methyl iodide with 2-octylpiperidine. Reaction of the addition product with ethyl iodide gave 2-octyl-N-ethyl-N-methylpiperidinium iodide (m.p. 138–139°; m.p. of mixture with authentic sample, 138–139°).

*Anal.* Calcd. for $C_{16}H_{34}NI$: I, 34.55. Found: I, 34.61.

The remaining distilland was distilled to give a fraction (6.8 g., b.p. 110–170° at 1 mm., $n^{20}D$ 1.4692, average mol. wt. 333), and a residue (8.6 g., average mol. wt. 429) remained.

CHICAGO 37, ILLINOIS

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

# The Thermal Rearrangement of Triarylmethyl Azides[1]

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A series of triarylmethyl azides of the type $p$-X-$C_6H_4(C_6H_5)_2CN_3$, where X = H, $CH_3O$, $CH_3$, Cl, $NO_2$ and $N(CH_3)_2$, has been prepared. On heating to 170–190° these substances evolve nitrogen to give mixtures of benzophenone anils. Analyses of the benzophenones from hydrolysis of the anils were used to determine migration aptitudes of the aryl groups. These migration aptitudes are relatively insensitive to the nature of the aryl group—$p$-anisyl, for example, was only 2.5 times better than phenyl. The unsubstituted azide in solution in dibutyl carbitol, nitrobenzene or hexadecane rearranges by a first-order process, the rate of which is little affected by the nature of the solvent. Similarly, the substituted azides in dibutyl carbitol rearrange at rates which are only slightly influenced by the nature of the substituent. In both series of rate runs there are substantial, but compensating, variations in energies and entropies of activation. Possible explanations of these facts are discussed.

The acid-catalyzed rearrangement of alkyl azides has been studied fairly extensively.[3-7] A thorough investigation of migration aptitudes in this reaction has been carried out by McEwen,[6] who used benzhydryl and 1,1-diarylethyl azides, sometimes as such and sometimes generated *in situ* from the carbinol or the olefin. Migration aptitudes were qualitatively similar to those found in the pinacol rearrangement,[8] but their range was much less. $p$-Anisyl, for example, had a migration aptitude of 6.5 in the benzhydryl azide rearrangement, compared to 500 in the pinacol rearrangement.

In contrast to the extensive investigations of the acid-catalyzed rearrangement, little is known of the thermal rearrangement. Triphenylmethyl azide rearranges on heating at around 180°, the product being benzophenone anil.[9] In the rearrangement of $p$-chlorophenyl-(diphenyl)-methyl azide,[9] the migration was claimed to be entirely statistical; *i.e.*, the product was two-thirds that of phenyl migration and one-third that of $p$-chlorophenyl migration. Our aims were to check this claim, to extend the study to other migrating groups and to determine the kinetics of the reaction. The intermediate I, which would result if nitrogen evolution preceded rearrangement, is the nitrogen analog of the carbenes.[10] Migrations to this uncharged, but electron-deficient, nitrogen atom might be expected to show interesting features.

$$Ar_3C{-}\underset{\bullet\bullet}{N}{:}\quad \text{I}$$

The only one of the desired azides which had been prepared and adequately characterized prior to the present work was triphenylmethyl azide itself.[11] Of the various methods available for the synthesis of triarylmethyl azides,[12-15] the action of hydrazoic and sulfuric acids on the carbinol[15] proved to be the simplest and also the best. The azides obtained in this manner were low-melting solids with the exception of the $p$-methoxy azide. This compound refused to crystallize and appeared to contain some unreacted carbinol. Preparations of the carbinol precursors of the azides are described under Experimental. Except for a new preparation of the $p$-nitro carbinol (treatment of diphenyl-($p$-nitrophenyl)-methane with N-bromosuccinimide followed by hydrolysis of the resulting bromide), standard procedures were used.

Experiments on the unsubstituted azide showed that it evolved nitrogen smoothly on heating to 170–200°. The residue, when chromatographed on alumina, gave 75% of benzophenone anil and an amorphous, dark brown material which could not be characterized. The anil was shown independently to be stable to the reaction conditions. The next step was to devise a procedure for analysis of the anil mixtures from the substituted azides. For this purpose the anils were hydrolyzed with a mixture of acetic and hydrochloric acids and the resulting benzophenone mixtures analyzed by comparison of their ultraviolet or infrared spectra with those of synthetic mixtures. Details of the spec-

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[1] This work was supported in part by the Office of Ordnance Research, U. S. Army.

[2] National Science Foundation Fellow, 1955–1957.

