Heterocycles by Cycloaddition. Part I. Cycloaddition–Extrusion–Ring Expansion Reactions of Five-membered Mesoionic Compounds with Diphenylcyclopropenone and Related Compounds: Preparation of Six-membered Heterocycles

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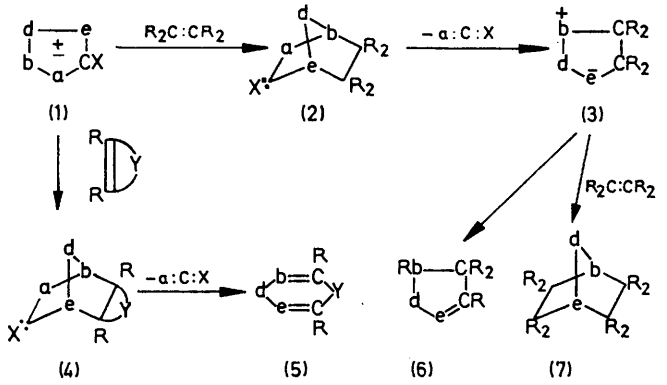
Cycloaddition–extrusion–ring expansion reactions of mesoionic oxazolones (9) and a thiazolone (15) with 2,3-diphenylcyclopropenylidene compounds (10) gave pyridin-4-one, -thione, and -imine, and 4-methylenedihydropyridine derivatives (12). The reactions of a mesoionic dithiolone (17) with cyclopropenylidene derivatives mainly gave thiopyranone and 4-methylenethiopyran derivatives (19).

THE cycloadduct (2) formed by the reaction of a five-membered mesoionic compound (1) with a dipolarophilic olefin generally fragments further under the reaction conditions to give a 1,3-dipolar intermediate (3), which ultimately gives a five-membered heterocycle (6) by migration of a substituent.[1] In a few cases, the 1,3-dipole (3) reacts further with the olefin to give a bridged bis-adduct (7).[2,3]

In the case of the reaction of a mesoionic compound with a strained dipolarophile, a third reaction route may be envisaged, in which fragmentation of the initial adduct (4) may be accompanied by simultaneous cleavage of the strained bond to afford a ring-enlarged product (5) as shown in Scheme 1. In this Scheme, a, b, d, e, and X of



