

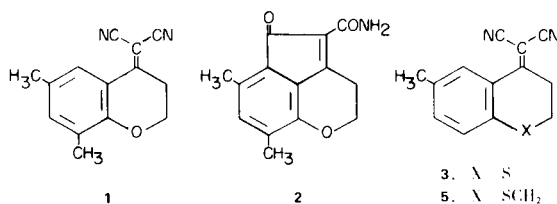
Ring Closure of a Chromanylidene malononitrile

S. W. Schneller*, D. R. Moore, and M. A. Smith

Department of Chemistry, University of South Florida, Tampa, Florida 33620

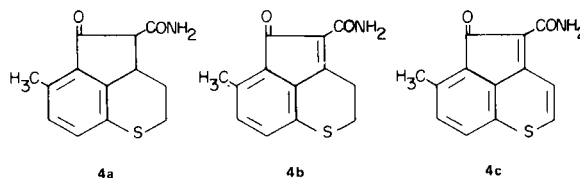
Received August 7, 1975

The acid mediated cyclization of various heterocyclic ylidene malononitriles has provided (1,2) a valuable means of building rings fused to heterocyclic moieties. This report now presents the first successful ring closure of a chromanylidene malononitrile (**1**).



Based on earlier studies (3) it was apparent that both the 6- and 8-positions of chroman-4-ylidene malononitrile would have to be blocked in order to realize fruitful results upon treatment with acid. By analogy to the investigations with thiochroman-4- (1a,b), 2,3,4,5-tetrahydrobenzo[*b*]-thiopin-5- (1c) and 2,3,4,5-tetrahydrobenzo[*b*]oxepin-5-ylidene malononitriles (1d) methyl substituents were chosen for this purpose. Thus treatment of compound **1**, prepared in the usual manner (1,2) from 6,8-dimethylchroman-4-one (**4**), with concentrated sulfuric acid (1a,b,c) produced a mixture of three products which, unfortunately, has so far resisted complete separation and is currently under investigation (5). However, in view of the recent successes (1d,2) with polyphosphoric acid as a cyclizing medium for heterocyclic compounds, **1** was treated with this reagent and found to yield the keto-amide **2** as the sole product. The structural assignment of **2** was based on spectral evidence (see Experimental) in comparison to similar keto-amides (1). Thin layer chromatographic comparison of **2** with the mixture obtained from sulfuric acid treatment of **1** indicates the definite presence of **2** (along with two other products (5)) in the latter product composition.

Since polyphosphoric acid did not promote the disproportionation of **1**, it was then applied to **3** which has produced (1a,b) the disproportionation products (**4a-c**). However, as before (1b), **4a-c** were obtained and their relative amounts were dependent on the reaction conditions in a manner similar to sulfuric acid (1b). This contrasting behavior between **1** and **3** in polyphosphoric acid is difficult to explain in view of the results reported by Tilak and



co-workers (6) for the acid promoted disproportionations with thiochromenes (6a), 1,2-dihydroquinolines (6b), and chromenes (6c).

Finally, treatment of **5** (1c) with polyphosphoric acid produced a red gummy intractable mass which resisted crystallization and, hence, identification.

EXPERIMENTAL (7)

6,8-Dimethylchroman-4-one (**4**) and its precursor, β -(2,4-dimethylphenoxy)propionic acid (**8**), were prepared by slight modifications of the reported (4,8) reaction conditions.

6,8-Dimethylchroman-4-ylidene malononitrile (**1**).

A 30 ml. benzene solution of 3.52 g. (0.02 mole) of 6,8-dimethylchroman-4-one, 2.0 g. (0.03 mole) of malononitrile, 2 ml. of glacial acetic acid, and 1.0 g. of ammonium acetate was refluxed with the assistance of a Dean-Stark trap until the calculated amount of water had been collected (7 hours). The orange reaction mixture was cooled, decanted from the malononitrile polymeric mass which was present, washed with water (2 x 100 ml.), dried over magnesium sulfate, and concentrated to dryness on a rotovaporator. The yellow solid which resulted upon cooling was recrystallized from methanol as yellow needles (96% yield), m.p. 137-139°; ir (potassium bromide): 4.45 μ (CN); ^1H nmr (deuteriochloroform): δ 2.17 (s, CH₃), δ 2.28 (s, CH₃), δ 3.07 (t, J = 6 Hz, CH₂), δ 4.38 (t, J = 6 Hz, CH₂), δ 7.36 (s, H-7), δ 8.11 (s, H-5).