[3] (a) T. Curtius and A. Darapsky, *J. prakt. Chem.*, **63**, 428 (1901); (b) T. Curtius and A. Darapsky, *Ber.*, **35**, 3229 (1902); (c) T. Curtius, *ibid.*, **45**, 1057 (1912); (d) T. Curtius and G. Ehrhart, *ibid.*, **55**, 1559 (1922).

[4] J. H. Boyer, F. C. Canter, J. Hamer and R. K. Putney, THIS JOURNAL, **78**, 325 (1956).

[5] (a) K. W. Sherk, A. G. Houpt and A. W. Browne, *ibid.*, **62**, 329 (1940); (b) S. N. Ege and K. W. Sherk, *ibid.*, **75**, 354 (1953).

[6] (a) C. H. Gudmundsen and W. E. McEwen, *ibid.*, **79**, 329 (1957); (b) R. F. Tietz and W. E. McEwen, *ibid.*, **77**, 4007 (1955); (c) D. R. Nielsen and W. E. McEwen, *ibid.*, **76**, 4042 (1954); (d) W. E. McEwen and N. B. Mehta, *ibid.*, **74**, 526 (1952); (e) W. E. McEwen, M. Gilliland and B. I. Sparr, *ibid.*, **72**, 3212 (1950).

[7] J. H. Boyer and F. C. Canter, *Chem. Revs.*, **54**, 1 (1954).

[8] W. E. Bachmann and J. W. Ferguson, THIS JOURNAL, **56**, 2081 (1934).

[9] J. K. Senior, *ibid.*, **38**, 2718 (1916).

[10] See footnote 9 of W. von E. Doering and L. H. Knox, *ibid.*, **78**, 4947 (1946).

[11] $p$-Chlorophenyl-(diphenyl)-methyl azide was obtained by Senior (ref. 9) as an uncrystallizable gum.

[12] H. Wieland, *Ber.*, **42**, 3020 (1909).

[13] I. Lifschitz and G. Girbes, *ibid.*, **61**, 1463 (1928).

[14] C. G. Swain, C. B. Scott and K. H. Lohmann, THIS JOURNAL, **75**, 136 (1953).

[15] C. L. Arcus and R. J. Mesley, *Chemistry & Industry*, 701 (1951).

trophotometric analyses are given under Experimental. In selected cases it was shown that chromatography of the anil mixtures caused no product fractionation and that the hydrolysis was quantitative.

The migration aptitudes determined in this fashion are recorded in Table I. With the exception of *p*-dimethylaminophenyl, reproducibility was good. Accuracy is difficult to assess and, although many precautions against systematic error were taken, we do not wish to assign too much quantitative significance to these figures. Around ±20% would seem a reasonable limit of error.

TABLE I

MIGRATION APTITUDES IN THE THERMAL REARRANGEMENT OF $p$-X-$C_6H_4(C_6H_5)_2CN_3$ AT 185°

| X | Migration aptitude[a] | Av. migration aptitude | Av. anil yield, % | Av. $N_2$ yield, % |
|---|---|---|---|---|
| $(CH_3)_2N$ | 4.6 | | | |
| | 8.8 | 6.7 | 70 | 86 |
| $OCH_3$ | 2.5 | | | |
| | 2.5 | | | |
| | 2.6 | 2.5 | 70 | .. |
| $CH_3$ | 1.8 | | | |
| | 1.8 | 1.8 | 66 | 97 |
| H | (1) | (1) | 75 | 95 |
| Cl | 0.34 | | | |
| | .38 | | | |
| | .46 | 0.39 | 43 | 94 |
| $NO_2$ | 0.20 | | | |
| | .20 | | | |
| | .20 | 0.20 | 75 | 100 |
| $CH_3O$[b] | 1.2 | | | |
| | 1.4 | 1.3 | .. | .. |
| $NO_2$[b] | 0.16 | 0.16 | .. | .. |

[a] Each figure represents an entirely separate run and not merely repeated analyses. [b] Reactions run in dibutyl carbitol solvent. [c] Since the starting azide was not pure, a nitrogen yield would be meaningless.

Since most of the kinetic runs (*vide infra*) were done in dibutyl carbitol, the *p*-methoxy and *p*-nitro azides were heated in this solvent and the products analyzed to see whether there was any significant solvent effect on migration aptitudes. Both migration aptitudes were lowered substantially (Table I), a fact difficult to explain in any simple manner. Since the solvent was removed *in vacuo*, preferential loss of one product through volatilization may have occurred.

