Regiospecific Annelations of Substituted Tropones with Ethane-1,2-dithiol

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2-Butyl-, 2-phenyl-, and 3-chloro-tropone were found to react with ethane-1,2-dithiol in methanol in the presence of boron trifluoride–ether † to give annelated products *via* addition of one sulphur atom to C-7 and replacement of the carbonyl oxygen by the other sulphur atom. The yields were low with the chloro-compound, but good in the other two cases. The same tropones were also found to react with boron trifluoride–ether alone in methanol to give, slowly, isolable equilibrium adducts of BF_3 addition to the carbonyl oxygen. These adducts reacted with ethane-1,2-dithiol to give the same annelated products mentioned above. A variety of other 2- and 3-substituted tropones, *viz* 2-hydroxy-, 2-methoxy-, 2-dimethylamino-, 3-methoxy-, and 3-dimethylamino-tropone, also gave isolable equilibrium adducts of BF_3 addition to the carbonyl oxygen which, however, were unreactive towards ethane-1,2-dithiol. Tropones like 2-tosyloxy-, 2-chloro-, and 2-methylthio-tropone are placed in a third category because they failed to react with either boron trifluoride–ether alone in methanol or with ethane-1,2-dithiol–boron trifluoride–ether in methanol.

RECENTLY we have discovered that tropone and either ethane-1,2-dithiol or propane-1,3-dithiol, under typical conditions for dithioacetalization of ketones (boron trifluoride-ether and methanol),[1] undergo (1 ⟶ 2) annelation instead.[2]

Our interest in such annelated cycloheptatrienes prompted us to synthesize other vicinally di-[3] or tri-substituted[4] cycloheptatrienes. As a further extension of such studies, we report here on the examination of our method of annelation with respect to the synthesis of fused cycloheptatrienes (2) carrying substituents at specific positions on the cycloheptatriene ring. We have examined the behaviour of various 2- and 3-substituted tropones towards ethane-1,2-dithiol in methanol at room temperature in the presence of boron trifluoride–ether. Although the desired annelation has been obtained in only a few cases, it is interesting to note that successful annelations were strictly regiospecific and, in some cases, also proceeded in good yield. Thus, 2-phenyltropone (3b)[5] gave 2,3-dihydro-9-phenyl-4a*H*-cyclohepta[*b*]-1,4-dithiin (4b) in 56% yield along with recovered tropone (3b) (40%). The annelation was slower than in the case of tropone (1), which gives compound (2a)[2] but, in contrast to the reaction with tropone (1),[2] no tars were noticed.

That the product has structure (4b) is supported by its elemental analysis and by the [1]H n.m.r. spectrum which shows a multiplet at δ 7.4 for the phenyl protons, a multiplet at δ 6.1—6.7 for the 6-, 7-, and 8-H protons, an ABX quartet centred at δ 5.55 for the 5-H proton, and a multiplet at δ 2.7—3.4 for both the 4a-H and methylene protons. On irradiation at the latter resonance, the ABX quartet became a doublet with $J_{5,6}$ 8 Hz. This observation, in accord with previous experience on related substances,[3] is most indicative of the proposed structure.

The case of the 9-butyl analogue (4a) was similar to that of (4b) as regards the regiospecificity and the [1]H n.m.r. structural evidence. The yield of compound (4a)

was 45%, while 40% of the unchanged tropone (3b) was recovered.

The last case concerns the 8-chloro-analogue (6) which was obtained from 3-chlorotropone (5).[6] Although the reaction of ethane-1,2-dithiol with compound (5) was faster than with either (3a) or (3b),‡ the yield of the annelated product (6) was low, *ca.* 15%, and much tar was also formed. § No other product having a cyclo-heptatriene structure could be found, besides compound (6), in the reaction mixture. The result is thus a regiospecific annelation.

That the product has structure (6) is supported by elemental analysis and by the [1]H n.m.r. spectrum which shows a multiplet at δ 5.7—6.6 for the 6-, 7-, and 9-H protons, an ABX quartet centred at δ 5.3 for the 5-H proton, and a multiplet at δ 1.9—3.1 for the 4a-H and methylene protons. Most significantly, on irradiation at δ 2.9, the ABX quartet became a doublet with $J_{5,6}$ 9 Hz. This is in accord with structure (6) for vicinal coupling between the 5-H and 6-H protons,[7] and rules out structure (8) which was a likely alternative to (6).[2,3b]

On treatment of compound (6) with trityl tetra-fluoroborate we obtained an alkylthiotropylium salt to which we assigned structure (7). In fact, on the basis of previous experience,[4] attack of the cation at S-4 rather than at the 4a-H protons was expected.

