1,3-DIPOLAR CYCLOADDITION REACTION OF AROMATIC N-OXIDE WITH HEXAFLUOROBUTYNE-2[1]

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Reaction of quinoline and isoquinoline N-oxides with hexafluorobutyne-2 (1) was examined. The former gave 2-(2-quinolyl)-3-trifluoroacetoxy-1,1,1,4,4,4-hexafluoro-2-butene, quinolinium trifluoromethyltrifluoroacetylmethylide, 2-(2,2,2-trifluoroethyl)quinoline and 2,3-bis(trifluoromethyl)furo[3,2-b]quinoline. The latter gave isoquinolinium trifluoroacetylfluorocarbonylmethylide and three pyrrolo[2,1-b]isoquinoline compounds which were probably formed by addition of the primarily formed ylide, isoquinolinium trifluoromethyltrifluoroacetylmethylide, to 1.

Some interesting results have been obtained from the 1,3-dipolar cycloaddition of aromatic N-oxides with acetylenic compounds[2]. We now wish to report the reaction of quinoline and isoquinoline N-oxides using hexafluorobutyne-2 (1) as an acetylenic component. Compound 1 has two electronegative trifluoromethyl groups and is a good dienophile and dipolarophile.

Thus, this study was undertaken in order to clarify the characteristics of the reactivity of the fluorine substituted acetylene and also to open a route to fluorine substituted

heteroaromatics.

Quinoline 1-oxide (2) was warmed with 1 in benzene at 70° for 3 hr. Repeated chromatographic separation of products on silica gel furnished four products shown in Chart 1; that is 2-(2-quinolyl)-3-trifluoroacetoxy-1,1,1,4,4,4-hexafluoro-2-butene (3) [7%; colorless needles; mp 127-8°; mass spectrum m/e: 403 (M^+); ^1H nmr ($CDCl_3$) δ: 7.2-7.8 (m); ^{19}F nmr[3] δ: -2.1 (5), +0.9 (broad), +3.3 (s); ir (KBr) cm^{-1}: 1720, 1680, 1150, 1130], quinolinium trifluoromethyltrifluoroacetylmethylide (4) [20%; pale yellow powder; mp 269-70°; mass spectrum m/e: 178 $(CF_3CCOCF_3)^+$, 129 (quinoline); ^1H nmr (DMSO-d_6) δ: 9.6-9.1 (m, 2H, 2- and 8-H), 8.67 (d, 1H, 4-H), 8.5-7.8 (m, 4H); ^{19}F nmr (DMSO-d_6) δ: 6.8, 16.7], 2,3-bis(trifluoromethyl)furo[3,2-b]quinoline (5) [2%; pale yellow cubes (sublimed at 140° at 5 mmHg); mass spectrum m/e: 305 (M^+); ^1H nmr ($CDCl_3$) δ: 8.20 (s, 1H, 9-H), 8.23 (d, 1H, 5-H); ^{19}F nmr δ: 0.05, -14.0 (both q, J_{FF}=8.1 Hz)] and 2-(2,2,2-trifluoroethyl)quinoline (6) [7%; colorless needles; mp 55-57°; mass spectrum m/e: 221 (M^+); ^1H nmr ($CDCl_3$) δ: 3.80 (q, 2H, CH_2-CF_3, J_{HF}=11 Hz); ^{19}F nmr ($CDCl_3$) δ: 0.8 (t, J_{HF}=11 Hz)].

