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A NEW APPROACH TO THE SYNTHESIS OF THIOPHENOPHANES. SYNTHESIS OF [n.1.1]PARACYCLO(2,5)THIOPHENOPARACYCLOPHANES

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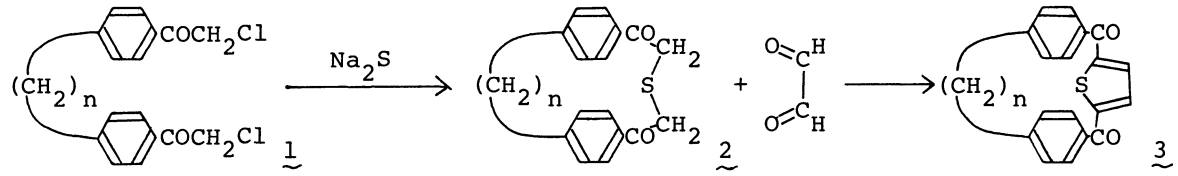
A new method for the synthesis of thiophenophanes which consists of cyclization of bischloroacetyl compounds with sodium sulfide and condensation of the resulting keto sulfides with glyoxal was developed. As an application a series of [n.1.1]paracyclo(2,5)thiophenoparacyclophanes (n=3,4,5,6,7,8,10) were synthesized.

In the synthesis of thiophenophanes carbon-carbon bond forming reactions have been utilized as critical ring-closing reactions. We wish to report a novel method for the synthesis of thiophenophanes in which a facile sulfide-bridging reaction is used in a critical cyclization step and the sulfur atom is subsequently incorporated into a thiophene ring.

Because of high reactivity of haloacetyl compounds cyclization of bishaloacetyl compounds by sodium sulfide was expected to be efficient and, as a matter of fact, several macrocyclic diketo sulfides have been reported[1]. However, to date, no further transformation of them has appeared in the literature. The methylene groups activated by both sulfide and carbonyl groups were considered to be suitable for the condensation with 1,2-dicarbonyl compounds affording thiophene rings as in the Hinsberg thiophene synthesis. We found for the open-chain model system of the type $RCOCH_2SCH_2COR$(R=alkyl, aryl) the condensation with glyoxal gave expected 2,5-diacylthiophenes efficiently under mild reaction conditions[2]. To investigate the applicability of these reactions to the synthesis of thiophenophanes we selected first the following [n.1.1]paracyclo(2,5)thiophenoparacyclophane system because the starting materials of various chain lengths(n) were readily available and the condensation of aroyl sulfides were found to be faster than that of alkanoyl sulfides[2].



1 2 3

The cyclization of 1,ω-bis(p-chloroacetylphenyl)alkanes 1, which were prepared readily by the Friedel-Crafts reaction of 1,ω-diphenylalkanes with chloroacetyl chloride in good yields[3], was carried out as follows. To a refluxing ethanol (1 L) were added simultaneously a solution of 1 (40 mmol) in benzene, dioxane, or tetrahydrofuran(250 mL) according to the solubility and a solution of sodium sulfide (40 mmol) in 80% ethanol (250 mL) over a period of 8-12 h under high dilution conditions

in an inert atmosphere. After refluxing for an additional 30 min the solvents were removed and the residue was chromatographed (silica gel, chloroform-benzene 1:1-1:2). The faster moving monomer 2 and the slower moving and less soluble dimer were collected and fractionally crystallized. Table 1 lists the yields of the products[4].

Table 1 Synthesis of Thiacyclophanes

	Monomer 2		PMR($CDCl_3$, ppm)		Dimer		PMR($CDCl_3$, ppm)	
n	Yield(%)	mp	δ Ar-H*	$COCH_2S$	Yield(%)	mp	δ Ar-H*	$COCH_2S$
3	29.3	169.5-170°	7.11	3.68	14.9	218-218.5°	7.49	3.91
4	24.2	183-184°	7.14	3.76	9.9	219-220°	7.52	3.96
5	42.0	117-117.5°	7.26	3.77	4.3	151-152°	7.47	3.93
6	56.7	131.5-132°	7.38	3.83	6.9	213.5-214°	7.54	3.96
7	55.2	126-126.5°	7.37	3.82	4.7	163.5-164°	7.54	3.93
8	47.9	114-115°	7.40	3.83	3.0	175.5-176.5°	7.55	3.96
10	56.5	85.5-86°	7.42	3.88	5.2	139.5-140.5°	7.55	3.93

* Quartet, AA'BB'.

All the monomers showed correct molecular ion peaks in the mass spectra while the dimers failed to give molecular ion peaks because of decomposition except for the lower members of the series(n=3,4). Yields of the monomers decreased gradually as the ring sizes became smaller. Attempted cyclizations to obtain the monomer 2 (n=2) were all unsuccessful.

