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THE SYNTHESES AND CONFORMATIONAL STUDIES OF [n](2,4)HETEROPHANES AND [7](3,5)PYRAZOLOPHANE

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Abstract—Synthetic sequences from (n + 3)-membered 2-cycloalkenones provide furan, thiophene and pyrrole derivatives bridged at the 2,4-positions by n-methylene chains (n = 6, 7, and 9) as well as a pyrazole derivative bridged at the 3,5-positions (n = 7). The molecular geometry as a function of the chain length has been investigated spectrometrically. The aliphatic chain of [7](2,4)pyrrolophane and [7](3,5)pyrazolophane is found to reside in the one side of the respective heteroaromatic rings even at 205°, whereas that of [7](2,4)thiophenophane flips up and down the thiophene ring upon heating, the energy barrier $\Delta G_c^{\ddagger}$ being 18·2 kcal/mol (T_c 111°C at 60 MHz). The conformational behaviour of the heptamethylene chain is thus dependent on the angle between the bonds connecting each heteroaromatic carbon with the benzylic one. Though the hexamethylene chain of the [6]-(2,4)heterophanes is fixed to the one side of the aromatic ring, the nonamethylene chain of the [9]-homologues is rapidly moving between the both sides even at room temperature. The red-shifts of the B-bands are attributed to the distorted, nonplanar heteroaromatic rings. The mass spectra of these heterophanes indicate the initial C(1)–C(2) fission of the polymethylene chain probably due to the steric strain of the systems.

In continuation of previous studies on heterophasnes,[1-5] we have synthesized [n](2,4)heterophanes (n = 6, 7, and 9) and [7](3,5)pyrazolophane to investigate the molecular geometry with respect to both the aliphatic chain conformation and the heteroaromatic ring distortion which should be dependent on the chain length variation. The hexamethylene chain of the [6](2,4)-heterophanes and the heptamethylene chain of [7]-(3,5)pyrazolophane are the shortest one, respectively, in the heterophane series synthesized heretofore.†‡

The syntheses of heterophanes

The key step of the synthesis is given in Scheme 1 and the intermediary 3-acetylcycloalkanones (**2a–c**) are obtained as shown in Scheme 2. The bromination of cyclodecanone ethylene acetal followed by dehydrobromination and hydrolysis gave *cis*-2-cyclodecenone (**1b**).[6]§ When the hydrolysis was performed under more drastic conditions, the isomerization to 3-cyclodecenone was observed.¶ The Michael addition of nitroethane[9] to **1b** and the successive Nef reaction[9a,10] gave 3-acetylcyclodecanone (**2b**) in a 70% total yield based on **1b**.

3-Acetyl-2-cyclononen-1-ol (**9a**) was prepared by the addition of lithium acetylide to **1a**, the acidic rearrangement of **7a**,[8a] and the final hydration of **8a** in the presence of mercuric sulphate. This is in sharp contrast to the behaviour of the 12-membered homologue **8c** which was hydrated and spontaneously cyclized to give a furanophane (**3cu**).[3] The oxidation of **9a** afforded 3-acetyl-2-cyclononenone (**10**), which was subsequently reduced to **2a**.

3-Acetylcyclododecanone (**2c**) was obtained as a by-product in the hydration reaction of **8c**. Alternatively, **2c** was prepared by the acid-catalyzed ring opening of 11-methyl[9](2,4)furanophane (**3cu**).[3]

The Paal–Knorr reaction of the 1,4-diketones afforded the corresponding heterophanes. Thiophenophanes (**3av**, **3bv**, and **3cv**) were prepared in 61, 51, and 70% yield, respectively, by treatment of the corresponding diketones with phosphorus pentasulphide. The most strained homologue, [6]thiophenophane (**3av**), formed a labile but distillable liquid.[1] The attempted dehydration of **2a** and **2b** to [6]- and [7]-furanophane, respectively, proved futile.†† Meanwhile, the ring-closure to [n]-

†H. H. Wasserman *et al.* have reported that a natural pigment called *metacycloprodigiosin* has a [9](2,4)-pyrrolophane framework. See Ref 6.

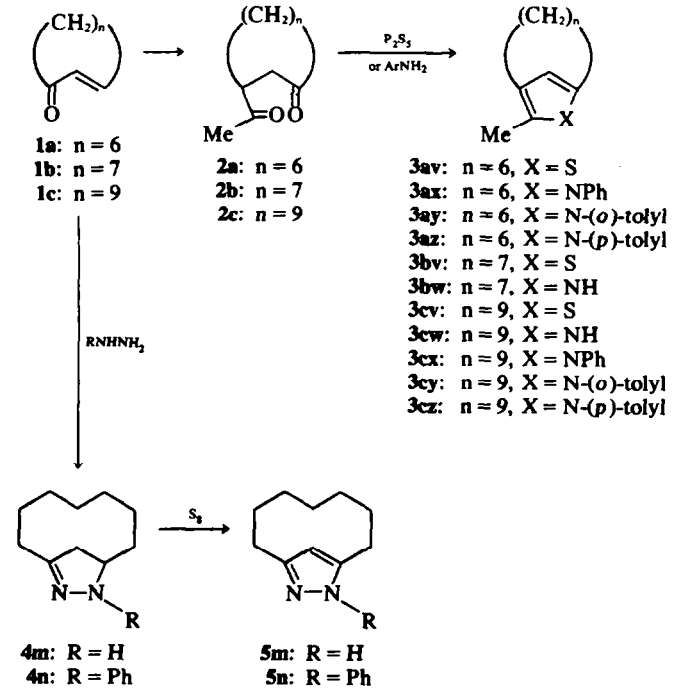
‡[9](2,4)Heterophanes are synthesized independently by G. Pagani *et al.* See Ref 7.

§The *cis–trans* isomerization proceeded in an acid medium and/or upon heating for distillation.

