Tetrahedron Vol 39, No. 16, pp 2691 to 2698, 1983
Printed in Great Britain

0040-4020/83 $3.00 + 00

A REMOVABLE FUNCTIONAL GROUP IN A PHOTOCHEMICAL MACROCYCLIC SYNTHESIS

REMOTE PHOTOCYCLIZATION WITH A PAIR SYSTEM OF PHTHALIMIDE AND 1,3-DITHIOLANYL GROUPS[1]

MASAO WADA, HIDEO NAKAI and YASUHIKO SATO*
Organic Chemistry Research Laboratory, Tanabe Seiyaku Co., Ltd., 2-2-50, Kawagishi, Toda, Saitama 335, Japan

and

YASUMARU HATANAKA and YUICHI KANAOKA
Faculty of Pharmaceutical Sciences, Hokkaido University, Kita-12, Nishi-6, Kita-ku, Sapporo 060, Japan

(*Received in Japan* 29 *September* 1982)

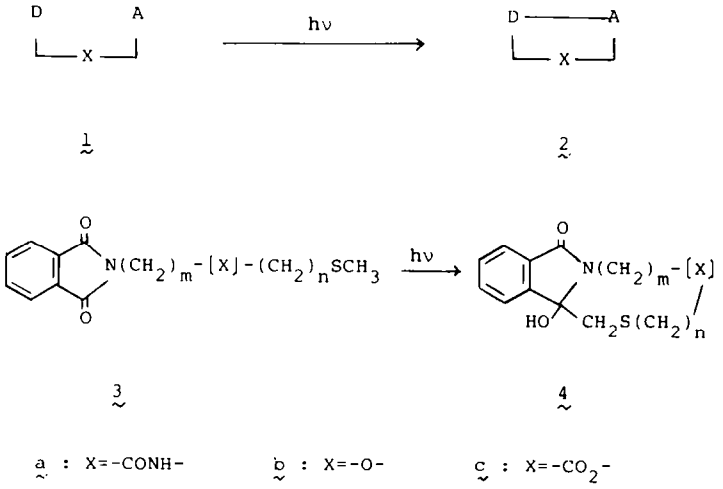
Abstract—Based on a regioselective remote photocyclization of a pair system consisting of a phthalimide group and a dithiolanyl group, a variety of aza-cyclic compounds with methylene, ester, or amide groups in their frameworks were synthesized. The dithiolanyl group provides a removable donor, which effects a needed reaction followed by removal to give a new carbon skeleton leaving little trace of the precursor form.

The importance of macrocyclic compounds in biological and chemical systems have recently attracted considerable attention.[2,3] Although many thermal reactions for the construction of macrocycles have been known, much less information is avialable for photochemical macrocyclic syntheses.[4]

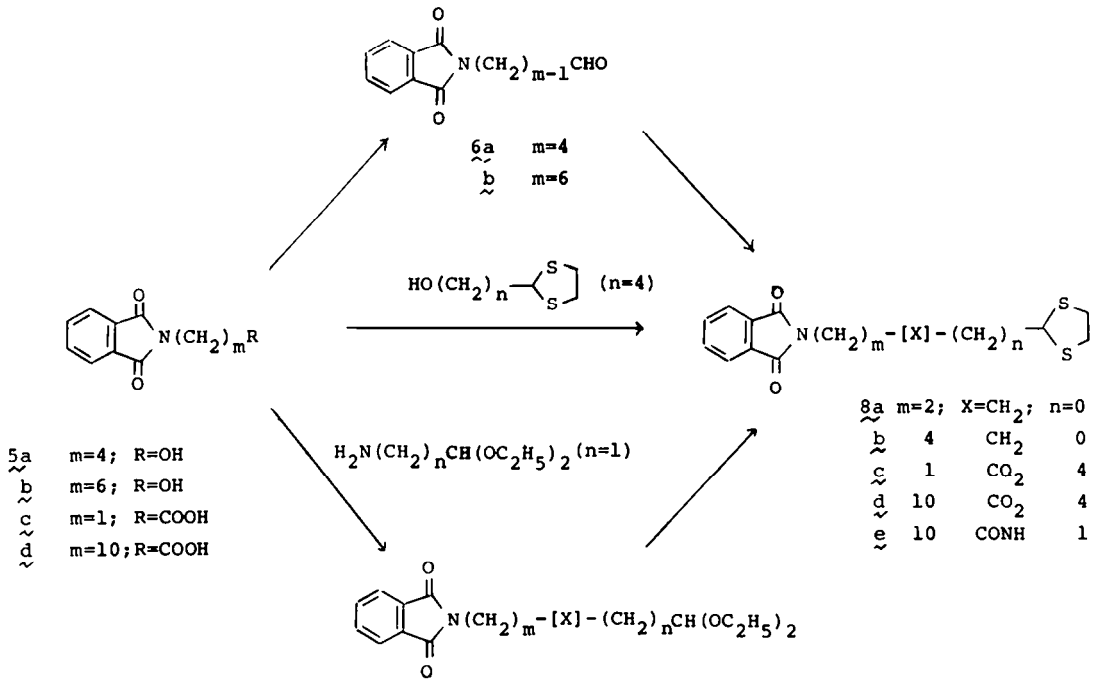
We have studied the application of "photolysis of donor–acceptor pair systems" for general synthetic purposes[5] (Scheme 1). In the approach with phthalimide (= 1,3(2H)-dioxo-2H-isoindole) as a typical acceptor (A), various donors (D) have been used such as sulfides,[6a] aromatics,[6b] anilines,[6c] amines,[6d] olefines,[6e] and indene.[6f] To see the scope and limitation of this method, a possible extent of structural variation of substrates (**3**) was explored, with the phthalimide-thiomethyl pair system, by systematically changing the connector portion (X) which combines the donor and the acceptor. Thus, a series of macrocycles (**4**) containing amides (**4a**),[7-9] ethers (**4b**),[8-10] and esters (**4c**)[8-9,11] have been photochemically synthesized.