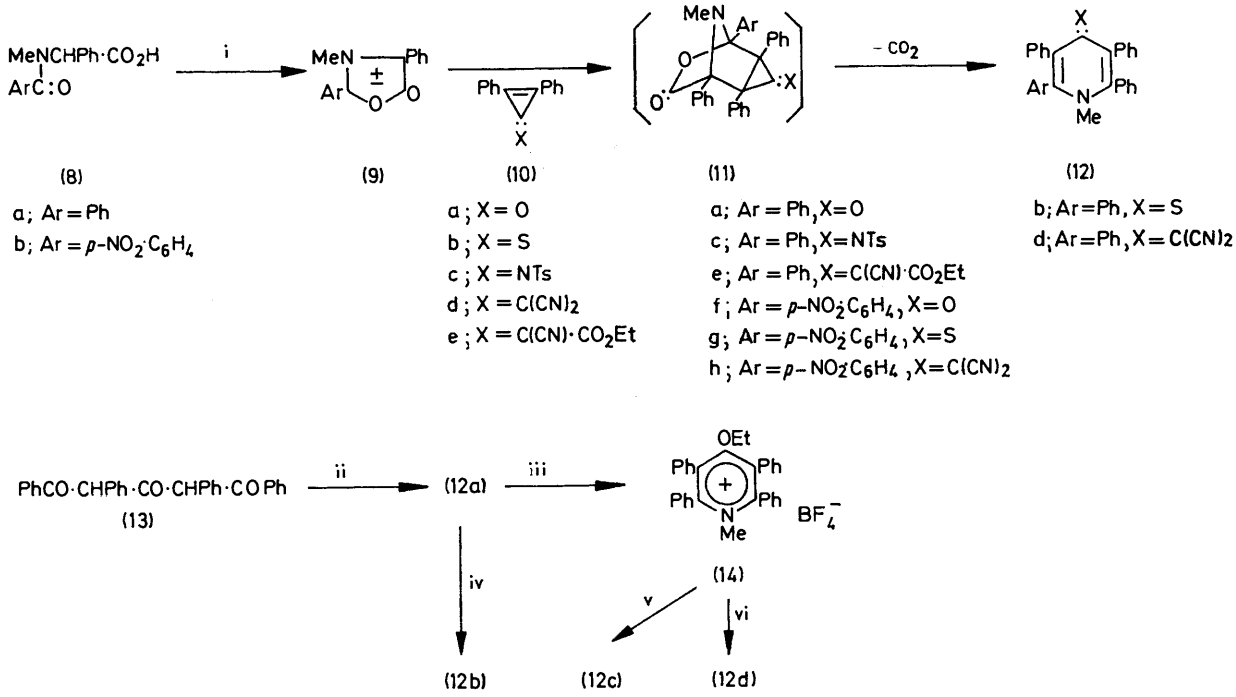
SCHEME 1

the ring system (1) may be any atoms or groups which satisfy the definition of mesoionic compound,[4] and Y may be any atom or group which provides sufficient energy in the resulting ring. This route has been realised recently by Martin and Hekman,[5] who showed that the reactions of a mesoionic oxazol-5-one with cyclopropene and cyclobutene give the corresponding six- and seven-membered heterocycles.

We describe here the cycloaddition–extrusion reactions of some five-membered mesoionic compounds with 2,3-diphenylcyclopropen-one, -thione, and -imine, and 3-methylenecyclopropene derivatives (hereafter referred to as cyclopropenylidene derivatives).[6] We hoped that these reactions would serve as a convenient procedure for the preparation of fully conjugated six-membered heterocycles. Further, the reactions have an added interest in view of the ability of cyclopropenylidene derivatives to undergo cycloaddition reactions across the 1,2- or the 2,3-position or across the exocyclic double bond depending on the nature of the other reagent, and the fact that diphenylcyclopropenone acts, in some cases, only as a masked diphenylacetylene.[7] During the present investigation, Potts and Baum [8] independently reported reactions of the same type; their results partly overlap with ours.

The mesoionic 3-methyl-2,4-diphenyloxazol-5-one (9a), prepared *in situ* from 2-(*N*-methylbenzamido)-2-phenylacetic acid (8a),[2] reacted readily with diphenylcyclopropenone (10a) to give 1-methyl-2,3,5,6-tetraphenyl-4(1*H*)-pyridone (12a). The assigned structure (12a) was supported by spectral data [$\nu_{max.}$ 1612 cm^{-1} (C:O); δ 7·03 and 7·18 (each 10H, s)], which eliminate the isomeric 2- and 3-pyridone structures, and confirmed by comparison with a sample prepared by the reaction of 1,2,4,5-tetraphenylpentane-1,3,5-trione (13) with methylamine. Similar *in situ* reactions of the oxazolone (9a) with diphenylcyclopropenethione (10b) and tosylimino- (10c), dicyanomethylene- (10d), and cyano(ethoxycarbonyl)methylenediphenylcyclopropene (10e) gave the corresponding dihydropyridine derivatives (12b—e) in acceptable yields (see Table). The structures of the dihydropyridines (12b—e) were supported by spectral data and in some cases by comparison with samples synthesised *via* different routes. The reaction of the pyridone (12a) with phosphorus pentasulphide gave the pyridinethione (12b). Treatment of the pyridone (12a) with triethyloxonium fluoroborate gave 4-ethoxy-1-methyl-2,3,5,6-tetraphenylpyridinium fluoroborate (14), which was then treated with toluene-*p*-sulphonamide or malononitrile in the presence of base to give the corresponding tosylimino- (12c) or dicyanomethylene (12d) derivative.

