Electrocyclic Aromatic Substitution by the Diazo Group. Part 4.[1] Periselectivity Studies on the Cyclisation of 1-Thienyl-3-diazoalkenes: a Route to 3*H*-Thieno[1,2]diazepines

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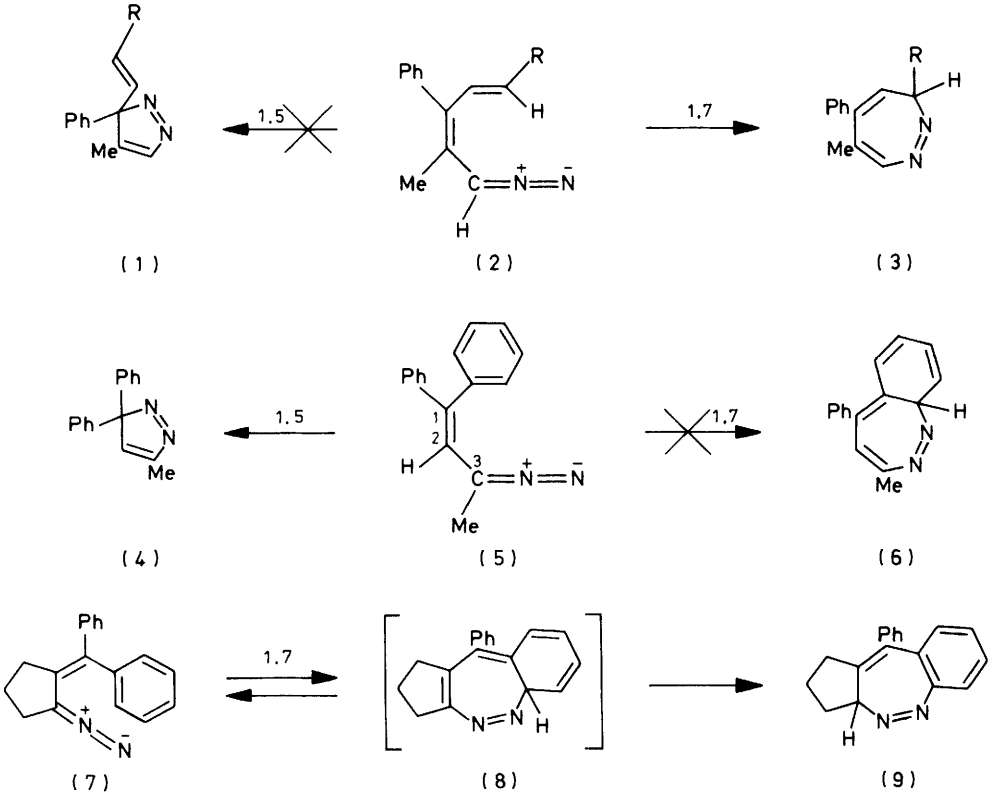
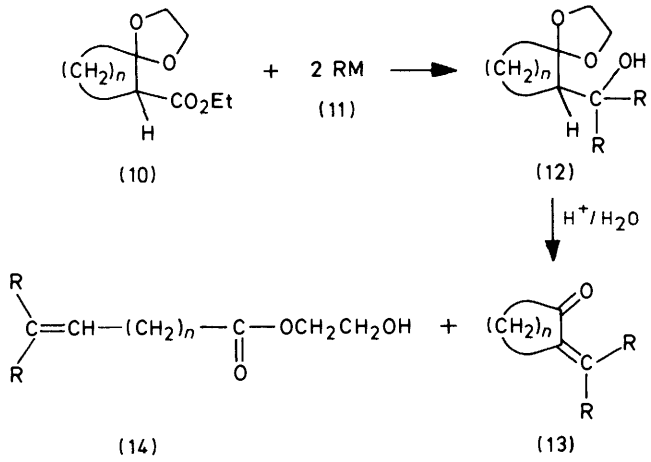
In the cyclisation reactions of the 1-thienyl-3-diazoalkenes (19) and (23) the thiophene ring is more reactive to 1,7 (8π-electron) electrocyclic substitution than the analogous arene ring in the 1-phenyl-3-diazoalkene (5). The 3,3-di-2-thienyl-3*H*-pyrazole (21b) undergoes thermal ring expansion to give the thienodiazepine (20b) in contrast to its diaryl analogue (4) which reacts by a primary [1,5] sigmatropic shift of the aryl group.

In recent studies on the electrocyclisation reactions of αβ,γδ-unsaturated diazo compounds we have shown that the mode of ring closure is strongly influenced by the nature of the γδ-double bond. In cases where it is olefinic in nature, *e.g.* in (2), the diazo compounds cyclise only *via* 1,7 closure to give 3*H*-1,2-diazepines, *e.g.* (3),[2] and produce no isolable quantities of the 3-vinylpyrazoles (1) † which would have resulted from the alternative 1,5 closure. The situation is reversed in compounds such as (5) in which the γδ-bond is part of an arene ring; these generally cyclise wholly by 1,5-closure to give 3*H*-pyrazoles, *e.g.* (4), rather than 1,2-benzodiazepines such as (6).[3] However in compounds of this type the periselectivity can be manipulated so that 1,7 cyclisation becomes competitive, by raising the activation energy for the 1,5 process by the fusion of a cyclopentyl ring at C-2,C-3 [3] or C-1,C-2.[4] Thus for the phenylalkene (7), only 1,7-cyclisation is observed, giving the 3*H*-1,2-benzodiazepine (9) in good yield. In this case the overall reaction is the substitution of an arene hydrogen by an azo group *via* a reversible 8π-electrocyclisation which gives the tricyclic compound (8), followed by a 1,5 sigmatropic hydrogen migration.[5]

The work described in this paper is concerned with the reactions of compounds of the same general type as (5) and (7) but containing thiophene rather than arene rings. It was undertaken to probe the reactivity of the thiophene ring to electrocyclisation, *i.e.* to discover whether in systems such as (19) and (23) the thiophene ring would be more susceptible to 1,7 ring closure than the benzene ring in (5) and so provide a general route to the thieno[2,3-*c*]- and thieno[3,2-*c*]-[1,2]diazepine systems, *e.g.* (20) and (24), which were unknown at the start of this investigation (but have since been prepared *via* the ring expansion of thienopyridinium *N*-imides [6,7]).

