Steric Effects in the *C*-Alkylation and Ring Expansion of Coumarins by Diazomethane

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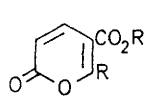
Diazomethane rapidly converts 3-acetylcoumarin, 3-cyanocoumarin, and their derivatives into the related 4-methylcoumarins. Since an acetyl group must rotate out of the plane of conjugation to allow the methyl group to enter, it is a less effective activating substituent than cyanide in alkylation reactions.

Substituents at the 5-position interfere with the methylation process so that 3-acetyl-5,7-dimethylcoumarin adds diazomethane giving a pyrazoline derivative (XIII) in the usual way. Methanol converts this pyrazoline into oxepin lactones, *e.g.* 3-acetyl-4,5-dihydro-4-methoxy-6,8-dimethyl-1-benzoxepin-2(3*H*)-one (XVIII). Thermolysis of the pyrazoline is unusual in regenerating some of the coumarin from which it was made; the main product, however, is a labile substance giving 3-acetyl-6,8-dimethyl-1-benzoxepin-2(3*H*)-one (XVII) when isolation was attempted

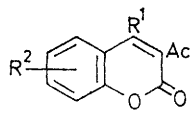
At −40° diazomethane and 3-acetyl-5,6-benzocoumarin give 1,11c-dihydro-3a-(2-methyloxiranyl)benzo[5,6]chromeno[3,4-*c*]pyrazol-4(3a*H*)-one (XXIV), but at 0° the sole isolable product is 8a-acetyl-11a,12-dihydro-11*H*-naphtho[1′,2′:6,7]oxepino[3,4-*c*]pyrazol-8(8a*H*)-one (XXII).

These results support the view that the ' direct ' methylation begins with an intermediate or transition state having the shape of a pyrazoline but at least one bond which is as much ionic as covalent in character. It continues with hydrogen migration because this restores the delocalisation energy of the coumarin system lost during the addition. The arguments also clarify some of the reasons for cyclopropane ring formation in certain related series.

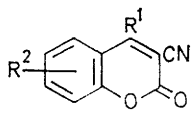
For a long time the smooth interaction of coumalic acid (2-oxopyran-5-carboxylic acid) (I) and diazomethane seemed anomalous because it included *C*-methylation giving the ester [1] (II). Many other efficient ' direct ' alkylations have now been recorded,[2-4] which apparently require that the ethylenic component must carry two electron-attracting substituents at the same end of the double bond. We have extended these studies into the coumarin series for preparative purposes and have obtained evidence supporting the view that ' direct ' alkylations involve very unstable pyrazolenic intermediates which, however, possess enough ionic character to permit steric effects to deflect the reaction into other channels.



(I) R = H
(II) R = Me



(III) R^1 = H
(IV) R^1 = Me



(V) R^1 = H
(VI) R^1 = Me

The action of diazomethane on coumarin itself is known to be slow.[5] We found the action on coumarin-3-carboxylic esters to be faster but unsatisfactory for our purposes; however, the derivatives (III) of 3-acetylcoumarin readily afforded the homologues (IV) (Table 1). The alkylation is much faster than is the methylation of most phenols; accordingly, the phenolic group of 3-acetyl-6-hydroxy-7-methoxycoumarin survived insertion of a methyl group into the 4-position. Though some of them have inconveniently low solubilities in ether, derivatives (V) of 3-cyanocoumarin give the related 4-methylcoumarins (VI) (Table 2) even more readily.

TABLE 1

Derivatives of 3-acetyl-4-methylcoumarin

Substituents R^2 in (IV)	Method	Yield (%)	M.p.	Found (%) C	Found (%) H	Formula	Reqd. (%) C	Reqd. (%) H
None	*a*	82	101°					
6-Methyl	*a*	78	145	72·3	3·5	$C_{13}H_{12}O_3$	72·2	5·6
7-Methyl	*a*	85	148	72·4	5·6	$C_{13}H_{12}O_3$	72·2	5·6
6-Methoxy	*a*	83	141	67·3	5·3	$C_{13}H_{12}O_4$	67·2	5·2
7-Methoxy	*a*	74	160	67·2	5·3	$C_{13}H_{12}O_4$	67·2	5·2
6-Hydroxy-7-methoxy	*a*	67	212	63·0	5·1	$C_{13}H_{12}O_5$	62·9	4·9
6-Acetoxy-7-methoxy	*		165	61·8	4·9	$C_{15}H_{14}O_6$	62·1	4·9

* By acetylation of 3-acetyl-6-hydroxy-7-methoxy-4-methylcoumarin; [*M* (mass spectrum) 290. $C_{15}H_{14}O_6$ requires 290].