[1] M. Ohta and H. Kato, 'Nonbenzenoid Aromatics,' vol. 1, ed. J. P. Snyder, Academic Press, New York, 1969, p. 117.
[2] H. Gotthardt and R. Huisgen, *Chem. Ber.*, 1970, **103**, 2625. This reaction actually gives the *endo,exo*-bis-adduct (m.p. 212—214°) in addition to the *exo,exo*-bis-adduct reported by Gotthardt and Huisgen (H. Kato and K. Morisaki, unpublished data).
[3] P. M. Weintraub, *Chem. Comm.*, 1970, 760.
[4] W. Baker and W. D. Ollis, *Quart. Rev.*, 1957, **11**, 15.
[5] H.-D. Martin and M. Hekman, *Angew. Chem. Internat. Edn.*, 1972, **11**, 926.
[6] Preliminary report, H. Matsukubo and H. Kato, *J.C.S. Chem. Comm.*, 1974, 675.
[7] K. T. Potts and J. S. Baum, *Chem. Rev.*, 1974, **74**, 189; M. L. Deem, *Synthesis*, 1972, 675.
[8] K. T. Potts and J. Baum, *J.C.S. Chem. Comm.*, 1973, 833.



SCHEME 2 Reagents: i, Ac_2O; ii, $MeNH_2$; iii, $Et_3O^+BF_4^-$; iv, P_4S_{10}; v, $TsNH_2$–NaOBu^t; vi, $CH_2(CN)_2$–NaOBu^t

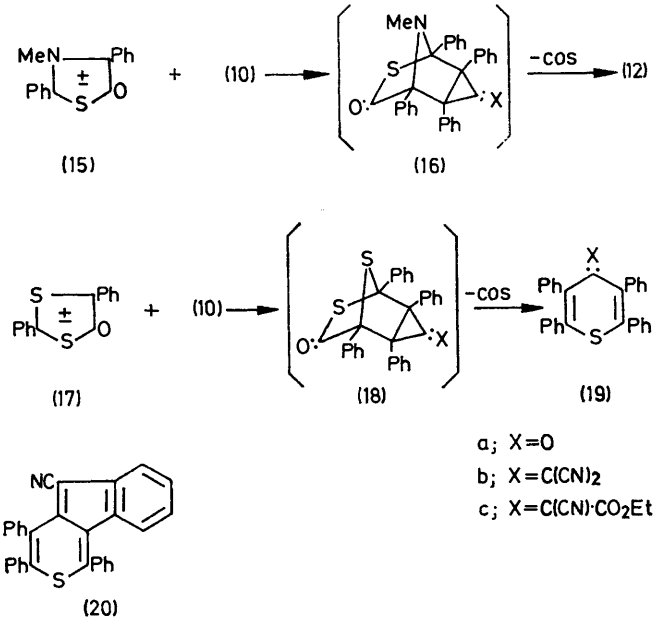
Similar *in situ* reactions of the mesoionic 3-methyl-2-*p*-nitrophenyl-4-phenyloxazol-5-one (9b) with the diphenylcyclopropenylidene derivatives (10a, b, and d) gave the corresponding 2-*p*-nitrophenylpyridine derivatives (12f, g, and h). This oxazolone (9b) is relatively stable, and it is possible to use it in isolated form.[9] The yield of (12g), however, was not improved by use of the isolated oxazolone (9b).

The pyridine derivatives (12a—e) could also be prepared in comparable yields by the reactions of cyclopropenylidene derivatives (10a—e) with the mesoionic 3-methyl-2,4-diphenylthiazol-5-one (15) [10] in refluxing xylene.

Lastly, the reactions of the mesoionic 2,5-diphenyl-1,3-dithiol-4-one (17) [11] with diphenylcyclopropenone (10a) and dicyanomethylenediphenylcyclopropene (10d) in xylene under reflux afforded 2,3,5,6-tetraphenylthiopyran-4-one (19a) [12] and the 4-dicyanomethylene-analogue (19b), respectively, though in relatively low yields.

In the case of the reaction of the dithiolone (17) with (10e), another product was formed (16%) in addition to that expected (19c). The by-product retained a cyano-substituent but no longer showed an i.r. carbonyl band, and the n.m.r. spectrum showed only a complex aromatic proton signal. From these spectral data and the combustion and mass analyses, the indeno[1,2-*c*]thiopyran structure (20) was assigned. Attempts at converting compound (19c) into (20) by pyrolysis were not successful.