† Or rearrangement products produced by group migrations in compound (1).





	(13) (%) *	(14) (%) *
a; n = 3, R = 2-Thienyl, M = MgBr	33	51
b; n = 3, R = 3-Thienyl, M = Li	22	46
c; n = 4, R = 2-Thienyl, M = MgBr	0	83
d; n = 4, R = 3-Thienyl, M = Li	0	75

* Yields based on (10)

Scheme 1.

Results and Discussion

The diazo compounds studied were all generated by the thermal decomposition of the sodium salts of tosylhydrazones at *ca.* 80 °C under aprotic conditions. Several of the β-thienyl-αβ-unsaturated ketones required as precursors to the tosylhydrazones did not prove easy to prepare by the routes used for their aryl analogues and these preparations are discussed in the next section.

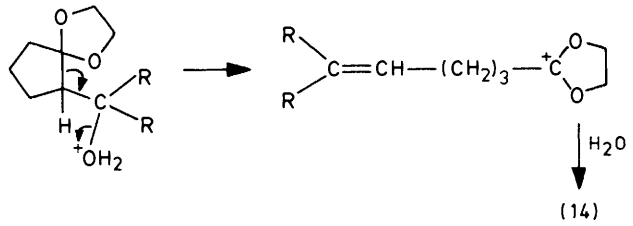
Preparation of β-Thienyl-αβ-unsaturated Ketones.—2-Di-2-thienyl- and 2-di-3-thienyl-methylenecyclopentanone (13a) and (13b) were prepared *via* reaction of the appropriate Grignard or organolithium reagent (11) with ethyl 1,4-dioxaspiro[4.4]nonane-6-carboxylate (10; n = 3) as shown in Scheme 1. The primary products (12), however, on treatment with acid gave not only the required ketones (13a) and (13b) but also the hydroxyesters (14a) and (14b) in substantial amounts. It seems likely that the latter are formed by the pathway shown in Scheme 2. Interestingly the diaryl analogues of (14) were not detected in the preparation of 2-diarylmethylenecyclopentanones by the same reaction.[3]

Attempts were made to apply the same low yielding but convenient procedure to the preparation of the analogous 2-dithienylmethylenecyclohexanones (13c) and (13d). However in these cases, although the first stage gave the required alcohol, subsequent acid hydrolysis gave only the hydroxyesters (14c) and (14d) even though this method had worked well for the preparation of 2-di-*p*-tolylmethylenecyclohexanone.[3] Other attempts to prepare (13c) and (13d) *via* directed aldol reactions of the anion of cyclohexanone dimethylhydrazone (15) with di-2-thienyl and di-3-thienyl ketones respectively, were also unsuccessful owing largely to difficulty in deprotection and dehydration and the ease with which the retro-aldol process takes place. However this method was successful for the preparation of 2-[phenyl(2-thienyl)methylene]-cyclohexanone (16), which was obtained as an inseparable mixture of *E* and *Z* isomers. Similarly the 4,4-dithienylbut-3-en-2-ones (17a) and (17b) were prepared by reaction of the anion of acetone dimethylhydrazone with di-2-thienyl and di-3-thienyl ketones respectively.

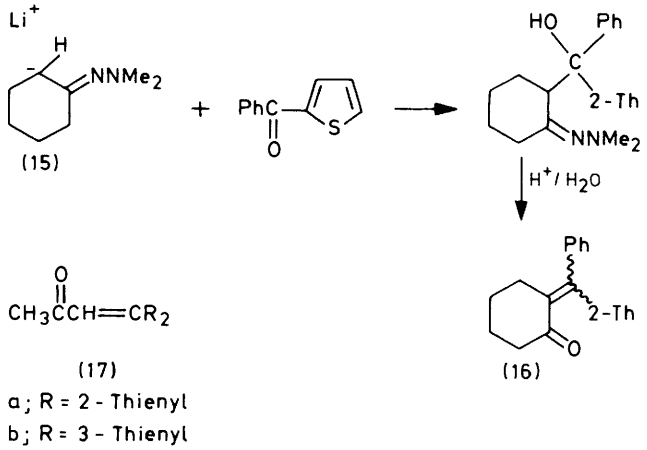
Cyclisation Reactions.—The first experiments on these systems were carried out with compounds (19a) and (23a). These are the direct thienyl analogues of (7) and so they were expected to undergo 1,7 cyclisation. In the event they did so very readily and gave only the thienodiazepines (20a) and (24a) respectively in high yields. It is notable that these reactions were complete in only 30 min under conditions where the aryl analogue (7) required *ca.* 7 h. Also, in the aryl case the red colour of the diazo compound persisted for many hours during the reaction whereas in the thermolysis of the tosylhydrazones (18a) and (22a) no red colour was observed at all, thus indicating that the faster formation of products (20a) and (24a) resulted from an increase in the rate of the cyclisation step rather than a more rapid generation of the diazo compounds from their tosylhydrazone salt precursors. It is also interesting that the tricyclic product (26) was not formed in the cyclisation of the diazo compound (23a), *i.e.* ring-closure occurred only at the 2-position of the thiophene ring although the 3-position is highly reactive in (19a). This parallels the recent observation that the thienylalkene (27) does not cyclise [8] and provides a further indication that the thiophene 3,4-bond lacks sufficient double bond character to participate in electrocyclisation.

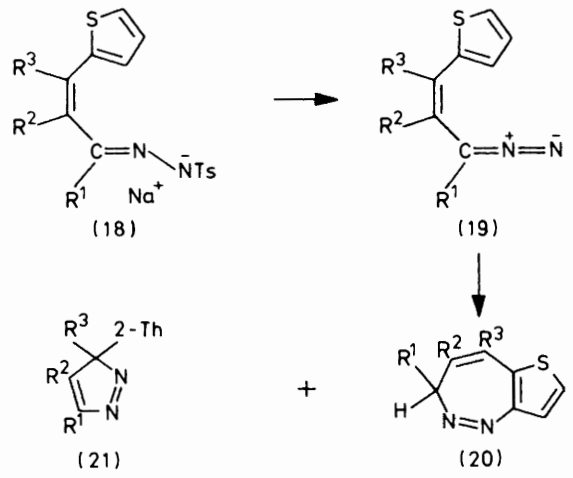
These cyclisations of the diazothienylalkenes (19a) and (23a) were carried out first to ensure (i) that the reactions of the thiophene systems did in fact parallel that of the benzene analogue (7) when subjected to the same steric constraint, and (ii) that the new 1,2-thienodiazepine systems were stable under the reaction and work-up conditions.