In this system, the imide CO and the sulfide Me groups provide the site for the formation of a new C–C bond, and as a result the thioether moiety is inevitably incorporated and left in the newly formed macrocyclic framework (**4**). In view of general synthetic methodology, it is advisable to have a functional group which effectively induces certain desired construction reaction, then at a proper stage can be removed or converted into the needed group for following reaction steps. We have briefly reported that 1,3-dithiolanyl group is a candidate for such a removal functional group,[12] and in the present work we wish to present a full account of this work.

The substrates **8a–e** were prepared as shown in Scheme 2. Alkanals **6a–b** and acetal **7** derived from **5a–b** and **5d** were ketalized (or transketalized) with ethane dithiol in the presence of BF_3-etherate to afford the substrates **8a–b** and **8e**, while **5c** and **5d** were esterified with 4-(1,3-dithiolan-2-yl)-butan-1-ol, 1-methyl-2-chloropyridinum iodide to afford **8c** and **8d** in good yields, respectively, as described in experimental section, Table 1 and 2. The assignment of these structures was made on



Scheme 1.



Scheme 2.

the basis of elemental analyses and their spectral properties.

Irradiation of the dithiolanyl derivatives **8** (4–11 mM) was achieved with 200 or 400 W high-pressure mercury lamp in a stream of argon for 25–360 min. As listed in Table 3, the cyclized product **9** was obtained as a major product (in some cases, accompanied by small amounts of **10**) after silica gel column chromatography in moderate yields (20–82%), as a result of C–C bond formation between the imide CO and the methine (and/or methylene) carbon(s) adjacent to the S atom(s).

For example, in the ^{1}H-NMR of **9a**† in $CDCl_3$ appeared a peak of an OH group at δ 6.46 as singlet, in place of the original methine part of dithiolanyl function of **8a**, and the peaks of two S-methylenes appeared at δ 2.80–3.40 (multiplet) with other methylenes, in support of the cyclol moiety. The IR signals of an OH group and an amide group in **9a** appeared at ν 3210 (OH) and 1665

†An aza-thiaspirocyclol obtained from **8a**.

Table 1. Prepartions and analytical data for the compounds (**8a–e**)

No	Compound*) m	X	n	Yield (%)	Method†)	mp (°C)	Formula	Analysis(%) Calcd (found) C	H	N	S	MS m/e (M^+)
8a	2	CH_2	0	89	A[a]	97–98	$C_{14}H_{15}NO_2S_2$	57.33 (57.26)	5.16 (5.31)	4.78 (4.81)	21.81 (21.83)	293
8b	4	CH_2	0	68	A[b]	82–83	$C_{16}H_{19}NO_2S_2$	59.80 (59.95)	5.96 (5.95)	4.36 (4.35)	19.92 (20.09)	321
8c	1	CO_2	4	99	B[c]	99–100	$C_{17}H_{19}NO_4S_2$	55.89 (56.13)	5.24 (5.19)	3.83 (3.80)	17.52 (17.66)	365
8d	10	CO_2	4	77	B[b]	45–46	$C_{26}H_{37}NO_4S_2$	63.52 (63.49)	7.59 (7.39)	2.85 (2.79)	13.02 (13.29)	491
8e	10	CONH	1	87	A[a]	124–125	$C_{23}H_{32}N_2O_3S_2$	61.59 (61.60)	7.19 (7.22)	6.25 (6.28)	14.27 (14.36)	448

*The following solvents were used for the recrystallization; a = EtOAc, b = ether–EtOAc, c = EtOAc–ether–hexane.

†Ether was used as the reaction solvent except for **8e** (in tetrahydrofuran-ethyl acetate).

Table 2. Spectral data for the compounds (**8a–e**)

Compd No	IR ν_{max}^{nujol} cm^{-1}	NMR ($CDCl_3$) δ	UV λ_{max} nm(ε)*
8a	1760,1710 1610	1.68-1.94(4H,m),3.20(4H,m),3.72(2H,m), 4.50(1H,m),7.60-8.00(4H,m)	220(48340),233(16870) 241(12260),293(2200)
8b	1760,1695 1605	1.20-2.10(8H,m),3.18(4H,s),3.65(2H,t,J=6.6Hz), 4.43(1H,t,J=6.3Hz),7.57-8.00(4H,m)	244(14330), 295(2290)
8c	1770,1740 1710,1610	1.39-2.10(6H,m),3.20(4H,s),4.15(2H,t,J=5.9Hz), 4.42(1H,m),4.42(2H,s),7.60-8.00(4H,m)	242(10345) 295(1980)
8d	1765,1725 1710,1610	1.10-2.00(22H,m),2.28(2H,t,J=6.5Hz), 3.21(4H,s),3.67(2H,t),4.05(2H,t,J=5.8Hz), 4.45(1H,t,J=6.5Hz),7.50-8.00(4H,m)	243(12440), 294(2135)
8e	3300,1770 1720,1550	1.10-1.90(16H,m),2.15(2H,m),3.18(4H,s), 3.41 and 3.65(4H,each t),4.59(1H,t,J=6.6Hz), 6.00(1H,br s),7.55-7.95(4H,m)	244(11530) 295(1980)

*Chloroform was used as the measurement solvent except for compound **8a** (in methanol).

