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CYCLOADDITION REACTIONS OF 6-CYANOBENZ[*a*]INDOLIZINES WITH ACTIVATED ALKYNES. FORMATION OF BENZO[2.2.3]- and [2.3.4]CYCLAZINES

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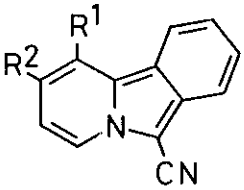
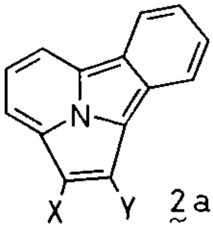
Abstract—Cycloaddition reactions of 6-cyanobenz[*a*]indolizines with activated alkynes such as dimethyl acetylenedicarboxylate, diacetylacetylene, methyl propiolate, methyl trimethylsilylpropiolate, methyl phenylpropiolate, and 4-phenyl-3-butyn-2-one were investigated.

Previously, we have described in full detail preparation of 6-cyanobenz[*a*]indolizines which are activated by means of aromatic stabilization in favor of the azomethine ylide structure.[1] Indeed, they readily undergo [8+2]cycloaddition with dibenzoylacetylene giving the 1,2-dibenzoylindolizino[3,4,5-*ab*]isoindoles.[1] In contrast, 3-cyanoindolizines only sluggishly reacted even with dimethyl acetylenedicarboxylate to afford the corresponding [2.2.3]cyclazines and/or a novel type of the 1:2 molar products.[2,3] We now report further examples of cycloaddition reactions of 6-cyanobenz[*a*]indolizines with electron deficient alkynes.

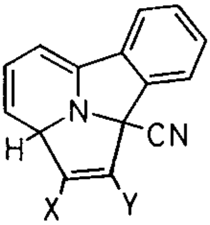
Reaction of 6-cyanobenz[*a*]indolizine (**1a**) with excess dimethyl acetylenedicarboxylate (DMAD) in refulxing toluene in the presence of Pd-C for 2 h gave (**2a**) (13%) along with the 1:1 adduct **3a** (7%).[4] Di-t-butyl acetylenedicarboxylate (DBAD) is potentially an acetylene equivalent since at high temperature of *ca.* 270°C t-butoxycarbonyl group was converted to hydrogen with extrusion of carbon dioxide and isobutylene.[5] Unfortunately, however, DBAD has often proved to serve as an acetylenedicarboxylic anhydride (C_4O_3) rather than an acetylene



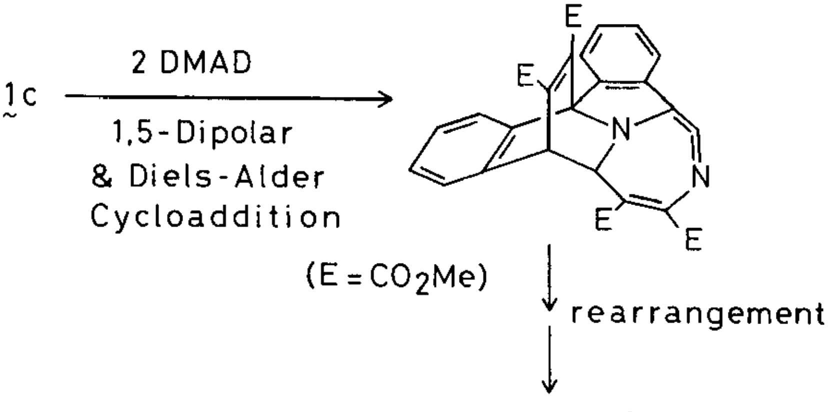
1 a : $R^1 = R^2 = H$
b : $R^1 = H, R^2 = Me$
c : $R^1 = \text{-(CH=CH)}_2\text{-} = R^2$

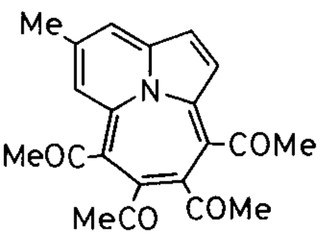


2 a : $X = Y = CO_2Me$
b : $X = Y = H$
c : $X = Y = CO_2Bu\text{-}t$
d : $X = Y = COMe$
e : $X = CO_2Me,\ Y = H$
f : $X = H,\ Y = CO_2Me$
g : $X = CO_2Me,\ Y = SiMe_3$
h : $X = SiMe_3,\ Y = CO_2Me$
i : $X = CO_2Me,\ Y = Ph$
j : $X = Ph,\ Y = CO_2Me$
k : $X, Y = Ph, COMe$



3 a : $X = Y = CO_2Me$
c : $X = Y = CO_2Bu\text{-}t$





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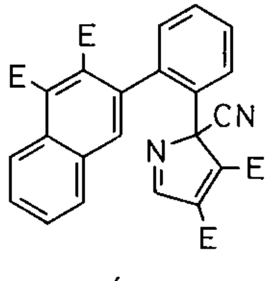