The rate of decomposition of triphenylmethyl azide was determined over the range 170–190° in three solvents by following nitrogen evolution manometrically. The decomposition obeyed the first-order rate law with good precision and the rate constant remained unchanged over a 2.5-fold variation in initial azide concentration. Of the three solvents used, dibutyl carbitol was the most convenient to purify and handle and consequently was used in work on rates of decomposition of the substituted azides. Each run on a given compound under a given set of conditions was repeated two or three times. Reproducibility was generally 1–2%. Rate constants are recorded in Table II. Each compound was investigated at three temperatures and the enthalpies and entropies of activation calculated from Arrhenius plots of the data (method of least squares). These values are given in Table III.

TABLE II

RATES OF REARRANGEMENT OF $p$-X-$C_6H_4(C_6H_5)_2CN_3$

| X | Solvent | $t$, °C.[a] | $10^4k$, sec.$^{-1}$ [b] |
|---|---|---|---|
| H | Nitrobenzene | 169.4 | 1.26 ± 0.01 |
| H | Nitrobenzene | 179.8 | 2.73 ± .01 |
| H | Nitrobenzene | 189.6 | 6.29 ± .13 |
| H | Hexadecane | 169.4 | 0.96 ± .01 |
| H | Hexadecane | 179.7 | 2.28 ± .02 |
| H | Hexadecane | 190.5 | 5.95 ± .16 |
| H | Dibutyl carbitol | 169.2 | 1.08 ± .02 |
| H | Dibutyl carbitol | 179.8 | 2.46 ± .02 |
| H | Dibutyl carbitol | 190.2 | 5.82 ± .07 |
| $CH_3$ | Dibutyl carbitol | 169.7 | 1.26 ± .01 |
| $CH_3$ | Dibutyl carbitol | 179.8 | 2.78 ± .01 |
| $CH_3$ | Dibutyl carbitol | 191.0 | 6.04 ± .09 |
| $CH_3O$ | Dibutyl carbitol | 169.6 | 1.80 ± .05 |
| $CH_3O$ | Dibutyl carbitol | 179.8 | 3.91 ± .02 |
| $CH_3O$ | Dibutyl carbitol | 190.5 | 8.25 ± .01 |
| $(CH_3)_2N$ | Dibutyl carbitol | 169.8 | 3.24 ± .02 |
| $(CH_3)_2N$ | Dibutyl carbitol | 179.8 | 6.55 ± .02 |
| $(CH_3)_2N$ | Dibutyl carbitol | 190.4 | 12.2 ± .1 |
| Cl | Dibutyl carbitol | 169.4 | 1.12 ± .01 |
| Cl | Dibutyl carbitol | 179.8 | 2.85 ± .03 |
| Cl | Dibutyl carbitol | 191.0 | 7.04 ± .04 |
| $NO_2$ | Dibutyl carbitol | 169.7 | 1.10 ± .01 |
| $NO_2$ | Dibutyl carbitol | 179.8 | 2.82 ± .04 |
| $NO_2$ | Dibutyl carbitol | 190.4 | 6.86 ± .04 |

[a] Temperature control was usually good to ±0.1°, but in a few experiments the range was wider (up to 0.3°). [b] Each constant is the average of two or more runs, with the indicated average deviations.

TABLE III

ENTHALPIES AND ENTROPIES OF ACTIVATION IN THE THERMAL REARRANGEMENT OF $p$-X-$C_6H_4(C_6H_5)_2CN_3$

| Solvent | X | $\Delta H^{\ddagger}$,[a] kcal./mole | $\Delta S^{\ddagger}$,[b] cal./mole-°C. |
|---|---|---|---|
| Nitrobenzene | H | 31.3 | −11.0 |
| Hexadecane | H | 34.3 | − 4.7 |
| Dibutyl carbitol | H | 32.0 | − 9.8 |
| Dibutyl carbitol | Cl | 33.8 | − 5.6 |
| Dibutyl carbitol | $NO_2$ | 34.3 | − 4.6 |
| Dibutyl carbitol | $CH_3$ | 29.0 | −16.1 |
| Dibutyl carbitol | $OCH_3$ | 28.9 | −16.0 |
| Dibutyl carbitol | $N(CH_3)_2$ | 25.4 | −22.5 |

[a] Calculated from slopes (method of least squares) of Arrhenius plots. Standard deviations averaged 1.1 kcal./mole. [b] From intercepts of Arrhenius plots. Standard deviations averaged 0.8 cal./mole-°C.

To facilitate discussion of the kinetic results, rates at 180.0° (taken from the Arrhenius plots), relative to triphenylmethyl azide in dibutyl carbitol, are given in Table IV. An immediately apparent feature of our results is the relative insensitivity of rates and migration aptitudes to the nature of the *p*-substituent. One might reasonably conclude that there is little or no aryl participation in the rate-determining step. In general outline at least, the evidence is consistent with a slow nitrogen loss to give the intermediate I, followed by a fast aryl-migration step.

