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A CONVENIENT SYNTHESIS OF POLYFUSED HETEROCYCLIC SYSTEMS FROM HETEROCYCLIC AMINES AND 2,3-DICHLORONAPHTHOQUINONE USING PHASE TRANSFER CATALYSIS

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Abstract – Some new polyfused heterocyclic systems were obtained by reacting 2,3-dichloronaphthoquinone with some dianionic ambident heterocyclic compounds containing N^-, S^-, C^- or O^- poles under phase transfer catalysis conditions.

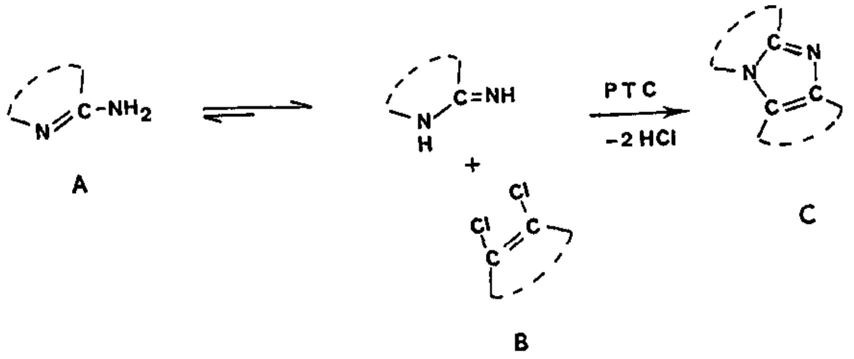
INTRODUCTION

The reaction of 2,3-dichloronaphthoquinone with variously 4-substituted 2-aminothiazoles was firstly reported by Issa et al.[1] Thiazoloaminoquinones were obtained in 40-50% yields by refluxing the starting materials in ethanol for 24 h. With 2-amino-4-alkylthiazoles a longer time of reflux is needed (36 h.) whereas the cyclized products were obtained. Simonov et al.[2] have also reported the reaction of 2,3-dichloronaphthoquinone with 2-mercaptobenzimidazole, 2-mercaptoimidazole, and 2-aminobenzimidazole, respectively. By refluxing in ethanol or dioxane, cyclized products (70%, yield) were obtained in the former two cases, while the benzimidazoquinone (44%, yield) was formed in the latter case. Dou et al.[15, 16] reported the reaction of certain dihalogeno derivatives (e.g. 1,2-, and 1,3-dichloroalkanes) with ethanedithiol, dimercaptobenzene and dianionic ambident heterocyclic compounds. They separated the corresponding fused heterocyclic systems and they gave the reactivity of the different anionic poles in the following order : $S^- > N^- \simeq C^- > O^-$.

Owing to the important development of the phase transfer catalysis technique in heterocyclic chemistry[3 - 17] we tried to apply this simple and rapid method to synthesize previously reported molecules as well as some new polyfused heterocyclic systems.

RESULTS AND DISCUSSION

When reacting an α-dihalogeno compound B with a 2-amino-azaaromatic base A, a fused heterocyclic system C is expected as seen in Scheme 1.



Scheme 1. General Formation Pathway of Fused Heterocyclic Systems

The above reaction scheme was applied to the condensation of 2,3-dichloronaphthoquinone with a variety of N-tautomeric heteroarylamines e.g. 2-amino-4-substituted thiazoles, 2-amino-5-substituted 1,3,4-thiadiazoles, 2-aminobenzothiazole, 2-aminopyridine, 2-aminobenzimidazole and 3,4-diaminopyridine.