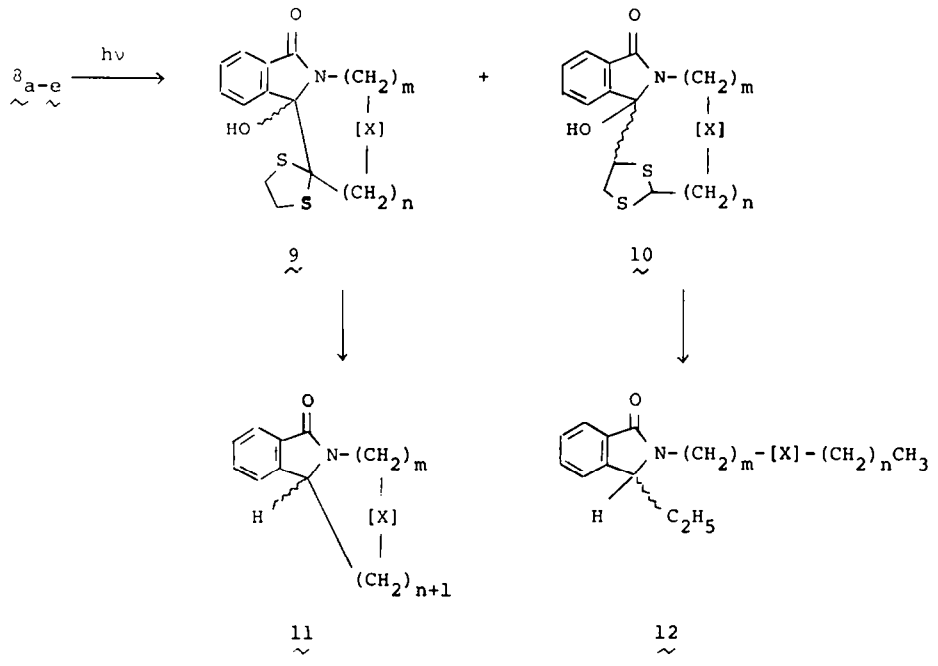
(amide CO), respectively. All other spectral and analytical data supported the structure **9a**. Compound **9a** was readily converted to the corresponding S-free compound **11a** [mass (MS) spectrum, *m/e* 187 (M^+)] through the treatment with Raney Ni (Scheme 3 and Table 6–7).

The irradiation of the substrates **8b–c** was performed in a similar manner (Table 3). The expected spiro-compound **9b** was obtained as a sole product from **8b**. From **8c**, the spirocyclol **9c** and the tetracyclic compound **10c** were obtained after silica gel column chromatography. Whereas the NMR spectra of **9b** and **9c** had a similar pattern to that described above, that of the minor product **10c** in which S-methylene group in involved showed peaks of two S-methine groups at δ 3.70–4.70 and 5.16 (accompanied by other methylenes), and an OH group at δ 6.74 as singlet, respectively. The IR signals of an OH group and CO groups of **10c** showed at ν 3250 (OH), 1735 (ester) and 1690 (amide) cm^{-1}, respectively. On heating with Raney Ni in ethanol, compounds **9b–c** were also converted to the S-free products **11b** and **11c**. On the other hand, similar treatment of the minor product **10c** afforded the open-chain compound **12c**. In the NMR spectrum of **12c**, the Me part of the Et function appeared at δ 0.59 (J = 7.4 Hz) as triplet peaks. When methanol and benzene were used as irradiation solvents for **8c**, spirocyclol **9c** and compound **10c** were obtained, each as a sole product, presumably due to unidentified solvent and conformational effects in the excited states.

Table 3. Photoproducts (**9** and **10**) from the compounds (**8**)

Compounds 8				Conditions				Products 9				Products 10			
	m	X	n	Weight g	Weight mmol	Solvent[a] [mM]	Time (min)	Yield (%)[b]	Ring size	mp (°C)		Yield (%)[b]	Ring size	mp (°C)	
a	2	CH_2	0	1.0	3.41	A[5]	25	82	6	242-243*					
b	4	CH_2	0	0.5	1.56	A[5]	25[c]	56	8	180-182*					
c	1	CO_2	4	1.5	4.11	A[6]	85[c]	26	10	231-233*		17	13	224-226*	
				1.0	2.74	M[11]	60	19	10						
				0.5	1.37	B[5]	360					12	13		
d	10	CO_2	4	1.5	3.06	A[4]	60[c]	53	19	160-161					
e	10	CONH	1	1.23	2.75	A[5]	60	20	16	178-180		12	19	185-188*	
				0.7	1.56	B[6][d]	130	25	16						

(a) The following abbreviations were used: A = acetone, M = methanol, B = benzene.
(b) Isolated yield.
(c) Irradiated with a 200 W high pressure mercury lamp.
(d) Irradiated through a Pyrex filter.
*Decomposed.



Scheme 3.

From substrate **8d**, thiaspirocyclol **9d** of 19-membered ring was obtained in a moderate yield. All the spectral and analytical data satisfied the structure **9d**. The thiaspirocyclol **9d** was readily converted into the S-free product **11d** [NMR: δ 4.57 (1H, triplet, J = 5.0 Hz, CH), mass spectrum, *m/e* 385 (M^+)] through a similar manner as described above, in support of the assigned structure. Likewise, irradiation of **8e** possessing an amide bond in their side chains afforded a mixture of cyclized compounds which were separated by silica gel column chromatography into **9e** and **10e**. In benzene, **8e** gave **9e** which was isolated as a single product without trace of **10e**. The spectroscopic data of **9e** and **10e** supported the cyclic structures (Experimental and Tables 4 and 5). The molecular weights of both compounds determined by the vapor-pressure method[13] and mass spectrometry were 440—456 and 448, respectively, both in agreement with the monomeric value (448). By a similar hydrogenolytic desulfurization,[14] compounds **9e** and **10e** were readily converted to the corresponding **11e** and **12e**, respectively.

