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AMINATION OF *p*-CYMENE WITH TRICHLORAMINE–ALUMINUM CHLORIDE[1,2]—VII

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Abstract—The direct amination of *p*-cymene with trichloramine aluminum chloride produced a mixture of bases in yields up to 61%. The product was composed of 2-, 3-, and 8-amino-*p*-cymene, 5-amino-*m*-cymene, and *m*- and *p*-toluidine. A compound was also formed which appears to be an N-chloro-8-amino-*p*-cymene. Several of the amines resulted from prior rearrangement and disproportionation of *p*-cymene. The product distribution was quite sensitive to changes in reaction conditions (temp, time and added water). Nuclear amination apparently occurs *via* a σ-substitution mechanism. Side-chain amination can be rationalized by a sequence involving intermediate formation of *p*-methyl-α,α-dimethylbenzyl cation which then suffers attack by a nitrogen-containing nucleophile.

INTRODUCTION

AS REVEALED in recent reports, the direct amination of aromatic compounds with N-halamines and Lewis acid catalysts leads to products of unusual orientation.[3-10] Monoalkylbenzenes, for example, gave the corresponding *m*-alkylanilines with trichloramine and aluminum chloride or aluminum bromide.[3-5] Dialkylbenzenes behaved similarly.[5,6] Halobenzenes and anisole produced, in addition to the *meta*-substituted aniline derivatives, products resulting from replacement of the substituent by an amino group.[8,9]

In an extension of dialkylbenzene amination, it was discovered that with *p*-cymene, a considerable amount of amination occurred at the α-carbon of the isopropyl side chain.[11] This finding appeared to possess potential significance in relation to the theoretical aspects of the amination reaction. In addition, it presented the possibility of a new synthesis of t-benzyl amines, a class of compounds which requires multistep procedures by classical techniques. This report deals with factors affecting nuclear and side-chain amination, and the theoretical implications.

[1] Paper VII, Chemistry of N-Halamines; from the Ph.D. thesis (1966) of R. J. H.

[2] For a preliminary account, see P. Kovacic, R. J. Hopper, S. S. Chaudhary, J. A. Levisky, and V. A. Liepkalns, *Chem. Comm.* No. 8, 232 (1966).

[3] P. Kovacic, C. T. Goralski, J. J. Hiller, Jr., J. A. Levisky, and R. M. Lange, *J. Am. Chem. Soc.* **87**, 1262 (1965).

[4] P. Kovacic, R. M. Lange, J. L. Foote, C. T. Goralski, J. J. Hiller, Jr., and J. A. Levisky, *J. Am. Chem. Soc.* **86**, 1650 (1964).

[5] P. Kovacic, J. A. Levisky, and C. T. Goralski, *J. Am. Chem. Soc.*, **88**, 100 (1966).

[6] P. Kovacic and J. A. Levisky, *J. Am. Chem. Soc.*, **88**, 1000 (1966).

[7] P. Kovacic and A. K. Harrison, *J. Org. Chem.* **32**, 207 (1967).

[8] P. Kovacic, J. J. Hiller, Jr., J. F. Gormish and J. A. Levisky, *Chem. Commun.* No. 22, 580 (1965).

[9] P. Kovacic and J. F. Gormish, *J. Am. Chem. Soc.* **88**, 3819 (1966).

[10] V. L. Heasley, P. Kovacic, and R. M. Lange, *J. Org. Chem.* **31**, 3050 (1966).

[11] J. A. Levisky, M. S. Thesis (1965), Case Institute of Technology.

RESULTS AND DISCUSSION

Reaction variables. The amination of *p*-cymene with trichloramine-aluminum chloride produced a mixture of amines derived from *p*-cymene itself or from its rearrangement and disproportionation products. An example reaction (Table 1,

TABLE 1. EFFECT OF VARIATION IN $AlCl_3$–NCl_3 RATIO WITH *o*-DICHLOROBENZENE SOLVENT[a]

$AlCl_3$: NCl_3; molar	Yield, %	Basic Product[b] Product distribution, mole %					Toluidine			
	Total	8-APC	8-APC	2-APC	3-APC	5-AMC	meta	para	*ar*-Cl-8-APC[c]	Residue, wt. %
1	13	12	91	0	0	0	0	0	9	—
1[d]	16	13	83	0	0	0	0	0	17	—
2[e]	46	19	41	15	18	19	5	2	trace	7
2	46	19	41	13	15	23	7	1	trace	9
3	61	28	46	11	12	22	7	2	trace	8

[a] NCl_3, 0·1 mole in ca. 210 ml of *o*-$C_6H_4Cl_2$; *p*-cymene, 1 mole; 0–10°; NCl_3 add'n time, 45 min; total reaction time, 90 min.

[b] APC = amino-*p*-cymene, AMC = amino-*m*-cymene.

[c] Formed indirectly.

[d] Total reaction time, 135 min.

[e] Extra dry (see Experimental).

