TABLE I[a]

SYNTHESIS OF SECONDARY AMINES

RRNCN ⟶ RRNC(=NH)OCH$_3$ ⟶ RRNH

I II III

Compd[b,c]	R	Disubstituted Cyanamides (I) Mp or bp, °C (mm)	Yield, %	O-Methylisoureas (II) Mp or bp, °C (mm)	Yield, %	Secondary amines (III) Mp or bp, °C (mm)	Yield, %
1	$(CH_3)_2C{=}CHCH_2$	146–148 (15)	63	142–144 (15)	75	92–94 (15)[d]	65
2	$(CH_3)_2C{=}CHCH_2CH_2$	96–98 (0.15)	55	92–94 (0.1)	63	116–118 (14)	61
3	$(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2$	166–168 (0.08)	61	165–168 (0.07)	76	134–137 (0.04)[e]	60
4	$(CH_3)_2C{=}CH(CH_2)_2CH(CH_3)CH_2CH_2$	154–157 (0.05)	72	147–149 (0.03)	81	123–125 (0.03)	71
5	Cyclopropylmethyl	141–143 (15)	90	74–75 (0.07)	83	63–64 (15)	85
6	Cyclobutylmethyl	157–159 (15)	75	85–88 (0.05)	78	97–98 (15)	83
7	Benzyl	55–56[f]	88	145–147 (0.05)	90	291–292 (760)[g]	65
8	3,4,5-Trimethoxybenzyl	85–86[h]	83	106–107[h]	43	87–88[i]	60
9	3,4-Methylenedioxybenzyl	106–107[h]	85	*j*	89	72–73[k]	78
10	CH_2 (o-$C_6H_4CH_2$)$_2$ (RR)	239–240[l]	69	151–152[m]	72	124–125[n]	80
11	$(CH_2)_2$ (o-$C_6H_4CH_2$)$_2$ (RR)	127–129[o]	72	118–119[m]	70	150–152[p]	91

[a] Satisfactory analytical values (±0.4% for C, H, and N) were reported for all compounds: Ed. [b] Consistent ir and nmr spectra were obtained for all products. [c] Yields are based on distilled or crystallized products, unless otherwise specified. Purity was also checked by vpc or tlc analyses, or by comparison with the literature data, when available. [d] Lit.[7] bp 80° (10 mm). [e] Lit.[8] bp 135–137° (0.03 mm). [f] Lit.[9] mp 47–50°. [g] Lit.[10] bp 298–300°. [h] Crystallized from Et_2O. [i] Crystallized from Et_2O–petroleum ether (bp 40–70°). [j] Waxy product. [k] Lit.[11] mp 72–73°. [l] Lit.[12] mp 239–240°. [m] Recrystallized from 50% aqueous EtOH. [n] Lit.[12] mp 124.5–125°. [o] Lit.[13] mp 128–129°. [p] Lit.[13] mp 152.5°.

ml of methanol was refluxed for 24 hr. The methanol was removed, water was added to the residue, and the mixture was extracted with ether. The ether layer was washed with water, dried over $MgSO_4$, and concentrated, and the residue was purified or used as crude product in the subsequent step.

The structure of these compounds was determined by ir and nmr spectra. For instance, the ir spectrum (film) of II-1 showed absorption at 3370 (NH), 1630 (C=N), and 1270 cm^{-1} (COC). The nmr spectrum (CCl_4) had peaks at δ 1.66, 1.72 [each 6 H, s, $(CH_3)_2C{=}$], 3.63 (3 H, s, $-OCH_3$), 3.70 (4 H, d, CH_2NCH_2), 4.57 (1 H, s, =NH), 5.15 (2 H, t, 2 =CH).

Secondary Amines (III).—A solution of 0.1 mol of the appropriate II in 80% acetic acid (300 ml) was refluxed for 24 hr. The reaction mixture was allowed to cool to room temperature and was then poured into ice–water. The mixture was washed with ether, the aqueous layer was made alkaline with 10% sodium hydroxide, and the basic material was extracted with ether. The ether extract was washed with water, dried over $MgSO_4$, and concentrated, and the residue was purified (Table I).