A comparison of migration aptitudes and rates

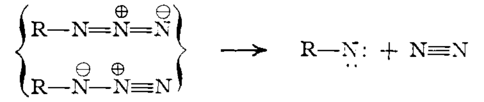
TABLE IV

RELATIVE RATES OF DECOMPOSITION OF $p$-$XC_6H_4(C_6H_5)_2CN_3$ AT 180.0°

| Solvent | X | Rate |
|---|---|---|
| Hexadecane | H | 0.94 |
| Nitrobenzene | H | 1.13 |
| Dibutyl carbitol | H | (1.00) |
| Dibutyl carbitol | Cl | 1.11 |
| Dibutyl carbitol | $NO_2$ | 1.07 |
| Dibutyl carbitol | $CH_3$ | 1.08 |
| Dibutyl carbitol | $OCH_3$ | 1.53 |
| Dibutyl carbitol | $N(CH_3)_2$ | 2.50 |

of rearrangement in the acid-catalyzed reaction led Gudmundsen and McEwen[6a] to conclude that nitrogen loss and rearrangement could not be concerted. The same approach to the present results was considered but rejected. Since neither our rates nor our migration aptitudes follow the Hammett equation, the graphical approach of McEwen does not yield a straight line. Even a qualitative comparison might be misleading, since the precision of the rate measurements is much superior to the precision of the migration aptitudes. Furthermore, our over-all rates apparently include a contribution from a non-rearranging side reaction, since nitrogen yields exceeded anil yields in all reactions (Table I). Finally, rates were determined in dibutyl carbitol and migration aptitudes in the absence of solvent. Our results on this point, though inconclusive, suggest that the solvent may alter migration aptitudes appreciably (*vide supra*).

In fact, closer examination of the evidence leads one to suspect the two-stage mechanism in spite of its surface plausibility. If the substituents exert a simple inductive effect on the rate of nitrogen loss, one might expect the rates to follow the Hammett equation. Instead, all substituted azides react faster than triphenylmethyl azide itself. Similarly, the variation of rate with solvent, though not large, is definitely in the direction of greater speed in the more polar solvents. If the azide went to a discrete intermediate I, there would be a charge dispersal in the transition state and the opposite behavior might be expected



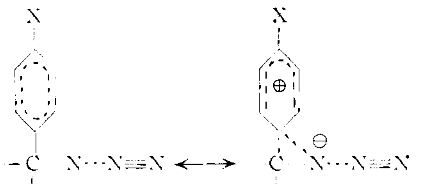
$$\left\{\begin{matrix} R{-}N{=}\overset{\oplus}{N}{=}\overset{\ominus}{N} \\ R{-}\overset{\ominus}{N}{-}\overset{\oplus}{N}{\equiv}N \end{matrix}\right\} \longrightarrow R{-}\ddot{N}{:} + N{\equiv}N$$

For reasons given below, it would be unwise to conclude too much from relative rates in this reaction, but the above deductions provide at least a starting point from which the remainder of the evidence can be discussed.

The enthalpies and entropies of activation vary over such a wide range that one can scarcely consider them to be determined solely by an inductive effect on nitrogen loss. The apparent insensitivity of rate to the nature of the $p$-substituent and the solvent is in fact a consequence of a linear relationship between enthalpies and entropies of activation, so that one nearly cancels the effect of the other. Such relationships have been observed by many other workers and have recently been reviewed.[16] A consequence of the relationship is that there will be an "isokinetic temperature," calculable from the slope of a $\Delta H^{\ddagger}$ *vs.* $\Delta S^{\ddagger}$ plot, at which all reactions following the relation will go at the same rate within the precision of the fit. The isokinetic temperature for the substituted azides in dibutyl carbitol is 188°. A linear relationship between $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ also exists for triphenylmethyl azide in the three solvents. Here the isokinetic temperature is 194°. Since our rates were determined at temperatures close to the isokinetic temperature in both instances, consideration of rates alone could lead to erroneous conclusions about the nature of the reaction.

The origins of isokinetic relationships are uncertain. Many are undoubtedly artifacts, but the spread of 9 kcal./mole in $\Delta H^{\ddagger}$ and 18 cal./mole-°C. in $\Delta S^{\ddagger}$, as well as the regular variation of $\Delta H^{\ddagger}$ with the electronic nature of the substituent, argue for the genuineness of our relation. A frequently-offered explanation is based on solvation, and this we feel is the source of the present isokinetic relationship.

