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bis-Isatoic anhydrides have been prepared in 20-40% yield by the treatment of sodio-isatoic anhydride with alkane dibromides and ditosylates.

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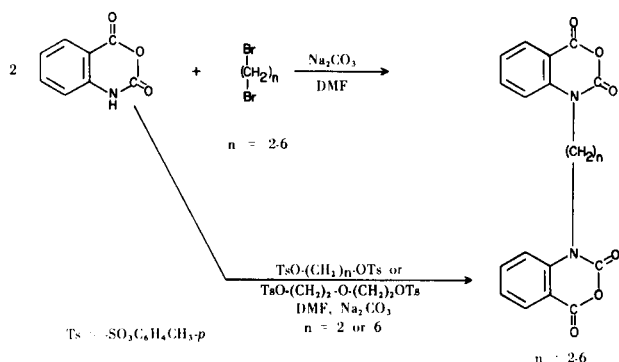
Isatoic anhydrides have been used in the preparation of a variety of anthranilic acid derivatives, many of which are intermediates in the preparation of heterocyclic materials (2-5). In addition, this molecule has been used to prepare aromatic amine monomers that have been polymerized with difunctional electrophilic reagents to give copolymers (6).

We wish to report our new investigations on the preparation of bis-isatoic anhydrides by the alkylation of sodioisatoic anhydride with 1,2-, 1,3-, 1,4-, 1,5-, and 1,6-dibromoalkanes. These materials 1-5 were prepared in approximately 40% yield (except 1 from dibromoethane, 20%) (7,8), and they were characterized by combustion analysis and infrared spectra (Nujol), which displayed two

prominent absorptions at 1715 ± 3 and 1770 ± 3 cm^{-1} . In addition, the synthesis of bis-isatoic anhydrides from ditosylates appears quite promising. The ditosylates of ethylene glycol, diethylene glycol, and 1,6-hexanediol were also treated with sodioisatoic anhydride to give bis-anhydrides 1, 5, and 6 in 25-40% yield (Table).

The synthesis of these bis-anhydrides using sodium hydride instead of sodium carbonate gave products in ca. 40% yield. Based upon the yields reported for mono-alkylations (7,8) of isatoic anhydrides, the yields reported here appear representative of the general procedure developed where the sodio-anhydride in dimethylformamide is treated with dibromide or ditosylate for 72 hours, which is followed by neutralization with ice water and ammonium chloride solution.

It has been our observation, as well as that of others, that isatoic anhydrides can be opened (with loss of carbon dioxide) with certain nucleophilic reagents (e.g., hydrazines) in nearly quantitative yield (9). This suggests the possibility of treating these bis-anhydrides with reactive difunctional reagents such as diamines and dithiols to give alternating copolymers, and the preparation of these polymeric materials is currently under investigation. The preliminary account for the preparation of (mono) quinazolinones could be expanded to the reaction of bis-anhydrides reported here (along with other bis-anhydrides),



Table

bis-Isatoic Anhydrides

Compound Number	Alkylating Agent	Empirical Formula	% Yield	M.p. (a) (°C)	Elemental Analysis (b)			
					C	H	N	
1	1,2-dibromoethane/ethylene glycol ditosylate	$\text{C}_{18}\text{H}_{12}\text{N}_2\text{O}_6$	20/25	354-355/ 358-359	Calcd.	61.37	3.43	7.95
					Found	61.17	3.68	8.06
2	1,3-dibromopropane	$\text{C}_{19}\text{H}_{14}\text{N}_2\text{O}_6$	40	255-260	Calcd.	62.30	3.85	7.65
					Found	62.19	3.96	7.76
3	1,4-dibromobutane	$\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_6$	42	286-288	Calcd.	63.16	4.24	7.36
					Found	63.35	4.47	7.48
4	1,5-dibromopentane	$\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}_6$	40	259-260	Calcd.	63.96	4.60	7.10
					Found	64.00	4.85	7.32
5	1,6-dibromohexane/1,6-hexanediol ditosylate	$\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}_6$	40/39	265-270/ 265-270	Calcd.	64.70	4.94	6.86
					Found	64.47	5.10	7.07
6	diethylene glycol	$\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_7$	25	220-226	Calcd.	60.61	4.07	7.07
					Found	60.40	4.36	7.23

(a) Melting point were taken in a Thomas-Hoover melting point apparatus in open capillary tubes and are uncorrected. (b) All combustion analyses were performed by Robertson's Laboratory, 73 West End Ave., Florham Park, NJ 07932.

with acyl hydrazines, followed by cyclization with dimethyl acetylenedicarboxylate to give *bis*-quinazolinones. Investigations concerning the potential of these molecules in polymer synthesis and general heterocyclic synthesis is currently in progress in our laboratory.

EXPERIMENTAL

Preparation of *bis*-Isatoic Anhydride.

The following method of preparation of *bis*-isatoic anhydrides from dihalides (or ditosylates) may be considered general. To 0.10 mole of isatoic anhydride dissolved in 300 ml. of *N,N*-dimethylformamide (DMF) was added 0.11 mole of anhydrous sodium carbonate. The flask was fitted with a drying tube (Drierite) and the mixture was stirred for 1 hour at room temperature. A 0.055 mole sample of dibromoalkane was then added, and the mixture was stirred 72 hours at room temperature. The mixture was then slowly poured into 500 ml. of ice water containing 50 ml. of 20% ammonium chloride solution. After 5 minutes of brisk stirring, the crude *bis*-anhydride was filtered through a Buchner funnel, and washed with ether (50 ml.). An analytical sample could be obtained after three recrystallizations from DMF. Infrared spectra (Nujol) of each *bis*-anhydride displayed two prominent absorptions at 1715 ± 3 and 1770 ± 3 cm^{-1} (Table).

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