All other 2- or 3-substituted tropones which have been investigated (including 2-hydroxy-, 2-tosyloxy-, 2- or 3-dimethylamino-, 2-chloro-, 2-methylthio-, and 2- or 3-methoxy-tropone), but excluding the case of 3-tosyloxytropone (which is dealt with later), failed to react with ethane-1,2-dithiol under the conditions used

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† Throughout this paper, 'ether' refers to diethyl ether.

‡ It should be stated that, whereas with either compound (3a) or (3b) the order of addition of the reagents is immaterial, in the case of the chloride (5) the addition of boron trifluoride–ether *must* precede that of ethane-1,2-dithiol. The reverse order of addition led to competitive nucleophilic substitution of chlorine by the thiol sulphur.

§ It should be remembered that 3-chlorotropone (5) is quite unstable *per se*, decomposing to give tars (ref. 6). The low yield of compound (6) may thus well reflect such intrinsic instability rather than any particular difficulty in the annelation.

with substrates (1), (3a, b), and (5). Since a prolonged reaction time in the case of 2-methoxytropone (4 d at room temperature) led only to a 2% disappearance of the tropone, this reaction is, clearly, devoid of any synthetic utility.

(1) → (2)

a ; n = 2
b ; n = 3

(3) → (4)

a ; R = Bu^n
b ; R = Ph

(5) → (6)

(8)   (7)
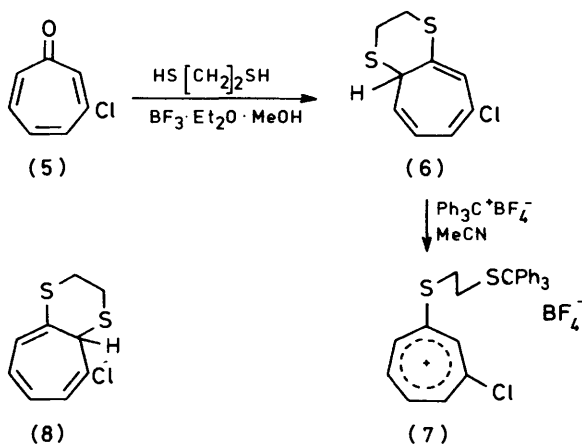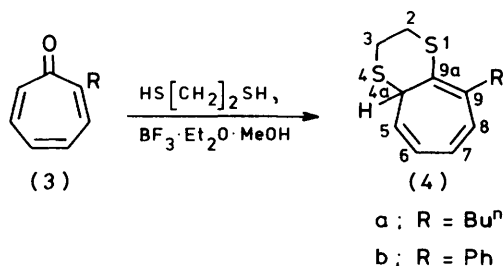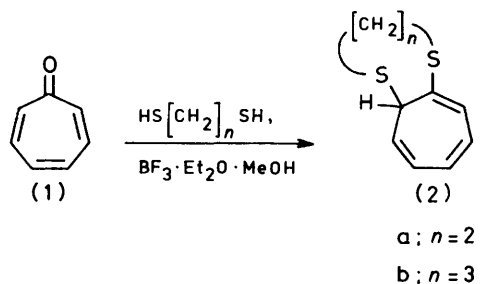
3-Tosyloxytropone is a special case. It did, in fact, react with ethane-1,2-dithiol in methanol at room temperature in the presence of boron trifluoride–ether. Although t.l.c. revealed a multitude of products, we failed to detect the presence of any annelated product of type (2).

In order to understand the factors determining the course of the reactions of tropones with dithiols, and to gain some guidance towards syntheses in this area, we studied the reactions of the aforementioned tropones with boron trifluoride–ether alone in methanol at room temperature.

