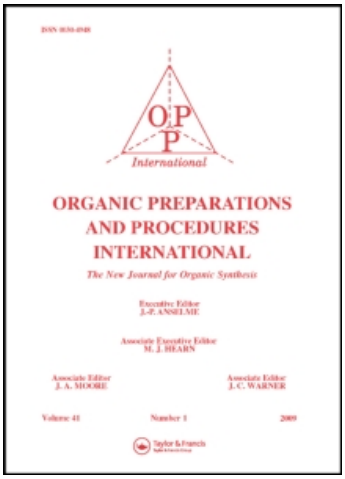

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NEW N,N'-*bis*(SUBSTITUTED PHENYLAZO)PIPERAZINES AND THEIR CLEAVAGE REACTIONS IN ACETIC ACID

Submitted by (5/19/99)

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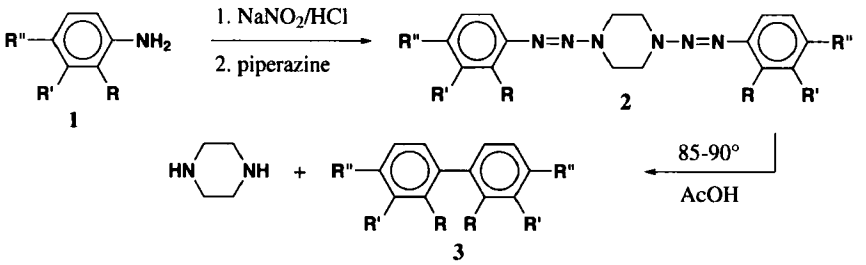
Piperazine derivatives have been are used as; anti-inflammatory,[1] andrenomedullary imaging agents,[2] as components in the amine-ketone photocoinitiation system,[3] calmodulin antagonist[4] and targeting agents for neuroblastoma.[5] In addition, the effects of these compounds have been studied in the area of cerebral circulation,[6] serotanin tyramine and benzylamine by porcine liver mitochondrial monoamine-oxidase[7] and on frog skeletal-muscle fibers.[8] The central thermo-regulatory,[9] antiarrhythmic,[10,11] electrophyssolagic and cardioprotective,[11] pharmacological,[12,13] agonist,[14] anxiolytic,[15] antagonistic,[16,17] and Ca-antagonistic activities[18] of some piperazine derivatives have also been investigated.



a) R,R',R" = H b) R = F, R', R" = H c) R, R' = H, R" = F d) R = Cl, R', R" = H e) R, R' = H, R" = Cl
f) R = Br, R', R" = H g) R, R' = H, R" = Br h) R = I, R', R" = H i) R, R' = H, R" = I
j) R = NO_2, R', R" = H k) R, R" = H, R' = NO_2 l) R, R' = H, R" = NO_2 m) R = CH_3, R',R" = H
n) R, R' = H, R" = CH_3 o) R = COOH, R', R" = H

In the present study, fifteen new N,N'-*bis*(substituted phenylazo)piperazine compounds (**2**) were synthesized. Upon heating in acetic acid, these compounds were converted related to substituted biphenyls.

EXPERIMENTAL SECTION

The substituted anilines and piperazine used in these reactions were supplied by Merck Co. All melting points were determined in sealed capillaries. FT-IR spectra were recorded on a Matson 1000 spectrometer. ^{1}H NMR spectra were obtained on a Varian EM-360 L (60 MHz) NMR spectrometer. Elemental analyses were carried out on a Leco-CHN 600 instrument.

TABLE 1. Yields, mps, IR and ^{1}H NMR Spectral Data of Compounds **2**

Cmpd	mp (°C)	Yield (%)	IR (KBr) (pipe. C-H) (cm^{-1})	^{1}H NMR (δ)
2a	124-125	51	2866, 2901	3.74(s, 8H); 7.12(s, 10 H) (CCl_4)
2b	125-126	59	2865, 2928	4.08(s, 8H); 7.05-7.31(m, 8H) (CCl_4)
2c	139-140	72	2880, 2920	3.92(s, 8H); 6.72-7.69(m, 8H) (CCl_4)
2d	84-86	81	2875, 2907	4.30(s, 8H); 7.17-7.91(m, 8H) (CCl_4)
2e	183-184	77	2858, 2916	3.84(s, 8H); 7.37(m, 8H) (DMSO-d_6)
2f	108-110	63	2858, 2897	3.80(s, 8H); 6.76-7.37(m, 8H) (DMSO-d_6)
2g	203	70	2857, 2914	4.08(s, 8H); 7.20-7.70(d, 8H) (DMSO-d_6)
2h	119-120	28	2858, 2922	4.06(s, 8H); 7.10-7.96(m, 8H) (DMSO-d_6)
2i	192-193	77	2858, 2922	3.67(s, 8H); 6.70-7.58(m, 8H) (DMSO-d_6)
2j	143-145	62	2857, 2927	3.94(s, 8H); 7.34-7.61(m, 8H) (CCl_4)
2k	167-168	42	2884, 2937	4.29(s, 8H); 7.21-8.41(s, 8H) ($CDCl_3$)
2l	198-200	80	2858, 2928	4.44(s, 8H); 7.20-7.73(m, 8H) (DMSO-d_6)
2m	104-105	72	2858, 2890	2.20(s, 3H); 3.68(s,8H); 6.70-7.45(m, 8H) ($CDCl_3$)
2n	148-149	97	2865, 2916	2.47(s, 3H); 4.10(s,8H);7.15-7.58(m, 8H) ($CDCl_3$)
2o	184-186	52	2832, 2928	3.57(s, 8H); 8.40(m, 8H); 9.96(s, 1H) (TFAA)