The cyclisation reactions of the diazo compounds derived from (18b), (18c), and (22b) were then examined. These were found to cyclise by both 1,5 and 1,7 ring closure to give mixtures of pyrazoles and diazepines whereas earlier work [3] had shown that the diaryl analogues gave only pyrazoles, *e.g.* (5) ⟶ (4). Thus, for example, the 2-thienyl derivative (19b) after a reaction time of 30 min gave the pyrazole (21b) (49%) and the diazepine (20b) (19%). When a similar experiment was

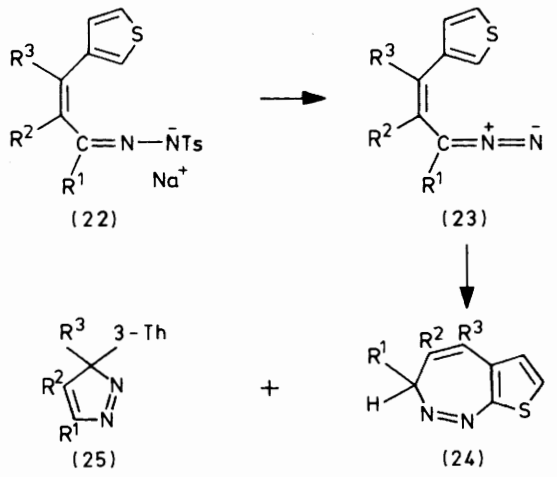


Scheme 2.





	(20) (%)	(21) (%)
a; $R^1,R^2 = (CH_2)_3$, R^3 = 2-Thienyl	85	0
b; R^1 = Me, R^2 = H, R^3 = 2-Thienyl	19 (see text)	49
c; $R^1,R^2 = (CH_2)_4$, R^3 = Ph (*E* and *Z* mixture)	10	85



	(24) (%)	(25) (%)
a; $R^1,R^2 = (CH_2)_3$, R^3 = 3-Thienyl	90	0
b; R^1 = Me, R^2 = H, R^3 = 3-Thienyl	8	43

monitored by h.p.l.c. it was found that the diazepine to pyrazole ratio increased as the reaction proceeded and it was subsequently shown that the isolated pyrazole (21b) when heated under reflux in 1,2-dimethoxyethane rearranged to give the diazepine. It would appear that the pyrazole is the kinetically favoured product but that prolonged heating gives the more thermodynamically stable diazepine *via* a reversal of the 1,5 cyclisation. A similar pyrazole to diazepine rearrangement has been observed previously for the 3-phenyl-3*H*-pyrazole (28).[4] This is not the normal thermal rearrangement process observed for 3-aryl-3*H*-pyrazoles but in the case of (28) it was argued that ring cleavage was facilitated by the ring strain imposed by the fused cyclopentyl ring. The usual mode of thermal rearrangement of 3-aryl-3*H*-pyrazoles involves a [1,5] sigmatropic migration of the aryl group, for example (4), the diaryl analogue of (21b), rearranges in two steps to give the aromatic pyrazole (29).[3] That the pyrazole (21b) fails to take a similar reaction path, and instead rearranges to give

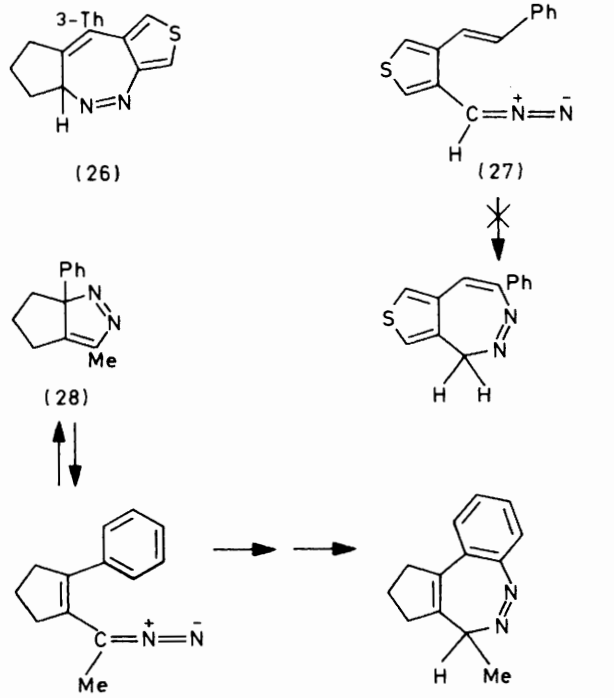
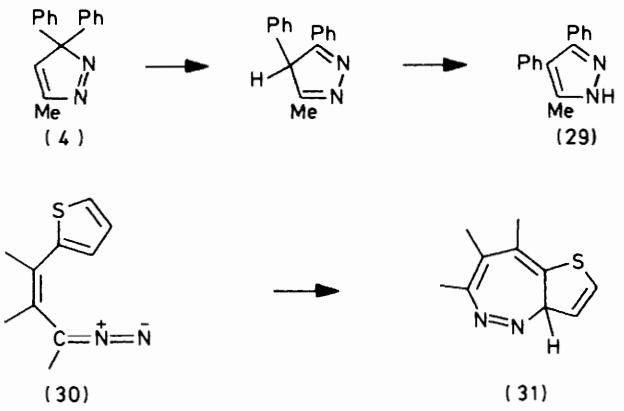


