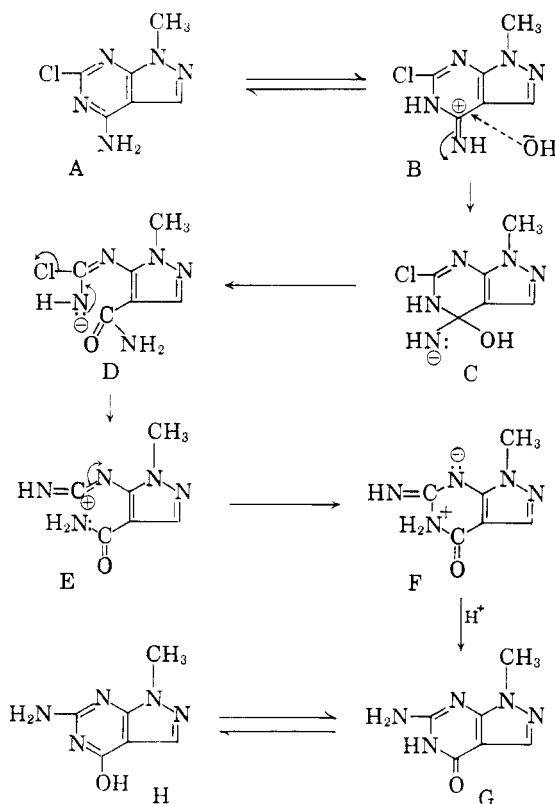A theoretical mechanism for this rearrangement involves a ring opening followed by ring closure as follows:

This type of rearrangement has previously been noted in the purine series. Fischer[5] observed that 6-amino-2-chloro-7-methylpurine (isomeric to I) rearranged in basic medium to give 7-methylguanine. It is interesting to note that in Fischer's case, although the 7-methyl group exerts a steric interference to the nearby amino group, the rearrangement was not influenced since the initial nucleophilic attack was at the *carbon* atom in the 6 position.

No rearrangement was observed in acid medium. When 4 - amino - 6 - chloro - 1 - methylpyrazolo-(3,4-d)pyrimidine (I) was refluxed in hydrochloric

acid, the expected 4-amino-6-hydroxy derivative (IV) was obtained.

EXPERIMENTAL

4-Amino-6-hydroxy-1-methylpyrazolo(3,4-d)pyrimidine (IV). This compound was prepared from 4-amino-6-chloro-1-methylpyrazolo(3,4-d)pyrimidine and concentrated hydrochloric acid as previously described.[4] The ultraviolet absorption spectra of this compound at pH 1 are 234 mμ (log ϵ = 4.10) and 251 mμ (log ϵ = 4.19); at pH 11.6, 247 mμ (log ϵ = 4.28) and 269 mμ (log ϵ = 4.11). The R_f value of the compound measured at 23° using n-propyl alcohol–1% ammonium hydroxide (2:1, volume ratio) is 0.55 (descending method). (Absorption spot was measured on Whatman #1 paper.)

6-Amino-4-hydroxy-1-methylpyrazolo(3,4-d)pyrimidine (II). This compound was prepared from 6-chloro-4-hydroxy-1-methylpyrazolo(3,4-d)pyrimidine and ethanolic ammonia as indicated in a previous paper.[4] The ultraviolet absorption spectra of this compound at pH 1 is 251 mμ (log ϵ = 4.34); at pH 11.6, 267 mμ (log ϵ = 4.29). The R_f value of the compound measured under the same conditions as for IV is 0.64.

Action of sodium hydroxide on 4-amino-6-chloro-1-methylpyrazolo(3,4-d)pyrimidine. Five g. of finely powdered 4-amino-6-chloro-1-methylpyrazolo(3,4-d)pyrimidine was added to 400 ml. of boiling water. To this suspension was added 20 ml. of 30% sodium hydroxide. The mixture was vigorously refluxed for 1 hr. The hot, clear solution was acidified with acetic acid. The white precipitate was filtered and re-dissolved in dilute hydrochloric acid, followed by reprecipitation with ammonium hydroxide. It was recrystallized from dimethyl formamide to give 3.1 g. (68%) of a white solid, m.p. >300°. The R_f value of this compound, measured under the same conditions as for IV, was identical with that of 6-amino-4-hydroxy-1-methylpyrazolo-(3,4-d)pyrimidine (II) prepared by the above procedure. The ultraviolet absorption spectra measured at pH 1 and pH 11.6 are also identical.

Anal. Calcd. for $C_6H_7N_5O$: C, 43.6; H, 4.3; N, 42.4. Found: (dried at 135° *in vacuo* for 6 hr.) C 43.3; H, 4.5; N, 42.4.

