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SYNTHESIS OF 3-SUBSTITUTED COUMARINS VIA SEQUENTIAL PERICYCLIC TRANSFORMATIONS OF α-ARYLOXYMETHYLACRYLIC ACIDS AND ENOPHILES

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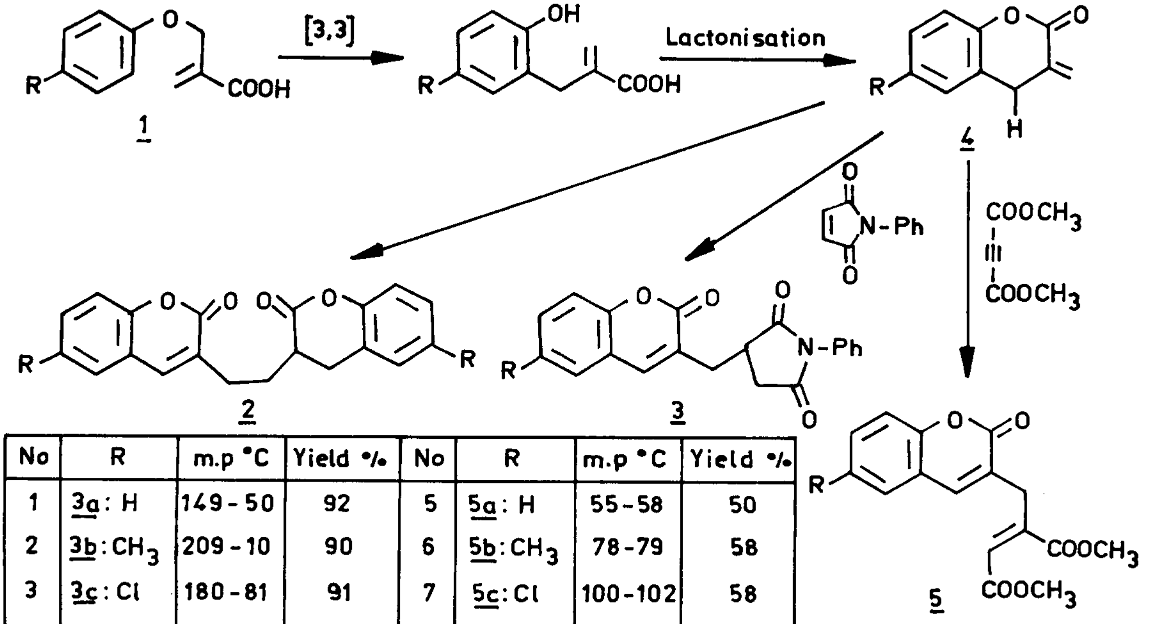
Summary: A new procedure for the synthesis of 3-functionally substituted coumarins via sequential Claisen and ene reactions of α-aryloxymethylacrylic acids and enophiles has been developed.

The ene synthesis has come into prominence over the recent years. However there appears to be no reports of ene reactions involving aryl allyl ethers or aryl allyl sulphides[1], which can undergo either competitive Claisen and ene or sequential Claisen-ene reactions[2]. In this communication, we would like to report a novel sequential Claisen-ene transformation of α-aryloxymethylacrylic acids in the presence of enophiles.

Thus refluxing 1[3](1eq 5 mmole) with excess of N-phenylmaleimide(NPM) or dimethylacetylenedicarboxylate(DMAD)(2eq 10 mmole) in 5 ml of o-dichlorobenzene(o-DClB b.p. 179°C) for 6h afforded the respective 3-substituted coumarins 3/5 in good yields. Analytical and spectral data of these products clearly established the structure assigned to them[4], vide Scheme and Table.



No	R	m.p °C	Yield %	No	R	m.p °C	Yield %
1	3a: H	149-50	92	5	5a: H	55-58	50
2	3b: CH_3	209-10	90	6	5b: CH_3	78-79	58
3	3c: Cl	180-81	91	7	5c: Cl	100-102	58
4	3d: OCH_3	195-97	90	8	5d: OCH_3	84-85	54

The whole transformation can be envisaged as a sequential Claisen rearrangement-lactonisation-ene reaction involving an initial Claisen rearrangement of 1, lactonisation of the resulting o-allylphenolic acid to give 3-methylene-3,4-dihydrocoumarin 4, which undergoes an ene reaction with NPM/DMAD to give the 3-substituted coumarins 3/5.

