Studies on Organic Fluorine Compounds. Part 23.[1] Diels–Alder Reactions of 1,2,3,4-Tetrakis(trifluoromethyl)-5-thiabicyclo[2.1.0]pent-2-ene

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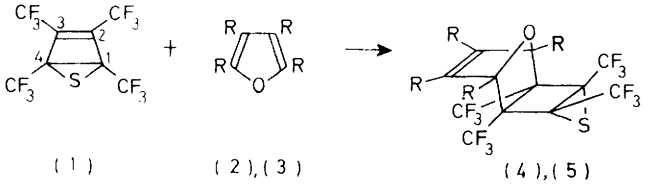
Diels–Alder reactions of Dewar thiophen (1) with acyclic and cyclic dienes have been examined. Butadiene gave the Diels–Alder adduct. Introduction of methyl groups at the 2- and/or the 3-position shortened the reaction time, and methyl groups on position 1 or 4 reduced the rate of the reaction. While cyclopentadiene and pyrrole reacted with compound (1) to give Diels–Alder adducts, substitution of the methylene group or at the nitrogen atom respectively, inhibited the reaction. From these results, the transition state of these Diels–Alder reactions is considered to be the *exo*-form. Cyclohexa-1,3-diene gave an adduct obtained by [4 + 2] reaction of the hexadiene and the thi-iran part of structure (1).

In a previous paper [2] we have reported that a strained double bond carrying trifluoromethyl groups reacts as a dienophile in the Diels–Alder reaction. Thus, 1,2,3,4-tetrakis(trifluoromethyl)-5-thiabicyclo[2.1.0]pent-2-ene [tetrakis(trifluoromethyl)Dewar thiophen] (1) reacts



(1) (2), (3) (4), (5)

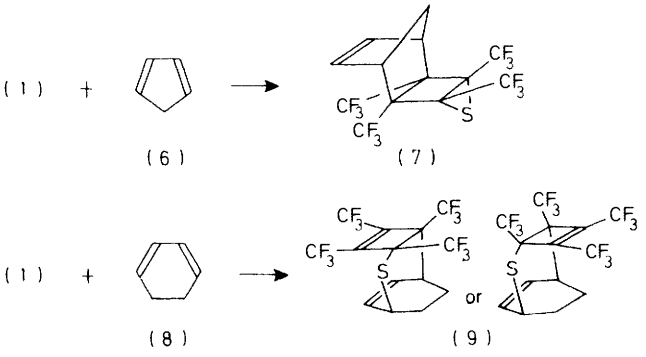
(2), (4) R = H
(3), (5) R = Me

with furans [(2) and (3)] to give Diels–Alder adducts [(4) and (5)]. A characteristic of this reaction is that (4) and (5) are *exo*-forms, contrary to the Alder rule.[3]

We have now investigated the scope and limitation of the Diels–Alder reaction of (1) with other cyclic and acyclic dienes.

First, the reaction with alicyclic dienes was examined. Cyclopentadiene (6) has non-aromatic and conjugated double bonds; it was therefore expected to be more reactive than furan. In fact the diene (6) reacted with (1) to give a 1 : 1 adduct (7), which did not show i.r. absorption near 1 700 cm^{-1}. This showed that the double bond of (1) had participated in the reaction. The high degree of symmetry observed in ^1H and ^{19}F n.m.r. spectra of (7) showed that the compound is 2,3,5,6-tetrakis(trifluoromethyl)-4-thiatetracyclo[5.2.1.$0^{2,6}$.$0^{3,5}$]dec-8-ene. Although these spectral data could not define the stereochemistry, it was tentatively assigned as *exo* by analogy with the furan adducts, determined by *X*-ray analysis.[4]

In contrast with this result, cyclohexa-1,3-diene (8) did not give a Diels–Alder adduct but a 1 : 1 adduct (9) by the participation of the thi-iran part of (1); the i.r. spectrum of the product showed a strong absorption at 1 720 cm^{-1} ascribable to a cyclobutene double bond bearing trifluoromethyl groups. Further, the ^1H n.m.r. spectrum showed peaks for two kinds of olefinic protons,



(1) + (6) → (7)

