Vaalburg and Mrs. H. D. Beerling-Van der Molen for technical assistance in the radioactivity measurements, to Mr. A. F. Hamminga for support in the CO determination, and to Gist-Brocades N.V., Delft, for a generous gift of two steroids.

Registry No.—**2a**, 35856-00-9; *endo*-**2b**, 3211-87-8; *exo*-**2b**, 3211-90-3; *endo*-**2c**, 62796-09-2; *exo*-**2c**, 62796-08-1; **2d**, 32730-85-1; **2e**, 766-05-2; **2f**, 56536-96-0; **2g**, 62796-10-5; **2h**, 57764-88-2; 17α-**2i**, 62796-11-6; 17β-**2i**, 62796-12-7; 3α-**2j**, 1251-67-8; 3β-**2j**, 1251-66-7; 3α-**2k**, 62796-13-8; 3β-**2k**, 62796-14-9; **2l**, 86-29-3; **2m**, 1823-91-2; **2n**, 42186-06-1; **2o**, 13310-75-3; **2p**, 62391-96-2; **2q**, 21101-85-9; **13e**, 52568-58-8; **14e**, 39031-25-9; 2,2-dimethyl-1,2,3,4-tetrahydronaphthalene-1-carboxamide, 62796-15-0; 4-tosyloxazole, 57764-94-0; $Tos^{14}CH_2N{=}C$, 62796-16-1; $^{14}CH_2O$, 3046-49-9; $Tos^{14}CH_2NHCHO$, 62796-17-2; TosMIC, 36635-61-7.

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(22) Tuinman[6b] has previously recommended for the same reason the use of 10 equiv of *t*-BuOK for reactions in DME–*t*-BuOH.
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Aminations with Ammonia and Formamide. Synthesis of Terephthalamic Acid and of *p*-Nitroaniline

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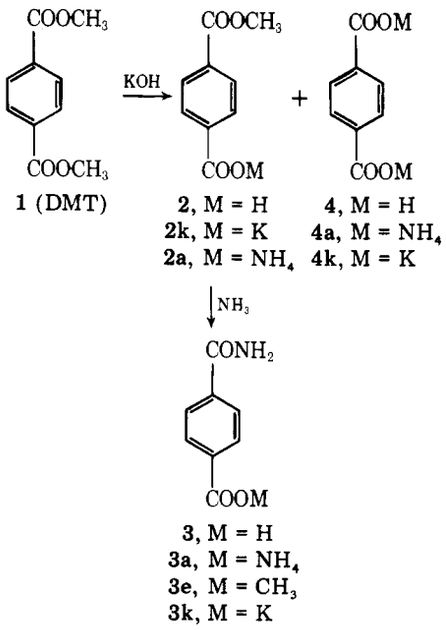
Ammonolysis of potassium methyl terephthalate (**2k**) to potassium terephthalamate (**3k**) is markedly accelerated by formamide solvent. No corresponding acceleration is seen with other amides, such as mono- or dimethylformamide or acetamide. Negligible hydrolysis to ammonium terephthalate (**4a**) occurs. An efficient procedure for the Hofmann conversion of potassium terephthalamate (**3k**) to *p*-aminobenzoic acid is reported. Ammonolysis of *p*-nitrochlorobenzene occurs rapidly in formamide solvent at 200–220 °C to furnish high yields of *p*-nitroaniline. *p*-Chlorobenzotrifluoride and 1,2,4-trichlorobenzene are not aminated under these conditions.

We sought to develop an economical synthesis of *p*-aminobenzoic acid from commercial dimethyl terephthalate (DMT, 1).[1] Attempts to half-ammonolyze DMT to methyl terephthalamate (**3e**) were unsuccessful, since all conditions tried formed excessive amounts of terephthaldiamide. However, half-hydrolysis of DMT by potassium hydroxide in

Scheme I



methanol proved to be quite selective, and potassium methyl terephthalate (**2k**) was isolated in about 90% yield (Scheme I).[2,3] The ammonolysis of **2k** to potassium terephthalamate (**3k**) in various media was investigated in detail, and the results form the subject of this paper.

Ammonolysis in 28% aqueous ammonia was examined first. At room temperature, ammonium methyl terephthalate (**2a**) required 20–24 h for complete reaction to ammonium terephthalamate (**3a**); 5–10% of diammonium terephthalate (**4a**) was also formed. However, heating the mixture at 50–100 °C accelerated hydrolysis of the ester group much more than ammonolysis, so that up to one-third of the product became **4a**. Addition of anhydrous ammonia to raise the concentration to 40–60% ammonia in water retarded both the hydrolysis and ammonolysis, but did not increase the selectivity appreciably. With the more basic potassium salt **2k**, hydrolysis became still more prominent.