When the reaction was carried out by refluxing 1eq of the acid 1 with 1eq of NPM/DMAD, the product consisted of mostly the self-ene dimer 2[5] of the 3-methylenecoumarin 4 and only about 5% of 3/5. Further support in favour of the mechanism came from the reaction of 4c[6] with 2eq of NPM/DMAD in refluxing o-DClB for 6h, which afforded the ene products 3c/5c, while refluxing with 1eq of NPM/DMAD gave only 2c.

With a view to check if the ene-dimer[7] could be used as a convenient source for generating the 3-methylenecoumarin 4 insitu by a retro-ene reaction which further could be trapped by an external enophile, the reaction was carried out by refluxing the ene-dimer 2c with excess of NPM/DMAD for more than 30h. In the event, the dimer 2c was recovered unchanged.

This route offers a novel entry into such systems proceeding from readily available starting materials and affording regiospecifically the coumarins which can be variously substituted in the benzene nucleas as well as at the 3-position. We are currently exploring the synthetic potentials of the 3-methylene-3,4-dihydrocoumarins.

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References and Notes

1. Examples of Intramolecular ene reactions involving allyl alcohols, propargyl alcohols & allyl amines have been well documented. D.F.Taber,Intramolecular Diels-Alder and Alder-ene reactions, Springer Verlag 1984, pg 61-94.
2. B.Gopalan, K.Rajagopalan, S.Swaminathan & K.K.Balasubramanian, Tetrahedron Lett., 18, 1507 (1975).
3. For Tandem Claisen-ene transformation, see F.E.Zeigler and J.J.Mencel, Tetrahedron Lett., 25(2) 123 (1984).
4. For 3b data: IR($CHCl_3$) 1710 cm^{-1}(lactone carbonyl) UV(MeOH) 280(logϵ 1.493) 320(logϵ 0.827) NMR($CDCl_3$) δ-values 2.3(s,3H),2.7-3.3(m,5H),6.8-7.2(m,ArH), 7.2(s,1H,benzylic H), MS m/z 347(M^+). ^{13}C-NMR(75 Mhz $CDCl_3$)20.54(q),32.76(t) 34.25(t),38.96(d),116.39(d),118.93(s),125.35(s),126.48(d), 127.45(d),128.60 (d),129.17(d),132.09(s),132.55(d),134.39(s),141.62(d),161.96(s),174.96(s), 177.9(s).
5. For 5b data: IR($CHCl_3$) 1720 cm^{-1}; UV(MeOH) 280(logϵ 0.826),325(logϵ 0.427) NMR($CDCl_3$) δ-values 2.2(s,3H),3.5(s,3H),3.6(s,3H),5.7(s,1H),6.7-6.9(m,ArH) 7.2(s,1H,benzylic H);MS m/z 317(M^+). ^{13}C-NMR(75 Mhz $CDCl_3$)20.59(q),34.83(t) 51.75(q),52.29(q),116.34(d),118.99(s),124.12(d),124.48(s),127.45(d),132.37 (d),134.18(s),140.80(d),144.01(s),151.82(s),161.01(s),165.15(s) & 167.73(s)
5. The sample was compared with an authentic sample of ene dimer prepared by the method reported in literature. See B.Gopalan,K.Rajagopalan,K.Sunitha & K.K.Balasubramanian, Tetrahedron, In print 1985.
6. K.Sunitha,K.Rajagopalan &K.K.Balasubramanian, Tetrahedron Lett.,25(29) 3125 1984.
7. A similiar strategy has been used to generate o-quinone methide by heating the corresponding dimer in xylene or mesitylene. M.S.Chauhan, F.M.Dean D.Malkind and M.L.Robinson, J.Chem.Soc., Perkin I, 120(1975).
8. All new compounds were characterised by analytical and spectral data.

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