Table. ^{13}C N.m.r. spectra of 3*H*-pyrazoles and 3*H*-1,2-diazepines

Compd.	δ/p.p.m. (from Me_4Si)
(20a)	C-6, -7, -8 27.0, 32.7, 32.9; C-5a 77.1; arom. and olefinic 123.5, 126.4, 126.7, 127.0, 128.4, 129.2, 135.7, 138.9, 140.1, 153.9
(24a)	C-6, -7, -8 26.8, 32.1, 32.9; C-5a 76.3; arom. and olefinic 124.5, 125.0, 125.5, 125.7, 126.5, 128.5, 133.1, 137.7, 138.7, 157.0
(20b)	Me 19.15; C-3 68.5; arom. and olefinic 120.0, 125.1, 126.1, 126.5, 127.0, 127.2, 127.4, 130.8, 140.9, 155.4
(24b)	Me 19.4; C-3 68.0; arom. and olefinic 119.7, 123.8, 125.6, 125.8, 125.9, 127.8, 130.8, 133.5, 139.4, 159.1
(20c)	C-6, -7, -8, -9 20.4, 23.4, 27.4, 28.1; C-5a 71.9; arom. and olefinic 124.3, 126.4, 126.8, 127.9, 128.5, 129.4, 129.5, 133.9, 139.2, 152.2
(21b)	Me 12.7; C-3 99.1; arom. and olefinic 125.6, 126.2, 126.6, 135.8, 137.8, 154.1
(25b)	Me 12.7; C-3 100.6; arom. and olefinic 122.5, 125.8, 126.7, 135.8, 136.1, 153.6
(21c)	C-4, -5, -6, -7 21.9, 22.1, 22.6, 22.8; C-3 100.7; arom. and olefinic 125.4, 126.5, 126.7, 128.1, 128.5, 136.5, 137.6, 150.3, 153.5

the diazepine (20b), suggests that the 2-thienyl group is less mobile than aryl in sigmatropic shifts. It was also found that the (21b) ⟶ (20b) isomerisation is a reversible process, thus the diazepine when heated at 80 °C for 2½ h was *ca.* 30% converted into the pyrazole. However in the case of the isomeric compounds (24b) and (25b), while the diazepine was readily converted into the pyrazole during 3 h at 80 °C, the pyrazole was recovered unchanged after 12 h at the same temperature. At 110 °C in refluxing toluene the pyrazole was slowly consumed during 24 h to give several unidentified products, but monitoring by h.p.l.c. showed that the diazepine was not formed.

In these reactions the diazepines and pyrazoles were identified by comparison of their ^1H and ^{13}C n.m.r. spectra



with those of aryl substituted analogues prepared previously.[1,4] Of these the ^{13}C n.m.r. spectra were the most useful (Table); the diazepines gave a characteristic peak for the saturated C next to the azo group in the range 68—77 p.p.m. while the saturated C in the 3*H*-pyrazole rings absorbed at 99—101 p.p.m.

These results show that in systems of types (19) and (23) the thiophene ring is more reactive to 1,7 electrocyclisation than a similarly placed arene ring but not sufficiently so to make this the kinetically favoured reaction path for (19b), (19c), and (23b). Thus, to obtain high yields of 3*H*-thieno-[1,2]diazepines from this reaction it is still necessary to incorporate some structural feature, as in (19a) and (23a), to inhibit pyrazole formation. It seems likely that the higher reactivity of the thiophene ring to electrocyclic substitution stems from its lower aromatic stabilisation energy which effects a reduction in the activation energy of the ring closure step, *e.g.* (30) ⟶ (31) compared to that for (5) ⟶ (6). The diazepine : pyrazole product ratio obtained in the cyclisation of the thienylalkenes (19b) and (23b) and the results of the diazepine ⇄ pyrazole interconversion experiments indicate that the thiophene ring is less reactive to 1,7 cyclisation at its 2- than at its 3-position in the internal competition with 1,5 cyclisation.

Experimental

^1H N.m.r. spectra were obtained on a Varian HA 100 spectrometer and ^{13}C n.m.r. spectra on a Varian CFT 20 spectrometer. All samples were run as solutions in deuteriochloroform and chemical shifts are recorded in p.p.m. downfield from internal tetramethylsilane. Mass spectra were obtained on an AEI MS902 instrument operated at 70 eV. High performance liquid chromatography (h.p.l.c.) analysis was carried out using 15 × 0.5 cm columns packed with 5μm Spherisorb silica and using u.v. detection at 254 nm. Preparative chromatography utilised the medium-pressure technique (<100 lb in^{-2})[9] and either 2.5 × 100 or 1.5 × 100-cm columns packed with Merck Kieselgel 60. Ether refers to diethyl ether.

Reagents and Starting Materials.—1,2-Dimethoxyethane (DME) and tetrahydrofuran were freshly distilled from calcium hydride under nitrogen as required. The following were prepared by literature routes: ethyl 1,4-dioxaspiro[4.4]-nonane-5-carboxylate,[10] ethyl 1,4-dioxaspiro[4.5]decane-6-carboxylate,[11] 3-bromothiophene,[12] di-3-thienyl ketone,[13] di-2-thienyl ketone,[14] 2-benzoylthiophene,[15] cyclohexanone *N*,*N*-dimethylhydrazone,[16] and acetone *N*,*N*-dimethylhydrazone.[17]

Unsaturated Ketones and their Tosylhydrazones.—2-*Di*-2-*thienylmethylenecyclopentanone*. A Grignard reagent was prepared from 2-bromothiophene (50.0 g, 0.30 mol) and magnesium (8.0 g, 0.33 mol) in ether (270 ml). The solution was cooled to 0 °C and a solution of ethyl 1,4-dioxaspiro[4.4]-nonane-6-carboxylate (28.0 g, 0.14 mol) in ether (75 ml) was added during 75 min with vigorous stirring. The mixture was boiled under reflux for 3 h, cooled, and aqueous ammonium chloride (300 ml, 25% w/v) was added with vigorous stirring. The ether layer was separated, dried, and evaporated under reduced pressure to give a yellow oil which on crystallisation from ethanol gave 1,4-*dioxaspiro*[4.4]*nonan*-6-*yl di*-(2-*thienyl*)-*methanol* (28.7 g, 64%), m.p. 81—82 °C (Found: C, 59.75; H, 5.6. $C_{16}H_{18}O_3S_2$ requires C, 59.6; H, 5.6%), $\nu_{max.}$ (Nujol) 3 460br cm^{-1} (OH).