Literature[7–13] melting points or boiling points of some of the compounds are also given in Table I.

Registry No.—I-1, 24339-01-3; I-2, 24339-02-4; I-3, 35211-92-8; I-4, 24339-03-5; I-5, 35140-75-1; I-6, 35140-76-2; I-7, 2451-91-4; I-8, 35140-78-4; I-9, 35140-79-5; I-10, 27016-63-3; I-11, 31486-22-3; II-1, 24339-04-6; II-2, 24339-05-7; II-3, 35191-83-4; II-4, 24381-82-6; II-5, 35140-84-2; II-6, 35191-85-6; II-7, 35140-85-3; II-8, 35140-86-4; II-9, 35140-87-5; II-10, 35140-88-6; II-11, 35191-86-7; III-1, 5122-42-9; III-2, 24339-06-8; III-3, 35146-71-5; III-4, 24381-83-7; III-5, 26389-68-4; III-6, 35146-74-8; III-7, 103-49-1; III-8, 35146-75-9; III-9, 6701-35-5; III-10, 16031-95-1; III-11, 31486-25-6.

Acknowledgment.—The authors are grateful to Professor S. Casadio for his interest in this work. They are also indebted to Dr. A. Gallazzi for physicochemical data.

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An Anomalous Reaction of Aceto-4- (or 6-) nitro-2,5-xylidides with Hydrochloric Acid

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Received October 19, 1971

In an attempt to prepare 4-nitro- and 6-nitro-2,5-xylidine by hydrolysis of a mixture of 4-nitro- and 6-nitro-2,5-acetoxylidide,[1,2] an oil was obtained which, upon steam distillation, fractionated into two components, neither of which contained nitrogen. Only a small amount of organic tars remained as a residue in the steam distillation flask.

The major component from the oil, melting at 82–84°, gave ir and nmr spectra having absorption bands identical with those of an authentic sample of

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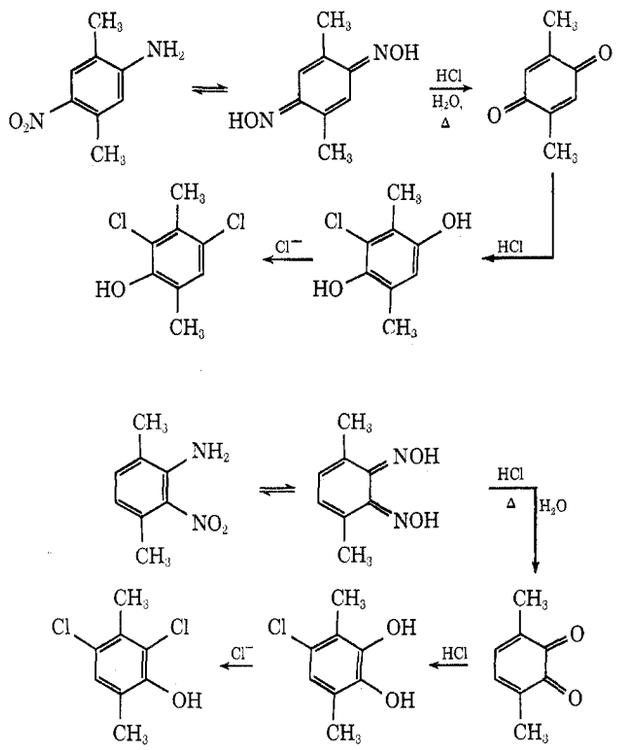

4,6-dichloro-2,5-xylenol.[3] The minor component, isolated by fractionation, and boiling at 220–222°, was identified as a dichloroxylene by mass spectrometry. The ir spectrum of the neat compound exhibited a strong absorption band at 850 cm^{-1}, typical of the aromatic CH wag of the isolated meta hydrogens of a 1,3,4,5-tetrasubstituted benzene.[4] The nmr spectrum of the compound in $CDCl_3$ had singlets for two methyl groups at δ 2.26 and 2.45. The two ring hydrogens were seen as a singlet at δ 7.05. Therefore, we have assigned it the structure of 2,6-dichloro-*p*-xylene (lit.[5] bp 220°).

