Chinese Chemical Letters Vol. 10, No. 12, pp. 1011–1012, 1999

Synthesis of Macrocyclic Arsinous Acid Esters

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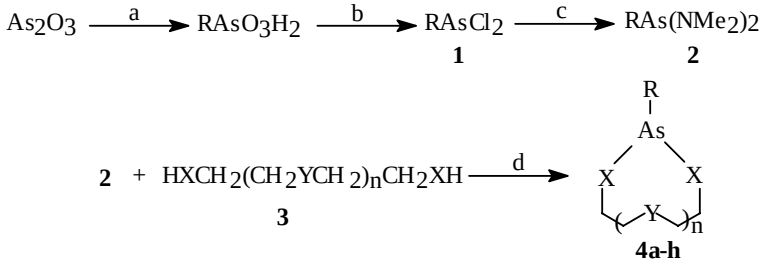
Abstract: The reactions of the bis (dimethylamino) alkylarsine with diols lead to the formations of macrocyclic arsinous acid esters. The synthesis of title compounds was described and their structures were characterized by elemental analysis, IR, ^{1}HNMR, and MS.

Keywords: Bis (dimethylamino) alkylarsine, macrocyclic arsinous acid ester, synthesis.

Macrocyclic arsinous acid esters are usually prepared by condensation of dichloroalkylarsines $RAsCl_2$ **1** with diols in the presence of organic alkali [1]. The method described here involves the transformation of intermediate from **1** to bis (dimethylamino) alkylarsine $RAs(NMe_2)_2$ **2** and the reaction of **2** with diols in dry THF to lead to the formation of title compounds. **2** can react smoothly with diols in the absence of organic alkali to generate corresponding macrocyclic arsinous acid esters **4** and dimethylamine which escapes from the reacting system as a gas in reflux. Although one more step, the yields of cyclization step of this method are higher than 70% and the target compounds are easy to purify. By this method , we synthesized five title compounds and their structures were characterized by elemental analysis, IR, ^{1}HNMR, and MS. Three macrocyclic arsinodithious acid esters are synthesized by the reaction of **2** with dithiols under the same conditions. The synthetic route of the target compounds is shown in **Scheme 1**.

Scheme 1 . Synthesis of Compounds **4a-h**



Conditions: a. NaOH, RX ; b. SO_2, HCl ; c. $H(NMe_2)_2$, Et_2O, -10^oC ; d. THF.

Table 1. Yields of Compounds **4a-h**

Compd	n	R	X	Y	Formula	Yield,%
4a	1	Me	O	O	$C_5H_{11}O_3As$	87
4b	2	Me	O	O	$C_7H_{15}O_4As$	72
4c	2	n-Pr	O	O	$C_9H_{19}O_4As$	70
4d	3	Me	O	O	$C_9H_{19}O_5As$	82
4e	3	Et	O	O	$C_{10}H_{21}O_5As$	70
4f	1	Me	S	O	$C_5H_{11}OS_2As$	51
4g	1	Me	S	S	$C_5H_{11}S_3As$	21
4h	2	Me	S	O	$C_7H_{15}O_2S_2As$	42

2 was prepared from arsenic trioxide over tree steps. Treatment of arsenic trioxide in aqueous caustic with alkyl halides gives in about 85% yields alkylarsonic acid $RAsO_3H_2$ which were reduced by sulfur dioxide in concentrated hydrochloric acid to generate dichloroalkylarsines[2,3]. The heterogeneous reaction of **1** with dimethylamine in dry ether under nitrogen atmosphere at -10^oC leads to the formation of **2** in 60% yield[4]. **3** was prepared by treatment of sulfourea with appropriate 1,ω-dichloro ether $ClCH_2(CH_2YCH_2)_nCH_2Cl$ (Y=O or S)[5].

Typical experimental procedure: Synthesis of 2-methyl-1,3,6,9,12-pentaoxa-2-arsacyclotetradecane **4d**. A solution of bis (dimethylamino) methylarsine (1.8g , 10 mmol) in THF (100 mL) and another solution of tetraethylene glycols (1.94g , 10 mmol) in THF (100 mL) were added dropwise simultaneously from separate constant addition funnels to a round-bottom flask initially charged with 200 mL of boiling THF with vigorous stirring. Finish the addition after 12 h and keep refluxing for 12 h . Removal of the solvent yielded an oil which was distilled in vacuum to give **4d** . yield: 82%; b.p. 140-143 ^oC/13.33Pa. $C_9H_{19}O_5As$ (Cald. C: 38.30, H: 6.78; Found. C: 39.79; H: 7.08); I.R. ν (2916, 2873, 1650, 1456, 1350, 1248, 1109, 1070, 937, 729, 649, 589); ^{1}HNMR (CCl_4) δ. 1.12 (3H, s, CH_3As), 3.5 (12H, s, $CH_2OCH_2CH_2OCH_2CH_2OCH_2$), 3.88 (4H, t, $2\times AsOCH_2$); M.S. *m*/*z*: 267 (M−15, 10.01), 223 (91.2), 179 (22), 135 (100), 90 (20.02), 45 (73).

2-methyl-6-oxa-1,3-dithia-2-arsacycloctane **4f**. Reaction of bis(dimethylamino)-methylarsine (1.8g, 10 mmol) and 3-oxa-1,5-pentanedithiol (1.4g, 10 mmol) as described for **4d** above gave, after concentrating workup, a pale yellow oil which was chromatographed on silica gel by using dichloromethane-ether (6:4) as eluant to yield **4f**. yield: 51%; I.R. ν (2910, 2850, 1651, 1105, 1071, 950, 890, 559); ^{1}HNMR (CCl_4) δ. 1.1(3H, s, CH_3As), 2.7(4H, t, $2\times SCH_2$), 3.4(4H, t, CH_2OCH_2); M.S. *m*/*z*: 226(M^+, 6), 213(100).

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Received 28 June 1999