This compound (10.0 g, 0.031 mol) in ethanol (100 ml) was heated to reflux, aqueous hydrochloric acid (30 ml, 1.7 vol%) was added and the mixture was boiled for 10 min. The ethanol was then evaporated off under reduced pressure and the residue, after dilution with water (100 ml), was extracted with ether. The ether solution was dried and evaporated under reduced pressure to give a yellow oil which on chromatography on silica (100 × 2.5 cm) gave (i) 2-*di*-2-*thienylmethylenecyclopentanone* (2.64 g, 33%) as yellow crystals, m.p. 90—91 °C (from ethanol) (Found: C, 64.4; H, 4.7. $C_{14}H_{12}OS_2$ requires C, 64.6; H, 4.65%), $\nu_{max.}$ (Nujol) 1 700 cm^{-1} (C=O); δ_H 1.98 (dist. quint, *J* 7 Hz, 4-H_2), 2.36 (dist. t, *J* 7 Hz, 3-H_2), 3.01 (t, *J* 7 Hz, 5-H_2), 6.9—7.2 (m, arom., 4 H), and 7.3—7.5 (m, arom., 2 H), and (ii) 2-*hydroxyethyl* 6,6-*di*-2-*thienylhex*-5-*enoate* (5.1 g, 51%) as a colourless oil (Found: C, 59.65; H, 5.55. $C_{16}H_{18}O_3S_2$ requires C, 59.6; H, 5.6%); $\nu_{max.}$ (film) 3 450 (OH) and 1 730 cm^{-1} (C=O); δ_H 1.78 (dist. quint., *J* 7 Hz, 3-H_2), 2.05 (s, OH), 2.1—2.5 (m, 2-H_2 and 4-H_2), 3.7—3.8 and 4.1—4.2 (m, OCH_2CH_2OH), 6.1 (t, *J* 7 Hz, 5-H), and 6.7—7.3 (m, arom., 6 H); δ_C 24.8, 29.1, and 33.6 (C-2, -3, -4), 61.6, 66.0 (OCH_2CH_2OH), 124.1, 125.2, 125.7, 126.8, 127.2, 127.7, 129.5, 130.5, 139.5, 146.5 (aromatic and olefinic), and 173.7 p.p.m. (C-1).

The 2-di-2-thienylmethylenecyclopentanone was converted into its p-*tolysulphonylhydrazone* by the usual method[3] in 87% yield, m.p. 193—195 °C (decomp.) (from ethanol) (Found: C, 58.8; H, 4.6; N, 6.5. $C_{21}H_{20}N_2O_2S_3$ requires C, 58.85; H, 4.7; N, 6.5%); $\nu_{max.}$ (Nujol) 3 270 cm^{-1} (NH).

2-*Di*-3-*thienylmethylenecyclopentanone*. A solution of 3-bromothiophene (10.0 g, 0.0615 mol) in ether (30 ml) was cooled to −70 °C and added with stirring to a solution of butyl-lithium (40 ml, 1.6M in hexane) at −70 °C under nitrogen. The mixture was stirred for 5 min and then ethyl 1,4-dioxaspiro[4.4]nonane-6-carboxylate (5.0 g, 0.025 mol) in ether (25 ml) cooled to −70 °C was added during 10 min. The solution was kept at −70 °C for 1 h and then water (75 ml) was added and the mixture allowed to warm up to room temperature. The mixture was extracted with ether and worked up in the usual way to give 1,4-*dioxaspiro*[4.4]*nonan*-6-*yl di*-(3-*thienyl*)*methanol* (2.9 g, 36%) as white crystals, m.p. 98 °C (from ethanol) (Found: C, 59.5; H, 5.5. $C_{16}H_{18}O_3S_2$ requires C, 59.6; H, 5.6%); $\nu_{max.}$ (Nujol) 3 460 cm^{-1} (OH).

This compound (5.0 g, 0.0156 mol) in ethanol (125 ml) containing dilute hydrochloric acid (5M, 0.65 ml) was boiled under reflux for 15 min and worked up as above to give (i) 2-*di*-3-*thienylmethylenecyclopentanone* (0.88 g, 22%) as yellow crystals, m.p. 78—80 °C (from ethanol) (Found: C, 64.5; H, 4.6. $C_{14}H_{12}OS_2$ requires C, 64.6; H, 4.65%); $\nu_{max.}$ (Nujol) 1 695 cm^{-1} (C=O); δ_H 1.94 (dist. quint, *J* 7 Hz, 4-H_2), 2.36 (dist. t, *J* 7 Hz, 3-H_2), 2.88 (t, *J* 7 Hz, 5-H_2), and 6.8—7.3 (m, arom., 6 H), and (ii) 2-*hydroxyethyl* 6,6-*di*-3-*thienylhex*-5-*enoate* (2.28 g, 46%) as a colourless oil (Found: C, 59.8; H, 5.6. $C_{16}H_{18}O_3S_2$ requires C, 59.6; H, 5.6%); $\nu_{max.}$ (film) 3 430 (OH) and 1 720 cm^{-1} (C=O); δ_H 1.76 (dist. quint, *J* 7 Hz,

3-H_2), 2.15br (s, OH), 2.20 (dist. q, *J* 7 Hz, 4-H_2), 2.34 (t, *J* 7 Hz, 2-H_2), 3.7—3.8 and 4.1—4.2 (m, OCH_2CH_2OH), 6.04 (t, *J* 7 Hz, 5-H), and 6.8—7.4 (m, arom., 6 H).

The 2-di-3-thienylmethylenecyclopentanone was converted into its tosylhydrazone by the usual method in 82% yield, m.p. 152—154 °C (decomp.). (A satisfactory analysis could not be obtained for this compound owing to occlusion of solvent, and in the mass spectrum the low abundance of the parent ion prevented an accurate mass measurement.)

