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# SYNTHESIS OF 3,4-DIARYL-1,2,4-TRIAZOLES FROM DIARYLIMIDOYL CHLORIDES AND DIAZOMETHYLLITHIUM.

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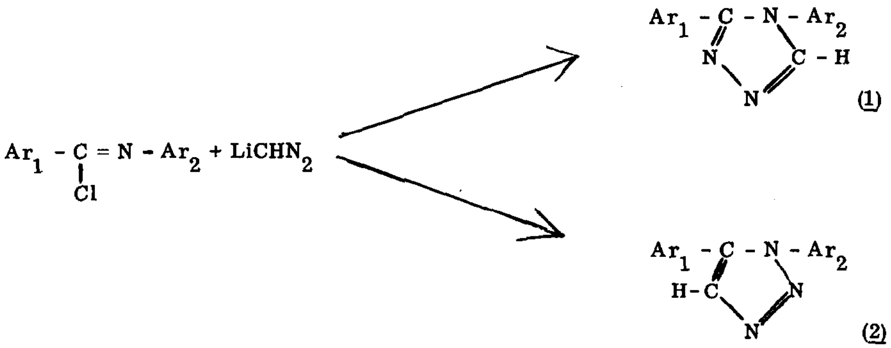
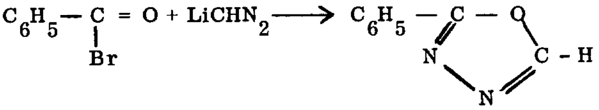
Imidoyl chlorides react readily with azide ion ($\bar{N} = \overset{+}{N} = \bar{N}$) to give 1,5-disubstituted tetrazoles[1] and we have investigated the synthetic utility and regioselectivity of parallel reactions with the isoelectronic diazomethyl ion ($\bar{C}H = \overset{+}{N} = \bar{N}$), supplied as diazomethyllithium[2], which could lead to disubstituted-triazoles.

If nucleophilic attack by diazomethyllithium upon diarylimidoyl chlorides is followed by cyclization, initial attack by the nitrogen terminus will lead to 3,4-diaryl-1,2,4-triazoles (1) and initial attack by the carbon terminus to 1,5-diaryl-1,2,3-triazoles (2)



| | a | b | c | d | e | f |
|---|---|---|---|---|---|---|
| $Ar_1$ | $C_6H_5$ | $C_6H_5$ | p-$CH_3C_6H_4$ | $C_6H_5$ | p-$CH_3OC_6H_4$ | p-$ClC_6H_4$ |
| $Ar_2$ | $C_6H_5$ | p-$CH_3C_6H_4$ | $C_6H_5$ | p-$CH_3OC_6H_4$ | $C_6H_5$ | $C_6H_5$ |

The probable regioselectivity can be predicted from a consideration of previously studied reactions at the analogous $sp^2$ hybridized carbon of acyl halides (RCOX). The parent diazomethane reacts to give high yields of the diazoketones ($RCOCHN_2$) formed with nucleophilic attack by the carbon terminus[3] but diazomethyllithium has been found to react with benzoyl bromide to give a 35% yield of 2-phenyl-1,3,4-oxadiazole[4], formed *via* initial nucleophilic attack by the nitrogen terminus:



By analogy, use of diazomethyllithium, rather than diazomethane, should favor formation of **1**. Although triazoles **2** can be conveniently constructed by a variety of reactions, incorporating within the 1,2,3-triazole ring the three nitrogen atoms of an aryl azide[5], only two methods for synthesis of **1** have been reported.[6,7]

We prepared an ether solution of diazomethyllithium in 70% yield [2,8] by interaction of diazomethane and methyllithium. The appropriate diarylimidoyl chloride[9] dissolved in methylene chloride (*ca* 0.5 *M*) was added, with stirring and in one portion, to an equimolar amount of the diazomethyllithium solution in ether (*ca* 0.4 *M*), at $0^{o}$ for systems **a**, **b**, **c**, and **f** and at $-20^{o}$ for systems **d** and **e**. After 30 minutes, the mixtures were allowed to warm to room temperature and to stand overnight. After treatment with ice-water and extraction with chloroform, the chloroform extract was dried over anhydrous magnesium sulfate, concentrated under reduced pressure, and chromatographed on a silica gel column using chloroform and 1-3% methanolic chloroform as eluents.