Those tropones which, like compounds (1), (3a, b), and (5), were found to give annelated products with

ethane-1,2-dithiol in the presence of boron trifluoride, also react with boron trifluoride alone to give, slowly and reversibly, boron trifluoride adducts. In the case of tropone (1) a crystalline 1 : 1 adduct with boron trifluoride (9) could be isolated in ca. 100% yield. Structure (9) can be assigned to the adduct on the basis of its elemental analysis and both the ^{1}H n.m.r. and u.v. spectra. The ^{1}H n.m.r. spectrum (CD$_3$OD) showed, besides the typical multiplet at δ 7.2—7.5 for tropone (1) (18%), a multiplet at δ 8.2—9.0 (82%) attributable to the adduct (9).[7] In parallel, the u.v. spectrum showed, besides the typical absorption band for tropone at 303 nm, an absorption band at 313 nm also attributable to the adduct (9).[7] On addition of boron trifluoride–ether to the solution, both the δ 7.2—7.5 multiplet and the u.v. band at 303 nm decreased in intensity, while, correspondingly, both the n.m.r. resonance and the u.v. absorption for the tropone–boron trifluoride adduct increased. These facts suggest an equilibrium between compound (1) and boron trifluoride which is much less displaced towards the product (9) than with the tropones dealt with below. This is indicated in the Table by ' slow ' and ' small K.'

In the case of compounds (3a, b) and (5) a similar situation was encountered, although no attempt was made to isolate the corresponding boron trifluoride adducts.

The other tropones in the Table, with one exception, can be classified into two groups. The exception concerns 3-tosyloxytropone which will be dealt with later. Thus, while the tropones of both groups fail to react with ethane-1,2-dithiol in the presence of boron trifluoride, those in the first group (2-tosyloxy-, 2-chloro-, and 2-methylthio-tropone) also fail to interact to any extent with boron trifluoride–ether alone in methanol. In fact, the u.v. absorption spectrum (in methanol) of the tropones of the first group did not appreciably change on addition of boron trifluoride–ether.

In contrast, the tropones of the second group (2-hydroxytropone, 2- and 3-methoxy-, and 2- and 3-dimethylamino-tropone) gave 1 : 1 adducts with boron trifluoride. With the exception of the oily adduct (11) from 2-methoxytropone, all other adducts [(10) from 2-hydroxytropone, (12) from 2-dimethylaminotropone, (13) from 3-methoxytropone, and (14) from 3-dimethylaminotropone] are crystalline. These equilibrium reactions differ from those leading to adduct (9) and its close congeners obtained from the tropones (3a, b) and (5) in being faster and more displaced towards the product; this is indicated in the Table by ' fast ' and ' large K.'

The evidence for the structure of the new adducts (10)—(14) is similar to that given above for adduct (9). The dimethylamino-cases (12) and (14) need a special comment, however. The u.v. absorption spectra of these adducts, showing absorption bands at $\lambda_{max.}$ 382 and 328 nm, respectively, for adducts (12) and (14) are closely similar to those of the corresponding methoxytropylium tetrafluoroborate salts for which immonium

structures have been proposed.[8]   Therefore, we suggest a large contribution of the immonium form in both adducts (12) and (14).   Also, we rationalize the observed magnetic equivalence of the two methyl groups in the adducts (12) and (14) by the same arguments used in the case of the 2- and 3-dimethylamino-methoxytropylium salts.[8]

Reactions of tropones,* or of their BF_3-adducts, in methanol at room temperature

Troponoid	A	B	C
Tropone	(2a) (50) [a]	slow, (9), (small K)	(2a)
2-Butyltropone	(4a) (45) [b]	slow, (small K)	(4a)
2-Phenyltropone	(4b) (56) [c]	slow, (small K)	(4b)
2-Hydroxytropone	NR	fast, (10), (large K)	NR
2-Tosyloxytropone	NR	NR	—
2-Methoxytropone	NR [d]	fast, (11), (large K)	NR
2-Chlorotropone	NR	NR	—
2-Dimethylaminotropone	NR	fast, (12), (large K)	NR
2-Methylthiotropone	NR	NR	—
3-Tosyloxytropone	[e]	slow, (small K)	NR
3-Methoxytropone	NR	fast, (13), (large K)	NR
3-Chlorotropone	(6) (15)	slow, (small K)	(6)
3-Dimethylaminotropone	NR	fast, (14), (large K)	NR

A: Reactions of tropones with ethane-1,2-dithiol–BF_3 to give the indicated annelated products (yield %). B: Reactions of tropones with BF_3, *via* either a slow or fast equilibrium addition of BF_3 to the carbonyl oxygen, to give the indicated adducts; (small K) = equilibrium little displaced towards product under given reaction conditions; (large K) = equilibrium strongly displaced towards product under given reaction conditions. C: Reactions of tropone–BF_3 adducts with ethane-1,2-dithiol to give the indicated annelated products.

* NR = no reaction.   [a] Ref. 2.   [b] Unchanged compound (3a) (40%) also recovered.   [c] Unchanged compound (3b) (40%) also recovered.   [d] See text.   [e] The tropone disappeared without giving annelated products.