The i.r. spectra in the 3-cyanocoumarin series show no marked dependence upon the presence of a 4-methyl group. In marked contrast, the spectra (Table 3) in the 3-acetylcoumarin series show a strong dependence resulting from the fact that the methyl group forces the acetyl group to rotate out of conjugation, as in analogous cases.[6,7] The values suggest that in 3-acetylcoumarin

[1] J. Fried and R. C. Elderfield, *J. Org. Chem.*, 1941, **6**, 577.
[2] J. Hamelin and R. Carrié, *Bull. Soc. chim. France*, 1968, (*a*) 2162; (*b*) 3000; (*c*) 2521; (*d*) 2513.
[3] J. Bastus, *Tetrahedron Letters*, 1963, 955.
[4] M. Alguerro, J. Bosch, J. Castaner, J. Castella, R. Mestres, J. Pascual, and F. Serratosa, *Tetrahedron*, 1962, **18**, 1381.
[5] E. Y. Spencer and G. F. Wright, *J. Amer. Chem. Soc.*, 1941, **63**, 2017.
[6] E. A. Braude and E. S. Waight, *Progr. Stereochem.*, 1954, 126, 144.
[7] R. N. Jones, W. F. Forbes, and W. A. Mueller, *Canad. J. Chem.*, 1957, **35**, 504.

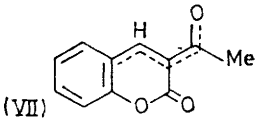
TABLE 2

Derivatives of 3-cyano-4-methylcoumarin

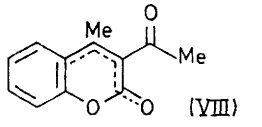
Substituents R^2 in (VI)	Method	Yield (%)	M.p.	Found (%) C	Found (%) H	Found (%) N	Formula	Reqd. (%) C	Reqd. (%) H	Reqd. (%) N
None	*b*	98	195°							
8-Methoxy	*c*	87	233	66·9	4·3	6·5	$C_{12}H_9NO_3$	67·0	4·2	6·5
6,7-Dimethoxy	*c*	41	244 *	63·4	4·4	5·8	$C_{13}H_{11}NO_4$	63·7	4·5	5·7
6-Methyl	*b*	88	206	72·1	4·3	7·0	$C_{12}H_9NO_2$ †	72·3	4·5	7·0
5,7-Dimethyl	*c*	56	218	73·2	5·4	6·5	$C_{13}H_{11}NO_2$	73·2	5·2	6·6

* With decomposition. † *M* (mass spectrum), 199.

only the acetyl group is strongly conjugated [see (VII)], whereas in the 4-methyl derivative only the lactone carbonyl group is effectively conjugated [see (VIII)]. The rotation is accompanied by loss of the fluorescence characteristic of 3-acetylcoumarins, by a reversion of the u.v. spectrum into one similar to that of coumarin itself (Table 4), and by a marked lowering of the rate of reaction with 2,4-dinitrophenylhydrazine.[8,9] In the n.m.r. spectrum of 3-acetylcoumarin, the 4-proton resonates at



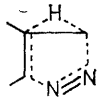
(VII)



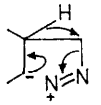
(VIII)

τ 1·52 and the acetyl protons at 7·28; introduction of the 4-methyl group, which absorbs at 7·42, destroys the former band and causes the chemical shift of the latter to rise to 7·56, a value comparable to that (7·55) found for ethyl 4-methylcoumarin-3-carboxylate.[10]

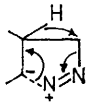
There is good evidence [2b,11,12] that ' direct ' methylations occur through thermally unstable pyrazolenic intermediates formed in the usual 1,3-dipolar cycloadditions. The collapse of a pyrazoline to a new olefin is now usually interpreted as a hydrogen shift concerted with nitrogen elimination in a cyclic mechanism which can be represented as in (IX) and is formally devoid of ionic character.[2a,b,13,14] However, some facts are hard to reconcile with such interpretations, especially the acceleration produced by increasing the dielectric constant of the solvent,[14] and the formation of by-products containing rings (dihydrofuran,[14] butenolide,[15] and cyclopentene [16]) not directly accessible through cyclic, non-polar arrangements. In the present work and in related studies we have also obtained results pointing to a considerable degree of ionic character of the kind which appears most clearly in the zwitterionic formulation (X). Representations such as (IX) and (X) are not mutually exclusive though they are often treated as if they were; we prefer to combine the two representations as in (XI), thus producing the symbol $+ \cdots -$ for a bond that is partly covalent, partly ionic, and only partly formed. In any particular example, the exact nature of such a bond will also depend on the adjacent substituents and on the solvent.



(IX)



(X)



(XI)

3-Acetyl-5,7-dimethylcoumarin (XII), in contrast to its analogues, added diazomethane giving the pyrazoline (XIII). No doubt the stability of this product is a consequence of the fact that a collapse to the 4-methylcoumarin (XIV) is opposed by the difficulty of forcing the two adjacent methyl groups into coplanarity. The