Purification of the crude **1(a-f)** obtained was by further column chromatography (Florisil-Celite column with chloroform and 0.5-3% methanolic chloroform as eluents) and by recrystallization from carbon tetrachloride-hexane.

Several general characteristics observed for compounds **1** are as follows:

*NMR*: The ring proton gives in chloroform-*d* a broad signal in the range δ8.28-8.35 and, in acetone-$d_6$, a much sharper signal in the range δ8.51-8.61[10]; IR (KBr) includes adsorptions at 3110-3120 $cm^{-1}$ [11] and at 1384-1392 $cm^{-1}$; *UV* (ethanol): λmax values are in the range 229-256 nm with ε values of about $10^4$.

The yields, melting points, and elemental analyses for individual compounds are presented in Table 1 and some of the more important spectral characteristics[12] are presented in Table 2.

Table 1. Characteristics of the 3,4-Diaryl-1,2,4-triazoles

| | | | Anal. | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Calcd, % | | | Found, % | | |
| Cpd. | Yield,% | mp,°C | C | H | N | C | H | N |
| 1a | 43 | 141 -142[a] | 76.00 | 5.01 | 18.99 | 75.76 | 5.27 | 18.78 |
| 1b | 36 | 151.5-152[b] | 76.57 | 5.57 | 17.86 | 75.94 | 5.59 | 17.68 |
| 1c | 35 | 165.5-166 | 76.57 | 5.57 | 17.86 | 76.52 | 5.54 | 17.74 |
| 1d | 29 | 121.5-122 | 71.69 | 5.21 | 16.72 | 71.52 | 5.43 | 16.62 |
| 1e | 33 | 141.5-142 | 71.69 | 5.21 | 16.72 | 71.28 | 5.03 | 16.53 |
| 1f[c] | 34 | 176 -176.5 | 65.76 | 3.94 | 16.43 | 65.70 | 3.94 | 16.36 |

[a] Lit.[6] mp 141-142°C. [b] Lit.[7] mp 143°C. [c] Anal. for Cl: Calcd, 13.87. Found, 13.92

Table 2. Some Spectral Characteristics of the 3,4-Diaryl-1,2,4-triazoles

| | NMR, δ | | IR(KBr),[a] | UV(EtOH) | |
|---|---|---|---|---|---|
| Cpd. | $\geqslant$CH | $CH_3$ | $cm^{-1}$ | $\lambda_{max}$, nm | $10^4\varepsilon$ |
| 1a | 8.58[b] | | 1389 | 236[d] | 1.51[d] |
| 1b | 8.51[b] | 2.39[b] | 1390 | 236 | 0.42 |
| 1c | 8.53[b], 8.44[c] | 2.31[b], 2.28[c] | 1385 | 244 | 1.70 |
| 1d | 8.39[c] | 3.79[c] | 1392 | 229 | 2.15 |
| 1e | 8.44[c] | 3.78[c] | 1389 | 256 | 1.64 |
| 1f | 8.61[b] | | 1384 | 246 | 1.90 |

[a] Includes peak at 3120 $cm^{-1}$ for 1e and peak at 3110 $cm^{-1}$ for remainder. [b] In acetone-$d_6$. [c] In 40% acetone-$d_6$: 60% chloroform-d (by wt.). [d] Lit: $\lambda_{max}$ 235.5 nm, ε1.47 x $10^4$ [M.R. Atkinson, E.A. Parkes, and J.B. Polya, *J. Chem. Soc.*, 4256 (1954)].

The known isomers 2a (mp[13] 113-114°) and 2d (mp[14] 85°) have melting points appreciably lower than the corresponding 1a and 1d. Although small amounts (< 5%) could have gone undetected, no evidence was obtained for any formation of compounds 2 and the formation of compounds 1 in reasonable yields supports the earlier observation[4] that nucleophilic substitution-cyclization reactions at a trigonal carbon initiated by attack of the anion derived from diazomethyllithium are initiated, to an appreciable extent, by attack of the nitrogen (rather than carbon) terminus.

## Acknowledgment

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## References and Notes

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