

Novel Synthesis of Indans, Tetralones, Condensed Benzocarbo-cyclic Nitriles and Condensed Pyridine-2(1*H*)-thiones from the Reactions of Cycloalkylidene-malononitriles with Arylmethylene(cyano)-acetamide and -thioacetamide

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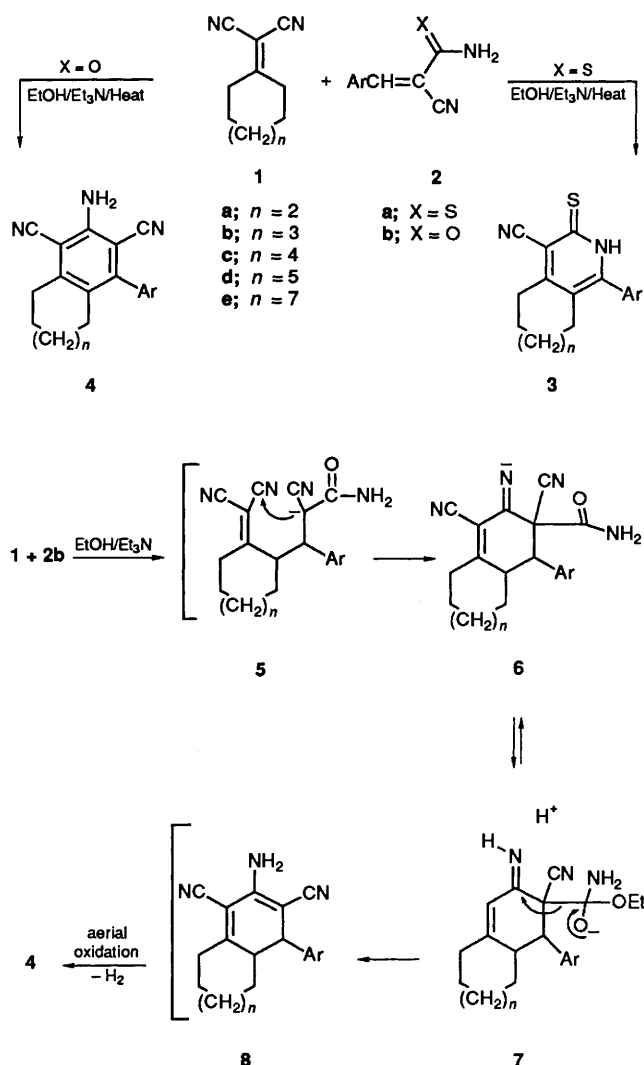
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A novel synthesis of indans, tetralones, condensed benzocarbo-cyclic nitriles and condensed pyridine-2(1*H*)-thiones from cycloalkylidenemalononitriles and arylmethylene(cyano)-acetamide and -thioacetamide is described.

α,β -Unsaturated nitriles are versatile reagents which have been extensively utilized in heterocyclic synthesis.¹⁻⁴ Recently, we reported the synthesis of pyridine-2(1*H*)-thiones and their condensed derivatives from the reactions of arylmethylene-cyanothioacetamides with appropriate active methylene compounds.^{5,6} We also described the novel reaction of cycloalkylidenemalononitriles **1a-c** with arylmethylene-cyanothioacetamides **2a** to produce the unexpected condensed pyridine-2(1*H*)-thiones **3** by a sequence initiated by the exchange reaction between the cycloalkylidene group of **1-c** and the arylmethylene group of **2a**. The unexpected course of the reaction between the cycloalkylidenemalononitriles **1** and **2a** prompted us to investigate how the cycloalkylidenemalononitriles **1** reacted with arylmethylene-cyanoacetamides **2b** in boiling ethanol containing catalytic amounts of piperidine. The products obtained were shown not to be the expected condensed pyridin-2(1*H*)-ones but the condensed benzocarbo-cyclic nitriles **4**. The latter structure was established on the basis of elemental analysis and spectral data (¹H NMR, IR and MS). Thus, the mass spectrum of **4e** was compatible with the molecular formula C₁₈H₁₅N₃ (M⁺, 273) and the ¹H NMR spectrum had signals at δ 6.4 (br, NH) and 7.18–7.55 (m, ArH). The formation of **4** is assumed to proceed *via* addition of the active methylene group of **1** to the double bond of **2b** to give the intermediates **5**, and then **8**, the latter finally being oxidized under the reaction conditions to the product **4**.

