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1,2,4-TRISUBSTITUTED 1,2,3-TRIAZOLIUM SALTS FROM NITRILIMINES AND ISOCYANIDES

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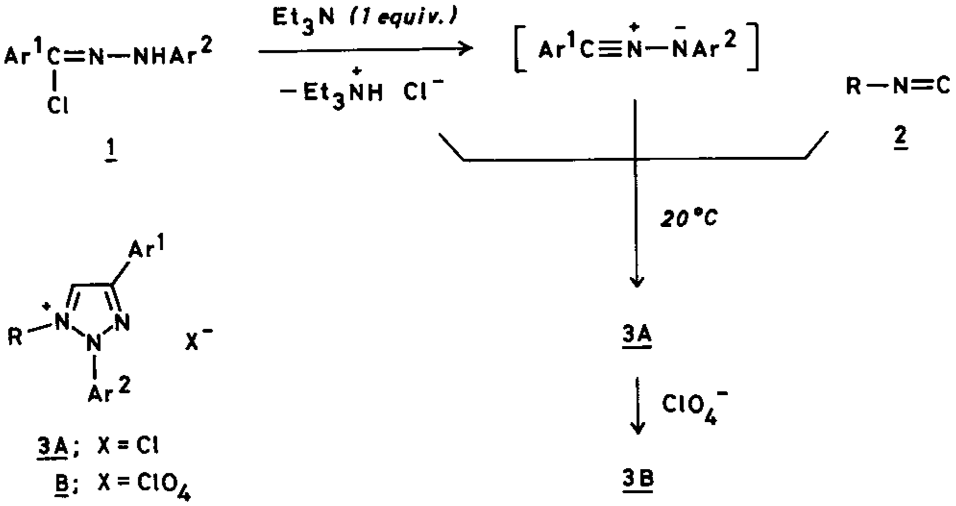
Abstract — Diarylnitrilimines (from 1 and triethylamine) react with alkyl isocyanides 2 to form, through proton transfer, the quaternary salts 3A. This constitutes a novel synthetic approach to the 1,2,3-triazolium ring having groups on adjacent nitrogens.

Several years ago Hiraki, Fuchita, and associates[1] have shown that nitrilimines and isocyanide-palladium(II) complexes undergo a [3+2] cycloaddition to give derivatives of 1,2,4-triazole. We now found that free isocyanides 2, in contrast to the aforementioned species, led to the 1,2,3-triazole series, viz. to quaternary salts of type 3 (Scheme 1). The change of regioselectivity in both reactions is best accounted for by the metal-induced alteration[2] of normal isocyanide reactivity. Since our reaction directly yields the chlorides 3A (as exemplified with 3Aa,c), the proton necessary for triazolium formation will be supplied by the triethylamine hydrochloride still present in the reaction mixture[3]. However, for preparative convenience the products, before isolation, were converted into the perchlorates 3B (Table). So, in a typical procedure (given for 3Bc) triethylamine (2 mM) was added at ambient temperature to a solution of N-phenylbenzohydrazonoyl chloride (1; $Ar^1 = Ar^2 = Ph$)[4] and cyclohexyl isocyanide (2; $R = c\text{-}C_6H_{11}$)[5] (2 mM each) in dry acetonitrile (50 ml)[6]; the mixture was allowed to stand for 24 h. Removal of the solvent gave a crystalline residue which was washed with ether and dissolved in the minimum amount of water (some insoluble material[7] was filtered off). Then aqueous perchloric acid (10 %) was employed to cause precipitation of crude 3Bc as a greenish-white solid (for yield see Table). Chromatography on acidic alumina (acetone as eluent), followed by addition of ether to the concentrated eluate, afforded colorless plates (for mp and further characterization data see Table and below).

Scheme 1



3A,B	Ar^1	Ar^2	R
a	Ph	Ph	Me
b	Ph	Ph	*i*-Pr
c	Ph	Ph	*c*-C_6H_{11}
d	4-MeC_6H_4	Ph	*i*-Pr
e	4-MeC_6H_4	Ph	*c*-C_6H_{11}
f	Ph	4-MeC_6H_4	*i*-Pr
g	Ph	4-MeC_6H_4	*c*-C_6H_{11}