Although the detailed mechanism of this remote photocyclization remains for further study, this cyclization

Table 4. Analytical and spectral data for the photoproducts (**9a–e**, **10c** and **10e**)

Compd No	Formula (M.W.)	Analysis(%) Calcd (found) C	H	N	S	Solvent†) (M.W.)[13]	MS m/e(M^+)	UV λ_{max}^{MeOH} nm(ε)
9a	$C_{14}H_{15}NO_2S_2$ (293.27)	57.33 (57.39)	5.16 (5.31)	4.78 (4.76)	21.81 (21.79)	(272)[a]	293	
9b	$C_{16}H_{19}NO_2S_2$ (321.32)	59.80 (59.73)	5.96 (6.24)	4.36 (4.48)	19.92 (19.74)	(328)[b]	321	240(4980)*
9c	$C_{17}H_{19}NO_4S_2$ (365.33)	55.89 (55.91)	5.24 (5.36)	3.83 (3.77)	17.52 (17.63)	(370)[b]	365	
10c	$C_{17}H_{19}NO_4S_2$ (365.33)	55.89 (55.86)	5.24 (5.35)	3.83 (3.79)	17.52 (17.65)		365	235(5870)*
9d	$C_{26}H_{37}NO_4S_2$ (491.52)	63.52 (63.37)	7.59 (7.49)	2.85 (2.95)	13.02 (13.15)	(490)[b]	491	247(5488)*
9e	$C_{23}H_{32}N_2O_3S_2$ (448.50)	61.59 (61.57)	7.19 (7.28)	6.25 (6.02)	14.27 (14.07)	(440)[c]	448	252(4790)*
10e	$C_{23}H_{32}N_2O_3S_2$ (448.50)	61.59 (61.38)	7.19 (7.05)	6.25 (5.99)	14.27 (13.98)	(456)[c]	448	

†The following solvents were used for the measurements; a = ethanol, b = methanol, c = chloroform.
*Shoulder.

Table 5. Spectral data for the photoproducts (**9a–e**, **10c** and **10e**)

Compd No	IR ν_{max}^{nujol} cm^{-1}	NMR (solvent) δ
9a	3210,1665	($CDCl_3$-d_6-DMSO); 1.40-2.30(3H,m),2.80-3.40(6H,m),4.16(1H,m), 6.46(1H,s),7.30-7.80(3H,m),8.00-8.20(1H,m)
9b	3260,1675	($CDCl_3$); 1.20-2.10(6H,m),2.10-2.70(2H,m),2.70-3.70(6H,m), 5.22(1H,s),7.36(3H,m),8.24(1H,m)
9c	3280,1750 1690,1675	($CDCl_3$-d_6-DMSO); 1.20-2.20(6H,m),3.08-3.80(4H,m),3.96-4.22(2H,m), 4.38(2H,d,J=11Hz),6.30(1H,s),7.20-7.80(3H,m),8.28(1H,m)
10c	3250,1735 1690	($CDCl_3$-d_6-DMSO); 1.20-2.00(6H,m),2.26(1H,q),2.99(1H,t), 3.70-4.70(5H,m),5.16(1H,d),6.74(1H,s),7.40-7.80(4H,m)
9d	3125,1730 1670	($CDCl_3$); 1.00-2.00(22H,m),2.33(2H,t),3.00-3.70(6H,m), 4.06(2H,m),4.65(1H,s),7.30-7.90(3H,m),8.20(1H,m)
9e	3290,3170 1680,1630	($CDCl_3$); 1.00-2.00(16H,m),2.20(2H,m),3.19(4H,m),3.60(4H,m), 4.80(1H,br s),6.44(1H,br),7.32-7.72(3H,m),8.10(1H,m)
10e	3230,3060 1680,1640	($CDCl_3$); 1.00-2.00(16H,m),2.19(2H,m),2.80-3.40(5H,m), 3.90(1H,m),4.32-4.60(3H,m),5.99(1H,t),7.30-7.70(4H,m)

would be rationalized by rapid electron transfer followed by proton transfer from the radical-cation of dithiolanyl group with favorable entropy factors by virtue of possible charge-transfer complex formation in the excited state (**13** and **14**: Scheme 4), in parallel with a general mechanism proposed for the phthalimide sulfide system (Scheme 1).[5,6a] To estimate the efficiency of this remote reaction, a quantum yield was measured in a typical case. The quantum yield value for the formation of **9d** from **8d** in acetonitrile was 0.032 ± 0.003.[15]

To explore a possible variation of the 1,3-dithiolanyl group, some homologous 1,3-dithianyl derivatives **15** were prepared and the photolysis was examined. Surprisingly, these derivatives failed to cyclize on irradiation, regardless to a very small difference in the ring size by a one C unit, giving no substantial amounts of the expected photoproducts and the substrates were quantitatively recovered. Recently formation of inter- and intramolecular radical cation complexes (**16** and **17**) has been observed during the oxidation of cyclic and open-

Table 6. Sulfur-free products (**11**, **12**) from the compounds (**9** and **10**)

Compd*) No	Method	Yield (%)	mp(°C)	Formula	Analysis(%) (found) C	H	N	Calcd C	H	N	IR $\nu_{max}^{(solvent)}$ cm^{-1}	MS m/e(M^+)
11a	A[a]	58	73-74	$C_{12}H_{13}NO$	76.97	7.00	7.48	(76.94	6.94	7.37)	(nujol);1670,1610	187
11b	A	49	oil	$C_{14}H_{17}NO$	78.10	7.96	6.51	(77.92	8.01	6.57)	(film);1680,1620	215
11c	A[b]	61	152-154	$C_{15}H_{17}NO_3$	69.48	6.61	5.40	(69.20	6.50	5.44)	(nujol);1730,1690	259
12c	A	73	oil	$C_{17}H_{23}NO_3$	70.56	8.01	4.84	(70.49	8.01	4.77)	(film);1740 1700	289
11d	B	58	oil	$C_{24}H_{35}NO_3$	74.76	9.15	3.63	(74.80	9.20	3.59)	(film);1730,1680	385
11e	A	47	oil	$C_{21}H_{30}N_2O_2$	73.64	8.83	8.18	(73.45	8.90	8.15)	($CHCl_3$);3450,1670	342
12e	A[b]	53	94-95	$C_{23}H_{36}N_2O_2$	74.15	9.74	7.52	(73.94	9.51	7.51)	(nujol);3400,3300, 3050,1670,1640	372

*The following solvents were used for the recrystallization; a = ether–hexane, b = EtOAc–hexane.

