

Heterocycles from Ylides. Part 7.¹ Reactivity of 3-Arylmethyleneindolin-2-ones with Stabilized Sulphur Ylides

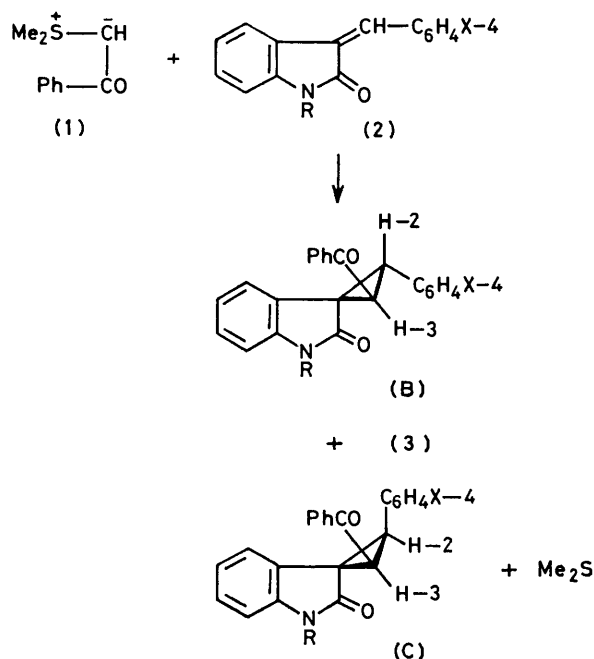
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3-Arylmethyleneindolin-2-ones react with carbonyl-stabilized sulphur ylides yielding spiro[cyclopropane-1,3'-indolin-2'-ones] whose structure and stereochemistry were assigned on the basis of spectroscopic data.

IN continuation of our studies² on the behaviour of sulphur ylides towards unsaturated systems we now report the reaction of carbonyl-stabilized sulphur ylides (1) with 3-arylmethyleneindolin-2-ones (2). Compounds (2) show a diene \longleftrightarrow dipole mesomerism³ and consequently can give products deriving from [1,2- or 1,4-dipolar] or [1,4-conjugate] (Michael type) addition reactions.

RESULTS AND DISCUSSION

Treatment of dimethylsulphonium phenacylide (1) with the 3-arylmethylene-1-methyl(or 1-acetyl)indolin-2-ones (2) in tetrahydrofuran solution, at room temperature, for 48 h gave, in all cases investigated, a mixture of two products. The basic components were isolated in a pure state by fractional crystallization and the compounds gave the same analyses.



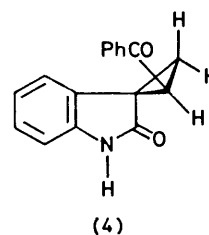
On the basis of spectroscopic data (i.r. and n.m.r.) oxiran and dihydrofuran derivatives, arising respectively from a [1,2- or 1,4-dipolar] addition reaction, were ruled out. The conclusion is that the reaction afforded, *via* a Michael-type addition reaction followed by a 1,3-elimination, a mixture of two isomeric spiro[cyclopropane-1,3'-indolin-2'-ones] (3a-f).

The reaction pathway was not influenced by the nature of the solvent (tetrahydrofuran, dimethyl sulphoxide, acetonitrile) or by the temperature (0, 25, or 60 °C). The structures were confirmed by i.r. (indolinone and benzoyl C=O stretching) and n.m.r. data (AB splitting pattern for the cyclopropane hydrogen atoms).

Although the structure of the spiro[cyclopropane-1,3'-indolinones] was confirmed spectroscopically, it was not possible to deduce their steric configurations from the n.m.r. data.

The coupling constants for 2-H and 3-H of the cyclopropane ring fall, for all the compounds, in the range 8–10 Hz, which makes it difficult to distinguish between the pairs of isomers. Graham⁴ reported that generally the coupling constants in substituted cyclopropanes are 8–9 Hz (*cis*) and 5–6 Hz (*trans*). Later, other authors⁵ attributed *cis* or *trans* configurations in substituted cyclopropanes on the basis that *cis* coupling constants are always greater than *trans* ones.