TABLE 2. Elemental Analyses of New Compounds (**2a-2o**)

Cmpd	C(Found)	N(Found)	H(Found)
2a	65.29(65.20)	28.55(28.50)	6.16(6.15)
2b	58.18(58.16)	25.44(25.40)	4.88(4.87)
2c	58.18(58.15)	25.44(25.41)	4.88(4.86)
2d	52.90(52.95)	23.14(23.11)	4.44(4.42)
2e	52.90(52.87)	23.14(23.10)	4.44(4.45)
2f	42.50(42.47)	18.59(18.62)	3.57(3.58)
2g	42.50(42.49)	18.59(18.57)	3.57(3.59)
2h	35.19(35.24)	15.39(15.41)	2.95(2.94)
2i	35.19(35.25)	15.39(15.41)	2.95(2.96)
2j	50.00(49.95)	29.15(29.11)	4.20(4.23)
2k	50.00(50.02)	29.15(29.10)	4.20(4.18)
2l	50.00(50.04)	29.15(29.19)	4.20(4.24)
2m	67.06(67.09)	26.07(26.07)	6.88(6.89)
2n	67.06(67.10)	26.07(26.10)	6.88(6.91)
2o	56.54(56.50)	21.98(22.01)	4.74(4.72)

TABLE 3. Yields, mps and ^{1}H NMR Spectral Data of Compounds **3**

Cmpd	mp. (°C)	lit mp. (°C)	Yield (%)	^{1}H NMR (δ)
3a	67-69	71[a]	24	7.77(s) (CCl_4+$CDCl_3$)
3b	oil	118.5-119.5[a]	–	7.28(m) ($CDCl_3$)
3d	57-59	60.5[a]	31	7.28(m) (CCl_4)
3e	144-147	148-149[a]	26	6.88(m) (TFAA)
3f	oil	81[a]	–	6.68-7.91(m) (TFAA)
3j	oil	127-128[a]	–	7.16-8.35(m) ($CDCl_3$)
3k	oil	200[a]	–	7.40-8.42(m) ($CDCl_3$)
3l	236-240	240-243[a]	29	8.47(m) (TFAA)
3m	oil	19.5-20.2[a]	–	1.80(s, 6H); 6.78(s, 8H) (CCl_4)
3n	oil	125[a]	–	2.34(s, 6H); 7.18(s, 8H) (CCl_4)

a) CRC Atlas of spectral data and physical constants for organic compounds, Ed.: S. G. Graselli, CRC Press., 1973.

Typical Procedure. N,N'-*bis*(2-Fluorophenylazo)piperazine.- A mixture of 2-fluoroaniline (5.55 g, 0.05 mole) and 13.5 mL of conc. HCl was cooled about to -10°; then 20 g of crushed ice was added and the mixture was diazotized by the slow addition of a solution of sodium nitrite (4.49 g, 0.065 mole) in 10 mL of water. The cold solution of diazotized amine (**CAUTION!**) was then added cautiously and slowly to a stirred solution of piperazine (2.15g, 0.025 mole) and allowed to warm up to room temperature to give a precipitate. The precipitate of N,N'-*bis*(2-fluorophenylazo)piperazine

(**2a**) was collected and crystallized (4.21 g, 51% yield) in alcohol-water. **CAUTION:** Compounds which bear the triazene moiety as part of their structure must be regarded as potentially carcinogenic and appropriate precautions taken to ensure that human contact does not occur.[19]

Cleavage Reaction of N,N'-*bis*(2-Chlorophenylazo)piperazine. Typical Procedure.- Acetic acid (15 mL) was added to 3.63 g (0.01 mole) of triazene compound (**2d**) and the mixture was heated to 85°-90° while continuously stirred. A gas (N_2) was vigorously evolved during dissolution. The evolution of the gas continued for about one hour. Then, 40 mL of 2.5 M NaOH solution was added in to the reaction mixture and product (**3a**) was extracted with $CHCl_3$. The chloroform extract was separated, evaporated to dryness and the oily residue obtained was crystallized in alcohol. Thus, 2,2'-dichlorobiphenyl (**3d**) was obtained in yield 31 % (0.69 g; mp. 57-59°).

Most arenediazonium salts are unstable at temperatures above 5°-10°, and very explosive in the dry state but aryltriazenes are generally crystalline compounds. These compounds are stable to air, light, and basic conditions[20] and they have been used for the synthesis of substituted aryl compounds by replacement of the triazene moiety with nucleophiles.[21-23] In this study, substituted biphenyls were obtained (or observed by pmr spectra) by cleavage reactions of piperazine triazene compounds in acetic acid.

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PHASE-TRANSFER CATALYZED ALKYLATION OF HYDROXY 9,10-ANTHRAQUINONES

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Substituted 9,10-anthraquinones have wide applications as dyes and in electron-transfer studies. Reduction of these compounds provides the corresponding substituted anthracenes[1] which also find numerous uses, for example as fluorescent probes. We were interested in 1-alkoxy and 1,8-