Many ammonolyses of esters reported in the literature use an organic cosolvent for either aqueous or anhydrous ammonia. Methanol usually gives the fastest rates and highest yields of amides.[4] In our hands, **2a** reacted sluggishly with anhydrous ammonia in methanol. At 130 °C about 80% conversion was obtained in 6 h, and about 5% of **4a** was also formed despite the anhydrous conditions. In dry dimethylformamide, conversion was nearly complete in 6 h at 130 °C, but 25% of the product was **4a**; the reaction was negligibly slow at 40 °C. The reaction was slightly faster in dimethyl sulfoxide at 130 °C and less **4a** was formed.

At this point it appeared that a protic solvent of high dielectric constant was required for rapid ammonolysis. Water fits this description, though hydrolysis is excessive at temperatures where the rate is practical. Formamide[5] was tried, and the search ended. When potassium (or ammonium) methyl terephthalate (**2k** or **2a**) was heated with excess anhydrous ammonia in formamide (500 mL/mol), almost complete conversion to **3k** (**3a**) was achieved in 2 h at 130 °C, or 1 h at 140 °C. Vigorous agitation is required. About 80% yield of almost pure **3k** was isolated merely by filtering the reaction mixture at room temperature. When the filtrate was used as solvent in a second reaction, the solubility losses disappeared and the yield reached 95%.

Curiously, although the **2k**, formamide, and ammonia were rigorously dry, the ammonolysis reaction invariably produced about 5% of terephthalic acid salt (**4**). This is not a simple hydrolysis by adventitious water, since addition of up to 5 mol of water/mol of **2k** did not increase the proportion of **4**. Indeed, the rate of ammonolysis was increased slightly, in keeping with literature statements.[6] In contrast to the acceleration caused by water, methanol caused a slight but definite retardation. In parallel experiments, **2k** with only ammonia and formamide gave 98% conversion, while a run to which 3 mol of methanol had been added (per mole of **2k**) gave only 85% conversion. Since methanol is a product of the ammonolysis, it is therefore desirable to strip out the methanol by heating under vacuum before reusing the filtrate.

Still faster rates would be desirable for a continuous commercial process, hence catalysts were sought. Imidazole is a powerful catalyst for many transformations of carboxylic acid derivatives.[7] In the formamide system, imidazole increased the rate considerably. Thus, in parallel runs at 130 °C for 30 min, conversion of **2k** to **3k** was 33% without catalyst and 82% with 7.3 mol % of imidazole. But when this additive was tested in the aqueous ammonia system first studied, no change in rate of either hydrolysis or ammonolysis was apparent either at 25 or 60 °C.

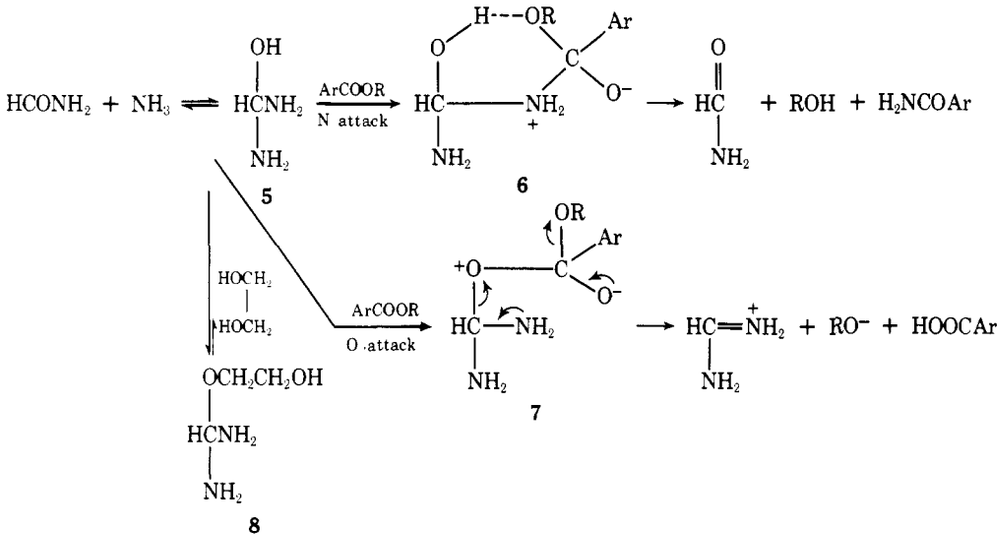
Polyhydric alcohols are known to promote ammonolysis of esters in aqueous dioxane;[4,8] ethylene glycol, glycerol, and sorbitol are increasingly effective. Day found it essential to have water present because of the low solubility of polyols in many anhydrous organic solvents. We found that both ethylene glycol and sorbitol are quite soluble in dry formamide. In parallel runs at 130 °C for 30 min, ethylene glycol gave 75% conversion and sorbitol 95%, compared to the 33% obtained without additive. Both polyols were used in the proportion of two hydroxyl groups per ester function. Unexpectedly, the "hydrolysis" to **4** observed in the formamide–ammonia system was almost completely suppressed by either polyol. Glycol has been used as solvent for the ammonolysis of polyesters such as poly(ethylene terephthalate).[9]