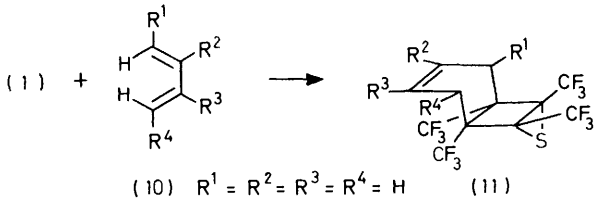
(1) + (8) → (9) or

two methine protons, and four methylenic protons, and the ^{19}F n.m.r. spectrum showed the presence of four

[1] Part 22, Y. Kobayashi, I. Kumadaki, and Y. Hanzawa, *Chem. and Pharm. Bull. (Japan)*, in the press.
[2] Y. Kobayashi, I. Kumadaki, A. Ohsawa, Y. Hanzawa, and M. Honda, *Tetrahedron Letters*, 1976, 2545.
[3] Y. Kobayashi, I. Kumadaki, A. Ohsawa, Y. Sekine, and H. Mochizuki, *Chem. and Pharm. Bull. (Japan)*, 1975, **23**, 2773.
[4] N. Kikutani, Y. Iitaka, Y. Kobayashi, I. Kumadaki, A. Ohsawa, and Y. Sekine, *Acta Cryst.*, 1975, **B31**, 1478.

kinds of trifluoromethyl group. From these data, the product was presumed to be 3,4,5,6-tetrakis(trifluoromethyl)-2-thiatricyclo[5.2.2.$0^{3,6}$]undeca-4,8-diene, although its stereochemistry could not be determined. The lack of formation of a Diels–Alder adduct might be due to steric repulsion between the two methylene groups of (8) and the trifluoromethyl groups of (1).

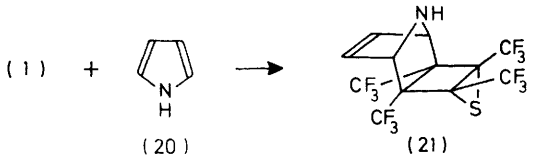
Next, the reaction of (1) with acyclic 1,3-dienes was examined. Butadiene (10) gave a Diels–Alder adduct (11), showing no cyclobutene double bond i.r. absorption and highly symmetrical ^{1}H and ^{19}F n.m.r. spectra. In this case, introduction of methyl groups at the 2- and 3-positions accelerated the reaction [see (12) and (14)], whereas two terminal methyl groups [in (18)] inhibited the reaction. This could be due to steric repulsion between the methyl groups and the trifluoromethyl groups. One terminal methyl group [in (16)] showed no apparent effect; acceleration by the electronic effect might in this case be cancelled by steric hindrance. These facts suggest that the transition state in the Diels–Alder reaction of (1) is an *exo*-form, as confirmed for the reaction with furans, since the inner methyl group should retard the reaction if the transition state were an *endo*-form. Acceleration by methyl groups at the 2- and 3-positions [of (10)] might be explained by the electron-donating effect of methyl groups and an increased proportion of the s-*cisoid* form of the 1,3-diene system.



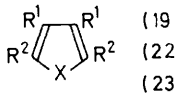
(10) $R^1 = R^2 = R^3 = R^4 = H$ (11)
(12) $R^1 = R^3 = R^4 = H$, $R^2 = Me$ (13)
(14) $R^1 = R^4 = H$, $R^2 = R^3 = Me$ (15)
(16) $R^1 = R^2 = R^3 = H$, $R^4 = Me$ (17)
(18) $R^1 = R^4 = Me$, $R^2 = R^3 = H$

To clarify the nature of the electronic effect, the reaction of 2,5-dimethyl-3,4-bis(trifluoromethyl)furan (19) was examined. Whereas furan and tetramethylfuran [(2) and (3)] gave Diels–Alder adducts [(4) and (5)], as reported earlier, (19) was unchanged under even more drastic conditions than in the case of (2). This means that the electron-attracting effect of the trifluoromethyl groups deactivates furan. Further, pyrrole (20), which is considered to be more aromatic than (2), reacted with (1) to give a Diels–Alder adduct (21), the structure of which must be the *exo*-form by analogy with the adducts from furans,[3] whereas *N*-methylpyrrole (22) was completely unchanged. As the electronic structures of (20) and (22) would be expected to be similar, a steric effect of the *N*-methyl group might account for the difference in reactivity.