TABLE 2. EFFECT OF VARIATION IN $AlCl_3$–NCl_3 RATIO WITH ETHYLENE DICHLORIDE SOLVENT[a]

$AlCl_3$: NCl_3, molar	Yield, %	Basic Product[b] Production distribution, mole %					Toluidine			
	Total	8-APC	8-APC	2-APC	3-APC	5-AMC	meta	para	*ar*-Cl-8-APC[c]	Residue, wt. %
1	18	17	94	0	0	0	0	0	6	17
2[d]	28	12	42	16	21	16	2	2	1	<20
2[e]	28	10	36	15	21	21	4	2	1	15
2	36	12	33	16	19	23	6	3	0	13
3[f]	32	10	31	17	19	24	6	3	trace	8
3[g]	46	11	24	27	41	trace	2	6	trace	11

[a] NCl_3, 0·1 mole in ca. 160 ml of ethylene dichloride; *p*-cymene, 1 mole; 0–10°; NCl_3 add'n time, 45 min; total reaction time, 90 min.

[b] APC = amino-*p*-cymene, AMC = amino-*m*-cymene.

[c] Formed indirectly.

[d] NCl_3, 0·025 mole in 36·5 ml of ethylene dichloride; *p*-cymene, 0·5 mole; NCl_3 add'n time = total reaction time, 22 min.

[e] *p*-Cymene, freshly distilled from sodium.

[f] Apparatus flushed with nitrogen during reaction.

[g] −25 to −35°.

entry 4), cited because it includes all the products in these categories, yielded the indicated compounds: 8-amino-*p*-cymene[2-amino-2(4-methylphenyl) propane or *p*-methyl-α,α-dimethylbenzylamine],2- and 3-amino-*p*-cymene, 5-amino-*m*-cymene, and *m*- and *p*-toluidine. An additional component, believed to be an N-chloro derivative of 8-amino-*p*-cymene, was also present. During GLPC of crude base containing this material, *ar*-chloro-8-amino-*p*-cymene was formed. A number of different conditions were studied to determine their effect on the reaction course. Several variables exerted a significant effect on the overall yield (Tables 1–3). The

TABLE 3. EFFECT OF TEMPERATURE[a]

Temp., °C	$AlCl_3$: NCl_3, molar	Yield, %	Basic Product[b] Product distribution, mole %								
		Total	8-APC	8-APC	2-APC	3-APC	5-AMC	Toluidine meta	Toluidine para	*ar*-Cl-8-APC[c]	Residue, wt. %
−30 ± 5	1	<8	5	57	0	0	0	0	0	43	
−30 ± 5[d]	1	<9	6	68	0	0	0	0	0	32	—
0–10[e]	1	17	16	93	0	0	0	0	0	7	9
33–38	1	19	18	93	0	0	0	3		4	9
−30 ± 5	2	37	21	58	14	19	0	0	7	2	13
−30 ± 5[d]	2	59	24	41	20	35	0	0	4	trace	15
0–10	2	46	19	41	14	17	24	6	2	trace	8
33–38	2	24	15	63	0	0	27	10	0	0	28
−30 ± 5	3	55	18	32	25	33	0	4	6	trace	16
0–10[f]	3	58	26	44	12	14	22	7	2	trace	9

[a] NCl_3, 0·1 mole in ca. 210 ml of *o*-$C_6H_4Cl_2$; *p*-cymene, 1 mole; NCl_3 add'n time, 45 min; total reaction time, 90 min.

[b] APC = amino-*p*-cymene, AMC = amino-*m*-cymene.

[c] Formed indirectly.

[d] Total reaction time, 135 min.

[e] Average of 3 runs.

[f] Average of 2 runs.

more detailed aspects concerning product distribution are discussed later. One of the most important requirements concerned the catalyst. In the absence of a promoter none of the amine was formed. An aluminum chloride–trichloramine ratio of at least two was necessary for efficient reaction.[3] At a ratio of 1, little or no heat was evolved after half the trichloramine was added, and unchanged halamine was present at the end of reaction. In contrast, at higher ratios, exothermicity characterized the entire addition period, and the final mixture was essentially devoid of halamine as evidenced by the potassium iodide test. The product from the equimolar catalyst–trichloramine reactions consisted of a mixture of 8-amino-*p*-cymene and presumably its N-chloro derivative. Apparently the absence of aromatic amines was the result of destruction by excess trichloramine. This then suggests that the side-chain base is more resistant to attack by trichloramine than are the nuclear isomers. The effect of excess trichloramine was evaluated in the following manner. An experiment was carried out under

the same conditions as those employing equimolar catalyst-trichloramine except that reaction was terminated immediately after half of the halamine was added (Table 2, entry 3). The resulting product distribution and yield were similar to those obtained at higher ratios by the standard procedure. The increased yield and the presence of aromatic amines is consistent with the apparent destruction of nuclear amine by excess trichloramine. Further support is found in the observation that *p*-toluidine was almost completely consumed by treatment with excess halamine at 0° for several hours.[9]

A slight solvent effect was operative since yields were about 10% higher in *o*-dichlorobenzene than in ethylene dichloride. Amination proceeded best in the −35° to 10° range. The rate of formation of 8-amino-*p*-cymene appears to be faster than that of nuclear amination. Increasing the time of reaction from 90 to 135 min benefited the yield of nuclear isomers only (Table 3).