Anal. Calcd. for C₁₄H₁₂N₂O: C, 75.00; H, 5.35. Found: C, 74.98; H, 5.65.

Reaction of **1** with Polyphosphoric Acid to Produce **2**.

To 150 g. of polyphosphoric acid warmed at 90° was added 3.0 g. (0.014 mole) of **1**. The mixture was mechanically stirred at 90° for 2.5 hours at which time the solution was poured over ice to produce orange-brown crystals. These crystals were filtered, air dried, and digested with 95% ethanol (to remove unreacted **1**). The resulting insoluble material was recrystallized from chloroform-ether to yield **2** as orange crystals (58.8% yield (9)), m.p. 214-217° dec.; ir (potassium bromide): 2.98 μ (NH₂), 5.85 μ (ketone C=O), 6.00 μ (amide C=O); ^1H nmr (trifluoroacetic acid): δ 2.29 (s, CH₃), δ 2.46 (s, CH₃), δ 3.50 (t, J = 6 Hz, CH₂), δ 4.61 (t, J = 6

Hz, CH₂), δ 7.11 (s, H-7); uv (absolute ethanol): λ max 237 nm, 266 nm.

Anal. Calcd. for C₁₄H₁₃NO₃: C, 69.12; H, 5.39. Found: C, 68.85; H, 5.50.

Compound **2** is also obtainable from treating 20.0 g. (0.089 mole) of **1** with stirred concentrated sulfuric acid (200 g.) at 75° for 1.5 hours and, subsequently, pouring over ice. Extensive silica gel column chromatography with chloroform of the resultant red precipitate produced only small amounts of **2** (5).
Acknowledgment.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their support of this research and to Mr. Lloyd Tillman for his involvement in the preparation of some of the starting materials.

REFERENCES

- (1a) E. Campaigne and C. D. Blanton, Jr., *Tetrahedron Letters*, 2489 (1964); (b) E. Campaigne, H. R. Burton, C. D. Blanton, Jr., and S. W. Schneller, *J. Heterocyclic Chem.*, **8**, 65 (1971); (c) S. W. Schneller and F. W. Clough, *ibid.*, **10**, 131 (1973); (d) S. W. Schneller and D. R. Moore, *J. Org. Chem.*, **39**, 1433 (1974).
- (2) S. W. Schneller and D. R. Moore, *J. Org. Chem.*, **40**, 1840 (1975).
- (3) E. Campaigne and C. D. Blanton, Jr., *J. Heterocyclic Chem.*, **7**, 1179 (1970).
- (4) A. B. Sen and S. B. Singh, *J. Indian Chem. Soc.*, **43**, 521 (1966).
- (5) We gratefully acknowledge Dr. Aaron Kossoy and Mr. Charles Underbrink and their associates of the Analytical Department of the Eli Lilly and Company for their assistance in our attempts to separate and identify the product mixture obtained from **1** and sulfuric acid. At present there is no definitive evidence that disproportionation similar to the sulfur series (1a,b) has occurred.
- (6a) B. D. Tilak and V. M. Vaidya, *Tetrahedron Letters*, 487 (1963); B. D. Tilak, H. S. Desai, C. V. Deshpande, S. K. Jain, and V. M. Vaidya, *Tetrahedron*, **22**, 7 (1966); (b) B. D. Tilak, J. Ravindranathan, and K. N. Subbaswami, *Tetrahedron Letters*, 1959 (1966); (c) B. D. Tilak and Z. Muljiani, *Tetrahedron*, **24**, 949 (1968).
- (7) Melting points were taken on a Mel-Temp capillary melting point apparatus and are uncorrected. The nmr spectra were obtained on a Varian A-60 spectrometer using TMS as an internal standard. Ir spectra were recorded on a Perkin-Elmer Model 337 spectrophotometer. The ultraviolet absorption spectrum was determined with a Cary Model 14 recording spectrophotometer using 1-cm. sample cells. The microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee.
- (8) R. Lichtenberger, J. Coré, and R. Geyer, *Bull. Soc. Chim. France*, 997 (1962).
- (9) An increase in reaction times (up to 10 hours) resulted in decreasing amounts of material recovery (i.e., **1** and **2**) apparently due to the acidic vulnerability of the chroman ether functionality.