The remarkable ability of formamide to promote ammonolysis of esters seems to be restricted to this solvent alone. Acetamide (D = 65[10]) gave 20% conversion of **2k** to **3k** under conditions where formamide (D = 109) gave 95%; addition of 1 mol of water to the acetamide system increased the hydrolysis to **4** substantially, but did not improve the 20% conversion to **3k**. N-Methylamides have enormous dielectric constants, but N-methylformamide (D = 200), N-methylacetamide (D = 165), and N-methylpropionamide gave no detectable **3k** under the standard conditions where formamide itself gave 95% of **3k**. Pyrrolidinone (butyrolactam), with a very high dipole moment resulting from the enforced cis configuration, was likewise inactive. Apparently, two protons on nitrogen and a high dielectric constant are both necessary.

Acids, esters, and other acid derivatives may sometimes be converted to amides by heating with formamide, acetamide, or their N-substitution products with or without acid or base catalysis.[11] To test this possible explanation for our formamide–ammonia ammonolysis, **2k** was heated with formamide without ammonia at temperatures to 180 °C for times known to be sufficient for complete conversion in presence of ammonia. In none of these experiments was **3k** detected.

The active ammonolytic reagent is believed to be the ammonia adduct of formamide, diaminomethanol (**5**, Scheme II). If one of the amino groups adds to the carbonyl of the ester to form the tetrahedral intermediate **6**, departure of methanol should be strongly promoted by hydrogen bonding to the hydroxyl function. Alternatively, if the hydroxyl group of **5** adds to the ester carbonyl, the tetrahedral intermediate **7** would dissociate to methanol, carboxylic acid, and formamidine. Formation and collapse of **7** explain the "hydrolysis" of the ester in the absence of free water. Promotion by glycols may result from formation of **8**, in which additional possibilities for three-dimensional hydrogen bonding exist. Failure

Scheme II



of N- or C-substituted formamides may be a result of a very unfavorable equilibrium in the first step, formation of **5**.

Since equal conversions (within experimental error) were obtained with either the ammonium or potassium salts (**2a** or **2k**), the reaction does not appear to be strongly catalyzed by either acid or base. A detailed study to confirm the proposed mechanism of this unusual reaction lay outside the scope of the present research.

Silylation of Terephthalamic Acid and Other Amides. Analysis of Acid Mixtures. The various combinations of **1**, **2**, **3**, and **4** encountered in this work were analyzed by GC. Unexpected chemistry was also encountered. A mixture of trimethylsilyl chloride and hexamethyldisilazane in pyridine (commercial Tri-Sil) forms the volatile trimethylsilyl esters from these acids quantitatively in 1 min at room temperature.[12] The amide function in **3** reacts erratically with Tri-Sil; depending on the time and temperature of silylation, four different peaks with quite variable areas were obtained from pure **3**. An amide may be O-monosilylated, N-monosilylated, or N,O-disilylated.[13] Subsequently, one or more of these may decompose to a nitrile. The first peak from **3** has the same retention time as trimethylsilyl *p*-cyanobenzoate.

The more powerful reagent *O,N*-bis(trimethylsilyl)acetamide (BSA) was ultimately used as the preferred silylating reagent for analysis of mixtures containing **3**. Pure **3** gave mostly the nitrile (3.6 min), but also variable small amounts of the 15.2- and 17.6-min peaks (Scheme III). The amount of **3** in amidation mixtures was computed from the total areas under the three peaks, corrected for the response factors determined with authentic mixtures. The precision of the method for mixtures of **2**, **3**, and **4** is about 3% relative.

Dennis[14] reported that dehydration of amides to nitriles by silylating reagents required temperatures near 200 °C; our nitriles may have been formed in the hot injection port. Some other aromatic amides were tested qualitatively. Benzamide with BSA yielded only a little benzonitrile; the main product was a single monosilyl peak. *m*-Toluamide also yielded but little nitrile; the main peak was a poorly resolved doublet, presumably a mixture of *O*- and *N*-monosilyl derivatives. By contrast, *p*-nitrobenzamide yielded only *p*-nitrobenzonitrile. *p*-Carbomethoxybenzamide (**3e**) yielded mostly nitrile plus a little monosilylamide as a chromatographic doublet. Evidently, an electron-attracting group markedly increases the rate at which aromatic amides are dehydrated by BSA, either because that group increases the acidity of the amide and thus the rate of disilylation, or because it accelerates the breakdown of the disilylamide.

