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Preparation of 4,5-Disubstituted-1,2,3-triazoles

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A recent publication (1) reports the synthesis of 1,2,3-triazoles by the addition of tropylium azide to acetylenes, followed by acid cleavage of the tropylium group. We report here the preparation of 1,2,3-triazoles (Table I) utilizing other azides which, after addition to an acetylene, provide a base-cleavable group.

The bromomethylphenyl acetates recently described (2) may be readily converted to the corresponding azides (Table II). Dipolar addition of these azides to acetylenes yields triazoles (Table III) which will undergo the amine exchange reaction generalized below. The initial deacetylated product need not be isolated but may be prepared by acid-catalyzed methanolysis if desired.

EXPERIMENTAL

Azidomethylphenyl Acetates (I-III). General Procedure.

To a solution of 0.275 mole of a bromomethylphenyl acetate in 1 l. of acetone was added a solution of 20 g. (0.3 mole) of sodium azide (40 g., 0.6 mole in the case of II) in 150 ml. of water. After the mixture had been stirred for 1 hour, it was poured onto 3 l. of ice and water. Filtration yielded the crude azide which was recrystallized from ethanol or from benzene-ligroin (b.p. 30-60°).

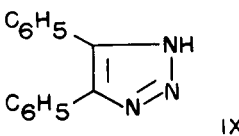
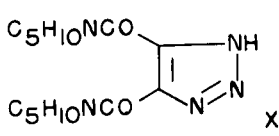
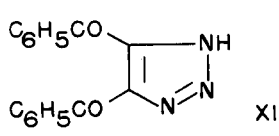
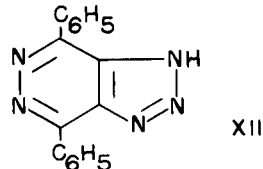
(4,5-Disubstituted-1H-1,2,3-triazol-1-ylmethyl)phenyl Acetates. General Procedure.

An azidomethylphenyl acetate was refluxed with a slight excess of an acetylene in toluene or xylene for 2-30 hours. When the characteristic azide peak at 2100 cm^{-1} disappeared, the mixture was cooled and the product crystallized. Recrystallization from benzene or toluene afforded pure samples.

(4,5-Disubstituted-1H-1,2,3-triazol-1-ylmethyl)phenols (IV and V).

TABLE I

4,5-Disubstituted-1,2,3-triazoles

Compound	M. p., °C	Yield, %	C	Analyses			Found	
				Calcd. H	N	C	H	N
 IX	139-140 [reported 138-139(a)]	19						
 X	248-249 (dec.)	30	57.7	7.3	24.0	57.8	7.5	24.0
 XI	167-169 [reported 164-165 (b)]	86	69.3	4.0	15.2	69.0	3.9	15.3
 XII	356 (dec.)	50	70.3	4.1	25.6	70.0	4.0	25.9

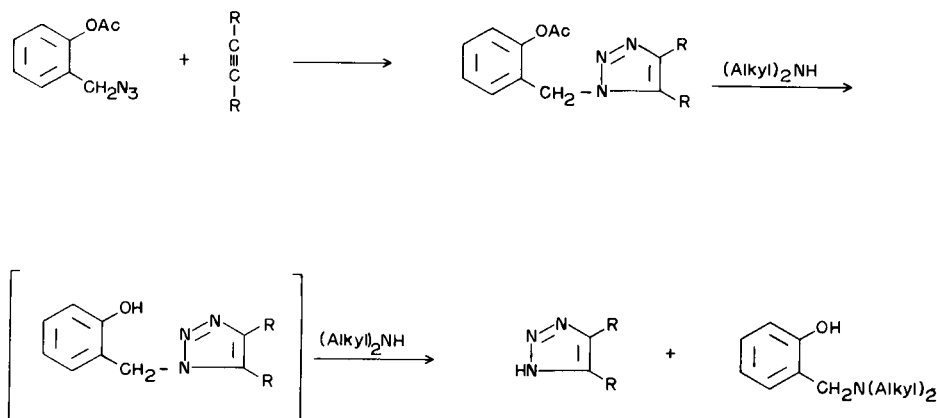
(a) R. Stolle, W. Munh, and W. Kind, *J. Prakt. Chem.*, 70, 440 (1904). (b) Ref. 1.