4,4-*Di*-2-*thienylbut*-3-*en*-2-*one*. Butyl-lithium (17.5 ml, 1.6M in hexane) was added to di-isopropylamine (2.02 g, 0.02 mol) at 0 °C with stirring under nitrogen. After 20 min at 0 °C a solution of acetone *N*,*N*-dimethylhydrazone (2.0 g, 0.02 mol) in tetrahydrofuran (15 ml) was added dropwise. After a further 30 min at 0 °C the solution was cooled to −70 °C and a solution of di-2-thienyl ketone (3.6 g, 0.0185 mol) in tetrahydrofuran (20 ml) was added slowly. After 1 h at −70 °C the reaction mixture was allowed to warm up to 0 °C and water (25 ml) was added. The mixture was extracted with methylene dichloride and the extract was dried and evaporated under reduced pressure to give an oil. The oil was dissolved in ethanol (40 ml), hydrochloric acid (1M, 40 ml) was added and the mixture was stirred overnight at room temperature. Extraction with methylene dichloride and removal of the solvent by evaporation under reduced pressure gave a yellow oil which was chromatographed on silica (2.5 × 100 cm) to give 4,4-*di*-2-*thienylbut*-3-*en*-2-*one* as a yellow oil (2.45 g, 57%) (Found: C, 61.6; H, 4.4. $C_{12}H_{10}OS_2$ requires C, 61.5; H, 4.3%); $\nu_{max.}$ (film) 1 650 cm^{-1} (C=O); δ_H 1.94 (s, Me), 6.58 (s, 3-H), 7.0—7.2 (m, arom., 4 H), and 7.3—7.5 (m, arom., 2 H); δ_C 29.7 (Me), 126.6, 127.0, 127.9, 128.4, 129.7, 129.9, 137.9, 139.3, 144.7 (arom. and olefinic), and 193.05 p.p.m. (C=O). *Tosylhydrazone* (89%), m.p. 142—143 °C (decomp.) (from methanol) (Found: C, 56.8; H, 4.4; N, 7.1. $C_{19}H_{18}N_2O_2S_3$ requires C, 56.7; H, 4.5; N, 7.0%), $\nu_{max.}$ 3 158 cm^{-1} (NH).

4,4-*Di*-3-*thienylbut*-3-*en*-2-*one*. A procedure similar to that above but using di-3-thienyl ketone gave 4,4-*di*-3-*thienylbut*-3-*en*-2-*one* (68%) as a yellow oil (Found: C, 61.6; H, 4.2. $C_{12}H_{10}OS_2$ requires C, 61.5; H, 4.3%), $\nu_{max.}$ (film) 1 650 cm^{-1} (C=O); δ_H 1.90 (s, Me), 6.56 (s, 3-H), and 6.9—7.4 (m, arom., 6 H); δ_C 29.8 (CH_2), 125.5, 125.7, 126.3, 126.5, 127.3, 128.6, 138.4, 142.4, 142.6 (arom. and olefinic), and 192.0 p.p.m. (C=O). *Tosylhydrazone* (87%), m.p. 157—159 °C (decomp.) (from methanol) (Found: C, 56.8; H, 4.5; N, 7.0. $C_{19}H_{18}N_2O_2S_3$ requires C, 56.7; H, 4.5; N, 7.0%), $\nu_{max.}$ (Nujol) 3 180 cm^{-1} (NH).

2-[*Phenyl*(2-*thienyl*)*methylene*]*cyclohexanone*. A solution of cyclohexanone *N*,*N*-dimethylhydrazone (1.4 g, 0.01 mol) in tetrahydrofuran (10 ml) was added slowly with stirring to lithium di-isopropylamide at 0 °C, prepared from butyl-lithium (1.27M in hexane, 8.0 ml) and di-isopropylamine (1.06 g, 0.01 mol). The solution was kept at 0 °C for 2 h, cooled to −70 °C and a solution of 2-benzoylthiophene (1.88 g, 0.01 mol) in tetrahydrofuran (10 ml) was added dropwise. After a further 2 h at −70 °C the solution was allowed to warm up to room temperature, water (25 ml) was added and the mixture was neutralised with dilute hydrochloric acid. Extraction with methylene dichloride and the usual work-up gave 2-[*hydroxy*(*phenyl*)(2-*thienyl*)*methyl*]*cyclohexanone* N,N-*dimethylhydrazone* (1.43 g, 41%), m.p. 101—102 °C (from ethanol) (Found: C, 69.4; H, 7.4; N, 8.6. $C_{19}H_{24}N_2OS$ requires C, 69.5; H, 7.4; N, 8.5%), $\nu_{max.}$ (Nujol) 3 320 cm^{-1} (OH). This compound (0.20 g, 0.0006 mol) was dissolved in ethanol (10 ml), hydrochloric acid (1M, 2.5 ml) was added and the mixture was stirred at room temperature for 24 h. The white precipitate formed was recrystallised from ethanol to give 2-*oxocyclohexyl*(*phenyl*)(2-*thienyl*)*methanol* (0.0869 g, 50%), m.p. 127—128 °C (Found: C, 71.5; H, 6.4. $C_{17}H_{18}O_2S$ requires C, 71.3; H, 6.3%); $\nu_{max.}$ (Nujol) 1 685 (C=O) and 3 400 cm^{-1} (OH). This compound (0.90 g, 0.0031 mol) was boiled under reflux in dry benzene (25 ml) with toluene-4-sulphonic acid (0.01 g) for 20 min. The usual work-up gave 2-[phenyl(2-thienyl)-methylene]cyclohexanone (0.71 g, 84%), m.p. 119—120 °C (from ethanol) (Found: C, 76.0; H, 6.1. $C_{17}H_{16}OS$ requires C, 76.1; H, 6.0%); $\nu_{max.}$ (Nujol) 1 670 cm^{-1} (C=O), δ_H 1.6—2.2 (m, *ca.* 4.9 H), 2.3—2.7 (m, *ca.* 2.5 H), 2.90br (t, *J* 6 Hz, *ca.* 0.6 H), and 6.7—7.6 (m, 8 H). The product consisted of two stereoisomers which could not be separated by chromatography. *Tosylhydrazone* (54%), m.p. 158—159 °C (decomp.) (from ethanol) (Found: C, 65.8; H, 5.6; N, 6.45. $C_{24}H_{24}N_2O_2S_2$ requires C, 66.0; H, 5.5; N, 6.4%), $\nu_{max.}$ (Nujol) 3 170 cm^{-1} (NH).

Attempted Preparations of 2-*Dithienylmethylenecyclohexanones*.—The methods used were similar to those described above for the cyclopentanone analogues.