Side-chain amination. We believe that the formation of side-chain amine occurs *via* abstraction of the isopropyl α hydrogen as hydride. The resulting carbonium ion then reacts with a nucleophilic nitrogen-containing moiety to form the amine eventually. This scheme is completely analogous to that proposed for side-chain attack in the presence of t-butyl cation as the hydride abstracting agent.[12] In the present case, chloronium ion is believed to be the precursor involved in carbonium ion generation.

$$Cl_3N + AlCl_3 \rightleftarrows Cl^{\delta+}Cl_2N^{\delta-}\cdots\cdots> AlCl_3 \qquad (1)$$

The same role for chloronium ion has been postulated for amination of methylcyclohexane leading to 1-amino-1-methylcyclohexane in good yield.[13] In the alkane case, the halonium species appears to be the only reasonable electrophile available for hydride abstraction. Transfer of hydride to bromonium ion has previously been proposed as a mechanistic feature of the uncatalyzed bromination of adamantane,

TABLE 4. EFFECT OF WATER[a]

H_2O, moles	$AlCl_3$: NCl_3, molar	Yield, %	Basic Product[b] Production distribution, mole %					Toluidine			
		Total	8-APC	8-APC	2-APC	3-APC	5-AMC	meta	para	*ar*-Cl-8-APC[c]	Residue, wt %
0[d]	2	46	19	41	15	18	19	5	2	trace	7
0·1	2	32	17	54	5	5	24	10	1	1	14
0·1	3	42	17	41	7	8	33	10	1	trace	4

[a] NCl_3, 0·1 mole in ca. 210 ml of *o*-$C_6H_4Cl_2$; *p*-cymene, 1 mole; 0–10°; NCl_3 add'n time, 45 min; total reaction time, 90 min.

[b] APC = amino-*p*-cymene, AMC = amino-*m*-cymene.

[c] Formed indirectly.

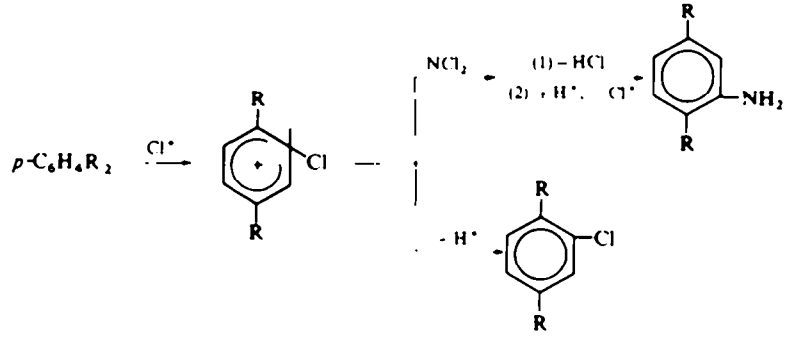
[d] Extra dry (see Experimental).

[12] P. Kovacic and R. J. Hopper, *Tetrahedron* 23, 3977 (1967).

[13] P. Kovacic and S. S. Chaudhary, *Tetrahedron* 23, 3563 (1967).

in which substitution occurs at the tertiary carbon.[14] On the other hand, other electrophiles capable of this type of interaction may be present in the *p*-cymene system. Although the isopropyl cation would seem to be the most likely possibility, there was no evidence for its participation in the amination sequence. No apparent correlation could be detected between rearrangement-disproportionation and the yield of 8-amino-*p*-cymene. In one case, the effluent gas was analyzed, with no indication of the presence of propane. Furthermore, the addition of isopropyl bromide proved inimical to the formation of side-chain amine.[12]

Nuclear amination. The route involved in this unusual mode of substitution has been discussed previously.[5-8] In the case of *p*-cymene, the same mechanistic picture (illustrated with a *p*-dialkylbenzene) can be employed to account for the nuclear amino-*p*-cymenes. Since the actual nucleophile is not known with certainty, NCl_2^- is used for simplicity.



(2)

(3)

The more hindered 3-amino-*p*-cymene was found to predominate over the corresponding 2-amino isomer. A fairly constant distribution of the two isomers, ca. 1·2, was obtained for the reactions at 0–10°, with some increase in the ratio at lower temperatures. According to the proposed mechanism (Eq. 2), it is clear that the factors governing orientation are more complex than in classical electrophilic substitution. The intermediate arenonium ion can lead to either the amino (Eq. 2) or chloro derivative (Eq. 3). It is altogether tenable, therefore, to expect that variation in conditions would affect the isomeric ratio. The predominance of 3-amino-*p*-cymene is consistent with the postulated initial electrophilic attack resulting subsequently in a distribution of amine isomers determined in part by the composition of the σ complexes.