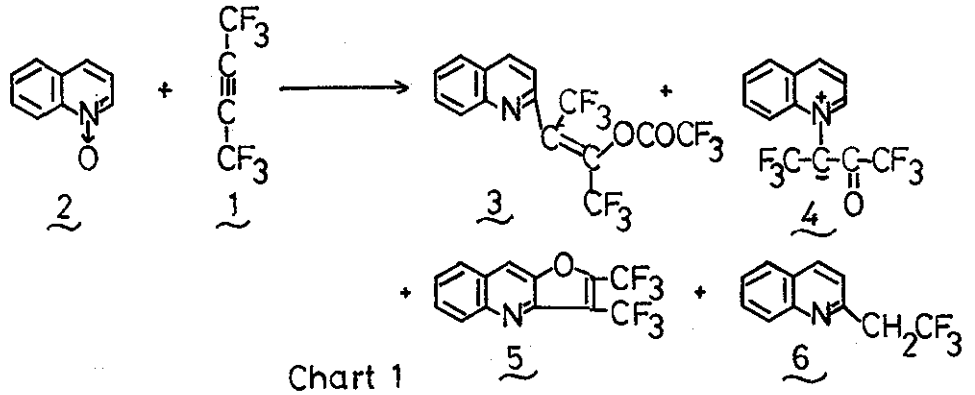

Chart 1

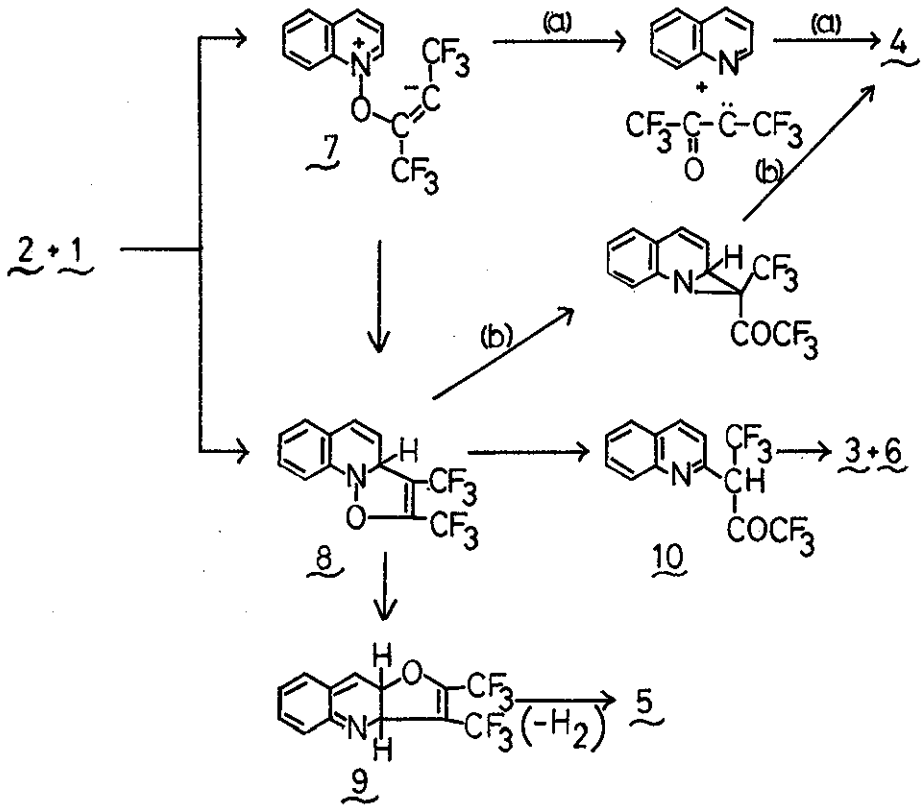

Chart 2

The mechanism for this reaction is tentatively postulated as shown in Chart 2. As for the formation of the ylide 4, two courses [(a) and (b)] might be conceivable. Course (a) involves the initial formation of the dipolar adduct (7), the consecutive collapse of 7 to quinoline and a carbene species and their recombination to 4[4]. Course (b) proceeds through a ring contraction of the 1:1 cycloadduct (8) to form aziridine intermediate which isomerizes to 4[5].

The cycloadduct 8 is also able to undergo two types of transformation different from course (b). The first one is rearrangement to dihydrofuro[3.2-b]quinoline (9) which is oxidized to product 5. The second is transformation into 2-substituted quinoline (10), and the trifluoroacetyl migration from one molecule of 10 to the other one (migration between two molecules of 10) to afford 3 and 6.

In connection with the formation of 5, the reaction of 3-bromoquinoline 1-oxide with 1 was carried out and 5 was obtained in 13% yield together with a minute amount of 4-bromo-1,2,3-tris-(trifluoromethyl)pyrrolo[1,2-a]quinoline (11); the furo-quinoline formation is apparently facilitated by the electron-drawing 3-bromo substituent. Product 11 is well assumed to be formed from the N-ylide (12) and 1. Actually, treatment of 4 with 1 gave the corresponding pyrroloquinoline (13) (Chart 3).