2-*Di*-2-*thienylmethylenecyclohexanone*. A Grignard reagent from 2-bromothiophene (10.0 g, 0.06 mol) and ethyl 1,4-dioxaspiro[4.5]decane-6-carboxylate (5.0 g, 0.025 mol) gave 1,4-*dioxaspiro*[4.5]*decan*-6-*yl di*-(2-*thienyl*)*methanol* (3.38 g, 43%), m.p. 96—97 °C (from ethanol at −50 °C) (Found: C, 60.75; H, 6.0. $C_{17}H_{20}O_3S_2$ requires C, 60.7; H, 6.0%), $\nu_{max.}$ (Nujol) 3 380 cm^{-1} (OH). A solution of this compound (1.0 g, 0.003 mol) in ethanol (25 ml) was heated to reflux, dilute hydrochloric acid (5M, 3 drops) was added and the mixture was boiled for 15 min. The usual work-up gave only 2-*hydroxyethyl* 7,7-*di*-2-*thienylhept*-6-*enoate* (0.83 g, 83%) as an oil (Found: C, 60.5; H, 5.85. $C_{17}H_{20}O_3S_2$ requires C, 60.7; H, 6.0%), $\nu_{max.}$ (film) 3 450br (OH) and 1 730 cm^{-1} (C=O), δ_H 1.2—1.8 (m, 3-H_2 and 4-H_2), 2.0br (s, OH), 2.1—2.5 (m, 2-H_2 and 5-H_2), 3.7—3.9 and 4.1—4.3 (m, OCH_2CH_2OH), 6.13 (t, *J* 7 Hz, 6-H), and 6.7—7.4 (m, arom., 6 H).

2-*Di*-3-*thienylmethylenecyclohexanone*. Reaction of 3-lithiothiophene with ethyl 1,4-dioxaspiro[4.5]decanecarboxylate at −70 °C gave 1,4-*dioxaspiro*[4.5]*decan*-6-*yl di*-(3-*thienyl*)*methanol* (54%), m.p. 102—103 °C (from ethanol) (Found: C, 60.6; H, 6.0. $C_{17}H_{20}O_3S_2$ requires C, 60.7; H, 6.0%); $\nu_{max.}$ (Nujol) 3 420 cm^{-1} (OH). Hydrolysis as described above gave only 2-*hydroxyethyl* 7,7-*di*-3-*thienylhept*-6-*enoate* (75%) as an oil (Found: C, 60.9; H, 5.9. $C_{17}H_{20}O_3S_2$ requires C, 60.7; H, 6.0%), $\nu_{max.}$ (film) 3 400br (OH) and 1 720 cm^{-1} (C=O); δ_H 1.3—1.8 (m, 3-H_2 and 4-H_2), 2.0—2.5 (m, 2-H_2, 5-H_2 and OH), 3.7—3.9 and 4.1—4.3 (m, OCH_2CH_2OH), 6.1 (t, *J* 7 Hz, 6-H), and 6.8—7.4 (m, arom., 6 H).

Preparation and Decomposition of the Tosylhydrazone Sodium Salts.—The sodium salts were prepared and dried as described previously [3] and decomposed in boiling dry DME in the dark under nitrogen. The reactions were continued until t.l.c. showed that all the reactant had been consumed. After cooling, the precipitated sodium toluene-*p*-sulphinate was filtered off and the other products isolated as described.

2-*Di*-2-*thienylmethylenecyclopentanone tosylhydrazone*. The hydrazone (1.0 g, 2.3 mmol) sodium salt in DME (75 ml) was boiled under reflux for 1 h. Evaporation of the filtrate gave a yellow solid which was recrystallised from ethanol to give 5a,6,7,8-*tetrahydro*-9-(2-*thienyl*)*cyclopenta*[f]*thieno*[3,2-c]-[1,2]*diazepine* (20a) (0.52 g, 85%), m.p. 120—121 °C as yellow crystals (Found: C, 61.5; H, 4.5; N, 10.2. $C_{14}H_{12}N_2S_2$ requires C, 61.8; H, 4.4; N, 10.3%), δ_H 2.0—2.8 (m, 6 H), 3.0—3.3 (m, 1 H), 7.0 (dd, *J* 5.3, *J*' 3.5 Hz, 4'-H), 7.10 (dd, *J* 3.5, *J*' 1.3 Hz, 3'-H), 7.15 (d, *J* 5.3 Hz, 3-H), 7.35 (dd, *J* 5.3, *J*' 1.3 Hz, 5'-H), and 7.45 (d, *J* 5.3 Hz, 2-H).

2-*Di*-3-*thienylmethylenecyclopentanone tosylhydrazone*. The hydrazone (1.0 g, 2.33 mmol) sodium salt in DME (75 ml)

was boiled under reflux for 0.5 h. Evaporation of the filtrate and recrystallisation from ethanol gave 5a,6,7,8-*tetrahydro*-9-(3-*thienyl*)*cyclopenta*[f]*thieno*[2,3-c][1,2]*diazepine* (24a) (0.52 g, 90%), m.p. 158—159 °C as yellow crystals (Found: C, 61.75; H, 4.4; N, 10.25. $C_{14}H_{12}N_2S_2$ requires C, 61.8; H, 4.4; N, 10.3%); δ_H 2.0—2.8 (m, 6 H), 3.0—3.2 (m, 1 H), 6.85 (d, *J* 5.3 Hz, 1-H), 7.0 (dd, *J* 5.3 Hz, *J*^{1} 1.3 Hz, 4^1-H), 7.20 (d, *J* 5.3 Hz, 2-H), 7.25 (dd, *J* 3 Hz, *J*^{1} 1.3 Hz, 2^1-H), and 7.35 (dd, *J* 5.3 Hz, *J*^{1} 3 Hz, 5^1-H).