The orientation in chlorination of *p*-cymene with chlorine-iron-acetic acid was 25% of 3-chloro- and 75% of 2-chloro-*p*-cymene, i.e. 3 to 1 in favor of the less hindered component. Analysis of the chlorocymene by-product from amination showed the same distribution (other isomers apparently derived from *m*-cymene were also present). In previous investigations of chlorination with this substrate, only the 2-chloro isomer was reported.[15-17]

From a straightforward extrapolation of the chlorination data, the ratio of 3- to 2-amino-*p*-cymene should be 3. However, the steric factor of the nitrogen-containing

[14] H. Stetter, J. Mayer, M. Schwarz, and K. Wulff, *Chem. Ber.* **93**, 226 (1960).
[15] R. J. W. LeFevre, *J. Chem. Soc.* 980 (1933).
[16] T. Kuan, *J. Chem. Soc. Japan* **52**, 473 (1931); *Chem. Abstr.* **26**, 5081 (1932).
[17] G. H. Swart and G. H. Stempel, Jr., British Patent 687,267 (1953); *Chem. Abstr* **48**, 3390 (1954).

nucleophile and competing deprotonation of the intermediate σ complex must also be taken into account. Prior studies lead us to believe that the nucleophile involved possesses less bulk than trichloramine.[5] Various possibilities are: Cl_2NH, $ClNH_2$, NH_3, or the corresponding amide ions. The steric factor of the actual participating entity might well be sufficient to interfere with entrance *ortho* to the isopropyl group, thus causing a reduction in the predicted amount of the more hindered isomer.

Before leaving the nucleophile topic, we wish to refer to a pertinent analytical treatment by Edwards and Pearson.[18] In a discussion of factors which affect nucleophilicity, they dealt with the aspects of basicity, polarizability, and the influence of an adjacent atom possessing unshared electrons. Conceivably, the nucleophile in our amination system may be appropriately endowed in terms of these essential features.

Additional elements of nuclear amination should be considered, notably the formation of 5-amino-*m*-cymene and *m*-toluidine. In the presence of a Friedel Crafts catalyst, *p*-cymene is susceptible to disproportionation,[19-22] leading to toluene and diisopropyltoluene, as well as rearrangement. Depending upon the conditions, the latter process yields *m*-cymene exclusively[21-23] or a mixture of the three isomers.[24] Since *m*-cymene and toluene can be generated initially, the presence of *m*-toluidine and 5-amino-*m*-cymene in the reaction product is not surprising. The formation of *m*-toluidine *via* toluene amination is well established.[4] In addition, *m*-dialkylbenzenes provide a particularly favorable situation in this reaction category. For example, the rate of amination for *m*-xylene is 49 times as fast as for toluene, and 7 times that of *p*-xylene.[6] Amination of *m*-cymene gave 5-amino-*m*-cymene in 26% yield.

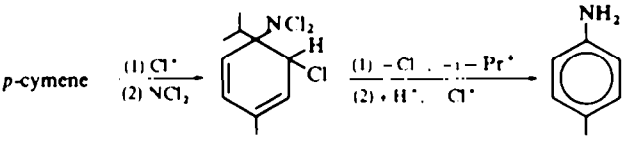
Previous work having established that rearrangement and disproportionation are dependent on such variables as time, temperature and cocatalyst, it is to be expected that the quantities of *m*-toluidine and 5-amino-*m*-cymene in the reaction products will be quite sensitive to changes in these conditions. Increases in the reaction time (Table 2) and temperature (Tables 2 and 3) enhanced the relative amounts of these bases. Table 4 shows that added water (co-catalyst) also facilitated rearrangement and disproportionation. In all cases the rearranged material is formed primarily at the expense of aromatic amine isomers derived from *p*-cymene.

These data shed some light on the question of the nature of the electrophile involved in the amination sequence. It appears logical that the amount of protonation and extent of rearrangement are directly related. However, no increase in the yield of 2- or 3-amino-*p*-cymene was noted when water was added. Hence a σ complex resulting from protonation does not seem a likely precursor for these two amines, which is in keeping with prior evidence of a similar nature in σ amination.[6,25]

In contrast with the present study, no more than very minor proportions of *p*-toluidine were observed from toluene amination in previous investigations under a variety of conditions including temperature variation. A possible mode of generation

[18] J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.* **84**, 16 (1962).
[19] A. W. Schorger, *J. Am. Chem. Soc.* **39**, 2671 (1917).
[20] A. Lacourt, *Bull. Soc. Chim. Belg.* **38**, 1 (1929); *Chem. Abstr.* **23**, 2431 (1929).
[21] D. A. McCaulay and A. P. Lien, U.S. Patent 2,770,662 (1956); *Chem. Abstr.* **51**, 7410 (1957).
[22] V. A. Koptyug, *Isomerization of Aromatic Compounds*, p. 17. D. Davey, New York, N.Y. (1965).
[23] D. E. Pearson, R. D. Wysong, and J. M. Finkel, private communication.
[24] H. I. Enos, Jr., U.S. Patent 2,744,149 (1956); *Chem. Abstr.* **51**, 468 (1957).
[25] P. Kovacic, K. W. Field, P. D. Roskos, and F. V. Scalzi, *J. Org. Chem.* **32**, 585 (1967).

is illustrated in Eq. 4.[26]



(4)

According to this mechanism, the yield of *p*-toluidine should be somewhat related to 2-amino-*p*-cymene production since both stem from the same intermediate σ complex. At the same time the amount of toluidine isomers should be unrelated. These views are consistent with the experimental facts (Tables 2–4).