In order to establish the true values of the *cis* and *trans* coupling constants in these compounds spiro[3-benzoylcyclopropane-1,3'-indolin-2'-one] (4) was pre-



pared. On examination of its n.m.r. spectrum (an AMX system for the cyclopropane protons) it was concluded that in these spiro[cyclopropane-1,3'-indolinones] the *cis* and *trans* coupling constants are very similar (see Experimental section). Thus it was necessary to use other criteria to determine the stereochemistry of the products.

Theoretically the reaction of ylide (1) with (*E*)- and (*Z*)-3-arylmethyleneindolin-2-ones (2) can give four stereoisomers † (*cis,trans*, *trans,trans*, *trans,cis*, and *cis,cis*) from a front or back attack of the ylide. In all cases, the same two products resulted starting from either (*E*)- or (*Z*)-arylmethyleneindolinones. This result

† In this paper *cis* and *trans* prefixes refer to the relative configuration of the substituents in the cyclopropane ring and the cyclic carbonyl group.

shows that the reaction is not stereoselective, which is easily explained on the basis of a two-step reaction mechanism. The first step involves a [1,4-conjugate]

$\alpha\beta$ -unsaturated compound and the ylide stabilizing group are both *trans* is the most favourable, as noted in other cases of cyclopropanation reactions.⁸

Physical data for the compounds

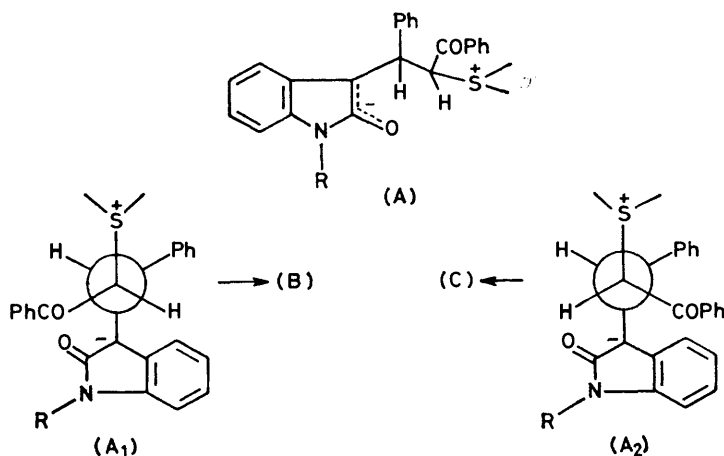
	R	X	Overall yield (%)	M.p. (°C)	δ		$J_{2,3}$ /Hz	$\nu_{\max.}$ (cm ⁻¹)	Ratio ^e (B) : (C)		
					H-2 ^d	H-3					
(3a)	CH ₃ CO	H	75	(B) 180—182 ^a (C) 126—128 ^b	4.37 3.80	4.13 4.02	8.5 9.5	1 735 1 750	1 700 1 710	1 670 1 675	2 : 1
(3b)	CH ₃ CO	OCH ₃	85	(B) 191—192 ^a (C) 150—152 ^a	4.32 3.75	4.09 3.98	8.5 9.5	1 750 1 750	1 720 1 720	1 675 1 690	1.8 : 1
(3c)	CH ₃ CO	NO ₂	94	(B) 180—182 ^a (C) 163—165 ^a	4.36 3.78	4.15 4.09	8.5 9.5	1 750 1 740	1 710 1 720	1 670 1 680	1.5 : 1
(3d)	CH ₃	H	60	(B) 190—191 ^c (C) 181—182 ^b	4.35 3.82	4.15 4.03	8.0 9.0		1 700 1 700	1 680 1 670	2.5 : 1
(3e)	CH ₃	OCH ₃	70	(B) 170—171 ^a (C) 166—167 ^a	4.29 3.75	4.04 3.95	8.0 9.0		1 700 1 680	1 680 1 660	3 : 1
(3f)	CH ₃	NO ₂	75	(B) 210—211 ^a (C) 194—195 ^a	4.32 3.87	4.10 4.04	8.0 9.0		1 700 1 690	1 675 1 670	3.5 : 1

^a From n-butanol. ^b From ethanol. ^c From methanol-di-isopropyl ether (1 : 1). ^d This proton is deshielded by the benzoyl group in the B isomers. ^e Calculated from the integration of the cyclopropane proton signals in the crude reaction mixture.

addition with the formation of a 1,3-zwitterion (A) and the second step a 1,3-elimination of dimethyl sulphide.