Let us assume that nitrogen loss does occur with some degree of aryl participation. The transition state may then be viewed as a resonance hybrid of the structures III and IV. The more electron-donating the $p$-substituent X is, the greater the degree of participation and hence the greater the contribution of IV. This process will lower the activation energy by aiding loss of nitrogen but, since IV possesses charge separation, more molecules of solvent will be "frozen" around the transition state and hence a lower (more negative) entropy of activation is to be expected. Similarly, increasing the polarity of the solvent should increase the contribution of IV and lead to the observed behavior of the entropies and enthalpies of activation.



III IV

An isokinetic relationship also has been reported in the thermal decomposition of $m$- and $p$-substituted benzazides.[17] Here the interpretation is complicated by resonance effects on charge distribution in the ground state, but otherwise the same factors may be operating as in our reactions.

The thermal decomposition of triarylmethyl azides thus is most reasonably viewed as proceeding with an appreciable degree of aryl participation. The apparent incursion of a non-rearranging side reaction does not constitute an objection, since participation does not necessarily lead to rearrangement.[18] Although the evidence is certainly suggestive, it is by no means conclusive and further studies of structure and solvent effects in azide decompositions would be desirable.

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[16] J. E. Leffler, *J. Org. Chem.*, **20**, 1202 (1955).

[17] Y. Yukawa and Y. Tsuno, THIS JOURNAL, **79**, 5530 (1957).

[18] S. Winstein, M. Brown, K. C. Schreiber and A. H. Schlesinger, *ibid.*, **74**, 1140 (1952).

## Experimental[19]

**Preparation of Triarylcarbinols.**—These were, with the exception of (*p*-nitrophenyl)-diphenylcarbinol, prepared by conventional procedures: (1) addition of the arylmagnesium bromide or aryllithium to benzophenone, (2) addition of phenylmagnesium bromide to the substituted benzophenone or (3) addition of phenylmagnesium bromide to the substituted methyl benzoate. The products so obtained were: (*p*-**Chlorophenyl**)-**diphenylcarbinol**, m.p. 85–86° (lit.[20] 85°); (*p*-**anisyl**)-**diphenylcarbinol**, m.p. 84° (lit.[21] 84°); **diphenyl**-(*p*-**tolyl**)-**carbinol**, m.p. 77.5–78.5° (lit.[22] 75–77°); (*p*-**dimethylaminophenyl**)-**diphenylcarbinol**, m.p. 89–90° (lit.[23] 87–88°).

**Diphenyl-(*p*-nitrophenyl)-carbinol.**—A mixture of 0.017 mole of **diphenyl-(*p*-nitrophenyl)-methane**[24] and 0.034 mole of N-bromosuccinimide was refluxed in 20 ml. of carbon tetrachloride for 1.5 hours. About half of the solvent was evaporated and the mixture filtered. Removal of the remaining solvent left an orange oil. The oil (presumably the bromide) was dissolved in 50% acetone–water and allowed to stand for several days. The mixture was extracted with hexane and the extract washed with sodium carbonate solution and dried. Removal of the hexane left pale yellow crystals which, on recrystallization from hexane, had m.p. 97.5–98.5° (lit.[25] 97–98°). The yield was 37% of purified product.

**Preparation of Triarylmethyl Azides.**—In a 3-neck flask fitted with stirrer and dropping funnel were placed 5 g. of sodium azide, 5 ml. of water and 20 ml. of chloroform (previously washed with concd. sulfuric acid). To this mixture was added a solution of 5 g. of the triarylcarbinol in 50 ml. of chloroform. The flask was cooled in an ice-bath and there was added dropwise 5 ml. of concd. sulfuric acid. After an hour, the reaction mixture was neutralized with sodium hydroxide and the chloroform layer removed. The solvent was removed and the residual oil taken up in hexane. Purification was by recrystallization from hexane, sometimes in combination with chromatography on alumina. Yields are of purified material and reflect difficulty of purification rather than amount actually produced.

**Triphenylmethyl azide** was obtained in 88% yield, m.p. 64–65° (lit.[12] 64°).

(*p*-**Chlorophenyl**)-**diphenylmethyl azide** was obtained in 77% yield, m.p. 50–51°. *Anal.* Calcd. for $C_{19}H_{14}N_3Cl$: C, 71.34; H, 4.42. Found: C, 71.33; H, 4.62.

**Diphenyl-(*p*-nitrophenyl)-methyl azide** was obtained in 39% yield, m.p. 62.5–63.5°. *Anal.* Calcd. for $C_{19}H_{14}N_4O_2$: C, 69.07; H, 4.27. Found: C, 69.06; H, 4.28.

**Diphenyl-(*p*-tolyl)-methyl azide** was obtained in 76% yield, m.p. 48–48.5°. *Anal.* Calcd. for $C_{20}H_{17}N_3$: C, 80.24; H, 5.72. Found: C, 80.17; H, 5.88.