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Amylsodium, Triethyl Amine, Sodium Hydroxide and the Metalation of Cumene[1]

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A previous paper[2] reported that the association of triethyl amine and sodium hydroxide (sodium chloride also was present) with amylsodium changed the polymerization of butadiene from a 1,2- to a

(5) E. Fischer, *Ber.*, **31**, 542 (1898).

1,4-process. This effect resembled alfin catalysis[3] where sodium isopropoxide and sodium chloride were associated with allylsodium. These added compounds must affect critically either the sodium reagent or the hydrocarbon, and one way to judge is to test another hydrocarbon in some other reaction. Accordingly, cumene was chosen because it is a key compound; it contains aromatic, primary and tertiary hydrogens, the last being attacked easily by free carbyls. Also, its alkyl group has steric and directive influences. Should the triethyl amine and sodium hydroxide alter the kind of reaction with cumene, their influence might be general —affecting the character of amylsodium itself; but if the type of reaction were unchanged, these compounds could reasonably have had a special influence upon the diene hydrocarbon so that its reaction, but not that of cumene, was changed. The latter proved to be the case.

The experiment began by preparing amylsodium from amyl chloride and sodium.[4] Then successively water (to form sodium hydroxide *in situ*), the amine, and cumene were added. After an alloted time the mixture was carbonated. The carboxylic acids were separated and in some cases were oxidized[5] in order to determine the positions metalated. Control tests in the absence of the hydroxide and of both the hydroxide and amine were made.

The results (Table I) show that the amine and sodium hydroxide reduced the percentage of total carboxylic acids, but that effect is one of degree and would be expected because another paper[6] will show that these compounds accelerate the decomposition of amylsodium. Within experimental error, however, the kind of metalation was unchanged; the distribution of the products at the various positions remained the same.

This behavior contrasts with the numerous tests upon butadiene. Therefore, the influence of the two added compounds can be interpreted as involving in some way the butadiene, so that its manner of chain growth was much less a 1,2-process. That effect might seem remarkable because the amine and the sodium hydroxide should enhance the polarity of the medium and, therefore, should cause more 1,2-polymerization (if any change occurred), that type of chain growth being credited[7] as symbolic for anionic polymerization; but the

TABLE I

YIELDS OF CARBOXYLIC ACIDS OBTAINED FROM THE METALATION OF CUMENE BY AMYLSODIUM UNDER A VARIETY OF CONDITIONS

Acids	Amylsodium with		
	No added compounds	Triethyl amine	Amine and hydroxide[a]
Total carboxyl,[b] %	85	67	16
Distributed as			
Caproic,[c] %	12	10	6
Isophth.,[d] %	29	30	31
Para-bz.,[e] %	52	53	56
Meta-bz.,[f] %	1	3	1

[a] Triethyl amine and sodium hydroxide. [b] The total percentage yield is calculated on the amyl chloride used in making amylsodium. The yield of formic acid, which would arise from decomposition of amylsodium to sodium hydride, is not included in this determination. [c] Caproic acid represents unchanged amylsodium. [d], [e] and [f] represent successively 5-isopropylisophthalic acid, *p*-isopropylbenzoic acid and *m*-isopropylbenzoic acid.

view adopted in this laboratory has been that these active organosodium salts can function as radical pairs[3,8] and that the added compounds, possibly by complexing with, or orienting of, monomer, can favor 1,4-polymerization.

This work also adds another example to a long list of fruitless attempts to metalate the isopropyl group with sodium reagents. Monometalation of either cumene[9] or 1,3-diisopropylbenzene[10] took place on the ring. In dimetalations the second sodium atom entered the ring in *m*-cumenylsodium[11] and *p*-isopropylbenzylsodium[11b] rather than replaced the tertiary hydrogen. *p*-Cumenylsodium[11a] resisted further metalation by amylsodium although a parallel reaction with *n*-butylbenzene[11b] showed no difficulty in a lateral attack. 2,6-Diisopropylanisole,[10] where an adjoining methoxy should favor metalation on the alkyl group (it did so when the alkyl group was methyl[12,13]), was metalated instead on the distant para position. 2,4,6-Trimethoxybenzene[12] was cleaved to a phenol instead of being metalated.

This resistance to metalation affects the interpretation of another reaction of cumene, namely, its alkylation with ethylene in the presence of organosodium compounds as promoters. That re-

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(13) A. A. Morton and A. E. Brachman, *J. Am. Chem. Soc.*, 76, 2980 (1954); R. L. Letsinger and A. W. Schnizer, *J. Org. Chem.*, 16, 869 (1951).

action has been pictured[14] as progressing through the intermediate phenyldimethyl carbanion, $C_6H_5C(CH_3)_2^-$, which adds to ethylene to form a new carbanion, $C_6H_5C(CH_3)_2CH_2CH_2^-$, which, in turn, abstracts a tertiary hydrogen from cumene to maintain the chain, while forming the final hydrocarbon, t-amylbenzene. With sodium reagents however, this alkylation should be on the nucleus instead of the tertiary carbon, because the carbanion is on the nucleus. Alkylation of p-cymene also should occur at the methyl group, because that position alone is metalated by either sodium[9b] or potassium[15] reagent; yet alkylation occurred at the isopropyl group.[14a] The above mechanism, therefore, can scarcely be correct.