TABLE 3

I.r. carbonyl frequencies (cm.$^{-1}$) of 3-acetylcoumarins

	Lactone CO	Acetyl CO
3-Acetylcoumarin	1736	1691
3-Acetyl-6-methylcoumarin	1732	1687
3-Acetyl-7-methylcoumarin	1737	1685
3-Acetyl-5,7-dimethylcoumarin	1720	1675
3-Acetyl-6-methoxycoumarin	1731	1686
3-Acetyl-7-methoxycoumarin	1732	1682
6-Acetoxy-3-acetyl-7-methoxycoumarin	1733	1670
3-Acetyl-4-methylcoumarin	1713	1708
3-Acetyl-4,6-dimethylcoumarin	1710	1699
3-Acetyl-4,7-dimethylcoumarin	1713	1699
3-Acetyl-4,5,7-trimethylcoumarin	1700	1700
3-Acetyl-6-methoxy-4-methylcoumarin	1708	1699
3-Acetyl-7-methoxy-4-methylcoumarin	1712	1699
6-Acetoxyl-3-acetyl-7-methoxy-4-methylcoumarin *	1720	1682

* And 1752 cm.$^{-1}$ (OAc).

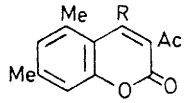
TABLE 4

U.v. spectra of three coumarins (*ca.* 10^{-4}M in ethanol)

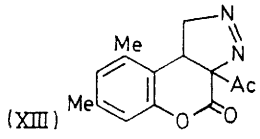
	$\lambda_{max.}$ (nm.)	log ε
Coumarin	275, 316	4·08, 3·77
3-Acetylcoumarin	300, 340	4·22, 4·01
3-Acetyl-4-methylcoumarin	282, 319	4·00, 3·77

[8] R. N. Lacey, *J. Chem. Soc.*, 1954, 816.
[9] F. M. Dean, A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 1950, 895.
[10] C. H. Schroeder and K. P. Link, *J. Amer. Chem. Soc.*, 1953, **75**, 1886.
[11] R. Huisgen, *Angew. Chem. Internat. Edn.*, 1963, 2, **11**, 633; R. Huisgen, R. Grashey, and J. Sauer, in ' Chemistry of the Alkenes,' ed. S. Patai, Interscience, London, 1964, ch. 11.
[12] H. Kisch, O. E. Polansky, and P. Schuster, *Tetrahedron Letters*, 1969, 805.
[13] T. V. van Auken and K. L. Rinehart, *J. Amer. Chem. Soc.*, 1962, **84**, 3736.
[14] D. E. McGreer, N. W. K. Chiu, and M. G. Vinje, *Canad. J. Chem.*, 1965, **43**, 1398; D. E. McGreer, N. W. K. Chiu, M. G. Vinje, and K. C. K. Wong, *ibid.*, 1965, **43**, 1407.
[15] P. Schuster, F. Wessely, and A. Stephen, *Monatsh.*, 1967, **98**, 1772.
[16] I. Tabushi, K. Takagi, M. Okano, and R. Oda, *Tetrahedron*, 1967, **23**, 2621.

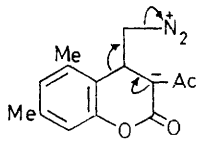
result supports the view that the 'direct' methylations involve first a cycloaddition and then a concerted elimination–hydrogen migration; had a simple ionic mechanism been involved at any point a zwitterion would have been formed and then, because of the inherent instability of such ions,[17,18] some product devoid of nitrogen. While coumarin (XIV) might not be accessible, no bar exists to aryl migration [see (XV)] and the formation of oxepin derivatives such as (XVI).



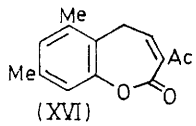
(XII) R = H
(XIV) R = Me



(XIII)



(XV)

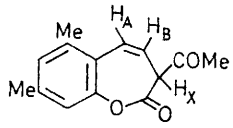


(XVI)

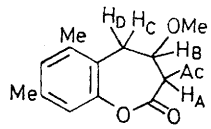
Significantly, aryl migration is readily induced by treating the pyrazoline with methanol or other hydroxylic solvents, and the products are indeed oxepin derivatives devoid of nitrogen. It seems that the incipient ionisation allowed for in (XI) is made real by solvation, and it follows that, had the system contained much water or methanol, the pyrazoline would not have been observed. Glass and silica also induce nitrogen eliminations of this kind in several of the pyrazolines studied, and since the reagent is difficult to free from hydroxylic compounds and is usually used in glass, some of the inconsistencies in the literature might be traceable to this source. We have previously clarified a related case.[19]

The methanolysis gives two products. One is the lactone (XVII), $\nu_{max.}$ 1738 (ester) and 1723 (Ac) cm.$^{-1}$ (no hydroxylic band). It enolises readily: in warm methanol it gives an intense ferric reaction and dissolves at once in aqueous alkali. The n.m.r. spectrum established the presence of an ABX system, the rather high coupling constant (J 10 Hz) for the ethylenic protons agreeing with their presence in a seven-membered ring. Probably the primary methanolysis product is the lactone (XVI), but prototropic shifts give the observed isomer. The second methanolysis product has structure (XVIII), established spectroscopically, and can be considered to result from the addition of methanol to the primary product (XVI).