These results show that the cycloaddition reactions of mesoionic compounds with cyclopropenylidene derivatives (10) took place as expected to give the initial cyclo-



SCHEME 3

adducts (11), (16), and (18), which underwent fragmentation with extrusion of carbon dioxide or carbon oxysulphide accompanied by cleavage of the three-membered

[9] H. O. Bayer, R. Huisgen, R. Knorr, and F. C. Schaefer, *Chem. Ber.*, 1970, **103**, 2581.

[10] R. Huisgen, E. Funke, F. C. Schaefer, H. Gotthardt, and E. Brunn, *Tetrahedron Letters*, 1967, 1809.

[11] H. Gotthardt and B. Christl, *Tetrahedron Letters*, 1968, 4743.

[12] K. W. Hubel and E. H. Braye, U.S.P., 3,280,017 (*Chem. Abs.*, 1967, **66**, 2462).

ring to give the fully conjugated six-membered heterocycles. The cycloaddition of the five-membered mesoionic compounds always occurred across the 2,3-double bond of the cyclopropenylidene derivatives irrespective of the nature of the exocyclic multiple bond and of the nature of the mesoionic ring system. In this sense, the behaviour of the cyclopropenylidene derivatives (10) towards mesoionic 1,3-dipoles is in strong contrast with that towards open-chain 1,3-dipoles, which show quite versatile behaviour depending upon the nature of the constituent heteroatoms.[6,7,13]

It may appear that the reactions of this type afford an attractive method for the preparation of a wide variety of fully conjugated six-membered heterocycles. However, the success of this method actually depends on the reactivity of the mesoionic ring system: the reactions of the mesoionic oxazolone (9) proceed readily at moderate temperature, but those of the mesoionic thiazolone (15) and dithiolone (17) require a long reaction time and a relatively high temperature. Further, with some other mesoionic ring systems, the expected cycloaddition–extrusion–ring expansion products were not obtained. Either the starting material was unchanged or a complex product mixture resulted from the reactions of diphenylcyclopropenone (10a) with 3-phenylsydnone, mesoionic 4-phenyl-1,3,2-oxathiazol-5-one, and mesoionic 2,3,5-triphenylthiazol-4-one; and cyclopropenethione (10b) did not react with the dithiolone (17). The u.v. and n.m.r. spectra and pertinent i.r. and mass spectra of compounds (12), (19), and (20) are available as Supplementary Publication No. SUP 21248 (3 pp.).

[13] H. Matsukubo and H. Kato, unpublished data.

EXPERIMENTAL

Unless otherwise stated, m.p.s were determined on a Yanagimoto hot-stage apparatus. U.v. and i.r. (KBr) spectra were recorded on Hitachi EPS-3T and EPI-G3 spectrophotometers. N.m.r. spectra were obtained on a JEOL JNM-4H-100 (100 MHz) spectrometer for solutions in deuteriochloroform (standard internal tetramethylsilane). Mass spectra were measured with a Hitachi RMU-6 spectrometer at 70 eV (direct inlet technique). Compounds stated to be identical were so on the basis of m.p., mixed m.p., and i.r. and n.m.r. spectral determinations.