3-Tosyloxytropone constitutes a special case even in respect to the reaction with boron trifluoride alone. This tropone at low concentrations (*ca.* 10^{-5}—10^{-4}M) seems to give slowly, and with a small K value (Table), a boron trifluoride-adduct with $\lambda_{max.}$ (MeOH) (log ε) 253 (4.20) and 297 nm (3.72).   However, when working at preparative concentrations, it proved impossible to isolate any definite product.   T.l.c. revealed a complex mixture, possibly resulting from the work-up procedure.

Although we have previously obtained some evidence for the elusive tropone dithioacetals in non-spiro cases,[3] we can best accommodate the majority of the above results in terms of the tropylium-ion route[2] to the annelated products.   Thus, annelation of the substrates (3a, b) and (5) can be viewed as proceeding *via* attack of the two sulphur atoms of ethane-1,2-dithiol at C-1 and C-7 of a species such as adduct (9) as in the case of tropone itself.[2]   The regiospecificity observed with

substrates (3a, b) and (5) may be viewed in terms of both electronic and steric contributions of the substituent favouring attack at C-7.

Following this reasoning, lack of annelation with aminotropones is attributed to the non-availability of a positively charged tropylium carbon for attack by the sulphur nucleophile because the positive charge is

(9) (10)

(11a) (11b)

(12)

(13)

(14)
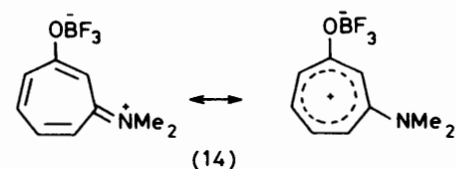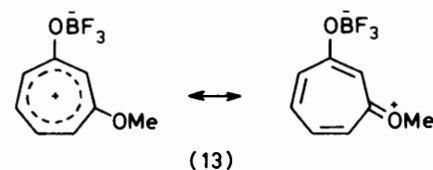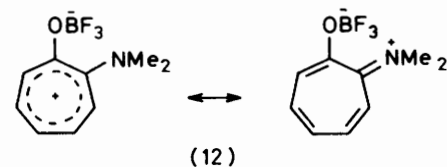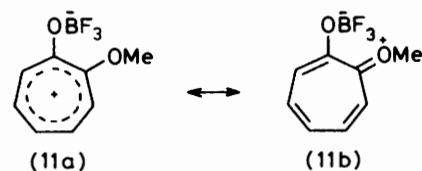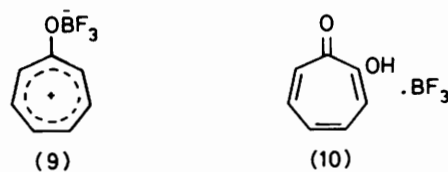
delocalised onto the immonium ion moiety.   This suggests that failure of both hydroxy- and methoxy-tropones to undergo annelation with ethane-1,2-dithiol may result from a large contribution of the oxonium-ion canonical structure, *e.g.* (11b) of 2-methoxytropone, while similar structures can be written for the adducts (10) and (13) of 2-hydroxytropone and 3-methoxy-tropone, respectively.

EXPERIMENTAL

[1]H N.m.r. spectra were taken with a Varian 360 (60 MHz) or a Joel SP100 (100 MHz) spectrometer.   Chemical shifts are given in δ (p.p.m.) values from SiMe$_4$ as internal reference.   I.r. spectra were recorded on a Perkin-Elmer 337 grating spectrometer and u.v. spectra on a Varian Techtron

635 spectrometer. Both analytical and preparative t.l.c. were carried out on Merck silica gel 60 F_{254} plates with adsorbent thicknesses of, respectively, 0.25 and 2 mm. Light petroleum refers to that fraction boiling in the range 30—50 °C.

