CONVENIENT METHOD FOR THE SYNTHESIS OF 2-SUBSTITUTED NAPHTHO[2,3-*g*]INDOLE-6,11-DIONES

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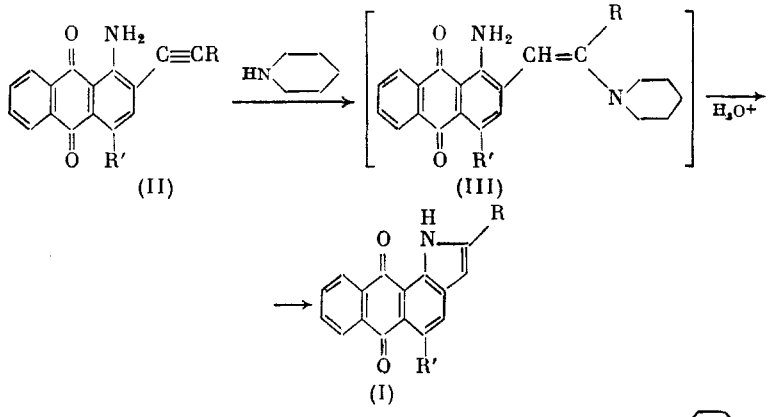
A convenient one-step method has been developed for the preparation of 2-substituted naphtho[2,3-g]indole-6,11-diones entailing the addition of piperidine to 1-amino-2-acetylenylanthraquinone and subsequent cyclization of the adduct with loss of the amine in the presence of dilute hydrochloric acid.

The preparation of 2-substituted naphtho[2,3-*g*]indole-6,11-diones (I) by the direct cyclization of 1-amino-2-acetylenylanthraquinones (II), as a rule, requires rather vigorous conditions. An advantage has been found for a two-step method for the synthesis of (I) entailing the addition of a secondary amine at the triple bond of acetylene (II) with subsequent cyclization of adduct (III) on silica gel [1]. We have found that the cyclization of intermediates (III) is also efficiently catalyzed by a mineral acid. This finding permitted us to develop a convenient one-step method for the preparation of (I).



(II) (III) (I)

$R' = NO_2$, $R = CMe_2OH$ (a); $R' = H$, $R = CMe_2OH$ (b); CH_2OPh (c), CH_2N⟨O⟩ (d).

After completion of the addition of the secondary amine or piperidine to (II) [2], the reaction mixture was diluted with benzene and shaken with 2-3% hydrochloric acid.

EXPERIMENTAL

The PMR spectra were taken on Varian XL-200 and Jeol FX 90Q spectrometers.

Substituted Naphtho[2,3-g]indole-6,11-diones (I). A sample of 0.001 mole (II) in 10 ml piperidine was stirred at 50-105°C until the starting compound disappeared as indicated by thin-layer chromatography on Silufol plates and diluted with 200 ml benzene. Then, 300 ml water and 15 ml concentrated hydrochloric acid were added and the mixture was vigorously agitated. The mixture turned from dark orange to yellow-orange. The organic layer was separated, washed with 300 ml water, and filtered through a fluted filter. The solvent was distilled off in vacuum. The residue was triturated in ether, filtered, and washed with ether and hexane.

Upon the isolation of (Id), the reaction solution was neutralized with 20 g Na_2CO_3. The product was extracted with three 200-ml portions of benzene and purified by preparative

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TABLE 1. Naphtho[2,3-g]indole-6,11-diones

Compound	Addition of piperidine		Yield, %	Mp, °C (solvent)	Chemical formula	Found/Calculated %			PMR spectrum in DMSO-d_6 (δ, ppm)
	T, °C	time, h				C	H	N	
(Ia)	50	0,7	51	254,5–256 (dec., toluene)	$C_{19}H_{14}N_2O_5$	65,32 65,14	4,11 4,03	8,23 8,00	1,58(CH_3), 5,86(OH), 6,66(H^3), 7,84–8,24 (H^{7-10}), 8,29(H^4), 11,45(NH)
(Ib)	90	2	78	188,5–190 (dec., (toluene–hexane)	$C_{19}H_{15}NO_3$	74,77 74,74	4,94 4,95	4,61 4,59	1,56(CH_3), 5,76(OH), 6,49(H^3), 7,78–8,20 (arom. H), 11,05(NH)
(Ic)	105	0,8	80	214,5–215,5 (toluene–hexane)	$C_{23}H_{15}NO_3$	78,32 78,17	4,24 4,28	3,90 3,96	5,35(CH_2), 6,73(H^3), 6,97–7,29, 7,80–8,17 (arom. H), 12,10(NH)
(Id)	105	17	19	164–165 (C_6H_6 – hexane)	$C_{21}H_{18}N_2O_3$	72,88 72,82	5,23 5,24	8,03 8,09	2,52 t(NCH_2), 3,72 (CH_2N), 3,75 t(CH_2O), 6,47(H^3), 7,73–7,80 ($H^{8,9}$), 7,87d, 8,01d ($H^{4,5}$), 8,22–8,31 ($H^{7,10}$), 10,66(NH) *

*In $CDCl_3$.

thin-layer chromatography on grade-II alumina with chloroform as the eluent. The reaction conditions for the addition of piperidine, yields, and physical indices for (Ia)-(Id) are given in Table 1.

1-Amino-2-(3-hydroxy-3-methylbutynyl)-4-nitroanthraquinone (IIa). A sample of 1.97 g 1-amino-2-iodo-4-nitroanthraquinone was condensed with 0.53 g 3-methyl-1-butyn-3-ol in 100 ml pyridine and 50 ml water in the presence of 30 mg $Pd(PPh_3)_2Cl_2$, 15 mg CuI, and 0.53 g Na_2CO_3 at 80°C for 10 min [3]. The reaction mixture was diluted with 300 ml benzene and treated with 500 ml water and 130 ml concentrated hydrochloric acid. Chromatography on 300 g grade-II alumina using $CHCl_3$ and 2:1 $CHCl_3$–ether as the eluents gave 1.34 g (76.6%) (IIa), mp 223-224.5°C (dec., from toluene). Found: C, 65.31; H, 4.04; N, 7.97%. Calculated for $C_{19}H_{14}N_2O_5$: C, 65.14; H, 4.03; N, 8.00%. PMR spectrum in DMSO-d_6 (δ, ppm): 1.61 (CH_3), 5.80 br.s (OH), 7.90-8.25 (arom. H).

1-Amino-2-(3-phenoxy-1-propynyl)anthraquinone (IIc) was synthesized from 3.49 g 1-amino-2-iodoanthraquinone by analogy to (IIa) with reagent concentrations four times greater at 90°C for 5 min. The yield of (IIc) was 2.80 g (79.3%), mp 165-166°C (from benzene–hexane). Found: C, 78.29; H, 4.32: N, 3.98%. Calculated for $C_{23}H_{15}NO_3$: C, 78.17; H, 4.28; N, 3.96%. PMR spectrum in $CDCl_3$ (δ, ppm): 5.02 (CH_2), 6.98-7.37, 7.66-7.77, 8.16-8.22 (arom. H), 7.54 (H^3, H^4).

The preparation of (IIb) and (IId) was described in our previous work [3].

LITERATURE CITED

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