THALLIUM SELECTIVE 6-METHYLPYRIMIDINE-2,4(1H,3H)-DIONE BASED PODANDS

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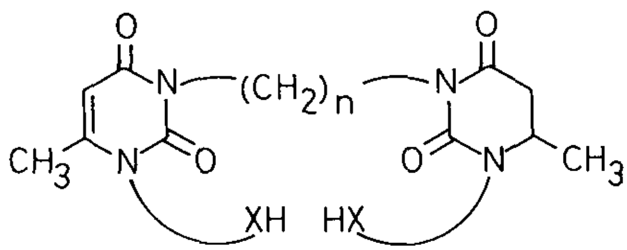
Abstract - Sequential reactions of dihalides and amino alcohols with 6-methyl-1,3-oxazine-2,4(3H)-diones provide title podands. 8a selectively extracts and transports Tl^+ picrate over Li^+, Na^+, K^+ and NH_4^+ picrates. Compounds (4), (6), and (8) are effective ionophores.

The significance of pyrimidine-2,4(1H,3H)-dione towards complexation (H^+) displayed remarkably in DNA and RNA strands[1] remains more or less untapped in case of synthetic ionophores.[2] Consequently we have designed podands (1) possessing (i) a carbon chain between N-3 of two pyrimidinediones and (ii) additional heteroatom bearing chains at their N-1. CPK models of (1)(n = 1 and 2) depict an overlapping of two C-2 carbonyl oxygens of pyrimidinedione moieties, which would inhibit cavity induced ligation and in podand (1) (n = 3) two oxygens



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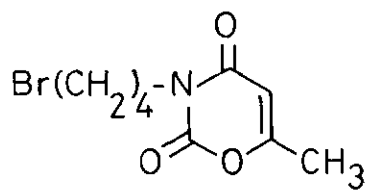

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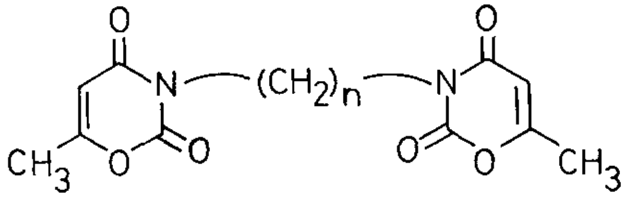

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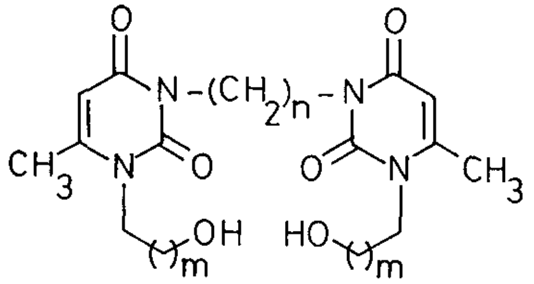
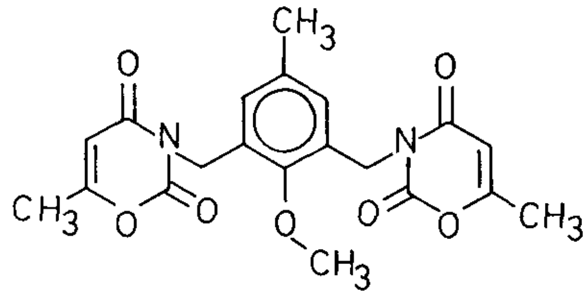
a n=4; b n=5; c n=6.



4a n = 4 m = 1
4b n = 4 m = 2
5a n = 5 m = 1
5b n = 5 m = 2
6a n = 6 m = 1
6b n = 6 m = 2



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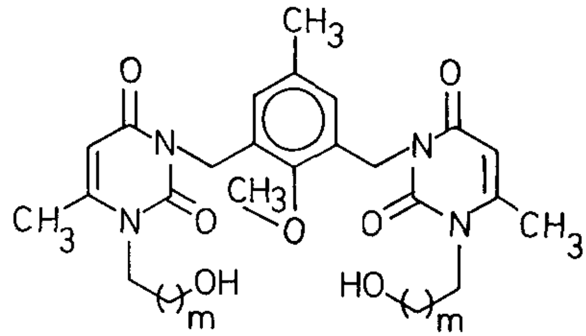

8a m=1 ; 8b m = 2

of pyrimidinediones are reasonably apart but it has relatively restricted flexibility for attaining a desired pseudocavity. However, podands (1)(n = 4, 5,6), in their CPK models, display considerable flexibility and could form adjustable pseudocavities with four hetero atoms. The incorporation of 2,6-dimethylene-1-methoxy-4-methylaryl group between two N-3 of two pyrimidinediones(8) leads to a cavitand type structure (CPK model) with an additional ligating site. Thus, we have initially synthesized podands (4-6) and (8) and investigated their extraction[3] and transport characters[4] towards picrates of Li^+, Na^+, Tl^+ and NH_4^+. The podand (8a) transports thallium(I) picrate nearly 25,14,10 and 8.5 times than K^+, Na^+ and NH_4^+ picrates respectively.