A third component was found as an impurity in the 2,6-dichloro-*p*-xylene fraction and was separated by preparative glpc. This compound was identified as 2,3,5-trichloro-*p*-xylene by mass spectrometry, based upon a parent peak of *m/e* 208 and an isotopic cluster pattern characteristic of three ring chlorines.[4]

Discussion

The results obtained during the attempted hydrochloric acid hydrolysis of the two acetonitroxylidides appear to be anomalous and certainly not general for nitroanilines. This was borne out by the fact that only the expected nitroanilines were obtained upon similar hydrochloric acid treatment of *o*- and *p*-nitroacetanilide and of aceto-4-nitro-2,6-xylidide.

Boyer, *et al.*,[6] demonstrated that, in 12 *N* hydrochloric acid and in the presence of copper, *o*-benzoquinone dioxime was rapidly isomerized to *o*-nitroaniline. They were not, however, able to show this same isomerization phenomenon with *p*-benzoquinone dioxime. Since these observations were published, Docken, *et al.*,[7] were able to show that, when *p*-benzoquinone dioxime was heated in polyphosphoric acid at 130–140°, it rearranged to *p*-nitroaniline.

Therefore, a suggested rationale which could account for the isolated products assumes that the appropriate nitroaniline, in acid solution, exists to some degree in equilibrium with the benzoquinone–dioxime. Hydrolysis of the benzoquinone dioxime to the analogous benzoquinone and subsequent reactions with hydrochloric acid would account for the formation of 4,6-dichloro-2,5-xylenol. Nucleophilic displacement of the hydroxyl group of 4,6-dichloro-2,5-xylenol by chloride ion can account for the presence of 2,3,5-trichloro-*p*-xylene. At present, however, we are not able to offer any rationale for the presence of 2,6-dichloro-*p*-xylene in the hydrolysate.

When the nitration, hydrolysis and separation, following the procedure of Van Helden, *et al.*,[8] was carried out using 7 *N* instead of 12 *N* hydrochloric acid, the expected 4- and 6-nitro-2,5-xylidines were obtained in reasonable yields. The different course of the reaction was attributed to the lower concentration of acid used in the reaction scheme.

Experimental Section[9]

Nitration of 2-Aceto-*p*-xylidide.—Following a modification of a procedure by Noelting and Thesmar,[1] a flask was fitted with a mechanical stirrer, thermometer, dropping funnel, and reflux condenser. To the flask was added 135 g (0.83 mol) of 2-aceto-*p*-xylidide and 225 mol of sulfuric acid, sp gr 1.84. The contents of the flask were cooled to 20° by means of an ice–water bath and a solution of 70 ml of HNO_3, sp gr 1.42, and 70 ml of H_2SO_4, sp gr 1.84, was added dropwise. The temperature of the reaction was controlled between 30 and 40° by means of ice cooling, and by controlling the addition rate of the acid solution. After acid addition, the reaction mixture was allowed to stir at room temperature for an additional hour, then poured over ice. The pale yellow product was collected and placed in a flask, 500 ml of concentrated hydrochloric acid was added while stirring, and the mixture was refluxed for 2 hr. Following this period, 800 ml of water was added and the product was subjected to steam distillation. There was obtained in the distillate 58 g of an orange oil. Fractionation of the oil gave 8 g of 2,6-dichloro-*p*-xylene, bp 220–222° (lit.[5] bp 222°), and 36 g of 4,6-dichloro-2,5-xylenol, mp 80–84° (lit.[3] mp 84°). The 4,6-dichloro-2,5-xylenol was further purified and gave 32 g of 4,6-dichloro-2,5-xylenol as pale yellow crystals, mp 82–84°. Glpc analysis of the 2,6-dichloro-*p*-xylene fraction resolved a peak amounting to ~2% of the total volatiles. Mass spectral analysis of this material revealed the structure to be 2,3,5-trichloro-*p*-xylene.

Registry No.—Aceto-4-nitro-2,5-xylidide, 6954-69-4; aceto-6-nitro-2,5-xylidide, 35182-75-3; hydrochloric acid, 7647-01-0; aceto-*p*-xylidide, 103-89-9.

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