Thermolysis of pyrazoline (XIII) gave, according to the n.m.r. spectrum, mainly the expected lactone (XVI), but this tautomerised so readily on silica that we could isolate only the isomer (XVII). Presumably steric effects are responsible, a methine group being more easily accommodated next to a methyl group than a methylene group can be. A little of the 4-methylcoumarin (XIV)



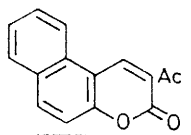
(XVII)



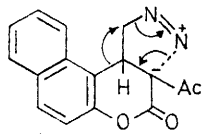
(XVIII)

was also found, but the most interesting minor product was the original coumarin (XII) (*ca.* 17%). It may be that the crowding caused by the 5-methyl group promotes this unusual thermal reversal of the addition reaction. Similar fissions produced by photochemical means are much better documented.[13,20,21]

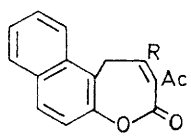
In 3-acetyl-5,6-benzocoumarin (2-acetylnaphtho-[2,1-*b*]pyran-3-one) (XIX) a methine group, though smaller than a methyl group, takes over the role of preventing a simple 4-methylation. Under the usual conditions at 0° the expected pyrazoline (XX) was not detected, apparently because it rapidly collapses as shown, and the resulting unsaturated lactone (XXI) at once adds a second molecule of the reagent giving pyrazoline (XXII), $\nu_{max.}$ 1750 (ester), 1718 (ketone) and 1520 (azo) cm.$^{-1}$. The pyrazoline exhibited proton resonance bands of the appropriate chemical shifts and intensities, but the complexities and overlapping of the splitting patterns prevented a full analysis, so the structure was confirmed by thermolysis in benzene which gave (in high yield) the methylated lactone (XXIII) with spectroscopic properties not permitting any other formulation.



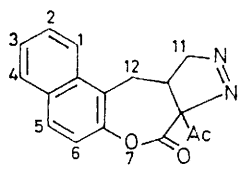
(XIX)



(XX)



(XXI) R = H
(XXIII) R = Me

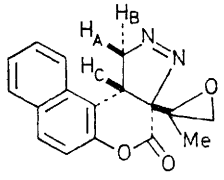


(XXII)

After efforts to isolate the initial pyrazoline (XX) were unsuccessful, the reaction was conducted at −40° for a period long enough for the excess of diazomethane to convert the acetyl group into an oxiran system, giving

[17] R. Huisgen and C. Ruchardt, *Annalen*, 1956, 601, 1.
[18] J. H. Bayless, A. T. Jurewicz, and L. Friedman, *J. Amer. Chem. Soc.*, 1968, **96**, 4466.
[19] F. M. Dean, P. G. Jones, R. B. Morton, and P. Sidisunthorn, *J. Chem. Soc.*, (*a*) 1963, 5336; (*b*) 1964, 411.
[20] M. Franck-Neumann, *Angew. Chem. Internat. Edn.*, 1968, **7**, 65; M. Franck-Neumann and G. LeClerc, *Tetrahedron Letters*, 1969, 1063.
[21] R. Moore, A. Mishra, and R. J. Crawford, *Canad. J. Chem.*, 1968, **46**, 3305.

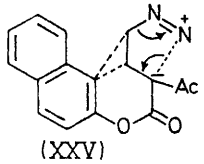
(XXIV). In effect, this product is a pyrazoline containing only one activating group; accordingly it is thermally insensitive and unaffected by methanol and silica, and readily isolated, though not in high yield. The compound has no ketonic i.r. band but absorbs at 1752 cm.$^{-1}$ (ester). The presence of the oxiran grouping is proved by the loss of a C_3H_5O fragment which provides the most prominent feature of the mass spectrum, loss of nitrogen from the molecular ion giving a fragment *m/e* 266·09372 which passes in a single stage to another, *m/e* 209·06019. In the n.m.r. spectrum, the methyl resonance appears as a doublet at τ 8·61 (J 0·6 Hz) because of slight coupling with the proton *trans* to it. In turn, the signal for this proton appears at τ 6·22 as a doublet (J 5 Hz) and its partner as a similar doublet at τ 7·20, with only the former showing the further slight splitting due to the methyl group. The protons of the nitrogen ring form an ABC system [see (XXIV)] with the following characteristics: τ_A 4·41, τ_B 5·56, τ_C 6·00; J_{AB} 18, J_{AC} 9, J_{BC} 6·5 Hz. The exceptionally low field at which proton A resonates indicates that it is near the plane of the naphthalene ring, and from this and the coupling constants follows the configuration shown in the diagram, the relative stereochemistry of the oxiran system being unknown.



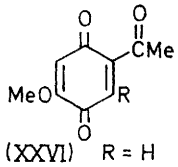
(XXIV)

Thus with diazomethane the benzocoumarin undergoes ring expansion under conditions which merely generate a pyrazoline from the dimethylcoumarin, yet there is little, if any, difference between them as far as stereochemistry or conformation is concerned. Hence it may be the ionic component of the system that plays the decisive part. As indicated in diagram (XXV), one bond is extensively ionised, the adjacent bonds will be affected in turn, and the naphthalene nucleus will be induced to migrate because of its low localisation energy [22] which makes it particularly susceptible to carbonium ion rearrangements.[23] The related oxiran (XXIV) corresponds to a situation in which the ionic character is much less important because there is only one electronegative group at the negative terminus; it is correspondingly stable.