(*p*-**Dimethylaminophenyl**)-**diphenylmethyl azide** was obtained in 42% yield, m.p. 79–80°. *Anal.* Calcd. for $C_{21}H_{20}N_4$: C, 76.79; H, 6.15. Found: C, 76.74; H, 6.10.

(*p*-**Anisyl**)-**diphenylmethyl azide** was an uncrystallizable oil. The infrared spectrum showed hydroxyl as well as azide absorption. Attempts to remove the hydroxyl-containing impurity by chromatography on alumina were unsuccessful. A nitrogen analysis gave N, 11.62; calcd. for $C_{20}H_{17}N_3O$: N, 13.32. Assuming the impurity to be unreacted carbinol, the oil is 87% azide and 13% carbinol.

**Kinetics of the Decomposition of Triarylmethyl Azides.**—The various solvents used were: nitrobenzene was Eastman Kodak Co. white label, m.p. 5–6°. Hexadecane (Eastman Kodak Co. practical) was heated on the steam-bath with concd. sulfuric acid for three days and distilled. A fraction boiling 90–100° (3 mm.), $n^{25}\text{D}$ 1.4360, was taken. Di-*n*-butyl carbitol (Carbide and Carbon) was dried over Linde 4A Molecular Sieves and distilled. A fraction of b.p. 64° (3 mm.), $n^{25}\text{D}$ 1.4258, was taken.

The reaction vessel was a 50-ml., r.b., flask connected by a capillary neck to a 3-way stopcock lubricated with Dow-Corning 200 silicone oil. One arm of the stopcock led to a capillary mercury manometer and the other could be opened to the atmosphere for sample introduction. The thermostat was a two-liter beaker filled with bath wax and surrounded by a heating mantle which provided continuous heating. In the bath were placed a thermometer, stirrer, knife-blade heater and thermoregulator. This arrangement usually kept the temperature within 0.1–0.2° of the set value.

In a run, the bulk of the solvent (14 ml.) was saturated with nitrogen and brought to thermal equilibrium in the reaction vessel. One milliliter of a solution of the azide in the same solvent (concentration calculated to give a final concentration of *ca.* 0.020 *M*) was injected through the stopcock with a hypodermic syringe. Several minutes was required for the reaction mixture to regain thermal equilibrium, so pressure readings were not started until 5–10 min. had elapsed. The Guggenheim differential method[26] was used to determine the rate constants.

**Rearrangement of Triphenylmethyl Azide.**—One gram of triphenylmethyl azide was placed in a test-tube and heated in an oil-bath at 185° for two hours. The dark residue was chromatographed on alumina using 50% benzene–pentane as eluent. The process was repeated using pentane as eluent. The yellow benzophenone anil, m.p. 110–112° (lit.[27] 112°), was obtained in an average yield of 0.67 g. (75%).

Stability of the anil to the conditions of the reaction was next demonstrated. A 0.50-g. sample of the anil was heated at 185° for two hours and the product (slightly darkened) was chromatographed to yield 0.46 g. (92%) of pure anil.

**Hydrolysis of the Anils.**—The procedure given for benzophenone anil was also applied to the substituted anils. To 0.2 g. of benzophenone anil were added 2 ml. of acetic acid, 5 drops of concd. hydrochloric acid and 5 drops of water. The mixture was left standing for several hours, diluted with a few ml. of water, made basic with dilute sodium hydroxide solution and extracted with ether. The ether solution was extracted with a little dilute hydrochloric acid and the aqueous layer made alkaline and treated with benzoyl chloride. There was obtained 0.15 g. of benzanilide (theoretical 0.154 g.). The solvent was removed from the ether layer and the residue dissolved in 95% ethanol for spectrophotometric analysis, using the benzophenone maximum at 254 mμ. In this manner the theoretical amount of benzophenone ($7.8 \times 10^{-4}$ mole) was shown to be present.

**Rearrangement of Substituted Triphenylmethyl Azides.**—The procedures for the rearrangement of the azides and hydrolysis of the products were essentially the same as for triphenylmethyl azide itself. It was shown in several cases that chromatography of the anil mixtures caused no product fractionation. This was done by rechromatographing and analyzing anil mixtures of known (previously analyzed) composition. In some cases the benzophenone mixtures were chromatographed as well. Impurities persisted through this treatment in a few instances and were dealt with as described under "Product Analysis."

The *p*-nitro and *p*-methoxy azides were also rearranged in dibutyl carbitol solution (about 0.3 *M*) to determine the effect of solvent on migration aptitude. Most of the solvent was removed *in vacuo* and the residue worked up by the procedure used for runs in the absence of solvent.