An unidentified material, presumably an N-chloro- or N,N-dichloro-8-amino-*p*-cymene, was generally obtained, for the most part in small quantities. However, this comprised a significant portion of the basic product in low temperature reactions involving an equimolar ratio of catalyst to trichloramine (Table 3, entries 1 and 2). Large amounts of aluminum chloride should facilitate decomposition since halogenation by N-halamines is subject to catalysis by Lewis acid.[27]

It was noted that the crude basic products, particularly those containing appreciable amounts of this component, deposited 8-amino-*p*-cymene hydrochloride on standing. Apparently the N-chloro compound is degraded slowly with formation of hydrogen chloride. In another experiment, the crude basic mixture (Table 3, entries 1 and 2) on GLPC yielded 8-amino-*p*-cymene and the derivative from nuclear chlorination (the position of attack was not ascertained). When the amination product was treated initially with potassium iodide and then subjected to GLPC, there was a 26% increase in 8-amino-*p*-cymene with no accompanying chlorinated material. Thus, it appears that the basic product bearing nuclear chlorine is not formed during the amination process, but is generated from an N-chloro intermediate during gas chromatography. Aromatic halogenation by N-halo compounds has ample precedent.[27–32]

A more comprehensive treatment of side-chain amination is described in the subsequent publication.[12]

EXPERIMENTAL[33]

Materials. *p*-Cymene, Eastman white label reagent, was used as supplied. *o*-Dichlorobenzene (technical material containing about 10% of the *para* isomer) was either redistilled over calcium hydride, or used without further purification (Eastman white label reagent). Technical ethylene dichloride was redistilled from calcium hydride before use. The other reagents were commercial materials which were used as obtained.

Analytical procedures. IR spectra were taken with Beckman IR-5A and IR-8 spectrophotometers

[26] A similar scheme is proposed by P. C. Myhre, G. S. Owen, and L. L. James (unpublished work) for the conversion of 1,3,5-tri-t-butylbenzene to 3,5-di-t-butylphenyl acetate on treatment with bromine in the presence of acetate ion.

[27] L. O. Brown and F. G. Soper, *J. Chem. Soc.* 3576 (1953).

[28] T. W. J. Taylor and W. Baker, Sidgwick's *The Organic Chemistry of Nitrogen*, p. 67. Clarendon Press, Oxford (1937).

[29] G. H. Coleman and W. A. Noyes, *J. Am. Chem. Soc.* **43**, 2211 (1921).

[30] M. D. Carr and B. D. England, *Proc. Chem. Soc.* 350 (1958).

[31] N. Stoll, *Bull. Soc. Chim. Belg.* **38**, 71 (1929); *Chem. Abstr.* **23**, 4456 (1929).

[32] P. Haberfield and D. Paul, *J. Am. Chem. Soc.* **87**, 5502 (1965).

[33] We are grateful to Mr. Joseph A. Levisky for his contributions to the scouting work in this area.

Quantitative analyses were made on the IR-8 instrument. GLPC was carried out with a home-made, thermal-conductivity unit unless otherwise specified. The various columns and conditions are listed in Table 5.

TABLE 5. GLPC CONDITIONS

Procedure	ft × 0·25 in	Packing	Temp, °C	He flow rate, ml/min
A	12	15% Carbowax 6000, 5% NaOH, on Chromosorb W, 35/60 mesh	185–190	85
B	5	30% Carbowax 6000, 2% NaOH, on Chromosorb G, 60/80 mesh	145–150	200
C	10	5% UCON 50-HB-5100, 2·5% NaOH, on Chromosorb G, 60/80 mesh	190	70
D	10	15% UCON 50-HB-5100, 5% NaOH, on Chromosorb W, 35/60 mesh	190	70
E	12	10% sodium dodecylbenzene sulfonate, 7% UCON HB-2000, 5% NaOH, on Chromosorb W, 35/60 mesh	55	14 psi
F	16	30% Dowtherm A on Chromosorb P, 60/80 mesh	30	25 psi
G	8	14% Carbowax 6000 on Chromosorb P, 35/60 mesh	120	120
H	14	15% Carbowax 6000 on Chromosorb P, 35/60 mesh	140	75
I	10[a]	15% Apiezon L on acid-washed Chromosorb P[b]	137	--[c]
J	9	20% SF-96 on acid-washed Chromosorb P, 60/80 mesh	150	86
K	6	2·5% UCON HB-2000, 5% NaOH, on Chromosorb, W, 60/80 mesh	188	42
L	12	20% Sodium dodecylbenzene sulfonate, 5% NaOH, on Chromosorb W, 35/60 mesh	165	120

[a] ¼ in.
[b] With Aerograph Hi-Fi instrument.
[c] 20 psi of N_2; 20 ml of H_2/min.