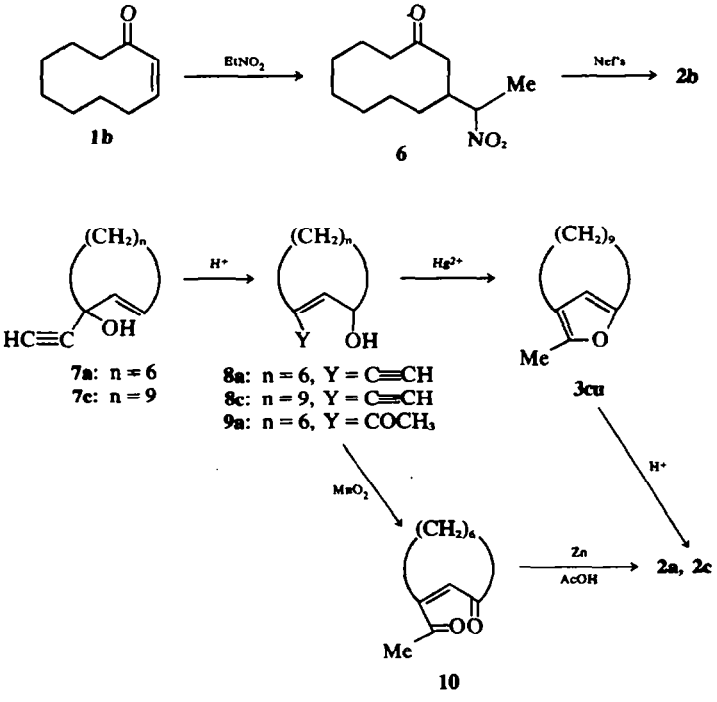
¶For the acid-catalyzed isomerization of medium-sized 2-cycloalkenones to 3-cycloalkenones, see Refs 8*b* and 8*c*.

[1]A [6]heterophane having a condensed heteroaromatic part has been reported, see Ref 11*a*.

††In the attempted synthesis of [7](2,4)furanophane, a crystalline product was obtained, whose molecular weight was equal to the dimer of the furanophane. No further structural study was made.



SCHEME 1.



SCHEME 2.

Table 1. Physical properties of heterophanes

Compound	b.p. (°C/mmHg) (m.p. (°C))	Formula	Calcd C%	Calcd H%	Calcd N%	Found C%	Found H%	Found N%
			(exact mass P^+)			(exact mass P^+)		
3av	68–74/3	$C_{11}H_{16}S$	(180·097)			(180·095)		
3ax	114–116/0·08	$C_{17}H_{21}N$	(239·167)			(239·163)		
3ay	129–130/2	$C_{18}H_{23}N$	85·3	9·2	5·5	85·2	9·2	5·3
3az	128–129/0·65	$C_{18}H_{23}N$	(253·182)			(253·176)		
3bv	120/3	$C_{12}H_{18}S$	74·2	9·3	—	74·4	9·4	—
3bw	(91–94)[a]	$C_{12}H_{19}N$	81·3	10·8	7·9	81·3	10·7	7·8
3cv	115/3	$C_{14}H_{22}S$[c]	75·6	10·0	—	75·7	10·2	—
3cw	(107–107·5)[a]	$C_{14}H_{23}N$	81·9	11·3	6·8	81·7	11·5	7·1
3cx	145/0·095	$C_{20}H_{27}N$	85·4	9·7	5·0	85·3	9·4	5·0
3cy	150/0·1 (46·5–47·5)[b]	$C_{21}H_{29}N$	85·4	9·9	4·7	85·2	9·9	4·9
3cz	150/0·08 (39–40)[b]	$C_{21}H_{29}N$	85·4	9·9	4·7	85·3	10·2	4·8
5m	(71·5–72·0)[a]	$C_{10}H_{16}N_2$	73·1	9·8	17·1	73·2	10·0	17·3
5n	125–130/0·08 (33–34·5)[a]	$C_{16}H_{20}N_2$	80·0	8·4	11·7	80·0	8·5	11·6

[a] Purified by sublimation.
[b] Recrystallized from n-hexane.
[c] Anal. for Sulphur, Calcd: 14·4. Found: 14·2.

(2,4)pyrrolophanes (**3bw**, and **3cw**) by treatment of the 1,4-diketones with either ammonium carbonate or ammonia gas in the presence of a catalytic amount of ammonium chloride was successful with [7]- and [9](2,4)pyrrolophanes, but failed with the [6]pyrrolophane. The latter ring closure was attained, however, by heating the diketone (**2a**) with aromatic amines in the presence of hydrochloric acid to afford the corresponding N-aryl[6](2,4)-pyrrolophanes (**3ax**, **3ay**, and **3az**). N-Aryl[9]-(2,4)pyrrolophanes (**3cx**, **3cy**, and **3cz**) were obtained analogously. The [7](2,4)pyrrolophane (**3bw**) formed unstable crystals having IR absorptions characteristic of the pyrrole ring.

Treatment of 2-cyclodecenone (**1b**) with hydrazine hydrate gave the corresponding pyrazoline (**4m**) as a labile oil. Freshly distilled **4m** was admixed with powdered S_8 and dehydrogenated at 210° to afford [7](3,5)pyrazolophane (**5m**) in a 75% yield. The highly strained phane **5m** formed a colourless solid.* N-Phenyl[7](3,5)pyrazolophane (**5n**) was prepared in a similar way by the action of phenylhydrazine.

The spectral properties of [n]heterophanes

The conformation of the aliphatic chains and the bridging effect on heteroaromatic ring. The PMR spectra of **3bw** and **5m** are shown in Figs 1 and 2. The highest field signal (δ −1·74 for **3bw** and δ −1·96 for **5m**) is ascribed to the magnetically shielded C(4)-H_x by assuming the fixed conformation **11** similarly as in the case of [7]metacyclophane systems.[5,12] The coalescence of

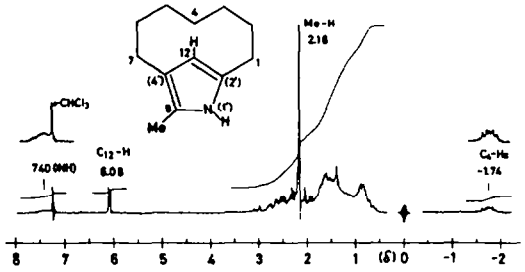


Fig 1. PMR spectrum of **3bw** (100 MHz, in $CDCl_3$, at 31·5°C).