The facts are beautifully accommodated, however, to the view of biradical activity along the lines used to explain alfin catalysis.[3] At first, ethylene coordinates with the cation of the promoter, Na^+-R, to give the complex salt, $[C_2H_4 \rightarrow Na]^+-R$. Next, dissociation to two radicals, $Na\cdot$ and $\cdot R$, occurs. Then the carbyl removes the tertiary hydrogen from cumene to give $C_6H_5C(CH_3)_2\cdot$ in a process typical for radicals, while atomic sodium converts the adjacent olefin into an anion-radical, $Na^+-CH_2CH_2\cdot$. Finally, the two radicals unite to form an end salt product, $Na^+-CH_2CH_2-(CH_3)_2CC_6H_5$, which serves as the promoter to start the cycle again and to form t-amylbenzene. The several steps are closely consecutive or almost simultaneous. In its fine detail the process provides good evidence for radial pair (atomic metal and carbyl)[3,8] activity rather than serves as an example of carbanion chemistry.

EXPERIMENTS

Metalation of cumene. In three experiments amylsodium was prepared in heptane from 1 g. atom of sodium sand and 0.5 mole of amyl chloride in the customary way.[4,12] To one preparation a mole of cumene was added. To a second was added one mole of cumene and 1.5 mole of triethyl amine which previously had been dried over amylsodium. To the third was added 4 ml. (0.22 mole) of water, followed by one mole of triethyl amine and 0.5 mole of cumene. Each mixture was heated quickly to 70° and kept there for 3 hr., with stirring at 10,000 r.p.m. After being cooled to room temperature, the contents were forced into a 4-liter Erlenmeyer flask filled to a quarter of its depth with powdered carbon dioxide. The reaction flask was rinsed twice with 200 ml. of heptane which likewise was carbonated.

The next day 300 ml. of water was added to dissolve the salts. When both layers had cleared the hydrocarbon portion was separated and extracted with 50 ml. of 10% aqueous sodium hydroxide, followed by 50 ml. of water. Next, the combined aqueous layer and extracts were extracted with four 150-ml. portions of ether, after which the aqueous portion was acidified with 50% (by volume) sulfuric acid. A white precipitate which appeared and the solution were extracted with four 150-ml. portions of ether. The ether

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extract was dried over Drierite, filtered and made up to 500 ml., from which a 5-ml. aliquot was titrated in order to determine the total carboxylic acid.

The ether solution was evaporated to about 50 ml. and 200 ml. of petroleum ether was added. Overnight, 5-isopropylisophthalic acid precipitated. It was washed, dried, weighed and recorded as dimetalated product. After being crystallized from ethanol-water, it was identified by its neutralization equivalent, 107 (calcd. 104), its melting point, 282–285° (lit.[16] 285°), the melting point of its dimethyl ester, 64–65° (lit.[11] 64–65°), and a mixed melting point with an authentic sample.

The petroleum ether decantate was evaporated to one-half its volume and cooled. The first crop of crystals had the correct neutralization equivalent for p-isopropylbenzoic acid and melted at 115–117° (lit.[9] 116–118°). Its amide melted at 152–153° (lit.[17] 153°).

The remaining petroleum ether in the mother liquor was evaporated and the acid residue was fractionated to remove caproic acid (b.p. 60°/4 mm.). An aliquot (1.5 g.) from the acid residue was oxidized with chromium trioxide according to the method developed by Bryce-Smith and Turner[5] for determining the amount of m-isopropylbenzoic acid and α-phenylisobutyric acid.

The yields calculated from these operations, with appropriate allowances for all samples removed, are recorded in Table I. They show that triethyl amine, and particularly triethyl amine with sodium hydroxide, decreased the amount of metalation of cumene. The loss is accounted for as decomposition of amylsodium,[1,8] although the formic acid was not measured. No product from metalation at the alpha carbon atom was observed.

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Transmetalation of Thiophene by the Ethylsodium-Diethylzinc Complex[1]

JEROME H. LUDWIG[2] AND HEINZ SCHULZE

In general, organosodium compounds will transmetalate with hydrocarbons if they can form an organometallic corresponding to a stronger acid. However, Morton and co-workers[3] have shown that this rule is not followed invariably (for example: Amylsodium metalates t-butylbenzene predominantly in the *para* position, but in the presence of sodium alcoholates *meta* metalation occurs preferentially). The mechanism of transmetalation is still the subject of discussion.[4] Its elucidation is made more difficult because sodium alkyls are insoluble in hydrocarbon solvents. Steric factors and

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