Table 7. Spectral data for sulfur-free products (11 and 12)

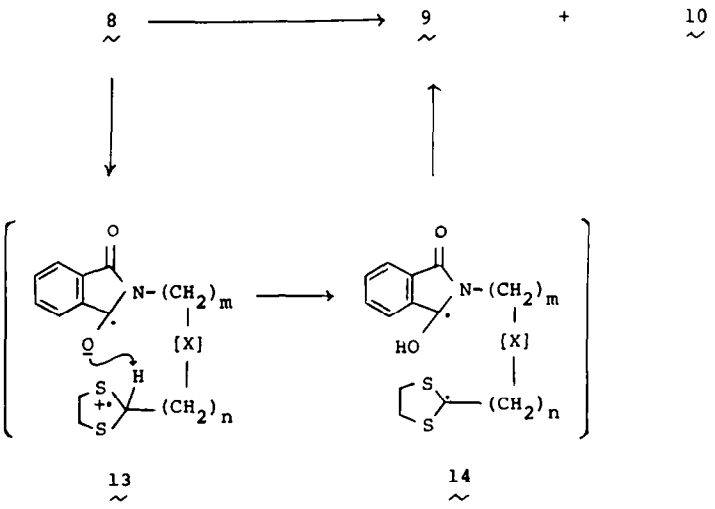
Compd No	UV $\lambda_{max}^{CHCl_3}$ nm(ε)*	NMR (solvent) δ
11a	247(5860), 270(3020)*	($CDCl_3$); 0.90-2.50(6H,m),2.67-3.25(1H,m),4.05-4.70(2H,m), 7.30-7.95(4H,m)
11b	251(4530),270(2890)* 280(1940)	($CDCl_3$); 1.00-2.50(10H,m),2.90-3.40 and 4.50-4.00(2H,each m), 4.53(1H,t,J=4.5Hz),7.35-7.95(4H,m)
11c	243(5610),270(1960)* 280(1430)	($CDCl_3$); 1.50(8H,m),4.00(1H,m),4.67(2H,t,J=3.4Hz), 3.64 and 5.18(2H,ABq,J=16.7Hz),7.30-8.00(4H,m)
12c	243(6260),270(2000)* 281(1560)	($CDCl_3$); 0.59(3H,t,J=7.4Hz),0.80-2.20(11H,m),4.13(2H,t,J=6.3Hz), 3.82 and 4.83(2H,ABq,J=18Hz),4.82(1H,t,J=4.4Hz),7.30-7.95(4H,m)
11d	248(6100),270(3230)* 280(2100)	($CDCl_3$); 1.34(24H,m),2.36(2H,t),3.53(2H,m),4.10(2H,t,J=5.2Hz), 4.57(1H,t,J=5.0Hz),7.20-8.00(4H,m)
11e	246(5070),268(2630)* 279(1710)	($CDCl_3$-d_6-DMSO); 1.00-2.00(16H,m),2.20(4H,m),2.80-3.80(4H,m), 4.56(1H,m),7.25(1H,br),7.35-8.00(4H,m)
12e	247(6970),269(3700)* 279(2470)	($CDCl_3$); 0.52(3H,t,J=8Hz),1.12(3H,t,J=8Hz),1.10-1.80(16H,m), 2.06(4H,m),3.28(2H,t each d,J=8 and 6Hz),4.00 and 3.05(2H,d each J=14 and 8 Hz),4.60(1H,s,J=4.0Hz),5.48(1H,br),7.28-7.60(3H,m), 7.80(1H,m)

*Shoulder.

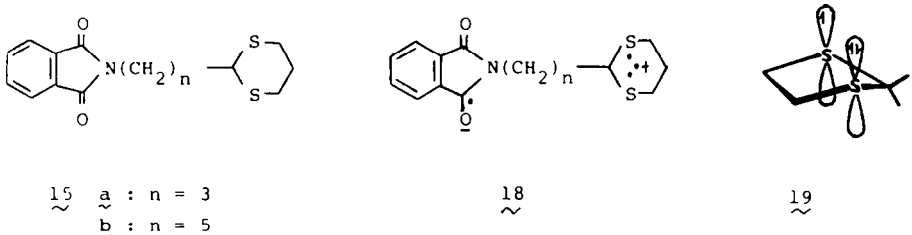
chain dithia compounds (the two S atoms not adjacent).[16] These species are characterized by a new S–S bond established by interaction of the unpaired *p*-electron from the oxidized S atom with the free *p*-electron pair of a second S atom (Scheme 5). Analogously, the above behavior of **15** may be rationalized by considering the involvement of a stable complex radical cation such as **18**, which is no longer capable of promoting a proton transfer required for the photocyclization to proceed (Scheme 4). By contrast, in the planar and rigid molecule of 1,3-dithiolanyl, the possible degree of *p*-orbital overlap is much too slight to allow for the formation of such a bond (**19**). This interpretation is in good agreement with the postulated mechanism shown in Scheme 4.

Thus the expected macrocyclic products were obtained as a result of C–C bond formation between the imide CO group and predominantly the S–methine group through this extensive Norrish type II photocyclization. The S–methine group is more reactive than the S–methylene group probably due to cumulative effects of the two adjacent S atoms of the dithiolanyl function. In some limited cases, compound **10** predominated presumably due to solvent and conformational effects in the excited states.