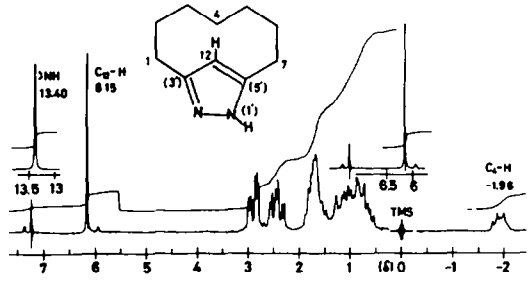


Fig 2. PMR spectrum of **5m** (100 MHz, in $CDCl_3$, at 31·5°C).

the H_x signal and the low-field counterpart H_y was not observed up to the temperature of 205° (60 MHz). So the heptamethylene bridge appears to be fixed to such an extreme conformation as **11**. N-Phenyl[7]pyrazolophane (**5n**) gave analogous PMR spectra. In contrast, the PMR spectra of [7]thiophenophane (**3bv**) were temperature-dependent (Fig 3). The one H signal of the C(4)-H_x

*For attempted synthesis of [6](3,5)pyrazolophane, see Ref 11*b*.

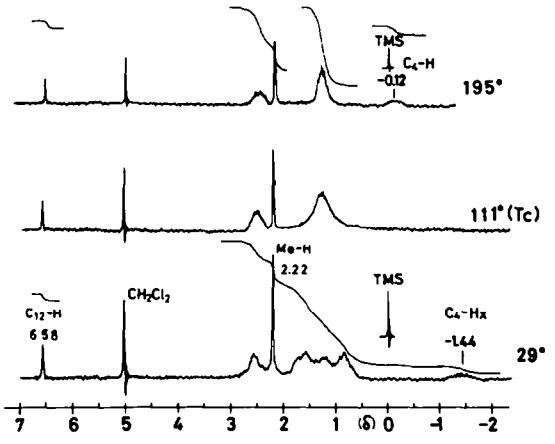
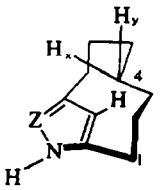
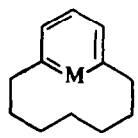


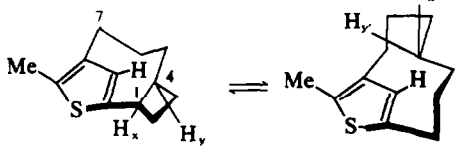
Fig 3. Temperature dependent PMR spectra of **3bv** (60 MHz, in C_4Cl_6). Flipping of the heptamethylene chain.



11a: Z = CH_3C
11b: Z = N



13a: M = N
13b: M = CH



12 **12'**

apparently disappeared at 111°C. This was ascribed to the coalescence of H_x, H_y signals, which reappeared as a 2H multiplet at higher temperature. Evidently, the equilibrium **12** ⇌ **12'** is frozen at room temperature, but is rapidly set up upon heating. The estimated activation energy data for this kind of equilibria of [7]heterophanes as well as of related [7]metacyclophane systems (**13a** and **13b**) are collected in Table 2. The barrier increases in the order: [7](2,6)pyridinophane (**13a**) < [7]metacyclophane (**13b**) < [7](2,4)thiophenophane (**3bv**) < [7](2,4)pyrrolophane (**3bw**), [7](3,5)pyrazolophane (**5m** and **5n**). The order is parallel to the increase of the angle ϕ defined in the formula attached to Table 2.

*The temperature-dependent PMR of **3cu** were reported, see Ref 3.

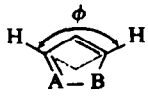
The PMR spectrum of [6]thiophenophane (**3av**) is shown in Fig 4. The small shielding effect suggests that the hexamethylene chain is compelled out of the shielding cone. This is consistent with the conformational inspection with the molecular models.

The PMR spectra of [9]thiophenophane (**3cv**) and [9]-pyrrolophane (**3cw**) are shown in Fig 5. The nonamethylene chain should be flexible at room temperature and flipping freely in analogy with [9]furanophane (**3cu**).*

The UV absorptions of the thiophenophanes (**3av**, **3bv**, **3cv**) are shown in Table 3. The B-bands experienced bathochromic and hypochromic shift as compared with those of 2,3,5-trimethylthiophene.[13] The shorter is the methylene chain, the larger is the red-shift and this is ascribed to the

Table 2. Energy barriers of the flipping of [7]heterophanes——— Relationship between $\Delta G_c^{\ddagger}$ and the bond angle ϕ

Compound	Solvent	T_c(°C)	$\Delta G_c^{\ddagger}$ (kcal/mol)	ϕ (°)
13a	$CFCl_3$	−75·5	9·0[f]	115[b]
13b	$CDCl_3$	−27·6	11·5[g]	120
3bv	C_4Cl_6	111	18·2[a]	140·5[c]
3bw	Ph_2O	> 205	>23	150·4[d]
5m	C_4Cl_6	>205	>23	153[e]
5n	C_4Cl_6	>205	>23	—



A = N or CH
B = NH or S

[a] $\Delta\nu$ = 158 Hz, k_c = 352 sec^{-1}; $k_c = \pi\Delta\nu/\sqrt{2}$, $\Delta G_c^{\ddagger} = 2{\cdot}303T_c(10{\cdot}319 - \log k_c + \log T_c)$. Assumption: $\Delta\nu = 2\ (\nu_{high} - \nu_{average})$. See Ref 5.