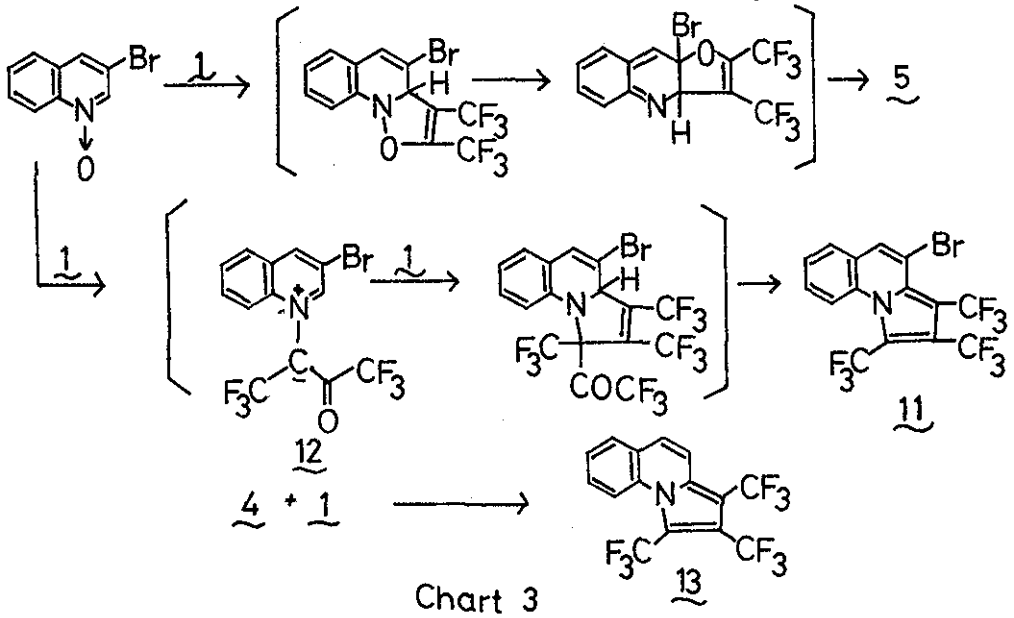

Chart 3

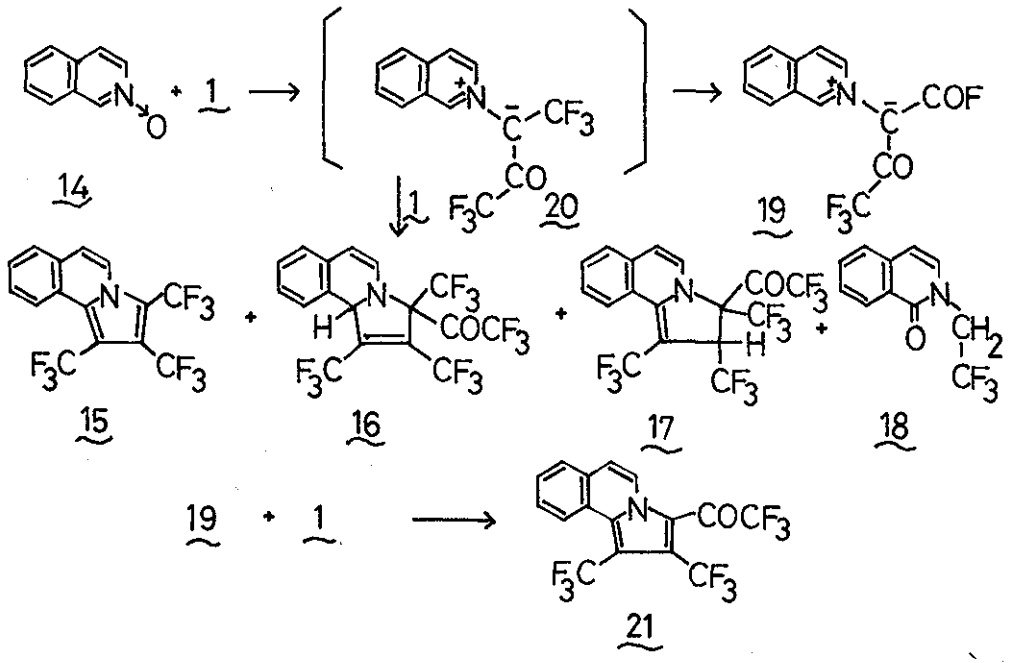

Chart 4

The reaction of isoquinoline 2-oxide (14) with 1 under the conditions showed rather different feautures as illustrated in Chart 4; that is, 1,2,3-tris(trifluoromethyl)furo[2,1-a]isoquinoline [pale yellow needles; mp 105°], 3-trifluoroacetyl-1,2,3-tris(trifluoromethyl)-3,10b-dihydrofuro[2,1-a]isoquinoline (16) [3%; mp 100°], 3-trifluoroacetyl-1,2,3-tris(trifluoromethyl)-2,3-dihydrofuro[2,1-a]isoquinoline (17) [3%; unstable yellow oil], 2-(2,2,2-trifluoroethyl)-1(2H)-isoquinolinone (18) [5%; pale yellow oil; bp_{20} 180°] and isoquinolinium trifluoroacetyltrifluoromethylmethylide (19) [30%; yellow needles; mp 213-5° (dec)].

Identification of these products was performed by elemental analyses, and the ^{1}H nmr, ^{19}F nmr and mass spectrometry.

All the products were apparently formed through the ylide (20) and no product, such as 3 and 6, resulting directly from the primary 1:1 cycloadduct was not isolated. This characteristic aspect might be ascribed to the steric effect of the 8-proton of isoquinoline ring and high electronegativity of the trifluoromethyl group. Product 16 is a 1,3-dipolar cycloadduct of the ylide 20 and 1, and the formation of 15 and 17 can be easily explained in terms of further transformation from 16. Compound 19 is formed by partial hydrolysis of 20, and treatment of 19 with 1 gave 1,2-bis(trifluoromethyl)-3-trifluoroacethylpyrrolo[2.1-a]isoquinoline (21) [pale yellow needles; mp 102-103°].

Above results show that the reaction of 1 with aromatic N-oxide is prone to form the ylide compounds, which would be useful for synthesis of trifluoromethylated compounds.

References

1. Dedicated to Professor R. B. Woodward on the occasion of his 60th birthday anniversary.
   Presented at the 8th Congress of Heterocyclic Chemistry, Kyoto, Japan, Oct. 1975.
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