Several other silylating reagents[15] (used in excess) were tested with **3** in various solvents. Only trimethylsilyldiethylamine $[(CH_3)_3SiN(C_2H_5)_2]$ yielded any significant amount of cyanobenzoic ester. The others gave varying proportions of the 12.5-, 15.2-, and 17.6-min peaks. This result suggests that nitrile formation indeed occurs during the silylation step, not in the injection port. Interestingly, the 12.5-min peak was never seen in the same chromatogram as the 15.2-min peak.

The column used in this work was 20% SE-30 silicone gum rubber on Chromosorb W AW-DMCS, 60–80 mesh. The carrier gas was helium; the temperature was 215 °C isothermal. The instrument was an Aerograph Model 202-B with a thermal conductivity detector.

Hofmann Degradation of 3 to *p*-Aminobenzoic Acid. The Hofmann degradation was first applied to terephthalamic acid by Toland and Heaton.[16] Since they began with a crude **3** of uncertain purity (prepared by oxidation of *p*-xylene with ammonium sulfate, hydrogen sulfide, and water), their yield of *p*-aminobenzoic acid based on **3** is uncertain; it averaged 75% based on chlorine. We studied the Hofmann reaction with **3k**, pure or containing known amounts of **4k**. *p*-Aminobenzoic acid was obtained consistently in 80–85% yield by careful attention to the factors discussed below.

The Hofmann reaction involves the following steps:

$$ArCONH_2 + NaOCl \rightarrow ArCONHCl \rightarrow ArCON(Cl)Na \rightarrow ArN{=}C{=}O$$

$$ArN{=}C{=}O + 2NaOH \rightarrow ArNH_2 + Na_2CO_3$$

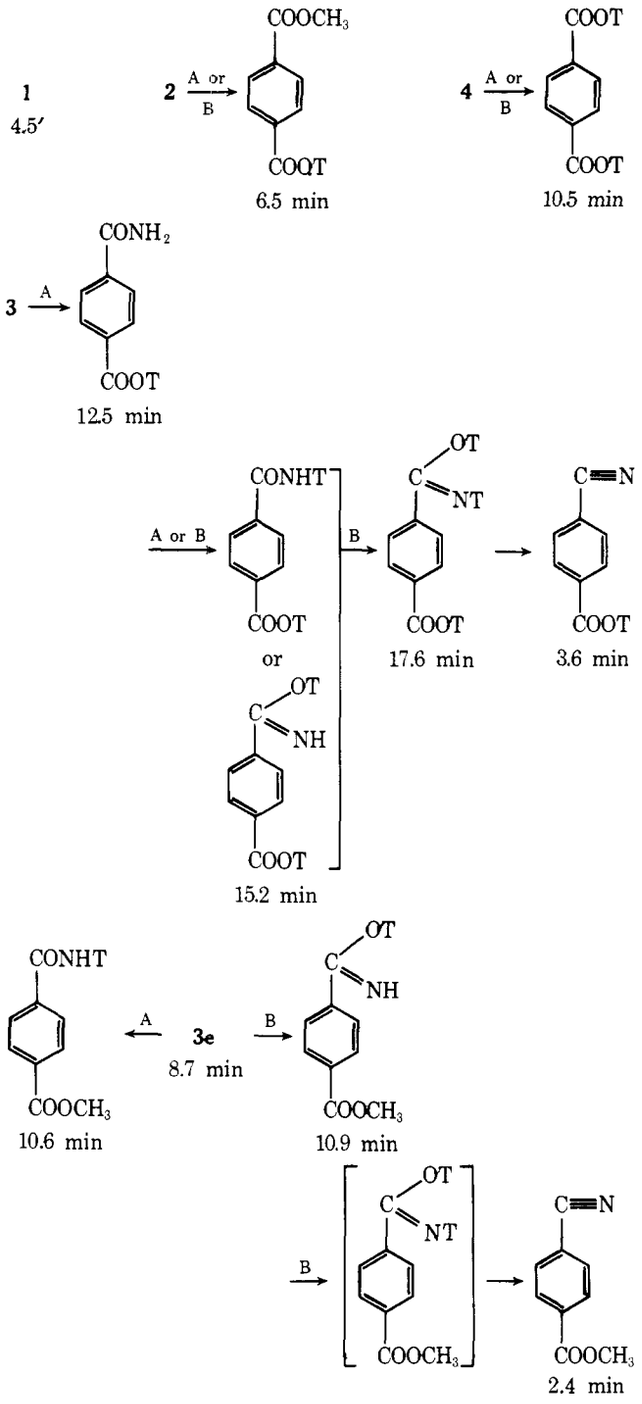
Overall:

$$ArCONH_2 + Cl_2 + 4NaOH \rightarrow ArNH_2 + Na_2CO_3 + 2NaCl + H_2O \quad (Ar = p\text{-}KOOCC_6H_4)$$