**Product Analysis.**—Migration aptitudes were determined by analyzing the benzophenone mixtures. The ultraviolet spectra of benzophenone and the substituted benzophenone differed sufficiently with three *p*-substituents: nitro, methoxyl and dimethylamino. Ultraviolet spectra of the pure standards and of the ketone mixtures were determined in 95% ethanol solution. The data were treated by the graphical procedure of Dewar,[28] which improves precision by utilizing many wave lengths and also allows the detection (and often the identification) of absorbing impurities. In this fashion the ketones from the *p*-nitro azide were found to contain no absorbing impurities while those from the *p*-methoxy azide were shown to be contaminated with a little (*p*-anisyl)-diphenylmethylcarbinol, which was then allowed for in arriving at a final value for the ketone analysis. The ketones from the *p*-dimethylamino azide contained an absorbing contaminant which could not be identified.

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[19] Melting points and boiling points are uncorrected. Analyses by Miss A. Smith and ultraviolet spectra by Mr. C. A. Whiteman.

[20] M. Gomberg and L. H. Cone, *Ber.*, **39**, 3278 (1906).

[21] A. Baeyer and V. Villiger, *ibid.*, **35**, 3027 (1902).

[22] H. H. Hatt, *J. Chem. Soc.*, 1630 (1929).

[23] P. Pfeiffer and H. Hoyer, *Ber.*, **65**, 919 (1932).

[24] A. Baeyer and R. Lohr, *ibid.*, **23**, 1622 (1890).

[25] A. Baeyer and V. Villiger, *ibid.*, **37**, 606 (1904).

[26] E. A. Guggenheim, *Phil. Mag.*, **2**, 1538 (1926); see A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 48.

[27] E. Knoevenagel, *J. prakt. Chem.*, [2] **89**, 1 (1914).

[28] M. J. S. Dewar and D. S. Urch, *J. Chem. Soc.*, 345 (1957).

The infrared spectra of the ketone mixtures from the *p*-chloro and *p*-methyl azides contained no peaks which were not attributable to one or both of the pure reference compounds, indicating the absence of any appreciable concentrations of absorbing impurities. The spectra of substituted and unsubstituted benzophenones differed sufficiently for accurate analysis only in the region 800–860 cm.$^{-1}$ (*p*-substituted phenyl). Since benzophenone itself was thus determined by difference, non-absorbing impurities could seriously affect the analysis. Consequently the spectrum of the unknown mixture in chloroform solution was determined and known mixtures prepared at such concentrations that the carbonyl absorption (1660–1670 cm.$^{-1}$) was essentially the same as that of the unknown. This correction was unnecessary for the products from the *p*-methyl azide, but did considerably improve the precision of the analyses for the products from the *p*-chloro azide.

In two cases (*p*-methoxyl and *p*-nitro), the identities of the anilines from hydrolysis of the anil mixtures were established. The anilines were converted to N-arylbenzamides by the Schotten–Baumann method. The ultraviolet spectra of these mixtures in 95% ethanol were compared with the spectra of authentic samples of the appropriate *m*- and *p*-substituted N-arylbenzamides again using the Dewar[28] procedure. Excellent straight lines were obtained when the mixtures were assumed to consist of N-arylbenzamide and *p*-substituted N-arylbenzamide, while the fit was completely unsatisfactory when *m*-substituted N-arylbenzamide was assumed to be present. One new compound, benz-*m*-anisidide, m.p. 110.5–111.5°, was prepared in the course of this work. *Anal.* Calcd. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.76. Found: C, 73.73; H, 5.74.

**Nitrogen Yields.**—A 100–200-mg. sample of the azide was heated at 186° for 4 hours in a test-tube connected to a mercury-filled gas buret. Readings were taken before the heating was started and after the reaction vessel had cooled to room temperature. Results (assuming one mole of nitrogen per mole of azide) are recorded in Table I and were reproducible to about 1%.

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# Amino Acids. VI. Preparation and Chemistry of ω-Carbalkoxyalkyl Isothiocyanates

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A series of ω-carbalkoxyalkyl isothiocyanates has been prepared from the corresponding amino acid ester hydrochlorides. Addition of the isothiocyanates to amines gave a number of unsymmetrical ω,ω′-disubstituted thioureas. Treatment of disodium ε-carboxypentyldithiocarbamate with basic lead acetate gave 1,3-di-(5-carboxypentyl)-thiourea as the major product as well as 5-carboxypentyl isothiocyanate. The reaction between 1-phenyl-3-(2-carboxyethyl)-thiourea and acetic anhydride gave a mixture of 3-phenyl-2-thiohydrouracil and 1-acetyl-3-phenyl-2-thiohydrouracil.