[b] B. Bak, L. Hansen and J. Rastrup-Andersen, *J. Chem. Phys.*, **22**, 2013 (1954).

[c] B. Bak, D. Christensen, L. Hansen-Nygaard and J. Rastrup-Andersen, *J. Mol. Spectrosc.*, **7**, 58 (1961).

[d] B. Bak, D. Christensen, L. Hansen and J. Rastrup-Andersen, *J. Chem. Phys.*, **24**, 720 (1956), calculated by using model III.

[e] J. Berthou, J. Elguers and C. Rerat, *Acta Crystallogr. Sect. B*, **26**, 1880 (1970); F. K. Larsen, M. S. Lehman, I. Søtofte and S. E. Rasmussen, *Acta Chem. Scand.*, **24**, 3248 (1970).

[f] See Ref 5.

[g] See Ref 12.

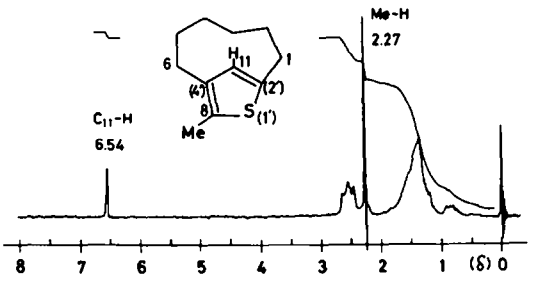


Fig 4. PMR spectrum of **3av** (60 MHz, in CCl_4, at 24°C).

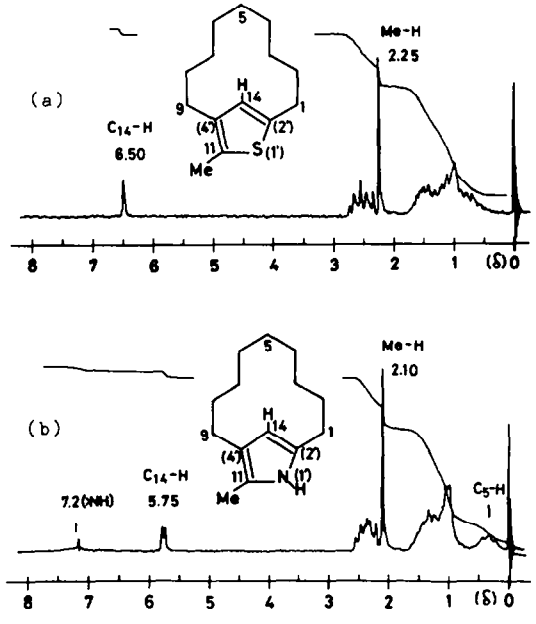
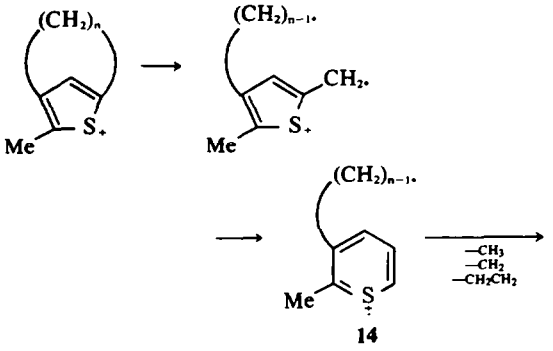


Fig 5. PMR spectra of **3cv** (a) in CCl_4 and **3cw** (b) in $CDCl_3$ at 24°C (60 MHz).

distortion of the thiophene ring introduced by the methylene bridges.[14] The UV absorptions of pyrrolophanes and pyrazolophanes listed in Table 3 showed the same red-shift.

In mass spectra (Experimental) of thiophenophanes (**3av**, **3bv**, and **3cv**), the large relative abundances of the parent peaks (P^+) is attributed to the thiopyrylium ion (**14**) possibly formed by the initial C(1)–C(2) fission of the thiophenophanes and the subsequent ring expansion.* The successive loss of methyl, methylene, or ethylene was observed. The MS of pyrrolophanes also is explained by assuming the intermediary pyridinium ion fragments.

*The relatively large $(P-1)^+$ of 2,3,5-trimethylthiophene was ascribed to the thiopyrylium ion produced by the loss of hydrogen from P^+. See Ref 15.



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EXPERIMENTAL

All the m.ps are uncorrected and yields are not optimized. PMR spectra (TMS internal standard) were obtained on a JEOL C-60-H and a Varian HA-100D spectrometer, IR on a Shimadzu spectrophotometer 27-G, UV on a Shimadzu MPS-50L spectrometer, and MS on a Hitachi RMU-6L spectrometer at 70 eV. The dynamic PMR spectra were determined on a JEOL C-60-H spectrometer at 60 MHz. Exact mass spectra were obtained on a Hitachi RMU-6D equipped with Nihon Denshi JEC-6 computer system at the Chemical Research Laboratories, Takeda Chemical Industries, Ltd., through the courtesy of Dr. T. Okada.

2-Bromocyclodecanone ethylene acetal. To a soln of cyclodecanone ethylene acetal (21·8 g, 0·11 mol) in anhyd ether (100 ml) cooled in an ice-bath, Br_2 (19·4 g, 0·12 mol) was added dropwise under stirring over a period of 2·5 h. The mixture was neutralized with sodium β-hydroxyethoxide prepared from Na metal (2·8 g, 0·12 g-atom) and ethylene glycol (*ca* 20 ml). Work-up, followed by fractional distillation, gave the bromide as a colourless liquid (22·8 g, 75%), b.p. 80°/0·04 mm, m.p. 38–38·5 (ethyl acetate). IR (neat): 1140, 1039, and 950 cm^{-1}. PMR (CCl_4): δ 4·47 (1H, d, d, $J = 8$, and 2 Hz, $\rangle$CH—Br), 4·01 (4H, A_2B_2, —OCH_2CH_2O—), and 2·6–1·2 (16H, m, main peak at 1·55). MS *m/e* 276, 278 (P^+). (Found: C, 51·9; H, 7·6. Calcd for $C_{12}H_{21}BrO_2$: C, 52·0; H, 7·6%).