Scheme 2

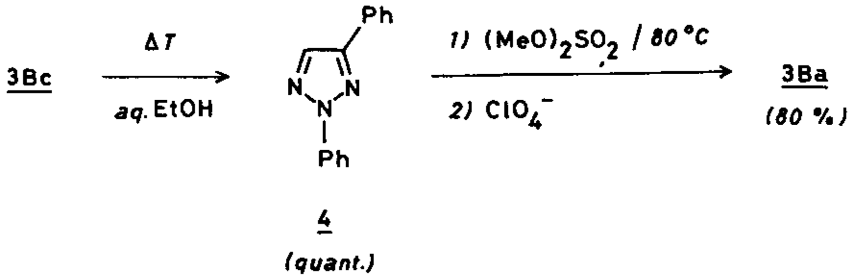


Table. 1-Alkyl-2,4-diaryl-1,2,3-triazolium Perchlorates 3B

compd	yield, % [a]	mp, °C (decomp.)	^{1}H nmr [b] [1-alkyl; 5-H]	anal. [c]
3Ba	63	180	4.30; 9.87	$[C_{15}H_{14}N_3]ClO_4$
3Bb	57	158-159	1.66 (d), 4.92 (m); 10.10 [d]	$[C_{17}H_{18}N_3]ClO_4$
3Bc	73	164	1.0-2.4 (m), 4.50 (m); 10.07 [e]	$[C_{20}H_{22}N_3]ClO_4$
3Bd	53	161	1.64 (d), 4.83 (m); 9.93 [f]	$[C_{18}H_{20}N_3]ClO_4$
3Be	73	148-150	1.0-2.5 (m), 4.46 (m); 9.92 [g]	$[C_{21}H_{24}N_3]ClO_4$
3Bf	70	178-179	1.64 (d), 4.88 (m); 10.07	$[C_{18}H_{20}N_3]ClO_4$
3Bg	58	175	1.0-2.5 (m), 4.50 (m); 10.07 [h]	$[C_{21}H_{24}N_3]ClO_4$

[a] Crude product. [b] Run in $(CD_3)_2SO$ solution; chemical shifts are δ relative to internal Me_4Si, unspecified signals are singlets. [c] Satisfactory analytical figures were obtained for all compounds listed in the table. C, H, N, Cl analyses; ± 0.3 %. [d-h] In $CDCl_3$ solution were found: 9.30, 9.33, 9.33, 9.37, and 9.50, respectively.

Regarding the scope of this new reaction, experiments with *tert*-butyl as well as phenyl isocyanide (2; R = *t*Bu, Ph) failed to furnish the respective products 3. This means, the synthetic utility rests on the preparation of those 1,2-disubstituted 1,2,3-triazolium salts that have a primary or secondary alkyl group attached to position 1. Our method may thus be viewed as a complement of earlier routes [8] to the rare class of 1,2,3-triazolium compounds bearing ligands (i.e. alkyl and / or aryl) on adjacent nitrogens.

Structural proof of 3 (which essentially aimed at exclusion of the isomeric 4-alkyl-1,3-diaryl-1,2,4-triazolium structure) is provided by (i) ^{13}C nmr (the spectrum of 3Bc lacked the high field shifted signal typical of C-2 of an unhindered *N*-phenyl group [9] : the four resonances attributable to C-2 and C-3 of the two phenyl substituents all appeared in the narrow range from δ 126.8 to 130.7 [10]) and (ii) thermolysis of 3Bc to give the known triazole 4 [11] which, on successive treatment with dimethyl sulfate [12] and aqueous lithium perchlorate, was transformed into the salt 3Ba obtained before (Scheme 2).

ACKNOWLEDGMENT

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REFERENCES AND NOTES

1. K.Hiraki, Y.Fuchita, and S.Morinaga, Chem.Lett., 1978, 1; Y.Fuchita, K.Hidaka, S.Morinaga, and K.Hiraki, Bull.Chem.Soc.Jpn., 1981, 54, 800.
2. A.Vogler, 'Coordinated Isonitriles' in 'Isonitrile Chemistry', ed. by I.Ugi, Academic Press, Inc., New York and London, 1971; p. 217-233.
3. A mechanistic study of the overall reaction is in progress.
4. Preparation analogous to the procedure described for 1 ($Ar^1 = 4\text{-}MeC_6H_4$, $Ar^2 = Ph$): D.L.Rector, S.D.Folz, R.D.Conklin, L.H.Nowakowski, and G.Kaugars, J.Med.Chem., 1981, 24, 532.
5. P.Hoffmann, G.Gokel, D.Marquarding, and I.Ugi, 'Isonitrile Syntheses' in 'Isonitrile Chemistry' (see ref. [2]); p. 9-39.
6. This solvent proved to be superior to chloroform, dichloromethane, nitromethane or benzene.
7. An investigation is currently underway.
8. a) Oxidative ring closure of substituted glyoxal arylhydrazone imines: B.Hirsch and E.Förster, Naturwissenschaften, 1963, 50, 374; B.Hirsch and A.Bassl, Z. Chem., 1963, 3, 351; A.Singh and B.Hirsch, Indian J.Chem., 1970, 8, 514. — Ligands at N-1 of the triazolium compounds made are aryl and (substituted) primary alkyl groups, respectively (note: the products mentioned in the foregoing references all have electron-withdrawing groups attached to C-4 of triazolium). b) Quaternization of 2-substituted 1,2,3-triazoles: M.Begtrup and K.V.Poulsen, Acta Chem.Scand., 1971, 25, 2087. — Methylation is dealt with only.
9. Cf. M.Begtrup, Acta Chem.Scand., 1973, 27, 3101; 1974, B 28, 61.
10. Measured in $CDCl_3$ solution (Me_4Si as internal standard). — Further resonances: δ 23.8, 24.9, and 32.2 (t; C-4, C-3, and C-2, respectively, of $c\text{-}C_6H_{11}$), 64.9 (d; C-1 of $c\text{-}C_6H_{11}$), 125.8 (s; C-1 of 4-Ph), 127.8 (d; C-5 of triazolium), 130.8 (d; C-4 of 4-Ph), 133.3 (d; C-4 of 2-Ph), 133.5 (s; C-1 of 2-Ph), and 149.9 (s; C-4 of triazolium).
11. Compared (ir) with an authentic sample (made according to H.El Khadem, M.M.El-Sadik, and M.H.Meshreki, J.Chem.Soc. C, 1968, 2097).
12. This reagent is reported to be unsatisfactory in quaternization of the related 2-phenyl-1,2,3-triazole [8b].

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