Other cyclic dienes, (23)—(25), which are usually regarded as 'good dienes' in the Diels–Alder reaction, were all unchanged after treatment with (1). The cyclobutenic double bond bearing trifluoromethyl groups is an electron-deficient dienophile, and (23) and (24) are electron-deficient dienes; therefore, the cumulative electronic effect is not favourable. In the case of (25), the



(20) (21)



(19) X = O, $R^1 = CF_3$, $R^2 = Me$
(22) X = NMe, $R^1 = R^2 = H$
(23) X = SO_2, $R^1 = R^2 = H$
(24) X = CO, $R^1 = R^2 = Ph$
(25) X = $C(OEt)_2$, $R^1 = R^2 = H$

bulkiness of the two ethoxy-groups seems to have inhibited the reaction.

To summarize, compound (1) is a good dienophile, and its Diels–Alder reaction is governed by electronic effects and by the steric bulk of the terminal substituents of the diene. The latter effect strongly suggests that the transition state is an *exo*-form.

EXPERIMENTAL

2,3,5,6-*Tetrakis*(*trifluoromethyl*)-4-*thiatetracyclo*[5.2.1.$0^{2,6}$.$0^{3,5}$]*dec*-8-*ene* (7).—To a solution of Dewar thiophen (1) [4] (1 000 mg) in CH_2Cl_2 (1 ml), cyclopentadiene (6) (319 mg) was added. The mixture was kept at room temperature for 25 min, then evaporated (vacuum line). The residue was recrystallized from MeOH to give wax-like *crystals* (7) (1 055 mg, 81.3%); m.p. 153—154°; $\nu_{max.}$ (KBr) 1 166 cm^{-1} (CF); δ_H ($CDCl_3$) 6.42 (2 H, s, 8- and 9-H), 3.51 (2 H, s, 1- and 7-H), 2.30 and 1.92 (both 1 H, ABd, *J* 10.8 Hz, CH_2); δ_F* ($CDCl_3$) −3.60 (6 F, s, 3- and 5-CF_3) and −2.52 (6 F, s, 2- and 6-CF_3); *m/e* 422 (M^+), 356 ($C_8F_{12}S$), and 66 (C_5H_6) (Found: C, 36.65; H, 1.4; F, 54.95; S, 8.2. $C_{13}H_6F_{12}S$ requires C, 36.95; H, 1.4; F, 54.05; S, 7.6%).

3,4,5,6-*Tetrakis*(*trifluoromethyl*)-2-*thiatricyclo*[5.2.2.$0^{3,6}$]-*undeca*-4,8-*diene* (9).—Cyclohexa-1,3-diene (8) (224 mg) was added to a solution of compound (1) (1 000 mg) in CH_2Cl_2 (2 ml) and the mixture was kept at room temperature for 7 days, then evaporated (vacuum line). The residue was recrystallized from MeOH to give prisms (184 mg, 15%); m.p. 81°; $\nu_{max.}$ (KBr) 2 950 (CH), 1 720 (C=C of cyclobutene), and 1 200 cm^{-1} (CF); δ_H ($CDCl_3$) 5.93 and 5.51 (both 1 H, m, olefinic H), 3.61 and 3.33 (both 1 H, m, methine H), and 2.11 (4 H, m, methylenic H); δ_F ($CDCl_3$) −3.18 (3 F, m) −1.75 (3 F, m), 0.19 (3 F, m), and 3.48 (3 F, m); *m/e* 436 (M^+).

1,6,7,9-*Tetrakis*(*trifluoromethyl*)-8-*thiatricyclo*[4.3.0.$0^{7,9}$]-*non*-3-*ene* (11).—A solution of compound (1) (2 000 mg) in n-pentane (15 ml) was sealed in a stainless-steel tube and buta-1,3-diene (10) (1.95 g) was added through a vacuum system. The tube was sealed and shaken at room temperature for 6 days. Pentane and the excess of (10) were evaporated off (vacuum line) and the residue was recrystallized from n-pentane to give needles (11) (1 612 mg, 70%); m.p. 176—178°; $\nu_{max.}$ (CCl_4) 1 165 cm^{-1} (CF), δ_H ($CDCl_3$) 6.03 (2 H, m, 3- and 4-H), 2.8 (4 H, m, 2- and 5-H_2);

* In p.p.m. to high field of internal $PhCF_3$.

δ_F ($CDCl_3$) −4.4 (6 F, s) and +4.0 (6 F, s) (Found: M^+, 409.996. $C_{12}H_6F_{12}S$ requires M, 409.999).