In our typical photochemical macrocyclic synthesis



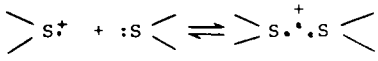
Scheme 4.



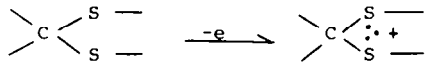
15 a : n = 3
b : n = 5

18

19



16



17

Scheme 5.

with the phthalimide–thiomethyl pair system **1**, **3**, the feature of the C–C bond formation remains the sulfide moiety in the C skeleton **4**. By contrast, the employment of the 1,3-dithiolanyl group as a new donor in place of a thiomethyl group, allows us to eliminate the remaining thioketal moiety after the construction of the new carbocycles, leaving little trace of the precursor group used in the cyclization stage. The present example of a removable functional group in a macrocyclic synthesis may suggest a new general strategy which places less restriction on the mode of carbon skeleton syntheses.

EXPERIMENTAL

All m.ps are uncorrected. IR spectra were taken on a Hitachi IR-215 (Nujol), UV spectra on a Hitachi 323, Mass (MS) spectra on a Hitachi RMS-4, NMR spectra on a JEOL MH60 [$CDCl_3$; $(Me)_4Si$ as an internal standard; the chemical shifts are expressed in δ (ppm), coupling constants (J) are given in Hz], unless otherwise specified. Then, the following abbreviations are used; s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad and sh = shoulder.

2-(4-*Hydroxybutyl*-2H-*isoindole*-1,3(2H)-*dione* (**5a**)[17a] was prepared by the described method, and then 2-(3-*formylpropyl*)-2H-*isoindole*-1,3(2H)-*dione* (**6a**; m.p. 72–74°)[17b] was prepared in a manner similar to that described for **6b**.

4-(1,3-*Dithiolan*-2-*yl*) *butan*-1-*ol*. BF_3–etherate (2 ml) was slowly added to a stirred soln of 2,3-dihydropyran (8.4 g, 0.1 mol) and ethane dithiol (12.5 ml, 0.15 mol) in ether (4 ml) at 0°. A vigorous reaction occurred and the temp. rose to 50°. After addition of BF_3–etherate, the mixture was stirred at 25° for 1 hr. The mixture was chromatographed on SiO_2 (hexane : EtOAc = 4 : 1) to give 9.56 g (54%) of a colorless oil, b.p. 141–142°/3 mmHg. (Found: C, 46.87; H, 7.90; S, 36.01. $C_7H_{14}OS_2$ requires: C, 47.18; H, 7.92; S, 35.92%.)

2-(6-*Hydroxyhexyl*)-2H-*isoindole*-1,3(2H)-*dione* (**5b**). A suspension of phthalimide (22 g, 0.15 mol), 6-bromo-1-hexanol[17c] (18.1 g, 0.1 mol) and K_2CO_3 (20.7 g, 0.15 mol) in DMSO (70 ml) was stirred at 25° for overnight and then heated at 55° for 6 hr. The mixture was poured into H_2O and acidified with conc HCl. After filtration of insoluble material, the filtrate was extracted with EtOAc. The extracts were washed with H_2O, dried and concentrated *in vacuo*. The residue was chromatographed on SiO_2 (benzene : EtOAc = 4 : 1) and recrystallized from EtOAc–hexane to give 19.2 g (78%) of **5b**, colorless plates, m.p. 50–51°. (Found: C, 67.88; H, 7.03; N, 5.72. $C_{14}H_{17}NO_3$ requires: C, 67.99; H, 6.93; N, 5.66%.)

1,3(2H)-*Dioxo*-2H-*isoindol*-2-*undecanoic acid* (**5d**), N-Ethoxycarbonyl phthalimide[17d] (21.9 g, 0.1 mol) was added to a stirred soln of 11-aminoundecanoic acid (20.1 g, 0.1 mol) and Na_2CO_3 (10.6 g, 0.1 mol) in H_2O (140 ml) at 25° for 1 hr. After insoluble material was filtered off, the filtrate was acidified and the ppt was collected by suction, washed with H_2O and dried to give 20.8 g (63%) of **5d**, colorless needles from ether, m.p. 90–91°. (Found: C, 68.66; H, 7.54; N, 4.32. $C_{19}H_{25}NO_4$ requires: C, 68.86; H, 7.60; N, 4.23%.)

2-(5-*Formylpentyl*)-2H-*isoindole*-1,3(2H)-*dione* (**6b**). CrO_3 (13.2 g, 0.12 mol) was added to a stirred soln of pyridine (19.2 ml, 0.24 mol) and CH_2Cl_2 (150 ml) at 25° under an argon. After stirring for 20 min, to the suspension was added a soln of **5b** (4.94 g, 0.02 mol) in CH_2Cl_2 (50 ml) and then the mixture was stirred for 30 min. The organic layer was decanted and the ppt was washed with CH_2Cl_2. The combined CH_2Cl_2 solns were washed with dil HCl and H_2O, dried and concentrated *in vacuo*. The residue was chromatographed on SiO_2 (hexane : EtOAc = 4 : 1) to give 4 g (82%) of **6b**, a colorless oil. (Found: C, 68.56; H, 6.06; N, 5.60. $C_{14}H_{15}NO_3$ requires: C, 68.55; H, 6.16; N, 5.71%.)