4

equivalent.[6] Thus, it is interesting to note that at 210°C in nitrobenzene for 4 h **1** with excess DBAD produced indolizino[3,4,5-*ab*]isoindole (**2b**) in 9% yield, whereas at about 100°C for 21 h in toluene gave a mixture of **2c** (14%) and the 1:1 adduct **3c** (42%). Curiously enough, isoindolo[1,2-*ab*]isoquinoline (**1c**) with DMAD gave the 1:2 molar adduct in 41% yield. The structure was tentatively assigned as **4**[7] that could be derived from the same type of an intermediate "proposed" in the novel formation of the pyrroles from 3-cyanoindolizines and DMAD.[3] Intriguingly, diacetylacetylene with 9-methyl-6-cyanobenz[*a*]indolizine (**1b**) gave the [2.3.4]cyclazine **5** albeit in 7% yield, while **1a** afforded the benzo[2.2.3]cyclazine **2d** in 8% yield.

As a matter of course, reactions of **1** with several unsymmetric alkynes were also examined. Trimethylsilylacetylene and phenylacetylene were inert to **1a** in refulxing toluene and xylene. **1a** with excess methyl propiolate in refulxing toluene for 34 h gave the benzo[2.2.3]cyclazine as a single product. Its regiochemistry was tentatively assigned as **2e** by an inspection of the mass fragmentation patterns of **2e** and the related [2.2.3]cyclazines.[8] Methyl trimethylsilylpropiolate with **1a** under similar conditions (72 h) afforded a mixture of **2e** [7](5%), **2f** (5%), **2g** (11%), and **2h** (14%).[8] An analogous reaction (45 h) of methyl phenylpropiolate with **1a** gave the corresponding cyclazines **2i** and **2j** in 52 and 6% yields respectively, their regiochemical assignments being based on the mass spectral fragmentation pattern.[8,9] Such desilylation during cycloaddition reactions is not unprecedent.[10] 4-Phenyl-3-butyn-2-one, likewise(72 h), underwent cycloaddition onto **1a** yielding a mixture of the regioisomers **2k** (48 and 7%). In this case, the regiochemical assignment could not be made.

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Tetrahedron Lett., 1987, **28**, 5707.

4. All the new compounds described in this paper had satisfactory elemental and/or exact mass analyses along with ^{1}H- and ^{13}C-nmr and ir spectra. Data of mp(°C): **2a**, 190; **2b**, 76-78; **2c**, 125; **2d**, 123-125; **2e**, 42-48; **2f**, 74-78; **2g**, 118-120; **2h**, 157-159; **2i**, 137-139; **2j**, 133-134; **2k**, 94-96 and 118-120; **3a**, 139-142; **3c**, 148; **4**, 179-180; **5**, 187-189.
5. D. Farquhar, T. T. Gough, and D. Leaver, J. Chem. Soc., Perkin Trans. 1, 1976, 341.
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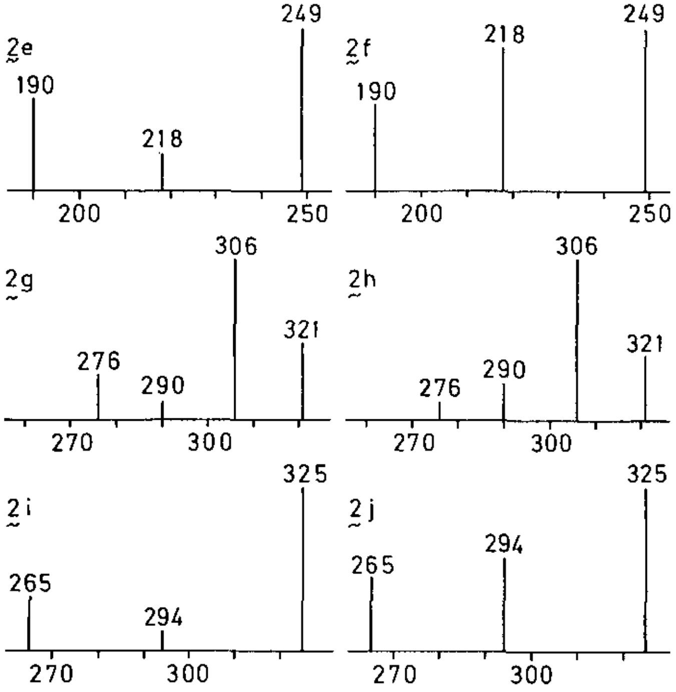
7. An X-ray analysis of this compound is envisaged.
8. Representative examples of mass spectral fragmentation patterns are followings:



9. Preliminary frontier orbital considerations based upon HMO calculations are in accord with such assignments. More sophisticated MO calculations like CNDO/2 are in progress.
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