3-*Methyl*-1,6,7,9-*tetrakis*(*trifluoromethyl*)-8-*thiatricyclo*-[4.3.0.$0^{7,9}$]*non*-3-*ene* (13).—2-*Methylbuta*-1,3-*diene* (12) (191 mg) was added to a solution of compound (1) (505 mg) in n-pentane (10 ml). The mixture was kept at room temperature for 3 days, then n-pentane and the excess of (12) were evaporated off (vacuum line). The residue was purified by column chromatography and preparative t.l.c. (SiO_2; n-pentane) to give an *oil* (13) (376 mg, 62.6%); $\nu_{max.}$ (CCl_4) 1 175 cm^{-1} (CF); δ_H ($CDCl_3$) 5.67 (1 H, m, 4-H), 2.73 (4 H, s, 2- and 5-H_2), and 1.83 (3 H, s, 3-CH_3); δ_F ($CDCl_3$) −5.4 (3 F, s), −4.4 (3 F, s), and 3.6 (6 F, s) (Found: M^+, 424.016. $C_{13}H_8F_{12}S$ requires M, 424.015).

3,4-*Dimethyl*-1,6,7,9-*tetrakis*(*trifluoromethyl*)-8-*thiatricyclo*-[4.3.0.$0^{7,9}$]*non*-3-*ene* (15).—2,3-Dimethylbuta-1,3-diene (14) (230 mg) was added to a solution of compound (1) (502 mg) in n-pentane (10 ml). The mixture was kept at room temperature for 1—2 days, then evaporated (vacuum line). The residue was purified by column chromatography (SiO_2; n-pentane) to give an *oil* (15) (532 mg, 78.2%); $\nu_{max.}$ (CCl_4) 1 180 cm^{-1} (CF); δ_H ($CDCl_3$) 2.73 (4 H, s, 2- and 5-H_2) and 1.78 (6 H, s, 3- and 4-CH_3); δ_F ($CDCl_3$) −5.2 (6 F, s) and 3.4 (6 F, s) (Found: M^+, 438.034. $C_{14}H_{10}F_{12}S$ requires M, 438.031).

2-*Methyl*-1,6,7,9-*tetrakis*(*trifluoromethyl*)-8-*thiatricyclo*-[4.3.0.$0^{7,9}$]*non*-3-*ene* (17).—*trans*-Penta-1,3-diene (16) (200 mg) was added to a solution of compound (1) (508 mg) in n-pentane (10 ml). The mixture was kept at room temperature for 6—7 days, then evaporated (vacuum line). The residue was passed through a silica gel column in n-pentane solution, and the product was recrystallized from n-pentane, and sublimed to give *prisms* (17) (97.6 mg, 16.1%); m.p. 138—140°; $\nu_{max.}$ (CCl_4) 1 160 cm^{-1} (CF); δ_H ($CDCl_3$) 6.0 (2 H, m, 3- and 4-H), 2.95 (3 H, m, 2-H and 5-H_2), and 1.35 (3 H, m, 2-CH_3); δ_F ($CDCl_3$) −4.8 (3 F, m), −3.6 (3 F, s), −2.4 (3 F, s), and 3.6 (3 F, m) (Found: M^+, 424.015. $C_{13}H_8F_{12}S$ requires M, 424.015).

2,3,5,6-*Tetrakis*(*trifluoromethyl*-4-*thia*-10-*azatetracyclo*-[5.2.1.$0^{2,6}$.$0^{3,5}$]*dec*-8-*ene* (21).—Pyrrole (20) (90 mg) was added to a solution of compound (1) (4.80 mg) in $CHCl_3$ (2.5 ml). The mixture was kept at room temperature for 30 min, then evaporated (vacuum line). The residue was purified by sublimation to give *prisms* (21) (400 mg, 70%); m.p. 78°; $\nu_{max.}$ (KBr) 1 161 cm^{-1} (CF); δ_H ($CDCl_3$) 6.65 (2 H, s, 8- and 9-H), 4.63 (2 H, s, 1- and 7-H), and 2.10br (1 H, s, NH); δ_F ($CDCl_3$) −2.92 (6 F, s) and −1.96 (6 F, s); *m/e* 404 (M − F), 356 ($C_8F_{12}S$), and 67 (C_4H_5N).

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