Tetrahedron Letters No. 15, pp 1227 - 1228, 1976. Pergamon Press. Printed in Great Britain.

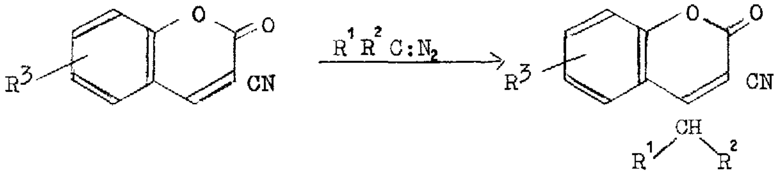
THE DIRECT C-ALKYLATION OF 3-CYANOCOUMARIN BY DIAZOALKANES.

Robert Clinging, Francis M. Dean,* Leonard E. Houghton and B.K. Park.
The Robert Robinson Laboratories, The University of Liverpool, L69 3BX

(Received in UK 20 February 1976; accepted for publication 1 March 1976)

The alkylation of activated alkenes with diazoalkanes is well known but has been little used synthetically.[1] During our studies on new applications of diazoalkanes we examined various 3-substituted coumarins,[2,3,4] and noted that the cyano group was highly efficient at promoting 4-methylation.[2] We now report that the cyano group is equally effective in inducing alkylation by diazoethane, 2-diazopropane, 3-diazopropene,[5] phenyldiazomethane and t-butyldiazomethane to give 4-alkylcoumarins (Table) in excellent yield whatever the bulk of the alkyl group. The contrast with the mixed products obtained with other activating groups[3,4] is marked. This simple technique is in particular useful for the preparation of hindered coumarins that are difficult to prepare by other methods,[6] and theory suggests that it could have much wider applicability.

The efficiency of the activation can be attributed to two factors. In the initial pyrazoline, the small bulk of the cyano group can be easily accommodated in the conformation required for proton migration (= alkylation),[4] even when R^2 = t-butyl. Secondly, the cylindrical symmetry of the cyano group allows it to conjugate fully with the nascent double bond as nitrogen is lost whereas other activating groups (e.g. acetyl) would have to rotate out of plane to accommodate the new substituent.[2]



R^1	R^2	R^3	Time	Temp.	Yield	m.p.
H	CH_3	H	0.33 h	0°	100%	140–141°[6]
H	CH_3	6-CH_3	0.33	0	85	198–199
H	CH_3	8-OCH_3	0.33	0	72	213–214*
CH_3	CH_3	H	0.50	0	100	157–158
H	$CH=CH_2$	H	1.50	20	97	123–124[5]
H	Ph	H	4.00	20	75	186–187
H	$C(CH_3)_3$	H	15.00	20	79	163–165

*Reaction performed in ethylene glycol dimethyl ether. In other cases the solvent was tetrahydrofuran - ether.

The i.r., u.v., n.m.r. and mass spectral spectra of all new compounds were consistent with the structures given.

References

1. F.M. Dean, in "Some Recent Developments in the Chemistry of Natural Products", ed. S. Rangaswami and N.V. Subba Rao, Prentice-Hall (India) New Delhi, 1972, p.71.
2. R. Clinging, F.M. Dean and L.E. Houghton, J. Chem. Soc. (C). 1970, 897.
3. R. Clinging, F.M. Dean and L.E. Houghton, J.C.S. Perkin I, 1974, 66.
4. F.M. Dean and B.K. Park, J.C.S. Perkin I, accepted for publication.
5. R. Clinging and F.M. Dean, J. Chem. Soc. (C), 1971, 3668.
6. C. Wiener, C.H. Schroeder and K.P. Link, J. Amer. Chem. Soc., 1957, 79, 5301.