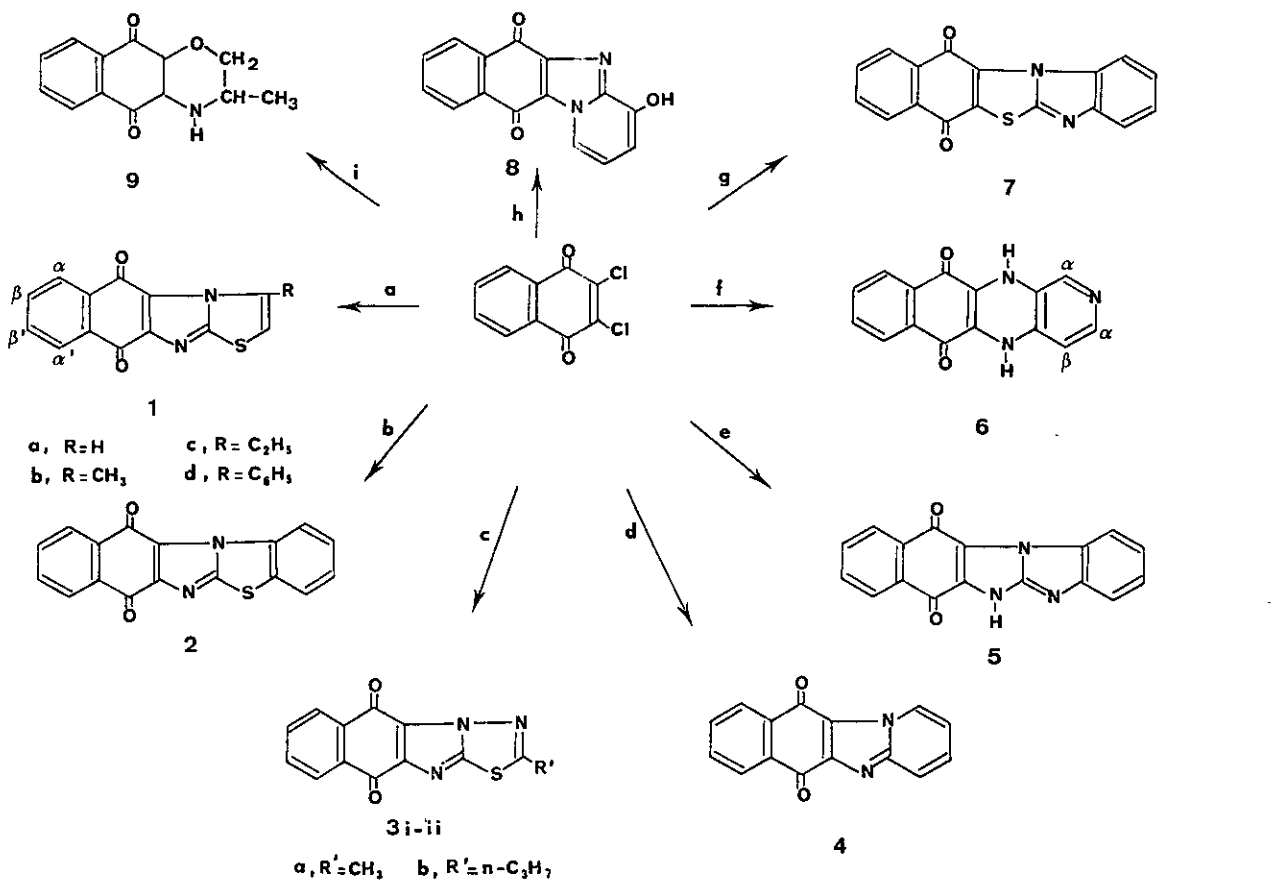
The reaction was also carried out with 2-mercaptobenzimidazole, 2-amino-3-hydroxypyridine, and 2-amino-1-propanol bearing nitrogen and sulphur or oxygen poles, respectively. The corresponding polyfused heterocyclic compounds 1 - 9 (see Scheme 2) were obtained in 65 - 90% yields by stirring the starting materials for 4 - 6 h to 60°C, under phase transfer catalysis conditions : e. g. 50% aqueous sodium hydroxide, benzene as the organic solvent and tetrabutylammonium bromide as the catalyst. This method was found to be more convenient than the one previously reported [2] owing to a shorter reaction time and increased yields.

The reactions were monitored by tlc. The structures of all products were determined on the basis of microanalyses, ^{1}H-nmr and ir spectral data.

In accordance with Dou's results we found that the reaction between 2,3-dichloronaphthoquinone and 2-amino-3-hydroxypyridine gave a compound which exhibits a clear OH band (both from ^{1}H-nmr and ir data) and contains no chlorine atom. This means that the reaction goes through the two nitrogen poles rather than the nitrogen and oxygen. However, with 2-aminopropanol, the nitrogen and oxygen poles are involved thus indicating that this dianionic ambident anion is reactive under PTC conditions.

EXPERIMENTAL

Melting points were determined using a Kopfler bank and are uncorrected. The ir spectra were recorded on a Pye Unicam SP 1200 spectrophotometer. ^{1}H-nmr spectra were obtained in DMSO-d_6 with a Varian A 60 spectrometer using TMS as internal standard, chemical shifts are expressed in δ ppm.



Scheme 2. Fused Heterocyclic Systems Obtained from Tautomeric Heteroarylamines and 2,3-Dichloronaphthoquinone

a : 2-amino-4-substituted thiazoles, b : 2-aminobenzothiazole, c : 2-amino-5-substituted 1,3,4-thiadiazoles, d : 2-aminopyridine, e : 2-aminobenzimidazole, f : 3,4-diaminopyridine, g : 2-mercaptobenzimidazole, h : 2-amino-3-hydroxypyridine, i : 2-amino-1-propanol.