2-Cyclodecenone ethylene acetal. A mixture of 2-bromocyclodecanone ethylene acetal (16·6 g, 60 mmol), potassium t-butoxide (72% K metal content, 14·1 g, 90 mmol) and dimethyl sulphoxide (80 ml, freshly distilled over calcium hydride) was stirred for 2·5 h at 80° under a nitrogen atmosphere. Work-up provided 2-cyclodecenone ethylene acetal as a colourless liquid (10·3 g, 88%), b.p. 100°/5 mm. IR (neat): 3006, 1107, 947, and 714 cm^{-1}. PMR (CCl_4): δ 5·86–5·08 (2H, m, olefinic), 3·86 (4H, m, —OCH_2CH_2O—), 2·30 (4H, m), and 1·45 (10H, m). MS *m/e* 196 (P^+). (Found: C, 73·7; H, 10·1. Calcd for $C_{12}H_{20}O_2$: C, 73·4; H, 10·3%).

2-Cyclodecenone (**1b**). A mixture of 2-cyclodecenone ethylene acetal (2·43 g, 12·4 mmol) in THF (35 ml) and 5% sulphuric acid (35 ml) was placed in a separatory funnel and was shaken vigorously for 5 min. The mixture was saturated with NaCl and the organic layer was separated. Extraction, followed by concentration and fractional distillation, yielded **1b** (1·20 g, 64% based on the acetal initially added or 97% based on the consumed acetal) along with the recovery of the starting material (0·84 g, 34%). The enone **1b** is a colourless liquid, b.p. 75°/2 mm.

Table 3. UV spectra of thiophenophanes, pyrrolophanes and pyrazolophanes (in EtOH)

Compound	λ_{max} nm (log ϵ)	Compound	λ_{max} nm (log ϵ)
3av[a]	251 (3·62)[b]	**3bw**	232 (3·82)
3bv	247 (3·56)	**3cw**	222 (3·83)
3cv	241 (3·81)	**3ax**	224 sh (3·96)
2,3,5-trimethylthiophane	237 (3·83)[c]	**3cx**	257 (4·00) 226 (3·51) 251 (3·30)
5m	222 (3·57)	**3ay**	230 (3·80) 287 (3·08)
[9](3,5)-pyrazolophane	217 (3·69)[d]	**3cy**	235 (3·92)
[10](3,5)-pyrazolophane	216 (3·69)[e]	**3az**	222·5 sh (3·69) 256 (3·66)
5n	259·5 (4·07)	**3cz**	218 sh (4·13) 228 sh (4·03) 247 (3·89)

[a] Reexamined in the present work. See Ref 1*a*.
[b] Additional absorption: λ_{max} 233 (3·87).
[c] This is taken in n-hexane, see Ref 13.
[d] See Refs 1*b* and 3.
[e] W. E. Parham and J. F. Dooley, *J. Amer. Chem. Soc.*, **89**, 985 (1967).

IR (neat): 3015, 1690, 1631, 1232, 1197, 1173, 932, 827, 792, 750, and 709 cm^{-1}. PMR (CCl_4): δ 6·27 (1H, d, J = 12 Hz, olefinic), 5·64 (1H, d, t, J = 12, and 8·5 Hz, olefinic), 2·5–2·1 (4H, m), and 2·0–1·0 (10H, m). MS *m/e* 152 (P^+). (Found: C, 78·7; H, 10·6. Calcd for $C_{10}H_{16}O$: C, 78·9; H, 10·6%).

Longer reaction time (0·5–5 h) or the use of stronger acid (30% H_2SO_4) resulted in the formation of *cis*-3-cyclodecenone in 80% yield. IR (neat): 3022, 1708, 1651, 739, and 725 cm^{-1}. PMR (CCl_4) δ 5·93–5·12 (2H, m, olefinic), 3·01 (2H, d, J = 7·5 Hz, —$COCH_2C$=), 2·5–1·1 (12H, m, peaks at 2·2 and 1·35). MS *m/e* 152 (P^+). (Found: C, 78·7; H, 10·7. Calcd for $C_{10}H_{16}O$: C, 78·9; H, 10·6%).

3-(1′-*Nitroethyl*)*cyclodecanone* (**6**). To a stirred soln of nitroethane (0·90 g, 12 mmol) in dry MeOH (30 ml), a soln of **1b** (1·0 g, 6·6 mmol) in dry MeOH (15 ml) and NaOMe–MeOH soln (0·30 g of Na in 15 ml of MeOH) were added simultaneously at a nearly equal rate over a period of 30 min. The mixture was stirred overnight and then treated with AcOH (50%, 2·3 ml) under cooling in an ice-bath. Work-up and distillation furnished a viscous oil **6** (1·1 g, 74%), b.p. 140°/0·13 mm. IR (neat): 1705, 1549, 1363, 1094, and 864 cm^{-1}. PMR (CCl_4): δ 4·57 (1H, quintet, J = 6·5 Hz, $\rangle CHNO_2$), 2·5 (4H, m), 2·1–1·2 (13H, m), and 1·5 (3H, d, J = 6·5 Hz, CH_3, each peak splitted into two peaks probably due to diastereoisomers $\Delta\nu = ca$ 1 Hz at 60 MHz). MS *m/e* 227 (P^+). (Found: C, 63·5; H, 9·1; N, 5·9. Calcd for $C_{12}H_{21}NO_3$: C, 63·4; H, 9·3; N, 6·2%).