6-Methyl-1,3-oxazine-2,4(3H)-dione with 1,4-dibromobutane[5] under solid-liquid phase transfer catalytic (PTC) conditions (CH_3CN-K_2CO_3-TEBA) gave two compounds. The lower R_f component (50%), mp 157°C, M^+ m/z 308, ^{1}H-nmr δ 1.50-1.87(m, 4H, CH_2CH_2), 2.17(s, 6H, $2XCH_3$), 3.88(t, J = 6.0 Hz, 4H, $2XNCH_2$), 5.67(s, 2H, 2X pyrimidine H), could be assigned the structure, 3,3'-(1,4-butanediyl)bis(6-methyl-1,3-oxazine-2,4(3H)-dione) (2a). The higher R_f component (5%), mp 68°C

M^+ m/z 263, 261(1:1) was found to be 3a. Similarly, 6-methyl-1,3-oxazine-2,4-(3H)-dione with 1,5-dibromopentane, 1,6-dibromohexane and 2,6-bis(bromomethyl)-1-methoxy-4-methylbenzene gave 2b(31%), mp 139°C; 2c (40%), mp 145°C, Lit.,[2b] 154-155°C; and 7(40%), mp 250°C, respectively. 2a with 2-aminoethanol and 3-aminopropanol-1 gave 4a (33%), mp 220°C, and 4b (46%), 187°C, respectively. Similarly, 2b, 2c and 7 on heating with 2-aminoethanol and 3-aminopropanol-1 gave 5a(39%), mp 134°C; 5b(50%), mp 100°C; 6a(36%), mp 194-195°C, Lit.,[2b] 207-208°C; 6b(21%), mp 165°C; 8a(19%), mp 105°C, and 8b(15%), mp 147°C, respectively.[6]

Podands |4(a,b) and 6(a,b)| with even number carbon bridge between two pyrimidinones show different trends in extraction experiments as compared with 5(a,b).

Table

Extraction ($x10^3$) ratio of metal picrate over podand in organic layer) and transport ($x10^8$ mol/24 h) (in parenthesis) rates of podands (4-6 and 8):

Podand	Li^+	Na^+	K^+	Tl^+	NH_4^+	Selectivity Ratios Tl^+/K^+	 Tl^+/Na^+	 Tl^+/NH_4^+	 Tl^+/Li^+
4a	– (7.5)	4.09 (14)	9.36 (50.5)	5.61 (–)*	4.36 (109)	1.66	3.81	3.58	–
4b	– (50.2)	3.09 (15.5)	5.08 (–)*	4.70 (27.1)	4.56 (12.4)	0.93	1.52 (1.75)	1.03 (2.19)	 (0.54)
5a	– (–)*	1.54 (–)*	1.39 (–)*	0.95 (13.9)	1.94 (9.1)	0.68	0.62	0.49 (1.52)	
5b	– (–)*	4.41 (–)*	4.39 (8.5)	4.32 (10.1)	4.26 (17.2)	0.98 (1.19)	0.98	1.01 (0.59)	
6a	– (26.1)	9.00 (46.0)	11.0 (20.1)	14.0 (35.1)	11.8 (32.5)	1.27 (1.75)	1.56 (0.76)	1.19 (1.08)	 (1.34)
6b	– (49.1)	8.3 (52.3)	11.9 (–)*	11.4 (50.8)	7.9 (34.3)	0.95	1.39 (0.97)	1.43 (1.48)	 (1.03)
8a	– (20.9)	2.4 (15.5)	2.7 (8.7)	8.4 (221)	2.6 (26)	3.05 (25.4)	3.5 (14.25)	3.28 (8.5)	
8b	– (42.3)	5.5 (54.1)	5.23 (45.3)	6 (104.5)	3.87 (50.3)	1.15 (2.31)	1.09 (1.93)	1.55 (2.07)	 (2.47)

*Not transported

Podands (4a) and (6a) with hydroxyethyl chain at N-1 extract metal picrates better than 4b and 6b possessing hydroxypropyl chain. But, 5a extracts metal picrates poorly than 5b. Further, podands (4) and (6) show selectivity towards

K^+ than Na^+ but 5a and 5b selectively extracts Na^+ than K^+. However, these podands transport metal picrates at poor rates. In general, the increase in lipophilicity in podands (6) in comparison with podands (5), results in better transport and extraction rates. Podands (4a), (5a) and (6a) with hydroxyethyl chain at N-1 of pyrimidinedione in general show selectivity towards Tl^+ picrate over K^+, Na^+ and NH_4^+ picrates. 8a extracts Tl^+ picrate nearly 3 times than Na^+, K^+ and NH_4^+ picrates and transports Tl^+ picrate nearly 25, 14, 8.5, and 10 times than K^+, Na^+, NH_4^+ and Li^+ picrates respectively. However, with 8b, the selectivity of transport is lowered.

Thus, the presence of two carbon unit chain at N-1 of pyrimidinedione in podands (4a), (5a), (6a), and (8a) favours the extraction and transport of metal picrates with selectivity towards Tl^+ picrate over Li^+, Na^+, K^+ and NH_4^+ picrates than their analogs (4a, 5b, 6b and 8b) with three carbon chains at N-1 of pyrimidinedione.

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5. Condensations of 6-methyl-1,3-oxazine-2,4(3H)-dione with diiodomethane, 1,2-dibromoethane and 1,3-dibromopropane failed.

6. All these compounds gave satisfactory spectral and analytical data.

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