NMR spectra were obtained on a Varian A-60 or A-60-A unit. Elemental analyses were performed by Dr. G. Weiler and Dr. F. B. Strauss, Oxford, England, or Galbraith Laboratories, Nashville, Tenn. M.ps and b.ps are uncorrected.

Preparation of trichloramine solution. A published procedure[3] (method B) was used with *o*-dichlorobenzene or ethylene dichloride as solvent.

Amination of p-*cymene*

General procedure. The apparatus consisted of a 1-l., 3-necked flask equipped with a mechanical stirrer, thermometer, dropping funnel, and drying tube. The *p*-cymene was taken with stirring to the desired temp which was maintained throughout the reaction. After introduction of the $AlCl_3$, the trichloramine soln (containing the requisite moles of halamine) was introduced through the dropping funnel. Stirring was continued until the total reaction time was reached. Work-up was according to a prior procedure.[3] Occasionally the crude, basic product deposited some amine hydrochloride on standing.

In one reaction, additional steps were taken to eliminate moisture ("extra dry"). The apparatus was flamed and purged with dry N_2. *p*-Cymene and the trichloramine soln were dried over $MgSO_4$ prior to use. $AlCl_3$, from a previously unopened bottle, was weighed under dry N_2 and introduced through a solid-addition funnel without exposure to the atmosphere.

When water was also employed, the additive was introduced following the $AlCl_3$. The addition was accomplished as rapidly as possible within the desired temp range. There was little change in the appearance of the reaction mixture.

The effluent gas from an amination was analyzed by a technique similar to that described elsewhere.[12] The IR spectrum of the trapped material was identical to that of the solvent, ethylene dichloride. Evidently, no significant amount of propane was present.

Basic products from p-*cymene amination.* Yield is calculated from an equimolar relationship between trichloramine and basic product. Yield data are based on the weight of distilled product or on GLPC analysis with 2- or 8-amino-*p*-cymene as external standards. Several reaction products were analyzed by both methods; the GLPC technique gave 3–5% higher yields.

The product distributions were determined by GLPC with procedures A, B, C, or D (Table 5). On cross-checking the methods, product distributions were found to agree within 3%. Procedures C and D were preferred because of the greater thermal stability of the UCON oil.

Standard mixtures of *m*-toluidine, 2- and 8-amino-*p*-cymene were gas chromatographed to determine the relative peak area/mole ratio for the components. Essentially the same areas were obtained for equimolar amounts of the amino-*p*-cymenes. The peak area of *m*-toluidine required a correction factor of 1·5; the same correction was applied for *p*-toluidine. Other amino-cymene isomers and *ar*-chloro-8-amino-*p*-cymene were assumed to have the same peak area/mole ratio, i.e. thermal conductivity, as 2- and 8-amino-*p*-cymene. Analyses were performed on the crude basic products since the distilled materials showed a slight decrease in the relative amounts of higher-boiling components. The separation characteristics were similar under all chromatographic procedures employed.

Characterization of 8-amino-*p*-cymene is described elsewhere.[12] The GLPC retention time and IR spectrum of pure 2-amino-*p*-cymene, obtained by GLPC, were identical to those of the authentic compound. The authentic material (Eastman, white label) required further purification by GLPC since about 10% of 3-amino-*p*-cymene was present. The retention time and IR spectrum (GLPC purification) of 3-amino-*p*-cymene were identical to those of the impurity in the authentic 2-amino isomer. Since the two isomers could not be separated by distillation, further characterization was carried out with the mixture. The combined product from three reactions (Table 3, entries 5, 6, and 9) was distilled with a 50-plate spinning-band column. A fraction (b.p. 90–94°/2·3 mm; lit.[34] 2-isomer, b.p. 110°/10 mm; lit.[35] 3-isomer, b.p. 238–242°/760 mm) was collected which contained 47% of the 2-isomer and 53% of the 3-isomer by GLPC analysis. This material was converted to a mixture of the corresponding phenols (see below). Pure 5-amino-*m*-cymene, obtained by GLPC collection, displayed a retention time and IR spectrum identical to those of the major product from amination of *m*-cymene.

For NMR analysis of the nuclear cymylamines, the combined basic products from several aminations was distilled through a 25-plate spinning band column. The NMR spectrum (TMS external standard) of a fraction (b.p. 130–130·5°/20 mm) which contained only 2- and 3-amino-*p*-cymene, and 5-amino-*m*-cymene (by GLPC analysis), was obtained. Integration of the spectrum showed the indicated bands (τ) with relative intensities, aromatic H (2·5–3·9), amino H (6·3–6·5); methyl H (7·5–7·8); isopropyl H (6·5–7·3 and 8·4–8·7) = 3:2:3:7.