The formation of a resonance-stabilized zwitterion explains the production of the same compounds in the same ratio starting from (*E*)- or (*Z*)-isomers.* The

To demonstrate that (B) is the *trans* isomer, photoisomerization tests on (3aB) and (3aC) were made. When irradiated in de-aerated benzene solution (3aC) converts almost quantitatively into the other isomer, but the reverse isomerization of (3aB) does not occur.



intermediate must exist long enough to allow for a rotation around the new C-C bond, a rotation that must take place to make the elimination of dimethyl sulphide possible.

The Newman projections and Dreiding models of intermediate (A) in the preferred conformations (A₁, A₂) necessary to the ring closure permit an evaluation of steric interactions and give indications of the stereochemistry in the final products. Trost's method,⁶ now widely used,⁷ for the prediction of the most probable isomers in cyclopropanation reactions with ylides, predicts the formation of two spiro[cyclopropane-1,3'-indolinones]: *cis*-phenyl-*trans*-benzoyl (B) and *trans*-phenyl-*trans*-benzoyl (C). This has been confirmed experimentally.

The configuration in which the activating group in the

* Isomerization of starting material and/or products has been excluded by suitable control.

The *cis* isomer is less stable than the *trans* and this observation is confirmed by the recent work of Decker⁹ on the photoisomerization of spiro[*cis*- and *trans*-2,3-bis-methoxycarbonylcyclopropane-1,9'-fluorene].

EXPERIMENTAL

N.m.r. spectra were recorded on a Varian A-60 spectrometer (solvent CDCl₃; SiMe₄ internal standard). I.r. spectra were recorded on a Perkin-Elmer 377 spectrophotometer for ca. 2% solutions in chloroform. Melting points were determined on a Buchi apparatus (capillary method). Elemental analyses for new compounds are available as Supplementary Publication No. 2234 (2 pp.).†

(*E*)- and (*Z*)-3-Arylmethyleneindolin-2-ones (2).—These were prepared by reported methods¹⁰ from 1-methyl- or 1-acetyl-indolin-2-ones and the appropriate aldehyde.

Preparation of Spiro[cyclopropane-1,3'-indolin-2-ones]

† For details, see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1977, Index issue.

(3a-f). *General Procedure*.—A solution of dimethylsulphonium phenacylide ¹¹ (1) (0.01 mol) in tetrahydrofuran (THF) (25 ml) was added to a stirred solution of the 3-arylmethyleneindolin-2-one (0.01 mol) in THF (50 ml). The mixture was stirred at room temperature for 48 h and the solvent was then evaporated off. The residue, which consisted of a mixture of the two isomeric spiro[cyclopropane-1,3'-indolin-2-ones] was recrystallized several times (see Table for solvents). In this way pure components were obtained.

Spiro[3-benzoylcyclopropane-1,3'-indolin-2-one] (4).—To a stirred solution of ylide (1) (0.3 g, 11 mmol) in THF (25 ml) was added a solution in THF (25 ml) of 3-methyleneindolin-2-one, obtained *in situ* from 3-bromo-2-oxoindolin-3-ylacetic acid ¹² (0.45 g, 16 mmol) and triethylamine (0.24 ml). The reaction mixture was kept overnight at room temperature. Triethylamine hydrobromide was filtered off and the solvent removed. The residue was crystallized from methanol, m.p. 190 °C (0.23 g, 80%); ν_{\max} 1720 and 1680 cm^{-1} (NCO and PhCO); δ 9.25 (s, 1 H, NH), 8–6.8 (m, 9 H, aromatic protons), 3.68 (t, 1 H, H_X), 2.52 [dd, 1 H, H_M , J_{MX} 7.7 Hz (*trans*)], and 2.16 (dd, 1 H, H_A , J_{AX} 8.7 Hz (*cis*)). Double-resonance studies at 100 MHz (Varian HD-100 spectrometer) gave the same results.

Photoisomerization of (3aC).—A solution of (3aC) (0.2 g) in benzene (50 ml) was thoroughly purged with nitrogen and

irradiated with a Phillips HPX 125-W medium-pressure lamp for 2 h. Removal of the solvent left a pale yellow residue which was crystallized from n-butanol. The product (0.15 g, 75%), m.p. 181–182 °C, showed no m.p. depression when mixed with an authentic sample of (3aB).

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