N - ((2,2 - *Diethoxy*)*ethyl*) - 1,3(2H) - *dioxo* - 2H - *isoindol* - 2 - *undecanamide* (**7**). A mixture of **5d** (8 g, 24.2 mmol), $SOCl_2$ (8 ml), DMF (0.1 ml) and $CHCl_3$ (30 ml) was refluxed for 2 hr. Removal of the solvent gave the crude acid chloride, which was used in the next reaction: A soln of the acid chloride in CH_2Cl_2 (50 ml) was added dropwise to a stirred soln of 2,2-diethoxyethylamine (3.22 g, 24.2 mmol), Et_3N (2.12 g, 24.2 mmol), CH_2Cl_2 (15 ml), and DMF (40 ml) at − 35° for 30 min. After stirring at 25° for 3 hr, the mixture was poured into dil HCl, and extracted with CH_2Cl_2. The extracts were washed with H_2O, 10% HCl, H_2O, 5% $NaHCO_3$ and H_2O successively, dried and concentrated *in vacuo*. The residue was recrystallized from benzene-hexane to give 5.55 g (51%) of **7**, colorless crystals, m.p. 66–67°. (Found: C, 67.24; H, 8.51; N, 6.36. $C_{25}H_{38}N_2O_5$ requires: C, 67.23; H, 8.58; N, 6.27%.)

General procedure for the preparations of the compounds (**8**) *and* (**15**)

Method A; *for* **8a–b**, **8e** *and* **15a–b**. BF_3–etherate (0.2 ml) was added to a suspension of **6a–b** or **7** (10 mmol) and ethane dithiol or 1,3-propane dithiol (1.3–2.0 eq.) in ether (15 ml) under ice-cooling. After stirring at 25° for 1–5 day, the mixture was concentrated *in vacuo*. The residue was dissolved in EtOAc or $CHCl_3$, washed with 5% $NaHCO_3$, 10% HCl and brine successively, dried and concen-

trated *in vacuo*. The residue was purified by recrystallization or after column chromatography on SiO_2 (hexane–EtOAc or $CHCl_3$–EtOAc) (Tables 1 and 2).

Method B; *for* **8c–d**. A suspension of **5c**[17e] or **5d** (15 mmol), 4-(1,3-dithiolan-2-yl)butan-1-ol (15 mmol), 1-methyl-2-chloropyridinum iodide[17f] and Et_3N (36 mmol) in CH_2Cl_2 (30 ml) was refluxed under an argon atmosphere for 7 hr. After removal of the solvent, the residue was purified by recrystallization (Table 1 and 2).

2-(3-(1,3*Dithian*-2-yl)*propyl*)-2H-*isoindole*-1,3(2H)-*dione* (**15a**). The product was recrystallized from EtOAc to give 69% of **15a**, colorless needles, m.p. 126–127°, IR (Nujol): 1760, 1700 cm^{-1}. UV (MeOH): 241 (ε 11890), 293 (2170). MS *m/e*: 307 (M^+), NMR ($CDCl_3$): δ 1.60–2.20 (6H, m), 2.70–3.00 (4H, m), 3.71 (2H, t, J = 6.5 Hz), 4.08 (1H, t, J = 6.5 Hz) 7.55–8.00 (4H, m). (Found: C, 58.66; H, 5.64; N, 4.65; S, 20.91. $C_{15}H_{17}NO_2S_2$ requires: C, 58.63; H, 5.58; N, 4.56; S, 20.83%.

2-(5-(1,3-*Dithian*-2-yl)*pentyl*-2H-*isoindole*-1,3(2H)-*dione* (**15b**). The product was recrystallized from EtOAc to give 59% of **15b**, colorless needles, m.p. 95–96°. IR (Nujol): 1760, 1700 cm^{-1}. UV ($CHCl_3$): 244 (ε 15010), 295 nm (2630). MS *m/e*: 335 (M^+), NMR ($CDCl_3$): δ 1.00–2.30 (10H, m), 2.70–3.00 (4H, m), 3.69 (2H, t, J = 6.6 Hz), 4.02 (1H, t, J = 6 Hz), 7.58–7.95 (4H, m). (Found: C, 60.82; H, 6.41; N, 4.15; S, 19.25. $C_{17}H_{21}NO_2S_2$ requires: C, 60.88; H, 6.31; N, 4.18; S, 19.09%.)

General procedure for the photolysis. A soln [300–700 ml (4–11 mM)] of **8** [0.5–1.5 g (1.37–4.11 mmol)] was irradiated with a 400 W high pressure mercury lamp at 10–20° under an argon bubbling, unless otherwise noted. After removal of the solvent *in vacuo*, the residue was purified by recrystalization or after SiO_2 column chromatography (Tables 3–5).

General procedure for the desulfurization (*Tables 6 and 7*).

Method A. A mixture of **9** (or **10**) (0.5 mmol) and Raney Ni (w-7, 3 ml) in EtOH (6 ml) was refluxed for 2 hr. After removal of the Raney Ni, the filtrate was concentrated *in vacuo*. The residue was purified by SiO_2 preparative TLC (developed with hexane–EtOAc or $CHCl_3$–EtOAc).

Method B. A mixture of **9d** (0.2 mmol) and Raney Ni (w-1, 6 ml) in acetone (12 ml) was refluxed for 5 hr. Purification was carried out according to the method A.

Quantum yields. Acetonitrile solns of a sample of **8d** (10 mM) in Pyrex tubes were degassed by five freeze-pump-thow cycles and sealed *in vacuo* at $\leqq 10^{-3}$ torr. Quantum yields were measured relative to 0.012 M potassium ferrioxalate actinometer[18] on parallel irradiation of samples of identical volumes (5 ml). Irradiations were performed on a merry-go-round apparatus with a Eikosha 500 W high pressure mercury lamp contained in a water-cooled, quartz immersion well. A chemical filter of 1.4 mM potassium chromate in 0.1% aqueous sodium carbonate[19] was used to isolate the 313 nm line. After the irradiation, the products were isolated by silica gel preparative TLC (Merck precoated PLC 60F-254, EtOAc:hexane = 2:3) and product formations were determined by measurement of optical densities in EtOH at 250 nm. Quantum yield of the formation of **9d** from **8d** was 0.032 ± 0.003.