3-*Acetylcyclodecanone* (**2b**). The nitro ketone **6** (396 mg, 1·74 mmol) was dissolved in a soln of NaOH (800 mg) in aq MeOH (MeOH 10 ml, water 3 ml) and stirred for 4 h at room temp under a N_2. The soln thus prepared was added dropwise to the vigorously stirred soln of H_2SO_4 (conc H_2SO_4 10 ml and water 50 ml) in MeOH (50 ml) at 0° over a period of 1 h and at room temp for additional 2 h. Work-up and distillation gave **2b** as a colourless oil (326 mg, 95%), b.p. 120°/1 mm. Spectroscopic and GLC, TLC analyses showed 100% pure. IR (neat): 1704, 1360, and 1167 cm^{-1}. PMR (CCl_4): δ 3·2–2·2 (5H, m), 2·14 (3H, s, CH_3), and 2·2–1·1 (12H, m, main peak at 1·35). MS *m/e* 196 (P^+). (Found: C, 73·3; H, 10·1. Calcd for $C_{12}H_{20}O_2$: C, 73·4; H, 10·3%).

3-*Acetyl-2-cyclononenol* (**9a**). A mixture of **8a**[6a] (4·34 g, 27 mmol), mercuric sulphate (a catalytic amount), 12% H_2SO_4 (26 ml), and dioxane (20 ml) was stirred at 95° under N_2 during 6 h. Work-up and distillation gave **9a** (3·02 g, 63%), b.p. 73°/3 mm. IR (neat): 3437, 3002, 1670, and 1034 cm^{-1}. PMR (CCl_4): δ 6·52 (1H, d, J = 7·8 Hz, olefinic), 5·40 (1H, m, methine), 4·85–4·30 (1H, m, OH), 2·33 (3H, s, CH_3), and 2·15–1·10 (12H, m). MS *m/e* 182 (P^+). (Found: C, 72·4; H, 10·2. Calcd for $C_{11}H_{18}O_2$: C, 72·5; H, 10·0%).

3-*Acetyl-2-cyclononenone* (**10**)

(a) *Oxidation of* **9a** *with active manganese dioxide.* Active MnO_2 (11·0 g, 0·13 mol) was added to a soln of **9a** (1·67 g, 9·2 mmol) in $CHCl_3$ (200 ml) and the mixture was stirred under N_2 at room temp during 3 h. Work-up and distillation afforded **10** (1·62 g, 98%), b.p. 100°/0·8 mm. IR (neat): 1680, 1658, 1354, 1210, and 1141 cm^{-1}. PMR (CCl_4): δ 6·81 (1H, s, olefinic), 2·80–2·43 (4H, C-4 and C-9 methylenes), 2·40 (3H, s, CH_3), and 2·24–0·87 (8H, m). MS *m/e* 180 (P^+). (Found: C, 73·0; H, 9·0. Calcd for $C_{11}H_{16}O_2$: C, 73·3; H, 9·0%).

(b) *The Brown oxidation of* **9a**. A mixture of sodium dichromate dihydrate (3·7 g), H_2SO_4 (2·8 ml), and water (22 ml) was added during 1 h to a soln of **9a** (6·75 g, 37·0 mmol) in ether. The mixture was stirred for an additional 2 h. Work-up and distillation gave **10** (4·55 g, 68%).

3-*Acetylcyclononanone* (**2a**). A mixture of **10** (4·99 g, 27·7 mmol), Zn powder (19·7 g), AcOH (200 ml), and water (114 ml) was stirred at room temp during 5 h. Work-up and distillation afforded **2a** (3·55 g, 70%), b.p. 124–134°/0·18 mm. IR (neat): 1707, 1355, and 1150 cm^{-1}. PMR (CCl_4): δ 2·18 (3H, s, CH_3), 2·90–0·92 (m, others). MS *m/e* 182 (P^+). (Found: C, 72·6; H, 9·7. Calcd for $C_{11}H_{18}O_2$: C, 72·5; H, 10·0%).

3-*Acetylcyclododecanone* (**2c**). A mixture of **3cu** (4·95 g,

24 mmol), conc H_2SO_4 (20 ml), AcOH (4 ml), water (40 ml), and dioxane (50 ml) was heated at 100° during 20 h. Fractional distillation afforded recovered **3cu** (2·2 g, 45%) and **2c** (1·2 g, 22%), b.p. 110°/0·13 mm, m.p. 70·0–71·0° (n-hexane). IR (KBr disk): 1695, 1347, 1159, 1150, 1051, and 731 cm^{-1}. PMR (CCl_4): δ 3·1–2·0 (5H, m), 2·13 (3H, s, CH_3), and 1·8–1·1 (16H, m, main peak at 1·30). MS *m/e* 224 (P^+). (Found: C, 74·9; H, 10·8. Calcd for $C_{14}H_{24}O_2$: C, 75·0; H, 10·8%).

9-*Methyl*[7](2,4)*thiophenophane* (**3bv**). A mixture of **2b** (50 mg, 0·255 mmol), finely powdered P_2S_5 (220 mg, 1·0 mmol) and dry toluene (4 ml) was stirred for 1·5 h at 100° under N_2. At the end of the period no starting material **2b** was detected and a new peak appeared on GLC assay. The mixture was treated with water (5 ml) and the aqueous layer was extracted with ether. The combined organic layer was washed, dried and evaporated. Distillation gave **3bv** as a colourless oil (25 mg, 51%). IR (neat): 3058, 1572, 1491, 1253, 1174, 1135, 1031, 867, 822, 712, and 666 cm^{-1}. MS *m/e* (relative abundance): 195 (15, $P^+ + 1$), 194 (100, P^+), 193 (14, $P^+ - 1$), 179 (59), 165 (41), 151 (71), 137 (75), 126 (35), 125 (78), 124 (95), 111 (80), and 91 (42).

9-*Methyl*[7](2,4)*pyrrolophane* (**3bw**). A mixture of **2b** (50 mg, 0·255 mmol) and a catalytic amount of ammonium chloride (*ca* 1 mg) was stirred under an atmosphere of ammonia at 95°. After 4 h foaming due to the water evolution ceased, and crystals began to appear on the surface of the mixture. Sublimation at 110°/9 mm gave **3bw** as colourless crystals (35 mg, 78%). IR (KBr disk): 3310, 3094, 1592, 1511, 1212, 831, 805, 795, 707, and 695 cm^{-1}. MS *m/e* (relative abundance): 178 (11, $P^+ + 1$), 177 (79, P^+), 176 (43, $P^+ - 1$), 162 (33), 148 (46), 134 (83), 120 (100), 108 (65), 94 (46), and 77 (18).