9-Butyl-2,3-dihydro-4aH-cyclohepta[b]-*1,4-dithiin* (4a).— To a stirred solution of 2-butyltropone (3a)[5] (0.064 g, 0.395 mmol) in dry methanol (7 ml) was added, under nitrogen, ethane-1,2-dithiol (0.1 ml, 1.19 mmol) and boron trifluoride-ether (0.1 ml, 0.81 mmol). After 2 d, the yellow mixture was evaporated to dryness under reduced pressure, the residue was taken up into chloroform, and the solution was washed with aqueous 5% sodium hydrogencarbonate and then twice with water. The chloroform phase was dried (Na_2SO_4), and evaporated under reduced pressure to small volume and the residue was subjected to preparative t.l.c. with light petroleum–diethyl ether (9 : 1) as developer. The R_F 0.73 band gave the *title compound* (4a) as an oil (0.039 g, 45%) (Found: C, 65.65; H, 7.5; S, 27.1. $C_{13}H_8S_2$ requires C, 65.49; H, 7.61; S, 26.89%); δ_H (CDCl₃) 5.9—6.6 (3 H, m), 5.55 (1 H, ABXq, which on irradiation at δ 3 became a doublet, $J_{5,6}$ 8 Hz), 2.3—3.5 (total 7 H, m, 2-H₂, 3-H₂, 4a-H, and α-CH_2 of the butyl chain), 1.3 (total 4 H, m, CH_2CH_2-CH_2CH_3), and 0.9 (3 H, t, J 7 Hz, CH₃); $v_{max.}$ (neat) 3 000, 2 955, 2 920, 2 855, 1 470, 1 420, 1 290, 910, 883, 757, and 735 cm⁻¹. The R_F 0.2 band gave unchanged starting material (3a) (0.0195 g, 40% recovery).

2,3-Dihydro-9-phenyl-4aH-cyclohepta[b]-*1,4-dithiin* (4b).— Following closely the procedure described above for compound (4a), the tropone (3b)[5] (0.070 g, 0.385 mmol) afforded, after work-up and preparative t.l.c. [light petroleum–diethyl ether (7 : 3) as developer, *compound* (4b) as a viscous oil (0.056 g, 56%) from the band with R_F 0.7. Repeated t.l.c. purification gave an analytically pure sample (Found: C, 69.5; H, 5.7; S, 25.1. $C_{14}H_{14}S_2$ requires C, 69.72; H, 5.46; S, 24.82%); δ_H (CDCl₃) 7.4 (5 H, m), 6.1—6.7 (3 H, m), 5.55 (1 H, ABXq, which on irradiation at δ 3 gave a doublet, $J_{5,6}$ 8 Hz), and 2.7—3.4 (5 H, m); $v_{max.}$ (neat) 3 100, 3 060, 3 020, 2 910, 1 600, 1 490, 1 440, 1 410, 1 365, 1 290, 1 130, 907, 800, 753, and 700 cm⁻¹. The R_F 0.14 band gave unchanged starting material (3b) (0.028 g, 40% recovery).

8-Chloro-2,3-dihydro-4aH-cyclohepta[b]-*1,4-dithiin* (6).— To a stirred solution of 3-chlorotropone (5) (0.21 g, 1.49 mmol) in dry methanol (25 ml) was added, under nitrogen, boron trifluoride–ether (3.0 mmol) and then ethane-1,2-dithiol (4.5 mmol). After 2 d, because of the formation of much tar, the procedure utilized for the synthesis of compounds (2a and b),[3b] which is particularly suited for extraction of products from tarry mixtures, was closely followed. Hence, careful work-up and preparative t.l.c. as developer (benzene) and extraction of the R_F 0.76 band gave the product (6) as an oil (0.048 g, 15%) (Found: C, 49.55; H, 4.2; S, 29.35. $C_9H_9ClS_2$ requires C, 49.87; H, 4.18; S, 29.58%); δ_H (C₆D₆) 5.7—6.6 (3 H, m), 5.3 (1 H, ABXq, which on irradiation at δ 2.9 became a doublet, $J_{5,6}$ 9 Hz), and 1.9—3.1 (5 H, m); $v_{max.}$ (neat) 2 960, 2 910, 1 555, 1 420, 1 260, 1 097, 1 054, 1 029, 886, 865, 822, and 790 cm⁻¹. No unchanged 3-chlorotropone was recovered from the reaction mixture.

1-Chloro-3-[(2-triphenylmethylthio)ethylthio]tropylium Tetrafluoroborate (7).—To a solution of trityl tetrafluoroborate (0.122 g, 0.37 mmol) in dry acetonitrile (5 ml) was added, at room temperature under nitrogen, an equimolar amount of compound (6). On addition of diethyl ether, the

salt (7) precipitated as yellow crystals (0.19 g, 94%), m.p. 162—163 °C (decomp.) (from acetonitrile) (Found: C, 61.5; H, 4.45; S, 11.75. $C_{28}H_{24}BClF_4S_2$ requires C, 61.49; H, 4.42; S, 11.73%); δ_H 7.8—8.2 (5 H, m, tropenylium protons), 7.0 (15 H, m, 3 × Ph), and 2.6 (4 H, m, 2 × CH₂).