4,4-*Di*-2-*thienylbut*-3-*en*-2-*one tosylhydrazone*. In this case after the preparation of the sodium salt further treatment was carried out as follows to ensure complete removal of the ethanol. After removal of the ethanol on the rotary evaporator (bath temperature <40 °C) the salt was dried under vacuum for 15 min and an aliquot of dry DME (25 ml) was added, the flask was swirled gently and then the DME was removed on the rotary evaporator and the salt was dried for 15 min under vacuum. This process was repeated with another aliquot of DME and finally the salt was dried under high vacuum over phosphoric oxide overnight. The tosylhydrazone (0.81 g, 2.02 mmol) salt in DME (25 ml) was boiled under reflux for 30 min. After evaporation of the filtrate the residue was chromatographed on silica (1.5 × 100 cm) to give (i) 5-*methyl*-3,3-*di*-2-*thienylpyrazole* (21b) (0.23 g, 49%) as colourless crystals, m.p. 73 °C (from light petroleum–benzene) (Found: C, 58.7; H, 4.1; N, 11.6. $C_{12}H_{10}N_2S_2$ requires C, 58.5; H, 4.1; N, 11.4%), δ_H 2.46 (d, *J* 1.6 Hz, Me), 6.9—7.1 (m, 5 H), and 7.2—7.3 (m, 2 H); and (ii) 3-*methyl*-5-(2-*thienyl*)-3H-*thieno*[3,2-c][1,2]*diazepine* (20b) (0.091 g, 19%) as yellow crystals, m.p. 97 °C (from ethanol) (Found: C, 58.4; H, 4.1; N, 11.4. $C_{12}H_{10}N_2S_2$ requires C, 58.5; H, 4.1; N, 11.4%); δ_H 2.15 (d, *J* 6 Hz, Me), 2.35 (m, 3-H), 5.40 (d, *J* 5.5 Hz, 4-H), 7.0 (dd, *J* 5.5, *J*^{1} 3.5 Hz, 4^1-H), 7.25 (m, 3^1-H), 7.30 (dd, *J* 5.5, *J*^{1} 1.25 Hz, 5^1-H), 7.34 (d, *J* 5.5 Hz, 8-H), and 7.53 (d, *J* 5.5 Hz, 7-H).

A similar experiment was monitored by h.p.l.c. and it was observed that both the pyrazole and diazepine were formed simultaneously but that the ratio of pyrazole : diazepine decreased as the reaction proceeded; after 90 min the reaction was worked up to give the pyrazole (34%) and diazepine (25%).

Thermal Rearrangement of the Pyrazole (21b) *and the Diazepine* (20b).—The pyrazole (0.163 g) in dry DME (25 ml) was boiled under reflux in the dark under nitrogen for 2½ h. Evaporation of the solvent and chromatography gave the recovered pyrazole (0.070 g, 43%), m.p. 73 °C and 3-methyl-5-(2-thienyl)-3*H*-thieno[3,2-*c*][1,2]diazepine (0.046 g, 28%), m.p. 96—97 °C. The identity of each product was confirmed by ^{1}H n.m.r.

The diazepine (20b) under the same conditions isomerised to give a mixture containing the pyrazole (21b) with a pyrazole : diazepine ratio of 1 : 2.5 (by ^{1}H n.m.r. and h.p.l.c.).

4,4-*Di*-3-*thienylbut*-3-*en*-2-*one tosylhydrazone*. The sodium salt of the tosylhydrazone (1.2 g, 3.0 mmol) was dried as above, DME (75 ml) was added and the mixture was boiled under reflux for 30 min. The usual work-up and chromatography gave (i) 3,3-*di*-3-*thienyl*-5-*methylpyrazole* (25b) (0.28 g, 43%) as colourless crystals, m.p. 85 °C (from light petroleum–benzene) (Found: C, 58.6; H, 4.15; N, 11.35. $C_{12}H_{10}N_2S_2$ requires C, 58.5; H, 4.1; N, 11.4%); δ_H 2.45 (d, *J* 1.6 Hz, Me), 6.8—7.0 (m, 3 H), and 7.1—7.3 (m, 4 H); and (ii) 3-*methyl*-5-(3-*thienyl*)-3H-*thieno*[2,3-c][1,2]*diazepine* (24b) (0.053 g, 8%) as a yellow oil which could not be crystallised (Found: *m/z* 246.028 888. $C_{12}H_{10}N_2S_2$ requires M^+ 246.028 539); δ_H 2.18 (d, *J* 6 Hz, Me), 2.5 (m, 3-H), 5.38 (d, *J* 5.5 Hz, 4-H), 7.0—7.2 (m, 2-H), and 7.25—7.4 (m, 3 H).

Thermal Rearrangement of the Pyrazole (25b) *and the Diazepine* (24b).—The diazepine (24b) (0.030 g) was heated at 80 °C in perdeuteriobenzene (0.5 ml) in an n.m.r. tube and the reaction was monitored by ^{1}H n.m.r. for 3 h by which time the diazepine had been wholly isomerised to the pyrazole (25b). The identity of the pyrazole was confirmed by h.p.l.c.

The pyrazole (25b) (0.025 g) in DME (10 ml) was heated under reflux for 12 h and monitored by h.p.l.c. No diazepine formation was observed and the pyrazole was recovered unchanged. In a similar thermolysis in toluene the pyrazole was slowly consumed during 24 h to give several unidentified products, but the diazepine (24b) was not detected by h.p.l.c. at any stage.

2-[*Phenyl*(2-*thienyl*)*methylene*]*cyclohexanone tosylhydrazone*. The tosylhydrazone (0.491 g, 1.12 mmol) salt in DME (40 ml) was boiled under reflux for 1 h. Filtration and evaporation of the filtrate gave an oil which was chromatographed on silica to give (i) 4,5,6,7-*tetrahydro*-3-*phenyl*-3-(2-*thienyl*)*indazole* (21c) (0.2561 g, 85%) as colourless crystals, m.p. 86—87 °C (from ethanol) (Found: C, 73.0; H, 5.8; N, 10.1. $C_{17}H_{16}N_2S$ requires C, 72.8; H, 5.75; N, 10.0%); δ_H 1.7—1.9 (m, 4 H), 2.3—2.5 (m, 2 H), 2.7—3.0 (m, 2 H), and 6.9—7.4 (m, 8 H); and (ii) 6,7,8,9-*tetrahydro*-10-*phenyl*-5a*H*-*benzo*[f]*thieno*-[3,2-c][1,2]*diazepine* (20c) (0.0287 g, 9.5%), m.p. 100—101 °C as yellow crystals (from ethanol) (Found: C, 72.6; H, 5.95; N, 9.7. $C_{17}H_{16}N_2S$ requires C, 72.8; H, 5.75; N, 10.0%); δ_H 1.6—2.7 (m, 8 H), 2.8—3.1br (m, 1 H), 7.0—7.4 (m, 5 H), 7.14 (d, *J* 5.5 Hz, 3-H), and 7.46 (d, *J* 5.5 Hz, 2-H).

Acknowledgements

We thank the S.E.R.C. for a studentship (T. K. M.).

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Received 4*th July* 1983; *Paper* 3/1144