TABLE 1

Preparation and properties of cycloadducts

Product	Reactants	Procedure T/°C [a]	Procedure t/h	Procedure Isolation [b]	Yield [c] (%)	Appearance (Recryst. solvent)	M.p. [d] (°C)	Formula	Analyses (%) † C	H	N
(12a)	(8a), (10a)	55	1	B (Me_2CO)	61	Needles	313—315 [e]	$C_{30}H_{23}NO$	86·5	5·55	3·35
	(15), (10a)	Rfl	7·5	A	55	(Me_2N·CHO)			(87·15)	(5·6)	(3·4)
(12b)	(8a), (10b)	55	1	A	61	Yellow prisms	341—342* [f]	$C_{30}H_{23}NS$	83·75	5·45	3·0
	(15), (10b)	Rfl	7·5	A	48	(Me_2N·CHO)	(decomp.)		(83·9)	(5·4)	(3·25)
(12c)	(8a), (10c)	60	1	B (Et_2O)	64	Plates	310·5—312·5	$C_{37}H_{30}N_2O_2S$	77·95	5·3	4·9
	(15), (10c)	Rfl	16	B (Et_2O)	39	(CH_2Cl_2–Et_2O)			(78·4)	(5·35)	(4·95)
(12d)	(8a,) (10d)	80	5	A, C ($CHCl_3$)	41	Yellow prisms	360—361 *	$C_{33}H_{23}N_3$	85·0	5·0	9·2
	(15), (10d)	Rfl	8	A	74	(Me_2N·CHO)	(decomp.)		(85·85)	(5·0)	(9·1)
(12e)	(8a), (10e)	80	1	B (Me_2CO)	65	Orange prisms	307·5—309 [g]	$C_{35}H_{28}N_2O_2$	82·3	5·55	5·7
	(15), (10e)	Rfl	5	A	73	(CH_2Cl_2–Et_2O)	(decomp.)		(82·65)	(5·55)	(5·5)
(12f)	(8b), (10a)	80	3·5	B (PhH)	53	Pale yellow prisms (CH_2Cl_2–Et_2O)	281—282	$C_{30}H_{22}N_2O_3$	78·85 (78·6)	5·1 (4·85)	6·15 (6·1)
(12g)	(8b), (10b)	80	8	B (PhH, Et_2O)	52	Orange–yellow prisms	307—309	$C_{30}H_{22}N_2O_2S$	75·7	4·6	5·9
	(9b), (10b)	Rfl	2·5	A	44	(CH_2Cl_2–Et_2O)			(75·95)	(4·65)	(5·9)
(12h)	(8b), (10d)	Rfl	9	B (PhH)	62	Yellow needles (CH_2Cl_2–Et_2O)	>330	$C_{33}H_{22}N_4O_2$	78·15 (78·25)	4·4 (4·4)	11·35 (11·05)
(19a)	(17), (10a)	Rfl	10	A	38	Pale yellow prisms (Xylene)	318·5—319 [h]	$C_{29}H_{20}OS$	83·25 (83·6)	4·75 (4·85)	
(19b)	(17), (10d)	Rfl	11	A	19	Yellow prisms (CH_2Cl_2–Et_2O)	305·5—306·5	$C_{32}H_{20}N_2S$	82·6 (82·75)	4·35 (4·35)	5·75 (6·05)
(19c)	(17), (10e)	Rfl	15	C (PhH)	8	Yellow prisms (EtOH)	186·5—187·5	$C_{34}H_{25}NO_2S$	79·85 (79·8)	5·1 (4·95)	2·7 (2·75)
(20)	(17), (10e)	Rfl	15	C (PhH)	16	Orange needles (Me_2CO)	295—295·5	$C_{31}H_{19}NS$	84·8 (85·1)	4·25 (4·4)	3·05 (3·2)

[a] Rfl: reflux. [b] Isolation procedures: A, crystals which separated on cooling were collected; B, solvent was distilled off and the residue triturated with the solvent shown in the parentheses; C, products were separated by column chromatography on silica gel with the eluant shown in parentheses. [c] Yields based on purified products. [d] M.p.s. with an asterisk were determined in a capillary tube. [e] Lit.,[7] 309—310°. [f] Lit.,[7] 320—322° (decomp.). [g] Resolidified at 313—315°. [h] Lit.,[12] 319—320°.

† Required values in parentheses. Some compounds gave consistently low carbon values but their purity was supported by spectral data and t.l.c. Mass spectra of all compounds gave consistent molecular ion peaks.

Cycloaddition Reactions of Diphenylcyclopropenylidene Derivatives (10) *and Mesoionic Oxazolones* (9) *prepared in situ. General Procedure.*—Under nitrogen, a solution of 2-(*N*-methylaroylamino)-2-phenylacetic acid (8) (0·3—0·55 g) in freshly distilled acetic anhydride (5 ml) was warmed at 55° for 5 min. An equivalent amount of cyclopropenylidene derivative (10) was then added, the resulting solution or suspension was warmed, and the products were isolated by appropriate procedures. The results are listed in the Table.