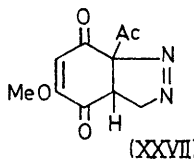
The importance of a second activating group appears in another way. Unlike 3-acetyl-5,7-dimethylcoumarin, and despite its 5-methyl substituent, 3-cyano-5,7-dimethylcoumarin undergoes 4-methylation with reasonable facility (Table 2). Although the cyanide and acetyl groups are similar in their ability to stabilise anionic centres [24] their shapes are very different, and the cyanide group is unaffected by the entry of a substituent at the 4-position which causes the acetyl group to rotate (a point made in another context by Wheland, Brownall, and Mayo [25]). Consequently the cyanide group but not the acetyl group is always fully able to promote hydrogen migration by interacting with the ethylenic bond as it is formed and, through it, with the electron-rich phenolic residue beyond. It follows that any electrophilic group can activate an ethylenic system towards attack by diazomethane, but that only cyanide should specifically favour the methylation reaction.



(XXV)

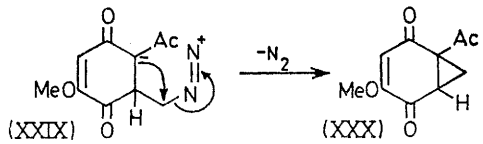


(XXVI) R = H
(XXVIII) R = Me



(XXVII)

We have not observed the formation of cyclopropane derivatives during these studies, although they are often reported as products from the reaction of diazomethane with highly activated ethylenic compounds.[24,13–16,26,27] Their origin remains unclear in most instances, but we refer to one which forms a useful complement to the present work. Derived from quinone (XXVI) and diazomethane, the pyrazoline [19b] (XXVII) suffers thermolysis in benzene to give nitrogen and the homologous quinone (XXVIII), presumably through a concerted hydrogen migration–nitrogen elimination reaction. In contact with methanol, however, it loses nitrogen without application of heat, no doubt because the dipolar ion (XXIX) is formed. In this, migrations yield no advantage. Migration of hydrogen serves at best to connect two electron-deficient centres with a third, as in quinone (XXVIII), while ring expansion requires migration of carbonyl to a cationic centre. Therefore the cyclopropane (XXX) is formed as shown.



(XXIX) (XXX)

EXPERIMENTAL

3-Acetyl-5,7-dimethylcoumarin, prepared from 2-hydroxy-4,6-dimethylbenzaldehyde by methods used before,[9] had m.p. 141° (from aqueous ethanol) [Found: C, 72·3; H, 5·5%;

[22] M. J. S. Dewar, *Rec. Chem. Progr.*, 1958, **19**, 1.
[23] G. W. Wheland, ' Advanced Organic Chemistry ', 3rd edn., Wiley, New York, 1960, ch. 12.
[24] H. C. Brown, D. H. McDaniel, and O. Häfliger, in ' Determination of Organic Structures by Physical Methods,' ed. E. A. Braude and F. C. Nachod, Academic Press, New York, 1955, ch. 14.
[25] G. W. Wheland, R. M. Brownall, and E. C. Mayo, *J. Amer. Chem. Soc.*, 1948, **70**, 2492.
[26] T. Sanjiki, M. Ohta, and H. Kato, *Chem. Comm.*, 1969, 638.
[27] A. Mustafa, W. Asker, A. H. Harhash, and A. M. Fleifel, *Tetrahedron*, 1965, **21**, 2215.

M (mass spectrum) 216. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%; *M*, 216], $\nu_{max.}$ 1720, 1675, 1620, and 1595 cm.$^{-1}$, τ 7·57, 7·45 (aromatic Me), 7·30 (Ac), 3·03br (2H, aromatic), and 1·33 (1H, s, 4-proton). The preparation of other derivatives of 3-acetylcoumarin has been reported previously: 3-acetyl-6-methylcoumarin, 3-acetyl-7-methylcoumarin, 3-acetyl-6-methoxycoumarin, 3-acetyl-7-methoxycoumarin, 3-acetyl-8-methoxycoumarin,[9] and 3-acetyl-5,6-benzocoumarin.[28]

3-*Acetyl*-6-*hydroxy*-7-*methoxycoumarin* was obtained by heating 2,5-dihydroxy-4-methoxybenzaldehyde (0·4 g.) in the minimum volume of ethanol with ethyl acetoacetate (0·34 ml.) and piperidine (1 drop) for 10 hr. Evaporation of the solvent left a solid which was sublimed at 150°/0·1 mm., giving the *coumarin* as bright yellow needles, decomp. *ca.* 200°, m.p. *ca.* 210° [Found: C, 61·6; H, 4·4%; *M* (mass spectrum), 234. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3%; *M*, 234]. The *acetate* gave pale yellow needles, m.p. 177—178° (from ethanol) (phase change at 174°), $\nu_{max.}$ 1750 (aryl acetate (CO), 1733 (coumarin CO), and 1670 (acetyl CO) cm.$^{-1}$ (Found: C, 60·6; H, 4·4. $C_{14}H_{12}O_6$ requires C, 60·9; H, 4·4%), τ (all singlets) 1·59 (1H, pyrone ring proton), 2·71 (1H, aromatic 5-proton), 3·01 (aromatic 8-proton), 6·09 (3H, OMe) 7·32 (3H, Ac), and 7·70 (3H, OAc).