Since our terephthalamic acid was already the salt **3k**, we conducted the N-chlorination in basic medium, rather than in acid as preferred by Zengel and Bergfeld.[9] N-Chlorination of **3k** was complete in about 10 min at 15–25 °C. Longer contact times permit hydrolysis of the *N*-chloroamide to salts of **4**. Blank experiments showed that **3k** suffered very little hydrolysis in this period. The rearrangement itself set in at about 50 °C, and the heat of reaction raised the temperature to 90 °C in a few minutes. Reaction was complete in 5–15 min under these conditions. Accordingly, the preferred conditions detailed in the Experimental Section provide 10 min for N-chlorination and 10 min at 90 °C for the rearrangement.

The quantity of sodium hydroxide is critical. The overall reaction requires 4 mol, two to neutralize the chlorine and two to neutralize the carbon dioxide. However, with only 4 mol of base, the yields were consistently about 10% lower than when

Scheme III[a]



[a] Abbreviations: reagent A = Tri-Sil; reagent B = BSA; T = $(CH_3)_3Si$.

5 mol were used, and the product was much darker. With <4 mol, the yields dropped further. Zengel and Bergfeld observed a similar minimum requirement. Excess hypochlorite apparently oxidizes the amine to colored by-products. A slight deficiency of hypochlorite avoids this problem.

The concentration of **3** in the reaction mixture was examined briefly, since it is directly proportional to equipment productivity. With concentrations in the range 0.85–1.0 M, the reaction proceeds well, and the reaction heat brings the temperature quickly to the preferred 90 °C. In the range 0.5–0.6 M, heating takes longer, but the yields are the same. In the more dilute solutions, the product is somewhat lighter colored. The more concentrated solutions are preferred for their higher productivity, and also because the solubility losses are less.

Urea formation from the intermediate isocyanate and product amine, frequently encountered in other Hofmann degradations,[17] was unimportant in the present study.

The crude product was always somewhat discolored. Decolorizing carbons did not remove all colored products. Common reducing agents such as sodium dithionite and stannous chloride were ineffective. Then we found that a trace of sodium borohydride at pH 7–8 destroyed the colored materials very efficiently.[18] However, even this reagent did not completely decolorize products prepared with excess hypochlorite.

Amination of Aryl Halides. The unusual potency of the formamide–ammonia combination for ammonolyzing esters suggested its use in nucleophilic displacements. Matthews and Cookson showed that octyl bromide reacted with formamide–ammonia to yield *N*-octylformamide, not *n*-octylamine.[19] They also stated that aryl halides did not react. Bredereck et al., as part of an extensive study of the properties of formamide,[11] observed that alkyl halides could form either the *O*- or *N*-alkylformamide, which subsequently decomposed. Specifically, 2,4-dinitrochlorobenzene reacted with formamide in 16 h at 150 °C to yield (after hydrolysis) 55% of 2,4-dinitroaniline. However, *p*-nitrochlorobenzene failed to react in 20 h at 115 °C. Neither reaction was performed in the presence of ammonia.

We assumed that failure in the latter case was a result of the low temperature, and heated *p*-nitrochlorobenzene in formamide at 180 °C. Polymeric material plugged the condenser, which we attributed to reaction followed by acid-catalyzed decomposition of formamide. Accordingly, we added ammonia to repress formamide decomposition, and heated *p*-nitrochlorobenzene with formamide *and ammonia* in an autoclave at 180 °C. We did not expect the excellent conversion of the halide to *p*-nitroaniline which took place.

The reaction was then examined in detail; selected results are given in Table I. The first entry shows again that formamide alone is ineffective. In the runs tabulated, and in others not shown, it was evident that 2–3 mol of formamide and 3–4 mol of ammonia sufficed to give nearly quantitative conversions of the halide. Heating for 1 h at 220 °C or 2 h at 200 °C was sufficient. The true yields were about 5% higher than those shown, the loss occurring during the isolation procedure.

A *p*-nitro group is sufficient to activate ring chlorine toward displacement by ammonia in formamide. However, a *p*-trifluoromethyl group (in *p*-trifluoromethylchlorobenzene) or one or two chlorines (in *p*-dichlorobenzene or 1,2,4-trichlorobenzene) were not sufficiently activating, since negligible conversions to the amines were obtained in several experiments under the conditions where *p*-nitrochlorobenzene was quantitatively converted. This new method is clearly not a panacea for amination of all aryl halides.