The toluidine isomers (*meta* and *para*) were identified by comparison of their GLPC retention times and IR spectra (from samples obtained by GLPC collection) with those of authentic materials.

Amination of m-*cymene.* *m*-Cymene was prepared from the *para* isomer essentially according to the method of Pearson *et al.*[36] (HF–BF_3 at dry ice temp). The product, b.p. 173–175°, proved to be identical to the authentic substance.[37]

The general procedure for amination was employed (similar to entry 4, Table 1, 0·7 × scale). The crude basic product was distilled (b.p. 72–155°/3 mm) to give 2·74 g (26% yield) of distillate with 8% residue by wt. GLPC analysis (Table 5, procedure A) of the distilled product showed the indicated composition: 5-amino-*m*-cymene, 72%; *m*-toluidine, 14%. The remaining 14% was a mixture which was not characterized. The distilled mixture was further purified by fractionation through a 25-plate spinning band column, b.p. 103–105°/4·8 mm. The distillate (87% pure by GLPC) was then converted to the corresponding phenol (see below). An analytical sample collected from the chromatograph was identical to 5-amino-*m*-cymene obtained from *p*-cymene amination. (Found: C, 80·29; H, 10·13; N, 9·14. Calc. for $C_{10}H_{15}N$: C, 80·46; H, 10·15; N, 9·39%.) The IR spectrum indicated 1,3,5-substitution,[38] with bands at 697 and 828 cm^{-1}.

[34] C. F. H. Allen and J. Van Allan, *Org. Syntheses* **22**, 9 (1942).

[35] F. Richter and W. Wolff, *Ber. Dtsch. Chem. Ges.* **63**, 1714 (1930).

[36] We are grateful to Professor D. F. Pearson for making available this procedure; see Ref. 23.

[37] We wish to thank Dr. D. A. McCaulay, American Oil Co., for this sample.

[38] L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, p. 79. Wiley, New York, N.Y. (1962).

Chlorocymenes. The neutral layer from work-up of the reaction mixture from *p*-cymene amination Table 1, entry 4) was washed with water and dried, wt 367 g. A portion, 291 g, was distilled at atm press through a 25-plate spinning-band column. A few drops of material, b.p. ca. 105°, were identified as toluene on the basis of the IR spectrum. The remaining 76 g was fractionated with the same column. The portion boiling at 45–52° 7·5 mm contained unchanged *p*-cymene. The IR spectrum of the cymene peak trapped from GLPC (Table 5, procedure G) showed no evidence for presence of the *meta* isomer. The spectra of known mixtures indicated that as little as 1% of *m*-cymene could be detected by this technique. Three fractions (6 g total wt; 0·17 mole extrapolated to total wt of the neutral fraction; b.p. 80–84°/7·5 mm) contained a mixture of four chlorocymene isomers. The NMR spectra of two of the fractions revealed the relative intensity, aromatic H : aliphatic H = 3 : 10. The spectra were quite complex but consistent with the predicted methyl H singlet and isopropyl H septet-doublet pattern. The elemental composition of one fraction was determined. (Found: C, 71·36; H, 7·81; Cl, 20·78. Calc. for $C_{10}H_{13}Cl$: C, 71·19; H, 7·77; Cl, 21·04%.)

An aliquot of the original neutral fraction was analyzed by GLPC to determine the relative amounts and retention times of the chlorocymene isomers. These were compared with the data from chlorination of *p*-cymene with molecular chlorine and from the chlorocymene fraction obtained in the amination of *m*-cymene (Table 6). Since resolution (GLPC) of the chlorocymene isomers was generally incomplete, no attempt was made to isolate pure materials for positive identification. Structural assignments are therefore somewhat tentative, being based primarily on GLPC retention times and analogy to prior reports. Based on GLPC retention times, entries 2 and 3 are probably 3- and 2-chloro-*p*-cymene, respectively. Entries 1 and 4 may well be derived from chlorination of *m*-cymene.

The chlorocymene fraction, b.p. 95–100°/18 mm; 30 g, 0·17 mole, from *m*-cymene amination was isolated and analyzed by the same procedures used for the neutral material from *p*-cymene. Three isomers were separated by GLPC (Table 6). The nmr spectrum of the mixed isomers was similar to the corresponding

TABLE 6. GLPC OF CHLOROCYMENES[a]

Retention time, min			Area, %		
From *p*-cymene amination	From *m*-cymene amination	From *p*-cymene chlorination	From *p*-cymene amination[b]	From *m*-cymene amination[c]	From *p*-cymene chlorination
60·3	60·3		7	26	-
63·3	63·0	64·4	18	13	25
67·4		68·3	50		75
70·0	69·8		25	61	—

[a] Table 5, procedure H.

[b] Relative peak areas: entry 2/entry 3 = 26/74, entry 1/entry 4 = 78/22.