Acknowledgements—We are grateful to Drs. S. Saito and T. Mizoguchi, Organic Chemistry Research Laboratory, Tanabe Seiyaku, Co., Ltd., for their encouragements. This work was supported in part by a Grant in Aid for Scientific Research (Project 57118006) from the Ministry of Education, Science and Culture (to Y.K.).

REFERENCES

[1a]Photochemistry of the phthalimide system. 33; Part 32: M. Machida, H. Takechi and Y. Kanaoka, *Tetrahedron Letters*, 4981 (1982); [b]Photoinduced reactions, 59; Part 58: Y. Kanaoka, Y. Hatanaka, E. N. Deusler, I. L. Karle and B. Witkop, *Chem. Pharm. Bull.* **30**, 3028 (1982).

[2a]P. Läuger, *Science* **178**, 24 (1972); [b]B. C. Pressman, *Ann. Rev. Biochem.* **45**, 501 (1976); [c]Y. A. Ovchinnikov, *Membrane-Active Complexenones*. Elsevier, Amsterdam (1974).

[3a]D. J. Cram and J. M. Cram, *Science* **183**, 803 (1974); [b]*Idem*, *Acc. Chem. Res.* **11**, 8 (1978); [c]J. M. Lehn, *Ibid.* **11**, 49 (1978); [d]H. Dugas and C. Penny, *Bioorganic Chemistry* (Edited by R. Frost), p. 225. Springer-Verlag, New York (1981).

[4a]M. A. Winnik, *Chem. Rev.* **81**, 491 (1981); [b]R. Breslow, *Chem. Soc. Rev.* **1**, 553 (1972).

[5]Y. Kanaoka, *Acc. Chem. Res.* **11**, 407 (1978).

[6a]Y. Sato, H. Nakai, T. Mizoguchi, Y. Hatanaka and Y. Kanaoka, *J. Am. Chem. Soc.* **98**, 2349 (1976); [b]Y. Kanaoka and H. Migita, *Tetrahedron Letters* 3693 (1974); [c]M. Machida, H. Takechi and Y. Kanaoka, *Heterocycles* **7**, 273 (1977); Idem, *Chem. Pharm. Bull.* **30**, 1579 (1982); [d]M. Machida, H. Takechi and Y. Kanaoka, *Heterocycles* **14**, 1255 (1980); [e]Y. Maruyama and Y. Kubo, *J. Am. Chem. Soc.* **100**, 7772 (1978); [f]M. Machida, K. Oda and Y. Kanaoka, *Heterocycles* **18**, 211 (1982).

[7]Y. Sato, H. Nakai, H. Ogiwara, T. Mizoguchi and Y. Kanaoka, *Tetrahedron Letters* 1889 (1976).

[8]Y. Kanaoka, Y. Hatanaka, Y. Sato, M. Wada and H. Nakai, *VIII IUPAC Symp. on Photochemistry*, Abstracts of Papers, p. 190. Seefeld, July (1980).

[9]Y. Sato, M. Wada, H. Nakai, Y. Hatanaka and Y. Kanaoka, *12th Symp. on Heterocyclic Chemistry*, Abstracts of Papers, p. 151, Tokyo, Oct. 1979.

[10]M. Wada, H. Nakai, Y. Sato and Y. Kanaoka, *Tetrahedron Letters* 3077 (1982).

[11]M. Wada, H. Nakai, K. Aoe, K. Kotera, Y. Sato and Y. Kanaoka. *Chem. Pharm. Bull.* **30**, 2275 (1982).

[12]M. Wada, H. Nakai, Y. Sato and Y. Kanaoka, *Ibid.* **30**, 3414 (1982).

[13]Hitachi-Perkin molecular weight measuring apparatus Model 115 (vapor-pressure method).

[14]G. R. Pettit and E. E. van Tamelen, *Organic Reactions*, (Edited by A. C. Cope), **12**, p. 356, Wiley, New York (1962).

[15]In preliminary studies with N-[(ω-methylthio)hexyl]-phthalimide,[3a] the quantum yield of cyclization was 0.05 (in CH_3CN; 313 nm). Relative efficiencies of **9d** were same order.

[16]K. D. Asmus, D. Bahnemann, C. H. Fischer and D. Veltwisch, *J. Am. Chem. Soc.* **101**, 5322 (1979).

[17a]S. Sugiura, S. Inoue, Y. Hayashi, Y. Kishi and T. Goto, *Tetrahedron* **25**, 5155 (1969); [b]F. E. King, P. L'Ecuyer and H. T. Openshaw, *J. Chem. Soc.*, 352 (1936); [c]E. F. Degering and L. G. Boatright, *J. Am. Chem. Soc.* **72**, 5137 (1950); [d]G. H. L. Nefkens, G. I. Tesser and R. J. F. Nivard, *Rec. Trav. Chem.* **79**, 688 (1960); G. H. L. Nefkens, *Nature* **185**, 309 (1960); [e]J. H. Billmann and W. F. Hartung, *J. Am. Chem. Soc.* **70**, 1473 (1949); [f]T. Mukaiyama, M. Usui, E. Shimada, and K. Saigo, *Chem. Lett.* 1045 (1975); K. Saigo, M. Usui, K. Kikuchi, E. Shimada and T. Mukaiyama, *Bull. chem. Soc. Japan* **50**, 1863 (1977).

[18]C. G. Hatchard and C. A. Parker, *Proc. Roy. Soc.* **A235**, 518 (1956).

[19]S. L. Murov, *Handbook of Photochemistry*, p. 99. Marcell Dekker, New York (1973).