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Synthesis of Novel Heteromacrocyclic Compounds from (*E*,*E*)-1,2-Diketone Dioximes and Dichloromethane

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(E,E)-1,2-Diketone dioximes, when treated with base in the presence of a phase transfer catalyst in dichloromethane, afford new heteromacrocyclic compounds in which oxime units are sequentially linked by methylene bridges.

Although a variety of macrocyclic polyether compounds such as crown ethers and cryptands have been reported in the literature,¹ there are few examples of heteromacrocycles containing oxime linkages except for Vögtle's macrocyclic monoand di-oximes² which are prepared from 1,2-diketone dioximes and oligomeric dichloroethylene glycol by the usual method,³ and a macrocyclic polyhydroximate formed *via* nucleophilic polymerization of acetonitrile oxide.⁴ Described herein is a new and convenient method for synthesizing the heteromacrocycles (2) and (3) by the sequential cyclic oligomerization of the 1,2-diketone dioximes (1) and dichloromethane, and the unique mode of this oligomerization.

The heteromacrocycle (2a) was obtained as follows. To a stirred suspension of (E,E)-butane-2,3-dione dioxime (dimethylglyoxime) (1a) (33 mmol), Bu^tOK (66 mmol), and 18crown-6 (3·3 mmol) in tetrahydrofuran (THF; 100 ml) was added dichloromethane (100 ml) at a rate to maintain a gentle reflux. After the addition was complete, the mixture



was refluxed for 18 h, cooled, and filtered. The solvent and excess of CH_2Cl_2 were then removed *in vacuo*. The residue was thoroughly washed with methanol and recrystallized from THF-MeOH. Pure (2a) was obtained in 20% yield as colourless crystals.

In the absence of 18-crown-6 no reaction takes place. However, the use of trioctylmethylammonium chloride as a phase transfer agent is comparatively effective in promoting the reaction. Thus, treatment of (1a) with Bu^tOK in THF-CH₂Cl₂ in the presence of 0·1 equiv. of the phase transfer agent under comparable conditions resulted in the isolation of pure (2a) in 21 % yield. (*E,E*)-2,5-Dimethylhexane-3,4-dione dioxime (1b) similarly afforded (2b) in 21 % yield upon treatment with Bu^tOK-18-crown-6. By contrast, (*E,E*)-octane-4,5dione dioxime (1c) gave (3) (40% yield), in which four oxime units are linked by methylene bridges.

In the ¹H n.m.r. spectra of (2a), (2b), and (3) (Table 1) the $-OCH_2O-$ protons appear as a singlet approximately at δ 5·50, and their ¹³C {¹H} n.m.r. spectra (CDCl₃) also exhibit only one singlet due to the methylene carbon at δ 99·45 p.p.m. for (2a) and δ 99·31 p.p.m. for (3) relative to Me₄Si. These observations indicate the equivalence of all the $-OCH_2O-$ groups, and they agree with the structures (2) and (3) illustrated. The extent of oligomerization was determined by the mass spectra of the products.

It is noteworthy that the mode of the cyclization is affected by the configuration of the oxime group. Thus, (Z,Z)-1,2dicyclohexylethanedione dioxime (1d) gave (4a), a previously unknown class of heterocyclic compound, in 66% yield via intramolecular cyclization of the 1:1 adduct of (1d) and CH₂Cl₂. Similarly, (Z,Z)-2,5-dimethylhexane-3,4-dione dioxime (1e) afforded (4b) in 47% yield along with a small amount (ca. 5%) of (5) containing two (Z,E)-oxime units. Table 1. Physical and spectral properties of cyclized products(2)--(5)

	¹ H N.m.r. (CDCl _a)			
	M.p or b.p.,		δ (others,	Mass
Producta	$t/^{\circ}C^{-1}$	δ(-OCH ₂ O)	J in Hz) ^e	$m/e (M^+)$
(2a)	270-271	5·74 (6H, s)	2·04 (18H, s)	384
(2 b)	140—148	5·63 (6H, s)	3·33 (6H, h, 7)	551 ^b
$\langle \mathbf{a} \rangle$	142 146	5 50 (011)	1.14 (36H, d, 7)	
(3)	143—146	5.10 (8H, s)	2.63 (16H, t, 7)	736
		1	0.94 (24U + 7)	m)
(4 a)	135—136	5·28 (2H, s)	0.84 (24H, 1, 7) 0.98—2.58	265ª
	(I mmHg)	5 00 (OTT)	(22H, m)	104
(4D)	(1 mmHg)	5·30 (2H, s)	2.68 (2H, n, 7) 1.25 (12H, d, 7)	184
(5)	82—83	5·55 (4H, s)	2.60 (4H, m)	368
			1.19 (12H, d, 7) 1.14 (12H, d, 7)	
Satisfactory elemental analyses were obtained. ^b M^+-1 h = heptuplet. ^d M^++1 .				

The (Z,E)-configuration (5) was assigned since the methyl signals of the two isopropyl groups appear at different chemical shifts as two sets of doublets in its ¹H n.m.r. spectrum. The heteromacrocycle (4b) was also formed from the (Z,E)-dioxime (1f) (R = Pr¹) in 16% yield, indicating that the $(Z,E) \rightleftharpoons (Z,Z)$ isomerization, when R = Pr¹, takes place during the reaction.[†] The physical and spectral properties of all the products obtained are listed in Table 1.

Although we have not yet fully examined the complexing properties of the macrocycles (2) and (3), some observations have been made with (2a). No incorporation of alkali metal cations was observed. However, when (2a) was treated in ether with 1 equiv. of Cu(ClO₄)₂·6H₂O at room temperature, a blue complex [m.p. > 280 °C (decomp.); i.r. (KBr) 3375 br. vs, 1610, 1070, and 995 cm⁻¹] which corresponds to the formula [LCu₂(ClO₄)₄]·3H₂O, L = (2a) was formed as a fine precipitate in 52% yield. The complex seems to be a binuclear macrocyclic Cu^{II} complex, a type which has attracted much attention in recent years.⁵ The complex tends to dissociate into the original components in polar solvents such as MeOH and acetone.

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[†] In the case of (E,E)-benzil dioxime (1g), 3,4-diphenylfurazan was formed (27%), formally via the $(E,E) \rightarrow (Z,E)$ isomerization followed by dehydration.