Cycloaddition Reactions of Diphenylcyclopropenylidene Derivatives (10) *and Mesoionic Compounds* (15) *and* (17). *General Procedure.*—A solution or suspension of the mesoionic compound (0·2—0·5 g) and an equimolar amount of diphenylcyclopropenylidene derivative (10) in xylene (5—10 ml) was refluxed, and the products were isolated by suitable methods. The results are shown in the Table.

1-Methyl-2,3,5,6-tetraphenyl-4(1H)*-pyridone* (12a).—A solution of 1,2,4,5-tetraphenylpentane-1,3,5-trione (0·31 g) and ethanolic 30% methylamine (0·5 ml) in ethanol (50 ml)

was kept overnight at room temperature. More ethanolic methylamine (0·5 ml) was added, and the solution was refluxed for 7·5 h. The solvent was distilled off and the residue was recrystallised from dimethylformamide to give prisms (12a) (0·13 g, 43%), m.p. 307—308·5°, identical with the sample prepared by cycloaddition.

1-*Methyl*-2,3,5,6-*tetraphenylpyridine*-4(1H)-*thione* (12b).—The pyridone (12a) (0·1 g) and phosphorus pentasulphide (0·06 g) in xylene (50 ml) were refluxed for 6 h. The organic solution was concentrated and the residue was recrystallised from dimethylformamide to give the pyridinethione (12b) (0·05 g, 48%), identical with the specimen prepared by cycloaddition.

4-*Ethoxy*-1-*methyl*-2,3,5,6-*tetraphenylpyridinium Fluoroborate* (14).—To a solution of triethyloxonium fluoroborate (5 g) in dichloromethane (10 ml) was added a solution of pyridone (12a) (1 g) in dichloromethane (15 ml). After stirring for 2 h, the solution was concentrated and the precipitate was recrystallised from ethanol to give the fluoroborate (14) (1·27 g, 99%) as needles, m.p. 268—273° (decomp.) (lit.,[7] 275—278°). This crude material was used without further purification. The u.v., i.r., and n.m.r. spectra agreed with those reported.[7]

1,4-*Dihydro*-1-*methyl*-2,3,5,6-*tetraphenyl*-4-*tosyliminopyridine* (12c).—A mixture of ethoxypyridinium fluoroborate (14) (0·1 g), toluene-*p*-sulphonamide (0·07 g), sodium t-butoxide [from sodium (0·01 g)], and t-butyl alcohol (12 ml) was refluxed for 3 h. The mixture was concentrated *in vacuo* and the residue was recrystallised from dichloromethane–ether to give the tosyliminopyridine (12c) (0·09 g, 84%), m.p. 310—312·5°, identical with the sample prepared by cycloaddition; $\lambda_{max.}$ (MeOH) 324 nm (log ε 4·112); $\nu_{max.}$ 1586 cm^{-1} (C:N); δ 7·35—7·02 (22H, m), 6·73 (2H, d, *J* 8 Hz), 3·14 (3H, s), and 2·19 (3H, s); *m/e* 566 (7%), 411 (81), and 397 (100).

4-*Dicyanomethylene*-1,4-*dihydro*-1-*methyl*-2,3,5,6-*tetraphenylpyridine* (12d).—The pyridinium fluoroborate (14) (0·1 g) was treated with malononitrile (0·025 g) by essentially the same procedure as described above to give the dicyanomethylenedihydropyridine (12d) (0·07 g, 80%), identical with the sample prepared by cycloaddition; $\lambda_{max.}$ (MeOH) 246 (log ε 4·309) and 383 nm (4·499); $\nu_{max.}$ 2180, 2155 (C:N), and 1584 cm^{-1} (C:C); δ 7·14br (10H, s), 7·06br (10H, s), and 2·98 (3H, s); *m/e* 461 (100%), 460 (81), and 118 (9).

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