Table 1. Synthesis of Some Heterocyclic Systems Containing Bridgehead Nitrogen Atom Using Phase Transfer Catalysis

Compound	mp °C	Yield %	Time h.	Colour	Mol. Formula Mol. Weight	Analyses Calcd./Found. C	H	N	ir λmax (cm^{-1})	nmr Spectral Data
1a	260^{d}	80	6	violet	$C_{13}H_6N_2SO_2$ (254.25)	61.40 61.52	2.37 2.42	11.01 10.95	1670 (C=O)	8.15-7.85(m, 2H, α, α'), 7.55-6.95(m, 4H)
1b	202	89	4	brownish red	$C_{14}H_8N_2SO_2$ (268.28)	62.67 62.74	3.00 2.94	10.44 10.60	1670 (C=O)	8.20-7.80(m, 2H, α, α'), 7.60-7.0(m, 3H), 3.70(s, 3H, CH_3)
1c	138	92	4	brownish red	$C_{15}H_{10}N_2SO_2$ (282.31)	63.81 63.94	3.57 3.51	9.92 10.03	1675 (C=O)	8.10-7.90(m, 2H, α, α'), 7.65-7.05(m, 3H), 4.15(q, 2H, CH_2), 1.42(t, 3H, CH_3)
1d	234	79	6	violet	$C_{19}H_{10}N_2SO_2$ (330.35)	69.07 69.11	3.05 3.00	8.48 8.52	1680 (C=O)	8.15-7.95(m, 2H, α, α'), 7.60-7.0(m, 8H)
2	212	65	6	violet	$C_{17}H_8N_2SO_2$ (304.31)	67.09 67.15	2.64 2.72	9.20 9.11	1675 (C=O)	8.05-7.85(m, 2H, α, α'), 7.75-6.9(m, 6H)
3a	205	83	6	reddish violet	$C_{13}H_7N_3SO_2$ (269.27)	57.98 57.90	2.62 2.70	15.60 15.71	1680 (C=O)	8.15-7.80(m, 2H, α, α'), 7.60-7.20(m, 2H, β, β'), 3.75(s, 3H, CH_3)
3b	251	85	6	violet	$C_{15}H_{11}N_3SO_2$ (297.32)	60.59 60.65	3.72 3.65	14.13 14.22	1680 (C=O)	8.10-7.80(m, 2H, α, α'), 7.65-7.15(m, 2H, β, β'), 4.00(q, 2H, CH_2), 1.85(t, 2H, CH_2), 1.35(q, 3H, CH_3)

Table 1. (Continued)

Compound	mp °C	Yield %	Time h.	Colour	Mol. Formula Mol. Weight	Analyses Calcd./Found. C	 H	 N	ir λmax (cm^{-1})	nmr Spectral Data
4	368^{d}	68	6	violet	$C_{15}H_8N_2O_2$ (248.23)	72.57 72.64	3.24 3.18	11.28 11.31	1675 (C=O)	8.25-8.00(m, 3H, α, α', N-CH), 7.65-6.90(m, 5H)
5	259	65	6	orange	$C_{17}H_9N_3O_2$ (287.27)	71.07 71.17	3.15 3.23	14.62 14.71	1675 (C=O) 3250(N-H)	10.16(s, 1H, NH), 8.20-7.95 (m, 2H, α, α'), 7.60-6.75 (m, 6H)
6	222	60	6	orange	$C_{15}H_9N_3O_2$ (263.25)	68.43 68.51	3.44 3.51	15.96 16.09	1680 (C=O), 3250 (N-H)	10.65(s, 1H, NH), 10.22(s, 1H,NH), 8.55(d, 1H, N=CH), 8.25-800(m, 2H, α, α'), 7.65-6.85(m, 4H)
7	265	85	6	red	$C_{17}H_8N_2SO_2$ (304.31)	67.09 67.14	2.64 2.61	9.20 9.17	1690 (C=O)	8.25-7.90(m, 2H, α, α'), 7.50-6.55 (m, 6H)
8	115-6	65	6	red	$C_{15}H_8N_2O_3$ (264.23)	68.17 68.08	3.05 3.11	10.60 10.70	1680 (C=O) 3500 (O-H)	8.35-8.05(m, 3H, α, α', O-H), 7.60-6.55(m, 5H)
9	210	75	6	yellow	$C_{13}H_{11}NO_3$ (229.22)	68.11 68.22	4.83 4.91	6.11 6.24	1675 (C=O) 3250 (N-H)	8.25-8.05(m, 2H, α, α'), 7.85-7.40 (m, 2H, β, β'), 6.33(s, 1H, NH), 4.35(d, 1H, C-H), 3.97(m, 2H, CH_2), 2.95(t, 3H, CH_3)

Qualitative thin layer chromatography analyses were carried out using nanoplates HPTLC silica 5μ with ethyl acetate - benzene (9 : 1) as eluent.

Phase Transfer Catalysis Heterocyclization. General Procedure — An equimolar mixture of 2,3-dichloronaphthoquinone and heteroarylamine **a** - **i** (0.03 mole) in benzene (100 ml), 50% aqueous sodium hydroxide (30 ml), tetrabutylammonium bromide (TBAB, 3 mmole) was stirred for 4 - 6 h at 60°C whereby a noticable change in colour from pale yellow to yellow, orange, brownish red, or violet was observed. After completion of the reaction monitored by tlc the mixture was left to cool and the organic layer was separated, washed throughly with water, and dried over anhydrous magnesium sulphate. The benzene was then evaporated in vacuo. The residue was washed with light petroleum ether or ether, and collected by filtration. In some cases, the expected polyfused heterocyclic compounds were precipitated during the course of the reaction. They were filtered off, washed throughly with water and crystallized from the appropriate solvent. Results are reported in Table 1.

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