In order to establish whether the reaction of **1** with arylmethylene-cyanothioacetamides **2a** could be extended to provide a general approach to pyridine-2(1*H*)-thiones, we allowed **2a** to react with a number of higher cycloalkylidenemalononitriles. Thus we found that cyclooctylidene **1d** and cyclodecylidene-malononitrile **1e** reacted with arylmethylene-cyanothioacetamides **2a** in boiling ethanol containing catalytic amounts of triethylamine to yield the pyridine-2(1*H*)-thiones **3**. Elemental analysis and spectral data (¹H NMR, IR and MS) established the structural assignment. Thus, the mass spectrum of **3a** was compatible with the molecular formula C₁₈H₁₈N₂S (M⁺, 294) and the ¹H NMR spectrum contained signals at δ 13.85 (br, NH) and 7.28–7.54 (m, ArH).

These results indicate that although addition of cycloalkylidenemalononitriles to the double bond of arylmethylene-cyano-acetamide or -thioacetamide leads to Michael adduct intermediates, the nature of the products depends on thermodynamic factors. Our conclusion concerning the base-catalysed exchange reaction between arylmethylene-cyano-acetamide or -thioacetamide and cycloalkylidenemalononitriles, therefore, seems justified.



Experimental

All m.p.s are uncorrected. IR spectra were obtained (KBr disc) on a Pye Unicam Spectra-1000. ¹H NMR spectra were measured on a Varian 400 MHz spectrometer for solutions in (CD₃)₂SO using SiMe₄ as internal standard. Analytical data were obtained from the Microanalytical Data Centre at Cairo University. The mass spectral IR, ¹H NMR and analytical results are available as a supplementary publication [Sup No.

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Table 1 Compounds 3a-h and 4a-u

Compound	n	Ar	Recryst. solvent	M.p./ °C	Yield (%)
3a ^a	5	Ph	AcOH	286	60
3b	5	p-ClC ₆ H ₄	EtOH	290	50
3c ^a	5	p-AcC ₆ H ₄	EtOH	275	50
3d	5	2-Furyl	EtOH	195	45
3e	7	Ph	EtOH	242	65
3f	7	p-ClC ₆ H ₄	MeOH	217	60
3g	7	p-AcC ₆ H ₄	Dioxane	227	55
3h	7	2-Furyl	EtOH	203	50
4a ^a	2	Ph	EtOH	220	85
4b ^a	2	p-Cl	EtOH	230	65
4c ^a	2	p-AcC ₆ H ₄	EtOH	195	80
4d ^a	2	p-O ₂ NC ₆ H ₄	EtOH	170	66
4e ^a	3	Ph	EtOH	227	70
4f ^a	3	p-ClC ₆ H ₄	EtOH	224	85
4g ^a	3	p-AcC ₆ H ₄	EtOH	185	80
4h ^a	3	p-O ₂ NC ₆ H ₄	EtOH-DMF	210	70
4i ^a	3	p-Me ₂ NC ₆ H ₄	EtOH	225	82
4j ^a	3	2-Furyl	EtOH	215	65
4k ^a	4	Ph	EtOH	205	90
4l ^a	4	p-ClC ₆ H ₄	EtOH	195	70
4m ^a	4	p-O ₂ NC ₆ H ₄	EtOH	155	80
4n ^a	4	p-O ₂ NC ₆ H ₄	EtOH-DMF	165	70
4o ^a	4	2-Furyl	EtOH	190	85
4p ^a	5	Ph	EtOH	175	65
4q ^a	5	p-ClC ₆ H ₄	EtOH	205	80
4r ^a	5	p-AcC ₆ H ₄	EtOH	210	65
4s ^a	5	p-O ₂ NC ₆ H ₄	EtOH-DMF	187	60
4t ^b	5	p-Me ₂ NC ₆ H ₄	EtOH	212	85
4u ^a	5	2-Furyl	EtOH	186	60

^a Yellow. ^b Orange.

56876 (10 pages)].* Compounds 1a-e were prepared following literature procedures.⁸

* For details of the Supplementary Publication Scheme, see 'Instructions for Authors (1992),' *J. Chem. Soc., Perkin Trans. 1*, 1992, Issue 1.

Cycloalkane Ring-fused 6-Aryl-3-cyanopyridine-2(1H)-thiones 3a-h.—Triethylamine (1 cm³) was added to a mixture of 1d, e and 2a (10 mmol) in ethanol (50 cm³) and the mixture was heated under reflux for 2 h; it was then set aside overnight. The resultant precipitate was filtered off and crystallized from the appropriate solvent (see Table 1).

Cycloalkane Ring-fused 2-Amino-4-arylisophthalonitriles 4a-u.—A few drops of piperidine were added to a mixture of 1a-e (10 mmol) and 2b (10 mmol) dissolved in ethanol (50 cm³) and the mixture was refluxed for 5 h. The precipitated solid product was then filtered off and crystallized from the appropriate solvent (See Table 1).

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