[c] Relative peak areas: entry 1/entry 4 = 70/30.

spectra of the chlorocymenes formed during *p*-cymene amination. Integration provided the relative intensities aromatic H : aliphatic H = 3 : 10. (Found: C, 71·42; H, 7·87; Cl, 20·77. Calc. for $C_{10}H_{13}Cl$: C, 71·19; H, 7·77; Cl, 21·04%.)

By analogy to the isomeric distribution in nitration of *m*-cymene,[39] entries 1 and 4 are tentatively designated as 4- and 6-chloro-*m*-cymene, respectively.

Preparation of chloro-p-cymene. p-Cymene (157 ml, 1 mole), glacial AcOH (150 ml), and Fe-filings (0·08 g) were placed in a 1-l., 3-necked flask equipped with a dropping funnel, thermometer, gas outlet, and mechanical stirrer. A soln of about 0·1 mole Cl_2 in 170 ml glacial AcOH was added dropwise in the dark during 1 hr below 35°. After being stirred overnight, work-up, including distillation through a 1-ft, helices-packed column, gave material, b.p. 180–210°, lit.[15] b.p. 213–214°/764 mm. Redistillation through a 25-plate, spinning-band column gave higher-purity material, b.p. 87–90°/11 mm. GLPC analysis for the isomer

[39] G. A. Olah and S. J. Kuhn, *J. Am. Chem. Soc.* **86**, 1067 (1964).

distribution was performed on undistilled product (Table 6). Based on prior reports,[13 17] the major component is 2-chloro-*p*-cymene. The other is apparently the 3-chloro isomer.

Preparation of carvacrol and thymol from the corresponding amines. A mixture, 4·5 g, of 2- and 3-amino-*p*-cymene (47 and 53%, respectively) from *p*-cymene amination was converted to the corresponding phenols by a published procedure.[5] After steam distillation, fractionation under N_2 provided a 51% yield of a carvacrol–thymol mixture, b.p. 130–135°/6 mm. Distillation at atm press gave a boiling range of 229–232°; lit.[40] (760 mm) carvacrol, b.p. 237·8°; thymol, b.p. 233°. An analytical sample was prepared by GLPC. (Found: C, 79·76; H, 9·78. Calc. for $C_{10}H_{14}O$: C, 79·95; H, 9·40%.)

GLPC analysis (Table 5, procedure I) showed the mixture to be 56% thymol, 43% carvacrol,[41] and 1% unknown. The composition and retention times were verified by chromatography of an authentic mixture of 56% thymol–44% carvacrol. The IR spectrum of the authentic mixture was identical to that of the product mixture. The NMR spectrum was a composite of the spectra of the individual components. Integration by triangulation of the doublets characteristic of isopropyl β-hydrogens (carvacrol, 8·89τ, J = 7·25 c/s; thymol, 8·82τ, J = 7·25 c/s; TMS internal reference) indicated a composition of 56% thymol and 44% carvacrol.

Preparation of sym-*thymol from* 5-*amino*-m-*cymene.* 5-Amino-*m*-cymene (1·13 g, 87% pure) from *m*-cymene amination was converted to the corresponding phenol by the method used in the previous section. The steam-distilled product was analyzed by GLPC (Table 5, procedure J) and the major component (m.p. 46–49°, lit.,[42] m.p. 50–50·5°) was found to have the same retention time and IR spectrum as for authentic material.[43]

Chlorination of 8-*amino*-p-*cymene.* 8-Amino-*p*-cymene was dissolved in glacial AcOH. After addition of a small quantity of Fe filings, an undetermined amount of Cl_2 was introduced and allowed to react in the dark at room temp for 4 days. The resulting mixture was poured into cold water, made basic with 50% NaOH aq, and extracted with ether. Following evaporation of ether from the dried extract, the crude product was analyzed by GLPC (Table 5, procedure D, 8 ft column at 200°). The nmr spectrum (TMS external reference) showed the indicated resonance (τ) and relative intensities: aromatic H (2·2, 3·1); methyl H (7·94); [amino H (8·67) + isopropyl β-H (8·92)] = 3:3:8. An analytical sample was prepared by GLPC. (Found: C, 65·21; H, 8·21; N, 7·32; Cl, 19·45. Calc. for $C_{10}H_{14}NCl$: C, 65·38; H, 7·68; N, 7·62; Cl, 19·32%.)

The product displayed the same GLPC retention time and infrared spectrum as the corresponding product derived from the amination reaction.

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[40] R. C. Weast, ed., *Tables for Identification of Organic Compounds* (2nd Edition). The Chemical Rubber Co., Cleveland, Ohio (1964).

[41] We are grateful to Dr. Fred Koch, Lubrizol Corp., for this sample.

[42] M. S. Carpenter and W. M. Easter, *J. Org. Chem.* **20**, 401 (1955).

[43] We wish to thank Midland Tar Distillers, Ltd. and Givaudan Corp. for the IR spectrum and a sample of the material.