Synthesis of the Tropone–Boron Trifluoride Adducts.—To a solution of the respective tropone in dry methanol (0.8M) was added, at room temperature under nitrogen, a slight molar excess of boron trifluoride-ether. After *ca.* 12 h the mixture was concentrated by evaporation under reduced pressure. In the case of the dimethylaminotropones and of 2-hydroxytropone, cooling of the concentrated mixture led to precipitation of crystalline adducts. In the other cases precipitation of crystalline adducts only occurred during prolonged cooling of the concentrated reaction mixture at −20 °C. The crystalline adducts were then filtered off and recrystallized from methanol. Because the adduct from 2-methoxytropone failed to crystallize, the solvent was decanted and the oily residue was washed several times with ether, whereby a yellow oil was obtained. Thus obtained was the *tropone–boron trifluoride adduct* (9) as crystals, m.p. 65 °C (from methanol) (Found: C, 44.0; H, 4.2. $C_7H_6BF_3O\cdot H_2O$ requires C, 43.81; H, 4.20%); δ_H (CD₃CN) 8.2—9.0 (m); δ_H (CD₃OD) 8.2—9.0 (m, adduct protons, 82%), 7.2—7.5 (m, free tropone protons, 18%); $\lambda_{max.}$ (MeOH) 313, 303, and 228 nm.

The *2-hydroxytropone–boron trifluoride adduct* (10); crystals, m.p. 158 °C (from methanol) (Found: C, 41.0; H, 3.9. $C_7H_6BF_3O\cdot H_2O$ requires C, 40.44; H, 3.88%); δ_H (CD₃CN) 8.7—7.5 (m); $\lambda_{max.}$ (MeOH) (log ε) 305 (3.86) and 358 nm (3.66).

The *2-methoxytropone–boron trifluoride adduct* (11); yellow oil; δ_H (CD₃OD) 7.6—8.4 (5 H, m) and 4.32 (2 H, s); $\lambda_{max.}$ (Me₃OH) (log ε) 237 (4.51), 305 (3.79), 320 (3.80), 337 (3.76), and 348 nm (3.77).

The *2-dimethylaminotropone–boron trifluoride adduct* (12); yellow crystals, m.p. 127 °C (from methanol) (Found: C, 46.3; H, 4.8; N, 6.0. $C_9H_{11}BF_3NO\cdot H_2O$ requires C, 46.00; H, 4.72; N, 5.96%); δ_H (CD₃OD) 7.2—7.7 (5 H, m) and 3.45 (6 H, s); $\lambda_{max.}$ (Me₃OH) (log ε) 253 (4.30) and 382 nm (3.89).

The *3-methoxytropone–boron trifluoride adduct* (13); crystals, m.p. 125 °C (from methanol) (Found: C, 43.8; H, 4.75. $C_8H_8BF_3O_2\cdot H_2O$ requires C, 43.29; H, 4.54%); δ_H (CD₃CN) 7.9—8.4 (4 H, m), 7.52br. (1 H, s), and 4.3 (3 H, s); $\lambda_{max.}$ (Me₃OH) (log ε) 292 nm (3.54).

The *3-dimethylaminotropone–boron trifluoride adduct* (14); pale yellow crystals, m.p. 112 °C (from methanol) (Found: C, 46.2; H, 4.75; N, 5.9. $C_9H_{11}BF_3NO\cdot H_2O$ requires C, 46.00; H, 4.72; N, 5.96%); $\lambda_{max.}$ (Me₃OH) (log ε) 265 (4.07) and 328 nm (3.72).

U.v. Monitoring of the Reactions of the Tropones with Boron Trifluoride.—To a *ca.* 10⁻⁵M solution of the tropone in dry methanol (3 ml), placed in a spectrophotometric cuvette, was added boron trifluoride–ether (two drops). The reaction of tropone (1), which was the reaction most accurately studied, proved to be very complex. In fact, u.v. monitoring of this reaction clearly revealed that it must proceed in at least two stages, as indicated by the appearance of an isosbestic point (λ 304 nm), followed by its disappearance, and the appearance of a second isosbestic point (λ 288 nm). T.l.c. of the reaction mixture gave a spot with R_F 0.6 [hexane–diethyl ether (85 : 15) as developer] which was extracted with methanol to give a product with the same u.v. spectrum as authentic adduct (9).

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