The second thiophene-forming cyclizations were slow compared to the open-chain compounds and the addition of a base solution at the rate used for the acyclic compounds brought about extensive formation of amorphous matter even for the largest and apparently unstrained thiacyclophane 2 (n=10). Thus, slow addition of a dilute solution of sodium alkoxide at room temperature was essential and the syringe pump technique was very helpful to obtain reproducible results. A typical experimantal procedure is as follows. To a solution of the thiacyclophane 2 (1 mmol) and glyoxal trimer dihydrate (168 mg, 2.4 mmol as a monomer) in dioxane (10 mL) and alcohol (50 mL) was added a solution of sodium alkoxide (0.2 M, 5 mL) with magnetic stirring over a period of 2 h at room temperature. After stirring for an additional 1 h the solvents were evaporated and the residue was acidified with dilute hydrochloric acid and extracted with chloroform. After washing with water the extracts were dried ($MgSO_4$) and passed through a column of silica gel (chloroform). The solvent was removed and the residue was crystallized from acetone to yield the thiophenophane 3. The yields of the thiophenophanes 3 are given in Table 2 along with some spectral data[4]. The yields were better in methanol in which the condensation was slower but decomposition was less pronounced than in ethanol, and reduced gradually from n=10 to n=4 and abruptly at n=3. Since the formation of thiophene ring apparently involves many intermediate steps, the conformational mobility of the $-COCH_2SCH_2CO-$ group may greatly affect the yield. The molecular models (CPK) indicate that for the thiacyclophane 2 (n=3) the conformation favorable for the condensation in which the sulfur is directed inward can no longer be adopted because of the large size of the sulfur atom and the molecule is rigid. Extra strain introduced on formation of the thiophene ring may also be the cause of the low yield.

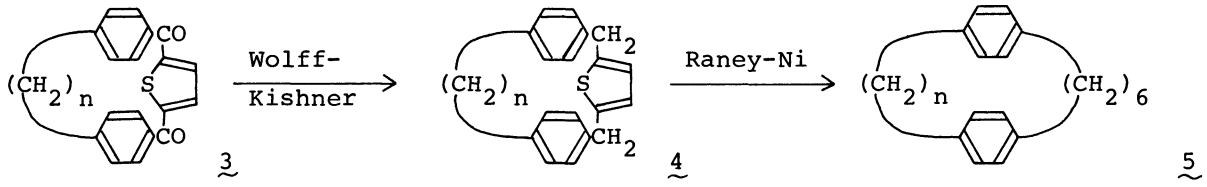
Table 2 Synthesis of Thiophenophanes 3

n	Yield (%) in EtOH	Yield (%) in MeOH	mp	IR ($CHCl_3$) $\nu_{C=O}$ (cm^{-1})	PMR ($CDCl_3$) δ 	PMR ($CDCl_3$) Ar-H* (ppm)
3	9.0	7.4	244-246°	1677	7.62	7.12 (s)
4	36.4	—	224.5-225.5°	1673	7.79	7.14 (q)
5	34.2	42.2	246-247°	1667	7.89	7.21 (q)
6	43.9	60.6	241.5-242.5°	1664	7.97	7.26 (q)
7	67.3	—	224-225°	1658	8.02	7.35 (q)
8	58.1	72.9	196.5-197.5°	1655	8.02	7.38 (q)
10	91.0	94.7	160.5-161.5°	1649	8.06	7.40 (q)

* s: singlet, q: quartet, AA'BB'.

The IR and PMR data of 3 indicate that fairly large conformational changes are brought about with the change in n, the situation of which is in good accord with the molecular model consideration[2].

The conversion of the carbonyl groups in the thiophenophanes 3 to methylene groups was effected readily by the Wolff-Kishner reduction as shown in Table 3[4].



3 4 5

Table 3 Synthesis of Thiophenophanes 4

n	Yield (%)	mp	PMR($CDCl_3$) δ Ar-H		$ArCH_2$  (ppm)
3	68.8	142.5-143.5°	6.77*	6.43	3.72
4	84.0	189-189.5°	6.87	6.57	3.83
5	91.1	230-230.5°	6.92	6.64	3.90
6	91.0	229.5-230.5°	6.96	6.67	3.94
7	94.9	193-193.5°	6.98	6.68	3.97
8	82.9	168-168.5°	7.00	6.69	3.98
10	68.7	143.5-144.5°	7.05	6.72	4.02

* Quartet, AA'BB'.

Thiophene ring has versatile synthetic possibilities, the simplest of which is reductive desulfurization. Thus, the reductive opening of the thiophene ring of the thiophenophanes 4 may lead to [n.6]paracyclophanes 5. As an example, [6.1.1]paracyclo(2,5)thiophenoparacyclophane was reduced readily by Raney nickel (W-2) in refluxing dioxane to [6.6]paracyclophane (mp 100-100.5°, lit[5]., mp 99.6-100.6°) in 80.9% yield.

Although this method may not be applicable when the conformation of a thiacyclophane is unfavorably restricted for the thiophene-forming condensation and excessive strain is built up in the molecule, versatile thiophenophanes which cannot be obtained otherwise may be synthesized. We are currently examining the applicability of the method to other systems.

References and Notes

1) a) T. Baccheti and L. Canonica, Gazz. Chim. Ital., 82, 243 (1952), Chem. Abstr., 47, 8718c (1952); T. Baccheti and L. Caprio, Gazz. Chim. Ital., 83, 832 (1953), Chem. Abstr., 49, 4679h (1954); b) F. Vögtle and R. G. Lichtenthaler, Synthesis, 480 (1972); F. Vögtle and R. G. Lichtenthaler, Angew. Chem. Int. Ed. Engl., 11, 535 (1972); R. G. Lichtenthaler and F. Vögtle, Chem. Ber., 106, 1319 (1973).
2) The details will be reported elsewhere.
3) For bischloro ketones 1 (n=3,4,5,10), see E. Gryszkiewicz-Trochimowski, O. Gryskiewicz-Trochimowski, and R. S. Levy, Bull. Soc. Chim. Fr., 1156 (1958). The other 1 were prepared analogously in 71-89% yields.
4) Satisfactory elemental analyses and spectral data were obtained for all new compounds.
5) J. Abell and D. J. Cram, J. Am. Chem. Soc., 76, 4406 (1954).

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