Experimental Section

Hydrolysis of Dimethyl Terephthalate (1) to Potassium Methyl Terephthalate (2k).[20] Powdered 1, 194 g, 1 mol, was dissolved in 3 L of boiling methanol; commercial briquets dissolve very slowly. A solution of 112.2 g of potassium hydroxide pellets (85% assay, 1.7 mol) in 1 L of methanol was added in 3–5 min to the boiling solution of 1. After about 2 min, solid began to precipitate. After 30 min of boiling, the mixture was cooled rapidly to 40 °C and filtered. The solid **2k** was washed with two portions of 40 °C methanol, each sufficient to cover the crystals, and two portions of 10 °C methanol, then dried. The product weighed 173 g (80%), and it contained about 1–2% of **1** and 2–5% of **4k**. The 1 can be removed with a chloroform wash, if required. Alternatively, using only 1.06 mol of potassium hydroxide, hydrolysis required about 6 h. When *sodium* hydroxide was used, the salt was much more voluminous, was difficult to wash and handle, and it retained a great deal of methanol.

The free acid **2**, obtained by acidifying an aqueous solution of **2k**, can be recrystallized from acetone, in which **4** is virtually insoluble.

Table I. Amination of *p*-Nitrochlorobenzene (PNCB) with Ammonia in Formamide[a]

Vessel[b]	PNCB, mol	$HCONH_2$, ratio[c]	NH_3, ratio[c]	Temp, °C	Time, h[d]	% convn[e]	% yield[f]
B[g]	0.2	5.5	None	220	0.5	1.3	
A	0.5	9.0	8.0	220	0.5	High	
A	0.65	9.0	2.0	210	0.5	46	
A	1.0	3.5	2.0	220	0.5	68	
B[h]	0.2	5.0	4.0	210	0.5	90	
A	1.0	3.0	3.0	225	0.75	97	88
B	0.25	2.0	4.0	210	3.0	100	93
A	1.0	2.5	4.0	200	2.0	99	87
A	1.0	2.25	4.0	220	1.0	100	89
A	1.0	2.0	4.0	210	1.5	99.7	93

[a] Details of procedure in Experimental Section. [b] Vessel A: 432 mL capacity; vessel B, 100 mL capacity. [c] Expressed as mol/mol PNCB. [d] Excluding heating and cooling times. [e] Calculated from GC analysis for PNCB and *p*-nitroaniline. [f] Calculated from weight of crude washed product. No correction is made for the 5% handling losses during isolation. [g] Heating a similar mixture at 230 °C for 2 h caused 76% disappearance of PNCB, but formed a great deal of tar. [h] The same results were obtained when 0.01 mol of sorbitol was added to this recipe.

For preparation of large amounts of **2k** in multiple runs, the methanol filtrate and washes were used as solvent for subsequent runs; only 1 mol of new potassium hydroxide was then needed. The yield of **2k** was almost quantitative, since solubility loss was eliminated. We did not determine whether impurity buildup placed any limit on the number of times the filtrate could be recycled.

Ammonolysis of 2 and Its Salts. Preparation of 3.[21] Orienting experiments showed that equivalent results were obtained with pure **2** (thus its ammonium salt), its sodium salt, or with chloroform-washed **2k**. The latter was used in practically all the present work; it was analyzed to determine the amount of **4k** present. Typically, a mixture of 218 g, 1 mol, of **2k** containing 2–5% of **4k**, 450–500 mL of commercial formamide (pure dry solvent gave equivalent results), and 200 g, 11.8 mol, of anhydrous ammonia were heated in a 1-L bomb with *strong agitation; slower reactions were obtained in a* conventional rocking autoclave. In our apparatus, the time required to reach 130–140 °C varied from 45 to 75 min, depending upon the operator. Optimal results were obtained in 2 h at 130 °C or 1 h at 140 °C (excluding heating and cooling times). The excess ammonia was vented at room temperature, and the product slurry was filtered. The solids were washed with acetone to remove formamide, which would interfere with the Hofmann reaction; methanol was a less satisfactory wash solvent. The bomb was rinsed with water, and the combined water, filtrate, and acetone washes were further diluted and acidified to recover additional **3** as the free acid. In the best runs, the crude washed **3k** weighed 175 g, 86%, and it contained 10–15% of **4** salts. About 23 g, 14%, of **3** was obtained from the filtrate and washes, and it contained about 30% of **4**. Evidently **4** salts are more soluble in formamide than **3k**. Alternatively, the salts in the filtrate could be precipitated with acetone, though not with methanol.

In other experiments, the formamide filtrate was reused directly with fresh make-up formamide for a second amidation. Product from reused formamide contained more **4** salts.

The procedure was similar when imidazole, glycols, or other additives were included.