8-*Methyl*[6](2,4)*thiophenophane* (**3av**). Treatment of **2a** (50 mg, 0·275 mmol) with P_2S_5 (267 mg) in toluene (4 ml) and the subsequent preparative TLC on silica gel (n-hexane) gave **3av** (30 mg, 61%). IR (neat): 3083, 1561, 1360, 1112, 1032, 871, 726, and 703 cm^{-1}.* MS *m/e* (relative abundance): 181 (18, $P^+ + 1$), 180 (100, P^+), 179 (20, $P^+ - 1$), 165 (46), 152 (38), 151 (55), 137 (95), 126 (32), 125 (53), 124 (54), 123 (35), 111 (60), 97 (38), and 91 (42).

8-*Methyl*-N-*phenyl*[6](2,4)*pyrrolophane* (**3ax**). A mixture of **2a** (194 mg, 1·1 mmol), aniline (164 mg, 1·8 mmol), and conc HCl (a catalytic amount) was heated at 80–100° under N_2 during 2 h. Distillation *in vacuo* afforded **3ax** (98 mg, 36%). IR (neat): 3075, 3050, 1596, 1528, 1502, 1384, 910, 760, 729, and 695 cm^{-1}. PMR ($CDCl_3$): δ 7·33 (5H, m, aromatic), 6·53 (1H, s, aromatic), 2·77–2·45 (4H, m, benzylic), 2·15 (3H, s, CH_3), and 1·9–1·2 (8H, m, main peak at 1·53). MS *m/e* (relative abundance): 240, (24, $P^+ + 1$), 239 (100, P^+), 238 (30, $P^+ - 1$), 224 (12), 210 (28), 196 (36), 184 (24), 170 (18), 118 (14), 105 (12), and 91 (11).

8-*Methyl*-N-(o-*tolyl*)[6](2,4)*pyrrolophane* (**3ay**). The compound **3ay** was prepared from **2a** (151 mg, 0·83 mmol) and *o*-toluidine (445 mg, 4·1 mmol). Distillation gave a pure sample of **3ay** (118 mg, 56%). IR (neat): 3078, 3046, 1604, 1578, 1527, 1502, 1385, 1184, 1151, 769, 758, and 728 cm^{-1}. PMR ($CDCl_3$): δ 7·22 (4H, m, aromatic), 6·29 (1H, s, aromatic), 2·75–2·45 (4H, m, benzylic), 2·02 (3H, s, CH_3), 1·89 (3H, s, CH_3), and 1·9–1·35 (8H, m, main peak at 1·52). MS *m/e* (relative abundance): 254, (19, $P^+ + 1$), 253 (100, P^+), 252 (39, $P^+ - 1$), 238 (55), 224 (46), 210 (48), 198 (33), 184 (27), 182 (30), 168 (12), 145 (14), 132 (15), 118 (16), and 91 (36).

8-*Methyl*-N-(p-*tolyl*)[6](2,4)*pyrrolophane* (**3az**). Treatment of **2a** (105 mg, 0·58 mmol) with *p*-toluidine (238 mg, 2·23 mmol) gave **3az** (54 mg, 37%). IR (neat): 3026, 1611, 1520, 1387, 1185, 1146, 824, and 731 cm^{-1}. PMR ($CDCl_3$): δ 7·15 (4H, s, aromatic), 6·47 (1H, s, aromatic), 2·75–2·45 (4H, m, benzylic), 2·40 (3H, s, CH_3 of benzene ring), 2·14 (3H, s, CH_3 of pyrrole ring), and 1·9–1·3 (8H, m, main peak at 1·55). MS *m/e* (relative abundance): 254 (19, $P^+ + 1$), 253 (100, P^+), 252 (40, $P^+ - 1$), 238 (16), 224 (44), 210 (51), 198 (34), 184 (25), 132 (18), 118 (14), 105 (13), and 91 (57).

11-*Methyl*[9](2,4)*thiophenophane* (**3cv**). A mixture of **2c** (100 mg, 0·446 mmol) and P_2S_5 (150 mg) was heated in a sealed tube under N_2 at 100° for 1 h. Distillation gave **3cv** (69 mg, 70%). IR (neat): 3057, 1573, 1493, 1211, 1130, 833, and 706 cm^{-1}. MS *m/e* (relative abundance): 223 (17, $P^+ + 1$), 222 (100, P^+), 221 (8, $P^+ - 1$), 207 (25), 193 (10), 179 (34), 165 (44), 151 (41), 137 (44), 126 (38), 125 (75), 124 (68), 111 (66), and 91 (34).

11-*Methyl*[9](2,4)*pyrrolophane* (**3cw**). A mixture of **2c** (100 mg, 0·446 mmol) and $(NH_4)_2CO_3$ (1 g) in a glass tube with xylene trap was stirred at 115–120° for 2 h, while an additional amount of $(NH_4)_2CO_3$ (3 g) was added. After cooling the reddish solid was sublimed (150°/0·1 mm) to afford **3cw** as colourless crystals (61 mg, 67%). IR (KBr disk): 3315, 3083, 1599, 1516, 1250, 1160, 1145, 800, 788, 708, and 688 cm^{-1}. MS *m/e* (relative abundance): 206 (16, $P^+ + 1$), 205 (98, P^+), 204 (53, $P^+ - 1$), 190 (27), 176 (23), 162 (46), 148 (58), 134 (41), 120 (84), 108 (90), 107 (100), and 94 (66).