TABLE II
Azidomethylphenyl Acetates

Compound	M. p., °C	Yield, %	C	Analyses				
				Calcd. H	N	C	Found H N	
3-Azidomethyl-5-phenylcatechol diacetate (I)	67-69	70	62.8	4.6	12.9	62.6	4.7	12.8
2,5-Bis(azidomethyl)hydroquinone diacetate (II)	111-113	72	47.3	4.0	27.6	47.5	3.9	27.4
2-Azidomethyl-3,5,6-trimethylhydroquinone diacetate (III)	118	97	57.8	5.9	14.4	58.0	5.8	14.4

TABLE III
(4,5-Disubstituted-1*H*-1,2,3-triazol-1-ylmethyl)phenols and Their Acetates

Compound	M. p., °C	Yield, %	C	Analyses				
				Calcd. H	N	C	Found H N	
3-(4,5-Diphenyl-1 <i>H</i> -1,2,3-triazol-1-ylmethyl)-5-phenylcatechol (IV)	217	60	77.3	5.1	10.0	77.0	5.0	9.8
IV as the Diacetate	176-177	66	74.0	5.0	8.3	74.2	5.1	8.3
3-(4,5-Dibenzoyl-1 <i>H</i> -1,2,3-triazol-1-ylmethyl)-5-phenylcatechol (V)	198-199	82	73.3	4.5	8.8	73.3	4.4	8.9
V as the Diacetate	176	80	70.8	4.5	7.5	71.0	4.5	7.5
2-(4,5-Dibenzoyl-1 <i>H</i> -1,2,3-triazol-1-ylmethyl)-3,4,6-trimethylhydroquinone diacetate (VI)	153-154	86	68.5	5.2	8.0	68.8	5.1	8.0
2,5-Bis(4,5-dicarbomethoxy-1 <i>H</i> -1,2,3-triazol-1-ylmethyl)-hydroquinone diacetate (VII)	179-183	100	48.9	4.1	14.3	48.9	4.1	13.9
2,5-Bis(4,5-dibenzoyl-1 <i>H</i> -1,2,3-triazol-1-ylmethyl)hydroquinone diacetate (VIII)	242-243	80	68.3	4.2	10.9	68.1	4.4	11.2



Deacetylation of the corresponding acetate was accomplished by refluxing in anhydrous methanolic hydrogen chloride for 2 hours. Evaporation and recrystallization from ethyl acetate-ligroin (b.p. 30-60°) (V) or from ethanol (IV) gave analytical samples.

4,5-Diphenyl-1,2,3-triazole (IX).

A solution of IV in piperidine was refluxed overnight. The solvent was removed under reduced pressure. The residue was slurried with benzene and filtered to remove the insoluble 3-piperidinomethyl-5-phenylcatechol. Removal of the solvent from the filtrate under vacuum gave a residue which, on treatment with 5% hydrochloric acid and filtration, gave IX. Recrystallization from ether-ligroin (b.p. 30-60°) afforded pure material (Table I).

4,5-Bis(piperidinocarbonyl)-1,2,3-triazole (X).

A solution of VII in piperidine was refluxed overnight. Removal of the solvent under reduced pressure gave a residue which was dissolved in ethanol. This solution deposited 2,5-bis(piperidinomethyl)-hydroquinone on standing. Filtration and removal of the solvent gave a residue which was dissolved in a minimum amount of methanol. Addition of ethyl acetate caused crystallization of X. Recrystallization from methanol afforded a pure product (Table I).

4,5-Dibenzoyl-1,2,3-triazole (XI). Method A.

A solution of 10 g. of VI in 100 ml. of 2,2-iminodiethanol was heated on a steam bath for 4 hours. The solution was poured into cold water and acidified with hydrochloric acid. Filtration gave an 86.5% yield of crude product, m.p. 166-168°. Recrystallization from ethyl acetate-ligroin (b.p. 30-60°) gave pure XI (Table I).

Method B.

A solution of V in piperidine was refluxed overnight. Removal of

the solvent gave an oil which crystallized on the addition of benzene. Recrystallization from ethanol gave an analytical sample of the piperidine salt of XI.

Anal. Calcd. for C₂₁H₂₂N₄O₂: C, 69.6; H, 6.1; N, 15.5. Found: C, 69.3; H, 6.0; N, 15.5.

The salt was then dissolved in methanol, acidified with hydrochloric acid, and poured into water to precipitate XI.

4,7-Diphenyl-1,2,3,5,6-pentaazaindene (XII). Method A.

A mixture of VI, hydrazine, and ethanol was refluxed for 6 hours. Removal of the solvent gave a residue which was slurried with methanol and filtered. Recrystallization from dimethylformamide gave pure XII (Table I).

Method B.

When VI was replaced with VIII in the above reaction, 2,5-dihydroxy-*p*-xylylene-1,1'-bis(4,7-diphenyl-1,2,3,5,6-pentaazaindene) was obtained which, after recrystallization from pyridine, had a m.p. of > 300°C.

Anal. Calcd. for C₄₀H₂₈N₁₀O₂: C, 70.6; H, 4.1; N, 20.6. Found: C, 70.5; H, 4.2; N, 20.4.

This compound, when treated with piperidine followed by hydrochloric acid, gave XII.

REFERENCES

- (1) J. J. Looker, *J. Org. Chem.*, 30, 638 (1965).
- (2) D. L. Fields, J. B. Miller, and D. D. Reynolds, *ibid.*, 29, 2640 (1964).

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