Derivatives of coumarin-3-carboxylic acid were prepared by standard methods. *Methyl* 5,7-*dimethylcoumarin*-3-*carboxylate* (5,7-*dimethyl*-2-*oxobenzopyran*-3-*carboxylate*) had m.p. 184° (subl.) (from aqueous acetone), $\nu_{max.}$ 1735, 1705, 1610, and 1560 cm.$^{-1}$ [Found: C, 67·0; H, 5·2; *M* (mass spectrum), 232. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%; *M* 232]. *Ethyl* 5,7-*dimethylcoumarin*-3-*carboxylate* (5,7-*dimethyl*-2-*oxobenzopyran*-3-*carboxylate*) had m.p. 128—128·5°, $\nu_{max.}$ 1760, 1710infl, 1605, and 1565 cm^{-1} [Found: C, 68·2; H, 6·0%; *M* (mass spectrum) 246. $C_{14}H_{14}O_4$ requires 68·3; H, 5·7%; *M*, 246] *Methyl* 5,6-*benzocoumarin*-3-*carboxylate* (*naphtho*[2,1-b]*pyran*-2-*carboxylate*) had m.p. 165° (from aqueous ethanol), $\nu_{max.}$ 1740, 1695, and 1570 cm.$^{-1}$ [Found: 71·0; H, 4·0%; *M* (mass spectrum) 254. $C_{15}H_{10}O_4$ requires C, 70·9; H, 4·0%; *M*, 254].

Derivatives of 3-cyanocoumarin were made according to the method of Baker and Howes [29] and purified from ethanol or acetone, either neat or aqueous. 3-*Cyano*-6-*methylcoumarin* had m.p. 205—206° [Found: C, 71·2; H, 3·9; N, 7·6%; *M* (mass spectrum), 185. $C_{11}H_7NO_2$ requires C, 71·3; H, 3·8; N, 7·6%; *M*, 185]. 3-*Cyano*-5,7-*dimethylcoumarin* had m.p. 228° (subl.) [Found: C, 72·3; H, 4·3; N, 7·2%; *M* (mass spectrum) 199. $C_{12}H_9NO_2$ requires C, 72·3; H, 4·5; N, 7·0%; *M*, 199]. 3-*Cyano*-6,7-*dimethoxycoumarin* gradually decomposed above 250° and no m.p. could be determined [Found: C, 62·3; H, 4·0; N, 6·2%; *M* (mass spectrum), 231. $C_{12}H_9NO_4$ requires C, 62·3; H, 3·9; N, 6·1%; *M*, 231]. 5,6-*Benzo*-3-*cyanocoumarin* (*naphtho*[2,1-b]*pyran*-2-*carbonitrile*) had m.p. 275—276° (subl.) [Found: C, 76·1; H, 3·2; N, 6·5%; *M* (mass spectrum), 221. $C_{14}H_7NO_2$ requires C, 76·0; H, 3·2; N, 6·3%; *M*, 221]: it proved nearly insoluble in the usual solvents and its behaviour towards diazoalkanes could not be studied. 3-Cyano-8-methoxycoumarin had m.p. 231—231·5° (lit.,[30] 224—226°), $\nu_{max.}$ 2260, 1720, 1706, 1610, and 1575 cm.$^{-1}$ (Found: C, 65·6; H, 3·4; N, 7·0. Calc. for $C_{11}H_7NO_3$: C, 65·7; H, 3·5; N, 7·0%).

Direct Alkylations.—Diazomethane was made from nitrosomethylurea by the distillation technique and purified by repeated treatment with fresh potassium hydroxide pellets during 4 hr. followed by slow redistillation in apparatus that had been very recently heat-dried. The method of use depended somewhat upon the solubility of the other reactant, as illustrated.

Method (a). 3-Acetylcoumarin (0·5 g.) dissolved in the minimum amount of ether (*ca.* 50 ml.) at 0° was treated at that temperature with diazomethane (*ca.* 0·5 g.) in ether. Steady nitrogen evolution was accompanied by separation of some of the product. After 20 min. the volatile materials were evaporated off under reduced pressure and the residue was crystallised from ethanol or aqueous ethanol giving 3-acetyl-4-methylcoumarin, m.p. 101° (lit.,[8] 102°).

Method (b). 3-Cyanocoumarin (0·5 g.) dissolved in tetrahydrofuran (20 ml.) was treated at 0° with diazomethane (*ca.* 0·5 g.) in ether (*ca.* 30 ml.). Work-up as in (a) and purification of the product from aqueous acetone supplied 3-cyano-4-methylcoumarin as fine needles, m.p. 195° (lit.,[10] 191—192°), $\nu_{max.}$ 2250, 1720, 1603, and 1565 cm.$^{-1}$.