Pure **3** can be separated from **4** by fractional neutralization of an aqueous solution of the salts. On a large scale, successive crops were taken at pH 6.6, 6.0, 5.0, and 4.0. The first was free of **4**. The subsequent crops could be carried back through the cycle for further separation of **4**. Acetone recrystallization was more convenient for small-scale purification. However, it was unnecessary to remove **4** from **3k** destined for the Hofmann reaction.

***p*-Aminobenzoic Acid by Hofmann Degradation of 3k.** Sodium hypochlorite was prepared by passing chlorine from a *trapped* cylinder into a flask (on a balance) containing 128 g (1.6 mol) of 50% sodium hydroxide solution, 50 mL of water, and 200 g of ice until 28.2 g, 0.4 mol, had been absorbed. The ice melted during the exothermic chlorine addition and held the temperature below 5 °C. The resulting mixture was diluted to 400 mL.

To 300 mL, 0.3 mol, of the above solution, 65.4 g, 0.3 mol, of analyzed **3k** (also containing about 10% of **4k**) was added in one portion. The temperature rose from 15 to 18 °C during the 4 min required for the solid to dissolve. After no longer than 10 min, the flask was immersed in a large bath of boiling water, with magnetic stirring. At about 50 °C, a vigorous exothermic reaction carried the temperature to 65 °C in 15 s and to 92 °C in 15 s longer; the total time from 18 to 92 °C was usually just over 2 min with the concentrations specified. The mixture was held 5 min longer in the boiling water, then adjusted to pH 8.0 with sulfuric acid, stirred with 3.0 g of Darco G-60 for 10 min, then filtered. The light tan solution was mixed with 1.0 g of sodium borohydride, which decolorized the solution completely. The pH was then brought to 4.0 to precipitate terephthalic acid. At this point, pressure filtration through a heated filter would remove the **4**; the solution crystallized in a steam-heated Büchner funnel. In one experiment the mixture was diluted with 800 mL of boiling water before filtration, which removed 8.1 g, 16%, of **4**. The chilled filtrate deposited 28.5 g, 69%, of *p*-aminobenzoic acid, mp 183.5–186.0 °C (*cloudy melt*). The filtrate was extracted with three 100-mL portions of ethyl acetate, which was evaporated to give 3.1 g of amino acid, mp 184–186.5 °C. The total product, 31.6 g, represented 77% of 0.3 mol or 85% of the 0.27 mol of **3k** actually contained in the crude material. When the total product was dissolved in 400 mL of hot ethyl acetate, an additional 1.7 g of **4** was insoluble; the total **4** was 9.8 g, 0.059 mol, 19.7%.

This general procedure could be modified by adding more or less of the reagents or additional water. In most experiments, the total acids were collected after chilling the pH 4 solution, and the **4** was separated by dissolving the dried crude acid in hot ethyl acetate and filtering through a tared funnel. Experiments showed that about 7% of the amino acid remained in the filtrate from the (undiluted) pH 4 solution; it could be recovered by ethyl acetate extraction.

Amination of *p*-Chloronitrobenzene. The experiments in Table I were performed in shaker tubes lined with Hastelloy C. The 400-mL tube was charged with 0.5–1.0 mol of PCNB, 2.0–4.5 mol of formamide, and the specified amount of other additive, if any. The tube was sealed, pressure-tested, and evacuated. The tube was chilled in a −80 °C bath, *connected to an ammonia cylinder through a flexible* copper coil, and placed on a balance. The desired amount of ammonia was transferred to the shaker tube, and the weight was checked by back-weighing the ammonia cylinder. The tube was then mounted in its heating jacket on a horizontal shaker (180 strokes/min) behind a steel barricade, heated to 200–220 °C as specified in Table I, and held for the desired length of time. The tube was allowed to cool. The times in Table I do not include heating and cooling times.

The tube was vented at room temperature through a trap into a water scrubber. The product was washed out with water, and the precipitated *p*-nitroaniline was collected and washed with water until free from chlorides, then dried. It was analyzed by GC on a 20% SE-30 silicone gum rubber column, using an F&M 500 instrument with TC detector. Response factors were determined for known mixtures of PCNB and *p*-nitroaniline. When the isolation procedure was carried out with a known weight of pure *p*-nitroaniline, about 5% of the material was lost. The tabulated yield figures are not corrected for this isolation loss.

The bulk of the formamide can be recovered for reuse if the pasty reaction product is filtered and washed with several small portions of methanol or ethanol. When the alcohol has been stripped out in vacuum, the residue can be used for another run after addition of make-up formamide. The alcohol-washed filter cake is washed with water to remove ammonium chloride.

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Registry No.—Terephthalamic acid, 6051-43-0; *p*-nitrochloro-

benzene, 100-00-5; ammonia, 7664-41-7; formamide, 75-12-7; *p*-nitroaniline, 100-01-6; *p*-aminobenzoic acid, 150-13-0.