A series of ω-carbalkoxyalkyl isothiocyanates were prepared as part of a study of functional derivatives of thiourea. The first two members of the series, namely, carbethoxy isothiocyanate and carbethoxymethyl isothiocyanate, have been known for some time. Carbethoxy isothiocyanate[1,2] was prepared by the reaction of ethyl chloroformate with potassium thiocyanate, while carbethoxymethyl isothiocyanate was prepared by treating ethyl glycinate with thiophosgene[3] and by pyrolysis of the ethyl carbethoxymethyldithiocarbamate.[4] Since the completion of the present work, Kjaer and Gmelin[5] have reported the isolation of 3-carbomethoxypropyl isothiocyanate as a component of a naturally occurring glycoside, glucoerypestrin.

The procedure used in preparing the carbalkoxyalkyl isothiocyanates listed in Table I was based on the earlier observations of Kaluza.[6] He found that N-substituted dithiocarbamates on pyrolysis gave the corresponding isothiocyanates. Recently, Hodgkins and Ettlinger[7] showed that carbethoxydithiocarbamates are decomposed into isothiocyanates readily at room temperature by aqueous alkali or by triethylamine in chloroform solution. They prepared the carbethoxydithiocarbamate in dioxane solution. It has now been found that replacement of the dioxane solvent with chloroform or methylene dichloride prevents the precipitation of triethylamine hydrochloride which eliminates the filtration step. Moreover, the amine could be used in the form of its hydrochloride if an additional equivalent of triethylamine were used in the reaction. Thus it was not necessary to isolate the reactive free amino acid esters.

TABLE I

CARBALKOXYALKYL ISOTHIOCYANATES, $ROOC(CH_2)_nNCS$

| R | $n$ | Yield, % | B.p. °C. | B.p. Mm. | $n^{25}D$ | $d^{20}_4$ | Formula | Carbon, % Calcd | Carbon, % Found | Hydrogen, % Calcd. | Hydrogen, % Found | Nitrogen, % Calcd. | Nitrogen, % Found | Sulfur, % Calcd. | Sulfur, % Found |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Methyl | 2 | 81.0 | 110–112 | 1.0 | 1.5036 | 1.193 | $C_5H_7NO_2S$ | 41.36 | 41.76 | 4.86 | 5.16 | 9.65 | 9.61 | 22.08 | 21.74 |
| Ethyl | 2 | 42.4 | 92–95 | 0.04 | 1.4904 | 1.132 | $C_6H_9NO_2S$ | 45.27 | 44.92 | 5.70 | 5.92 | 8.80 | 8.56 | 20.12 | 19.75 |
| Methyl[a] | 3 | 81.2 | 64–67 | .17 | 1.5059 | 1.135 | $C_6H_9NO_2S$ | 45.27 | 45.06 | 5.70 | 5.65 | 8.80 | 8.67 | 20.12 | 19.95 |
| Methyl | 5 | 36.9 | 120–122 | .30 | 1.5000 | 1.101 | $C_8H_{13}NO_2S$ | 51.30 | 51.66 | 7.00 | 7.06 | 7.48 | 7.84 | 17.13 | 17.30 |
| Methyl | 10 | 59.8 | 166–168 | .1 | 1.4879 | 1.022 | $C_{13}H_{23}NO_2S$ | 60.65 | 61.01 | 9.01 | 9.07 | 5.44 | 5.45 | 12.46 | 12.36 |

[a] Kjaer and Gmelin[5] report b.p. 70° (0.2 mm.), $n^{25}D$ 1.5066.

5-Carboxypentyl isothiocyanate was prepared by the lead acetate process.[8] The disodium salt of 5-carboxypentyldithiocarbamate on treatment

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(1) A. E. Dixon and J. Taylor, *J. Chem. Soc.*, **93**, 697 (1908).

(2) C. W. Capp, A. H. Cook, J. D. Downer and I. Heilbron, *ibid.*, 1342 (1948).

(3) T. B. Johnson and E. H. Hemingway, THIS JOURNAL, **38**, 1550 (1916).

(4) T. B. Johnson and A. G. Renfrew, *ibid.*, **47**, 242 (1925).

(5) A. Kjaer and R. Gmelin, *Acta Chem. Scand.*, **11**, 577 (1957).

(6) (a) L. Kaluza, *Monatsh.*, **30**, 717 (1909); (b) **33**, 364 (1912).

(7) J. E. Hodgkins and M. G. Ettlinger, *J. Org. Chem.*, **21**, 404 (1956).

(8) M. Delepine, *Compt. rend.*, **144**, 1125 (1907).