was washed with water three times and dried over anhydrous magnesium sulfate. After the solvent was removed under reduced pressure, the residue was subjected to column chromatography on silica gel (300 mesh) with chloroform as eluent to give the *corresponding 2,2-dibutyl-N,N'-disubstituted malonamide* derivatives.

2,2-Dibutyl-*N,N'*-bis(2-pyridyl)malonamide (6): yield 63%; mp 96–97 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) 0.87 (6 H, t, J = 7 Hz, CH_3), 1.33 (8 H, m, $CH_2CH_2CH_2CH_3$), 2.07 (4 H, m, $CH_2CH_2CH_2CH_3$), 7.08 (2 H, dd, J = 5 and 7 Hz, Py-H^5), 7.73 (2 H, dd, J = 8 and 8 Hz, Py-H^4), 8.28 (2 H, d, J = 8 Hz, Py-H^3), 8.32 (2 H, d, J = 5 Hz, Py-H^6), and 9.56 (2 H, s, NH) ppm; precise mass found 368.219, calcd for $C_{21}H_{28}N_4O_2$ 368.221; IR (KBr) 3160 (NH), 1675 (C=O) cm^{-1}; UV ($CHCl_3$) λ_{max} = 277 nm, $\epsilon \times 10^{-3}$ = 17.2. Anal. Calcd for $C_{21}H_{28}N_4O_2$: C, 68.45; H, 7.66; N, 15.21. Found: C, 68.57; H, 7.68; N, 15.23.

2,2-Dibutyl-*N,N'*-bis(2-pyridylmethyl)malonamide (7): yield 75%; colorless liquid; ^{1}H-NMR (300 MHz, $CDCl_3$) 0.83 (6 H, t, J = 7 Hz, CH_3), 1.26 (8 H, m, $CH_2CH_2CH_2CH_3$), 1.94 (4 H, m, $CH_2CH_2CH_2CH_3$), 4.61 (4 H, d, J = 5 Hz, pyridyl-CH_2), 7.17 (2 H, dd, J = 5 and 7 Hz, Py-H^5), 7.27 (2 H, d, J = 8 Hz, Py-H^3), 7.64 (2 H, dt, J = 2 and 8 Hz, Py-H^4), 8.40 (2 H, broad, NH), and 8.52 (2 H, d, J = 5 Hz, Py-H^6) ppm; precise mass found 396.253, calcd for $C_{23}H_{32}N_4O_2$ 396.252; IR (neat) 3330 (NH), 1665 (C=O) cm^{-1}; UV ($CHCl_3$) λ_{max} = 261 nm, $\epsilon \times 10^{-3}$ = 7.6. Anal. Calcd for $C_{23}H_{32}N_4O_2$: C, 69.67; H, 8.14; N, 14.13. Found: C, 69.27; H, 8.23; N, 14.17.

2,2-Dibutyl-*N,N'*-bis(2-(2-pyridyl)ethyl)malonamide (8): yield 71%; colorless liquid; ^{1}H-NMR (300 MHz, $CDCl_3$) 0.78 (6 H, t, J = 7 Hz, CH_3), 1.03 (4 H, m, $CH_2CH_2CH_2CH_3$), 1.17 (4 H, m, $CH_2CH_2CH_2CH_3$), 1.74 (4 H, m, $CH_2CH_2CH_2CH_3$), 2.40 (1 H, s, H_2O), 2.99 (4 H, t, J = 6 Hz, pyridyl-CH_2CH_2), 3.67 (4 H, m, Py-CH_2CH_2), 7.14 (2 H, dd, J = 5 and 7 Hz, Py-H^5), 7.17 (2 H, d, J = 8 Hz, Py-H^3), 7.60 (2 H, dt, J = 2 and 8 Hz, Py-H^4), 8.11 (2 H, broad, NH), and 8.52 (2 H, d, J = 5 Hz, Py-H^6) ppm; precise mass found 424.282, calcd for $C_{25}H_{36}N_4O_2$ 424.284; IR (neat) 3340 (broad, NH and OH), 1650 (C=O) cm^{-1}; UV ($CHCl_3$) λ_{max} = 262 nm, $\epsilon \times 10^{-3}$ = 5.8. Anal. Calcd for $C_{25}H_{36}N_4O_2 \cdot {}^1/_2H_2O$: C, 69.25; H, 8.60; N, 12.92. Found: C, 69.07; H, 8.77; N, 12.82. Water could not be removed from the hydrated product even after it was dried overnight at 100 °C in vacuo (0.1 Torr).

2-Benzyl-*N*-(8-quinolyl)-*N'*-(2-pyridylmethyl)malonamide (9). In a similar manner to that described above for the preparation of **3**, malonamide **9** was obtained in 22% yield when benzylmalonic acid was used instead of dibutylmalonic acid; mp 144–145 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) 3.44 (2 H, d, J = 8 Hz, Ph-CH_2), 3.66 (1 H, t, J = 8 Hz, C-H), 4.56 (2 H, d, J = 5 Hz,

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pyridyl-CH_2), 7.0–7.6 (11 H, m, aromatic-H and NH), 8.14 (1 H, dd, J = 1 and 8 Hz, Q-H^4), 8.48 (1 H, d, J = 5 Hz, Py-H^6), 8.74 (1 H, dd, J = 4 and 4 Hz, Q-H^7), 8.86 (1 H, dd, J = 1 and 4 Hz, Q-H^2), and 10.74 (1 H, s, NH) ppm; precise mass found 410.172, calcd for $C_{25}H_{22}N_4O_2$ 410.174; IR (KBr) 3310 (NH), 1690 and 1645 (C=O) cm^{-1}; UV ($CHCl_3$) λ_{max} = 318 nm, $\epsilon \times 10^{-3}$ = 6.7. Anal. Calcd for $C_{25}H_{22}N_4O_2$: C, 73.15; H, 5.40; N, 13.65. Found: C, 72.83; H, 5.28; N, 13.55.