Method (c). A solution of 3-cyano-8-methoxycoumarin (0·4 g.) in diethylene glycol dimethyl ether (60 ml.) at 0° was treated with diazomethane (*ca.* 0·5 g.) in ether (*ca.* 25 ml.) and set aside for 20 min. Volatile materials were removed under reduced pressure, and light petroleum (b.p. 40—60°) was added slowly to the residual solution to precipitate the product, which crystallised from benzene giving 3-*cyano*-8-*methoxy*-4-*methylcoumarin* as cream-coloured needles, m.p. 233° (Tables 2 and 3).

3a-*Acetyl*-1,9b-*dihydro*-7,9-*dimethylchromeno*[3,4-c]*pyrazol*-4(3aH)-*one* (XIII).—A solution of 3-acetyl-5,7-dimethylcoumarin (1·5 g.) in ether (400 ml.) was mixed at 0° with one of diazomethane (*ca.* 2 g.) also in ether (120 ml.) and after 25 min. volatile material was removed under reduced pressure without application of heat. The *chromeno*-[3,4-c]*pyrazole* gradually separated as needles (1·7 g.) which, after being washed with ether, were satisfactorily pure. The compound decomposed readily at 54—56° and had $\nu_{max.}$ 1743 (lactone), 1720 (ketone), and 1568 (azo) cm.$^{-1}$ (Found: C, 65·1; H, 5·7; N, 10·9. $C_{14}H_{14}N_2O_2$ requires C, 65·1; H, 5·5; N, 10·9%). The compound decomposed slowly and effervesced in contact with hydroxylic solvents. It was not stable enough to give a reliable, reproducible n.m.r. spectrum.

The chromeno[3,4-*c*]pyrazole (1·5 g.) was added to methanol (50 ml.). When the effervescence had subsided, the solution was set aside for 45 min. and then evaporated leaving a pale yellow oil that solidified slowly. This material was separated by chromatography on silica (40 g.) from benzene into two main components, the total of which was reproducible but the ratio of which varied. The first to leave the column formed a crystalline solid (*ca.* 0·60 g.) that was purified from light petroleum (b.p. 60—80°) and supplied 3-*acetyl*-4,5-*dihydro*-4-*methoxy*-6,8-*dimethyl*-1-*benzoxepin*-2(3H)-*one* (XVIII) as needles, m.p. 104—104·5° (Found: C, 68·8; H, 6·7. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%), $\nu_{max.}$ 1735 (lactone), 1720 (ketone), 1625 and 1580 (aromatic) cm.$^{-1}$, τ 3·09 and 3·16 (aromatic), 7·69 (narrow band, aromatic Me), 7·82 (Ac), and 6·62 (OMe), 7·34 (q, H_D), 6·78 (q, H_C), 5·55 (octuplet, H_B), and 6·53 (d, H_A); first-order analysis gives J_{AB} 8, J_{BC} 2·5, J_{BD} 4, and J_{CD} 15 Hz.

The second component also formed crystals (*ca.* 0·15 g.),

[28] K. Bartsch, *Ber.*, 1903, **36**, 1966.
[29] W. Baker and C. S. Howes, *J. Chem. Soc.*, 1953, 119.
[30] E. C. Horning and M. G. Horning, *J. Amer. Chem. Soc.*, 1947, **69**, 968.

and these separated from wet ethanol giving 3-*acetyl*-6,8-*dimethyl*-1-*benzoxepin*-2(3H)-*one* (XVII) as needles, m.p. 89·5—90·5°, displaying an intense green colour with ferric ions in ethanol (Found: C, 72·9; H, 6·1; N, 0·0. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%), τ 3·0 (2H, aromatic), 7·66 (6H, 2 aromatic Me), and 7·71 (Ac), and 6·20 (m, H_X), 3·57 (m, H_B), and 3·07 (m, H_A); first-order analysis gave J_{AB} 10, J_{BX} 5·5, and J_{AX} 1·5 Hz.

Thermolysis of Chromenopyrazole (XIII).—The pyrazole (freshly prepared; 0·70 g.) was warmed (without solvent) on a steam-bath until evolution of gas occurred. After 15 min., the residual melt was allowed to cool; it then partly solidified. Chromatography on silica with benzene as solvent gave two fractions. The first was an oil that later solidified and supplied the benzoxepin-2(3*H*)-one (XVII) (0·33 g., 52%), identical with an authentic specimen. The next fraction supplied a mixture of two coumarins (total 0·16 g., 28%) shown by n.m.r. spectroscopy to consist of 3-acetyl-5,7-dimethylcoumarin (0·094 g., 17%) and 3-acetyl-4,5,7-trimethylcoumarin (0·064 g., 11%). Repeated chromatography separated these two, though not efficiently. The former was identical with authentic material. From ethanol, 3-*acetyl*-4,5,7-*trimethylcoumarin* crystallised as needles, m.p. 149—150° (Found: C, 73·0; H, 6·2. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%), τ 7·64 (3H, Ac), 7·50, 7·48, and 7·33 (9H, 3 nuclear Me), and 3·08 and 3·00 (2H, aromatic).