11-*Methyl*-N-*phenyl*[9](2,4)*pyrrolophane* (**3cx**). This was prepared from **2c** (90 mg, 0·40 mmol) and aniline (112 mg, 1·2 mmol) by a similar method as described in the preparation of **3ax**. The pure sample of **3cx** (102 mg, 90%) was obtained by distillation. IR (neat): 3060, 3043, 1600, 1519, 1501, 1342, 1072, 791, 775, 745, and 700 cm^{-1}. PMR ($CDCl_3$): δ 7·5–7·0 (5H, m, aromatic), 5·92 (1H, s, aromatic), 2·55–2·25 (4H, m, benzylic), 1·94 (3H, s, CH_3), 1·8–0·9 (12H, m, main peak at 1·15), and 0·8–0·2 (2H, m). MS *m/e* (relative abundance): 282 (22, $P^+ + 1$), 281 (100, P^+), 280 (27, $P^+ - 1$), 266 (17), 252 (12), 238 (22), 224 (39), 210 (27), 195 (52), 184 (58), 183 (43), 182 (39), 170 (40), 141 (17), 118 (13), and 91 (13).

11-*Methyl*-N-(o-*tolyl*)[9](2,4)*pyrrolophane* (**3cy**). The reaction of **2c** (100 mg, 0·446 mmol) and *o*-toluidine (143 mg, 1·34 mmol) gave **3cy** (110 mg, 83%). IR (neat): 3073, 3032, 1606, 1583, 1500, 1340, 1115, 794, 776, 747, and 724 cm^{-1}. PMR ($CDCl_3$): δ 7·18 (4H, m, aromatic), 5·93 (1H, s, aromatic), 2·6–2·0 (4H, m, benzylic), 2·00 (3H, s, CH_3), 1·82 (3H, s, CH_3), and 1·7–0·3 (14H, m, main peak at 1·2). MS *m/e* (relative abundance): 296, (23, $P^+ + 1$), 295 (100, P^+), 294 (24, $P^+ - 1$), 280 (13), 266 (10), 252 (20), 238 (41), 224 (22), 210 (37), 198 (55), 184 (26), 182 (46), 168 (11), 167 (10), 132 (9), and 91 (28).

11-*Methyl*-N-(p-*tolyl*)[9](2,4)*pyrrolophane* (**3cz**). A mixture of **2c** (100 mg, 0·446 mmol) and *p*-toluidine (143 mg, 1·34 mmol) was treated as in the case of **3az**, yielding 124 mg (94%) of **3cz**. IR (neat): 3040, 1617, 1580, 1515, 1344, 1106, 832, and 790 cm^{-1}. PMR ($CDCl_3$): δ 7·08 (4H, m, aromatic), 5·90 (1H, s, aromatic), 2·5–2·25 (4H, m, benzylic), 2·35 (3H, s, CH_3 of benzene ring), 1·92 (3H, s, CH_3 of pyrrole ring), 1·7–0·9 (12H, m, main peak at 1·15), and 0·7–0·25 (2H, m). MS *m/e* (relative abundance): 296 (25, $P^+ + 1$), 295 (100, P^+), 294 (30, $P^+ - 1$), 280 (18), 266 (13), 252 (23), 238 (40), 224 (26), 210 (46), 198 (58), 197 (41), 184 (39), 168 (7), 132 (12), 105 (11), and 91 (31).

3,5-*Heptamethylene*-2-*pyrazoline* (**4m**). A soln of **1b** (1·14 g, 7·5 mmol) and hydrazine hydrate (80%, 940 mg,

*Reexamined in the present work. See Ref 1*a*.

15·0 mmol) in EtOH (30 ml) was heated to reflux for 1·5 h. Evaporation of the solvent, followed by distillation, gave **4m** as a colourless oil (685 mg, 55%), b.p. 80°/0·12 mm. The product **4m** was so labile that it did not give the correct analyses. The structure was ascertained by conversion to **5m**. The spectroscopic data were consistent with the structure given. IR (neat): 3290, 1622, 1339, 1298, 935, 837, and 745 cm^{-1}. MS *m/e* 166 (P^+).

[7](3,5)*Pyrazolophane* (**5m**). Freshly distilled **4m** (250 mg, 1·5 mmol) was admixed with finely powdered S_8 (55 mg, 1·7 mmol) and the mixture heated at 210° under N_2 for 2 h. Work-up and preparative TLC on silica gel (benzene:EtOAc = 3:1) afforded **5m** as colourless crystals (185 mg, 75%). IR (KBr disk): 3190, 3155, 3102, 3022, 1575, 1215, 1028, 898, 840, 808, and 711 cm^{-1}. MS *m/e* (relative abundance): 164 (76, P^+), 149 (8), 135 (43), 121 (22), 110 (50), 109 (32), 108 (20), 96 (100), 95 (60), 94 (65), 82 (54), 81 (30), and 65 (23).

N-*Phenyl*[7](3,5)*pyrazolophane* (**5n**). A soln of **1b** (304 mg, 2·0 mmol) and phenylhydrazine (238 mg, 2·2 mmol) in dry EtOH (10 ml) was treated as above. Concentration gave **4n**, IR (neat): 1600, 1500, 1255, 748, and 693 cm^{-1}. MS *m/e* 242 (P^+). The crude **4n** was subjected to dehydrogenation with S_8 (64 mg, 2·0 mmol). Work-up and preparative TLC on silica gel (benzene) afforded **5n** (300 mg, 63%). IR (neat): 3050, 1598, 1550, 1500, 1217, 1033, 894, 763, and 696 cm^{-1}. PMR (CCl_4): δ 7·34 (5H, m, aromatic), 6·29 (1H, s, aromatic), 2·95 (2H, m, benzylic), 2·41 (2H, m, benzylic), 1·9–0·6 (9H, m), and −1·66 (1H, m, one of C(4) protons). MS *m/e* (relative abundance): 240 (100, P^+), 211 (11), 816 (15), 172 (29), 171 (33), 158 (28), 157 (24), 135 (16), 130 (23), 119 (13), 93 (40), and 77 (79).

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