Transport of Metal Ions through Liquid Membranes. The transport experiments were carried out by using a U-type glass cell across the chloroform liquid membrane from the buffered aqueous source phase (pH 6.2) containing one or several kinds of metal ions of Cu(II), Ni(II), Co(II), and Zn(II) to the receiving phase containing 0.05 M sulfuric acid. The cell was kept at 25.0 ± 0.2 °C, and each phase was mechanically agitated at 200 rpm.[11] The amount of both metal ions transported into the receiving phase and metal ions remaining in the source phase was determined by atomic absorption spectroscopy.

General Procedure of Solvent Extraction. The following was poured into a 20-mL sample tube with screw cap: 5 mL of an aqueous solution containing 1 mM transition-metal ions (Cu(II), Ni(II), Co(II), or Zn(II)) and 5 mL of chloroform solution containing 1 mM malonamide derivative. The aqueous solution ranged from pH 6.2 to 1.4 and was adjusted by using both 1 M sodium acetate and 0.2 M acetic acid (or 1 N hydrochloric acid). The mixture was shaken vigorously for 24 h at 25 °C. The concentration of the remaining metal ions in aqueous solution was determined by atomic absorption spectroscopy. The concentration of the extracted metal ions was calculated from these values.

Registry No. 1, 123038-39-1; 3, 144436-25-9; 4, 131356-13-3; 5, 131356-14-4; 6, 144436-26-0; 7, 131356-15-5; 8, 131356-16-6; 9, 139424-08-1; $Bu_2C(CO_2H)_2$, 2283-16-1; $PhCH_2CH(CO_2H)_2$, 616-75-1; 8-aminoquinoline, 578-66-5; 2-aminopyridine, 504-29-0; 2-(aminomethyl)pyridine, 3731-51-9; 2-(aminoethyl)pyridine, 2706-56-1.

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Conrotatory and Disrotatory Reaction Paths for Thermal and Photoinduced Ring-Closing Reactions of 1,3,5-Hexatriene and Its Isoelectronic Analogs

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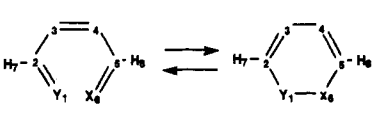
The reaction pathways for the thermal and photocyclizations of 1,3,5-hexatriene and its isoelectronic analogs **1** into 1,3-cyclohexadiene and respective heterocyclic dienes **2** have been investigated by use of the semiempirical MINDO/3 method. The main conclusions are as follows: (1) The transition-state structure of the symmetry-forbidden thermal reaction **1a** ↔ **2a** corresponding to the conrotatory reaction path has been located and found to be asymmetric. (2) The photocyclizations of 1,3,5-hexatriene (**1a**) and its isoelectronic analogs **1b–d** proceed as diabatic reactions that include internal conversion from the first excited singlet state (S_1) to the ground-state (S_0) potential energy surface (PES). (3) The photocyclizations of 1,3,5-hexatriene (**1a**) and 2,4-pentadienal imine (**1b**) may occur as "hot state" reactions through population of the vibrationally excited levels on the S_0 energy surfaces. The photoreaction **1d** ↔ **2d** is expected to be susceptible to triplet sensitization. (4) For the cyclizations of π-heteroanalogs of 1,3,5-hexatriene, containing terminal carbonyl, thiocarbonyl, or aldimine groups, two reaction channels similar to the dis- and conrotatory reaction paths of the **1a** ↔ **2a** reaction were revealed by calculations of both the ground and singlet excited electron states. The energy-preferred pathways correspond to the symmetry-allowed reaction modes, although the energy difference between the "allowed" and "forbidden" transition-state structures is smaller relative to 1,3,5-hexatriene. The orientation of the C2–H and C5–H bonds relative to the C1–X6–C5 plane serves as the structural criterion for assignment of the reaction channel to either dis- or conrotatory type. (5) Monoheterosubstitution in **1a** decreases the energy difference between the cyclic and polyene forms, although the ring-closed form remains more stable. Heteroatom substitution of both terminal methylene groups in **1a** reverses the order of relative stability of the valence isomers. Finally, the calculations show that heteroatom substitution lowers the energy barriers to cyclization of **2a** and **3a** in the S_0 and T_1 electron excited states.

Introduction

The thermal and photochemically induced ring closure of 1,3,5-hexatriene to 1,3-cyclohexadiene (**1a**) ↔ (**2a**) are key steps in the biosynthesis of the vitamin D series (the provitamin D ↔ previtamin D interconversion)[1,2] as well as the basic reactions defining the mechanisms of thermochromic and photochromic behavior of fulgides and fulgimides,[3] [10]-annulenes,[4] and diarylethylenes.[5] The analogous transformations of compounds in which the terminal methylene group is substituted by the isoelectronic oxygen or nitrogen atoms form the basis of the photo- and thermochromic behavior of such classes of compounds as spiropyrans,[6] chromenes,[7] spirooxazines,[8] dihydroquinolines,[9] and others.



1 2

a) X=Y=CH_2 ; b) X=NH,Y=CH_2; c) X=O, Y=CH_2; d) X=Y=O

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