

## On the 2,5-Diaryltetrazole Synthesis of Dimroth and Merzbacher (1,2)

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Benzaldehyde phenylhydrazone and phenyl azide gave 2,5-diphenyltetrazole and aniline when heated in ethanolic sodium ethoxide. Benzaldehyde *p*-bromophenylhydrazone and phenyl azide gave 2-*p*-bromophenyl-5-phenyltetrazole and aniline. No *p*-bromoaniline was formed. These observations of Dimroth and Merzbacher (5) and analogous qualitative observations (6-8) identify the aryl group of the azide utilized in the reaction with that of the aryl amine produced.

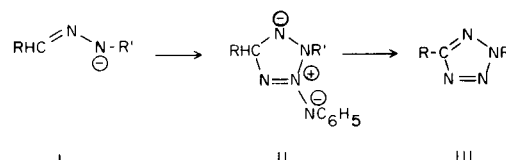
We have reconfirmed this result and made it quantitative through a  $^{14}\text{C}$ -labeling experiment.

From phenyl azide and benzaldehyde  $1\text{-}^{14}\text{C}$ -phenylhydrazone was obtained 2,5-diphenyltetrazole (1.0221  $\mu\text{C}/\text{mmole}$ ) and aniline (0.0086  $\mu\text{C}/\text{mmole}$ ). Thus, 99.17% of the radioactivity found in the two products resided in the tetrazole, demonstrating that at least this proportion of the reaction occurs with incorporation of the *N*-aryl group of the hydrazone as the *N*-aryl group of the tetrazole.

This result, unlike those obtained earlier (5-8), is not subject to the uncertainties associated with basing conclusions on the isolation of only one of two possible products in less than quantitative yield.

Although the 0.83% of label in the aniline derivative might be taken as indicating a minor pathway involving a 1,3-cycloaddition of phenyl azide with the C-N double bond of the hydrazone, followed by elimination of aniline, this is not a necessary conclusion. A slight contamination of the benzanilide by a radioactive impurity or an unsuspected minor elimination of  $^{14}\text{C}$ -aniline through base-catalyzed decomposition of benzaldehyde  $1\text{-}^{14}\text{C}$ -phenylhydrazone could account for the observed activity.

The mechanism of the tetrazole synthesis has not been the subject of investigation or public speculation. The view of the reaction that we are tentatively adopting as a guide to further experimentation postulates a 3+2-cycloaddition between the anionic species I and phenyl azide. This cycloaddition of a 4  $\pi$ -electron system across the terminal nitrogens of the azide would be allowed to be a concerted process (9). Tautomerization and elimination of  $\text{C}_6\text{H}_5\text{NH}_2$  would convert the initial cycloadduct II to the isolable 2,5-disubstituted tetrazole III.



## EXPERIMENTAL (10)

Benzaldehyde  $1\text{-}^{14}\text{C}$ -Phenylhydrazone.

From 5.7 g. (0.0394 mmole) of phenylhydrazone- $1\text{-}^{14}\text{C}$  hydrochloride (1.26  $\mu\text{C}/\text{mmole}$ ; Tracerlab; Waltham, Massachusetts), 5.778 g. (39.96 mmole) of unlabeled phenylhydrazone hydrochloride, and 6.367 g. (60 mmole) of benzaldehyde was obtained 3.60 g. of benzaldehyde  $1\text{-}^{14}\text{C}$ -phenylhydrazone after four recrystallizations from 95% ethanol. The product had an activity of 0.9724  $\mu\text{C}/\text{mmole}$  after three recrystallizations, and 0.9784  $\mu\text{C}/\text{mmole}$  after four.

Benzaldehyde phenylhydrazone, dissolved in the solution for liquid scintillation counting, appeared faintly yellow; this coloration probably caused inefficient detection of radioactivity and a low determination of specific activity for the compound.

2,5-Diphenyltetrazole- $^{14}\text{C}$ .

Benzaldehyde  $1\text{-}^{14}\text{C}$ -phenylhydrazone (1.96 g., 0.01 mole; 0.978  $\mu\text{C}/\text{mmole}$ ), 0.54 g. of sodium dissolved in 10.8 ml. of methylcellosolve, and phenyl azide (1.25 g., 0.01 mole) were combined and heated to reflux at  $105\text{-}110^\circ$  for 7 hours. The reaction mixture was cooled, diluted with 18 ml. of 2*N* hydrochloric acid, and filtered. The filtrate was saved and the precipitate obtained was recrystallized seven times from absolute methanol. The white needles of 2,5-diphenyltetrazole had m.p.  $101\text{-}102^\circ$  [lit (5) m.p.  $101\text{-}102^\circ$ ]; 0.45 g. (20.2% yield). The tetrazole had an activity of 1.0206  $\mu\text{C}/\text{mmole}$  after the sixth recrystallization and 1.0221  $\mu\text{C}/\text{mmole}$  after the seventh.

## Benzanilide.

The filtrate from the synthesis of 2,5-diphenyltetrazole- $^{14}\text{C}$  was neutralized with 20% sodium hydroxide and extracted with ether. The ethereal solution was concentrated and treated with 1.75 ml. (2.1 g., 0.015 mole) of benzoyl chloride and 8 ml. of 20% sodium hydroxide. The benzanilide obtained was recrystallized five times from 95% ethanol: it had m.p.  $160\text{-}161^\circ$  [lit (11) m.p.  $161^\circ$ ], 0.72 g. (36.5% yield based on benzaldehyde  $1\text{-}^{14}\text{C}$ -phenylhydrazone); 0.0086  $\mu\text{C}/\text{mmole}$  after the fourth recrystallization and after the fifth.

## REFERENCES

- (1) Part XXII in a series on cycloadditions. Part XXI: J. A. Kapecki and J. E. Baldwin, to be published.
- (2) Supported in part by National Science Foundation Grant GP-5226 and Public Health Service Research Grant GM-14381.
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- (5) O. Dimroth and S. Merzbacher, *Chem. Ber.*, **40**, 2402 (1907).
- (6) O. Dimroth and S. Merzbacher, *ibid.*, **43**, 2899 (1910).
- (7) F. D. Chattaway and G. D. Parkes, *J. Chem. Soc.*, 113 (1926).
- (8) S. Y. Hong and J. E. Baldwin, *Tetrahedron*, **24**, 3787 (1968).
- (9) R. Hoffmann and R. B. Woodward, *Accounts Chem. Res.*, **1**, 17 (1968).
- (10) Specific activities were obtained by the channels ratio method with a Packard Tri-Carb Liquid Scintillation Spectrometer, Model 3203. The scintillation solution contained 5 g. of 2,5-diphenyloxazole per liter of toluene. We thank Dr. R. F. Nystrom for his help with the  $^{14}\text{C}$ -analyses.
- (11) "Handbook of Chemistry and Physics," Chemical Rubber Publishing Co., Cleveland, Ohio.

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