References and Notes

(1) The classical synthesis involves nitration of toluene (36% para), separation of isomers, oxidation of *p*-nitrotoluene, and reduction of the nitro group. It is not a route adaptable to large-scale manufacture of pure *p*-aminobenzoic acid because of heavy losses to unwanted isomers.
(2) The potassium salt was much easier to handle than the sodium salt.
(3) The crude product contained up to 5% each of unchanged DMT and potassium terephthalate.
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(20) This procedure is adapted from one originally devised by R. H. Sullivan.
(21) All pressure reactions must be conducted behind a suitable steel barricade with remotely actuated controls.

β-Thioxo Ketones. 2.[1] Preparation and Structure of Some Five- and Six-Membered 2-Acylcycloalkanethiones and 2-Thioacylcycloalkanones

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2-Acetylcyclohexanethione, 2-thioacetylcyclopentanone, and 2-benzoylcyclopentanethione have been synthesized by acid-catalyzed reaction of the corresponding β-diketones with H_2S, while 2-thioacetylcyclohexanone was obtained by Claisen condensation of cyclohexanone with ethyl thionoacetate. ^1H NMR, IR, and UV spectroscopic investigations have shown that these β-thioxo ketones exist as equilibrium mixtures of the tautomeric (*Z*)-enethiol and (*Z*)-enol forms, which interconvert very rapidly by intramolecular chelate proton transfer. The direction of enolization/enethiolization is determined by the relative stabilities of the respective endo- and exocyclic C=C double bonds. A small equilibrium concentration of the (*E*)-enethiol form was recognized only for 2-thioacetylcyclopentanone. Methylation as well as acetylation of the β-thioxo ketones resulted in exclusive formation of the respective *S*-methyl and *S*-acetyl derivatives.

It has been demonstrated recently[1,3] that thioacetylacetone[1,3] and similar open-chain α-unsubstituted β-thioxo ketones[1] exist in solution as equilibrium mixtures of the tautomeric (*Z*)-enol and (*Z*)-enethiol forms, which interconvert very rapidly by intramolecular chelate proton transfer. The two tautomers are distinguishable as individuals in the electron[1,3] and vibrational[1] spectra, whereas the very fast interconversion gives rise to a ^1H NMR spectrum where the positions of the resonance signals are weighted averages of the chemical shifts of the separate tautomers.[1] This suggests a very low activation energy barrier to the tautomeric interconversion. Furthermore, for all compounds investigated,[1,3] the equilibrium was found to depend distinctly on the nature of the solvent. It was therefore anticipated that properties which may influence the stability of the alternative types of C=C double bonds also must determine the position of the tautomeric equilibrium. Six-membered homocyclic compounds possessing an exocyclic C=C double bond are generally considerably less stable than prototropic isomers having an endocyclic C=C double bond, whereas the opposite is true for five-membered ring compounds.[4,5] It might therefore be expected that 2-acetylcyclohexanethione (**1**) would exist predominantly as the enethiol tautomer (**1C**), whereas the enol tautomer (**2D**) should predominate for the isomeric 2-thioacetylcyclohexanone (**2**).[3] For monothio analogues of 2-acylcyclopentanones a considerable contribution of the tautomer possessing an exocyclic C=C double bond would be expected. The purpose of the present work was primarily to demonstrate the fulfillment of these expectations, but also to extend generally our present knowledge of the tautomeric and structural properties of β-thioxo ketones.

Synthesis. 2-Acetylcyclohexanethione (**1**) was obtained as the only product by the acid-catalyzed reaction of 2-acetylcyclohexanone with H_2S under conditions very close to those applied successfully in the synthesis of thioacetylacetone.[1] It is noteworthy that no 2-thioacetylcyclohexanone (**2**) was formed by this reaction. The latter compound was, however, easily synthesized by Claisen condensation of cyclohexanone with ethyl thionoacetate.[6] 2-Thioacetylcyclopentanone (**3**) was obtained in a low yield by reaction of the corresponding β-diketone with H_2S in acidic acetonitrile solution. The product was isolated from the crude reaction mixture as its lead complex, which was decomposed to the free ligand by dilute sulfuric acid. The crude reaction mixture was not further investigated, but very probably a main component was 1,3-dimethyldicyclopentano[5,9,7,10]-2,4,6,8-tetrathiaadamantane (a formal dimer of 2-thioacetylcyclopentanethione), which in an earlier investigation[7] of this reaction was isolated as the only product. The reaction of 2-benzoylcyclopentanone with H_2S in acidic acetonitrile solution afforded as the only product 2-benzoylcyclopentanethione (**4**), which was also purified via its lead complex.