To confirm that 3-acetyl-5,7-dimethylcoumarin is formed by thermolysis and is not present as an impurity in the starting pyrazoline (which is too unstable to be fully purified if it is not already satisfactory), a new sample was prepared and divided into two portions. One of these (89 mg.) was thermolysed as before; the other (123 mg.) was treated with cold methanol until gas evolution ceased; the solvent was then removed *in vacuo*. The two oils so made were dissolved in deuteriochloroform and scanned in the n.m.r. spectrometer. That from thermolysis showed a band at τ 1·33 characteristic of 3-acetyl-5,7-dimethylcoumarin, its relative intensity corresponding to a yield of about 17%. That from methanolysis showed no such signal. Thus this coumarin is formed by thermolysis and is neither present as an impurity nor formed by methanolysis.

3-*Acetyl*-5,6-*benzocoumarin* (2-*Acetylnaphtho*[2,1-b]*pyran*) *and Diazomethane*.—(a) *At* −40°. A solution of 3-acetyl-5,6-benzocoumarin (1·54 g.) in methylene chloride (130 ml.) cooled to *ca.* −50° was mixed with diazomethane (*ca.* 1·5 g.) in ether (70 ml.), also at that temperature, and kept overnight at −40° in the dark. Removal of the solvents under reduced pressure left an oil which was taken up in benzene and partially reprecipitated by the gradual addition of light petroleum (b.p. 60—80°). This gave a yellowish, semicrystalline mass, which was removed, and a solution which slowly deposited a colourless crystalline solid. Evaporation of the mother liquor furnished an oil. The semicrystalline mass and the oil were repeatedly reprecipitated by petroleum from their solutions in benzene until no more of the colourless crystalline product could be procured. This product (186 mg.) was purified from methylene chloride–light petroleum (b.p. 60—80°) giving (3a-*RS*,9b-*SR*)-1,11c-*dihydro*-3a-(2-*methyloxiranyl*)*benzo*[5,6]*chromeno*-[3,4-c]*pyrazole*-4(3aH)-*one* (XXIV) as needles effervescing at 140—141·5° (Found: C, 69·6; H, 4·7; N, 9·5. $C_{17}H_{14}N_2O_3$ requires C, 69·4; H, 4·8; N, 9·5%).

(b) *At* 0°. The coumarin (1·5 g.) in freshly dried dichloromethane (50 ml.) was cooled to 0° and diazomethane (*ca.* 1·5 g.) in ether (100 ml.) also at 0° was added; the mixture was kept in ice for 35 min. The filtered solution was concentrated under vacuum without application of heat until a yellow glass had formed, and this was taken up in freshly dried benzene. Light petroleum (b.p. 40—60°) was added cautiously to precipitate a gum from which the solution was decanted; the latter was kept in a sealed vessel. The gum was twice again dissolved in benzene and precipitated with light petroleum. Each of the three decanted solutions so obtained gradually deposited a semicrystalline powder (combined yield 0·45 g.) which crystallised from dichloromethane–light petroleum (b.p. 60—80°) giving (8a-*RS*, 11a-*RS*)-8a-*acetyl*-11a,12-*dihydro*-10*H*-*naphtho*[1′,2′-6,7]-*oxepino*[3,4-c]*pyrazol*-8(8aH)-*one* (XXII) as prisms, m.p. 101—102° (decrepitation above 95°) (Found: C, 69·5; H, 4·9; N, 9·5. $C_{17}H_{14}N_2O_3$ requires C, 69·4; H, 4·8; N, 9·5%), τ 7·58 (Ac), 5·53 ($N{\cdot}CH_2$), and complex patterns between 6·2 and 7·1 (two benzylic protons and one other). Chromatography of the residual gums recovered 3-acetyl-5,6-benzocoumarin (0·08 g.).

This oxepinopyrazole (0·15 g.) was pyrolysed in freshly dried benzene (25 ml.) at the b.p. for 4 hr.; evaporation of the solvent then left an oil that crystallised under light petroleum (b.p. 60—80°) and then crystallised from that solvent to give 3-*acetyl*-2-*methylnaphtho*[2,1-b]*oxepin*-4(1H)-*one* (XXIII) as needles, m.p. 85°, $\nu_{max.}$ 1708 (unsaturated ester), 1688 (unsaturated ketone), and 1610 and 1600 (aromatic and ethylenic) cm.$^{-1}$ (Found: C, 76·6; H, 5·2. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3%). The most important fragmentations of the molecular ion (*m/e* 266) were losses of keten and acetoacetyl (or their equivalents) to give ions *m/e* 224 and 182, respectively. The n.m.r. spectrum showed a six-proton multiplet extending from τ 1·83 to 2·76. The acetyl and vinylic methyl resonances coincide at 7·70, and the ring methylenic resonance occurs at 6·20.

[9/1458 *Received, August 26th,* 1969]