Reaction of Difluorocarbene with 2-Benzylidenecyclohexanones to afford Phenylfluorofurans

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Summary Difluorocarbene reacted with several 2-benzylidenecyclohexanones giving phenylfluorofurans: trans-1benzoyl-2,2-difluoro-3-phenylcyclopropane, when heated for $1\frac{1}{2}$ h at 216°, gave 3-fluoro-2,5-diphenylfuran in high yield.

CARBENES and carbenoids rarely react with unsaturated systems to afford products formally derived by or via 1,4-addition.¹ However diffuorocarbene reacts with the 2-methoxymethylene ketone (I) giving both isomers of the dihydrofuran (II) (combined yield 70%),² and "ethoxycarbonylcarbene" reacts with the 2-methoxymethylene ketone (III) to afford the furan (IV) (29%), presumably via the dihydrofurans (V).³ Recent work⁴ suggests that the reagent in the latter case initially attacks the carbonyl group of the substrate. We now report that furan derivatives



are also obtained when 2-benzylidene-5x-cholestan-3-one

(VI) and some related ketones are treated with diffuorocarbene; they are not, however, formally derived by or via 1.4-addition.



Treatment of 2-benzylidene-5 α -cholestan-3-one (VI) in refluxing triglyme (ca. 216°)⁵ with 30 equiv. of difluorocarbene generated by the thermal decomposition of sodium chlorodifluoroacetate,6 afforded, after column chromatography, one main product, m.p. 172-174°, (29%)[†] which was identified as the phenylfluorofuran (VII) from the following data. The molecular weight (high-resolution mass spectrometry)[‡] and C, H, and F analyses were in agreement with the formula $C_{35}H_{49}FO$. The only signals in the ¹H n.m.r. spectrum (solution in CDCl₃) at lower field than $\delta 2.70$ p.p.m. were due to a phenyl group. The i.r. spectrum (solution in CHCl₃) contained no carbonyl band, but had bands at 1654 and 1607 cm⁻¹. The i.r. spectra of several polyfluorofurans have bands in this region.⁷ The base peak in the mass spectrum was the molecular ion. A prominent peak (40%) at m/e 188 is attributed to a retro-Diels-Alder cleavage and a metastable peak at m/e70.2 supports this.⁸ The u.v. spectrum, λ_{max} (EtOH) 220, 226sh, 274sh, 286, and 298sh nm (log e 3.85, 3.80, 4.19, 4.29, and 4.16), is similar to that of 2-phenylfuran§ and unlike that of 3-phenylfuran.¶

 17β -Benzoyloxy-2-benzylidene-5 α -androstan-3-one (VIII) and 2-benzylidenecyclohexanone reacted similarly with diffuorocarbene to afford, respectively, the furan (IX), m.p. 221–223°, (52%)[†] and the furan (X), a gum, (8%)[†] which were identified in a similar manner to (VII).

The phenylfluorofurans probably arise by 1,2-addition of the carbene to the olefinic double bond followed by thermal



rearrangement of the adduct and loss of hydrogen fluoride. This is supported by the observation that when a solution of trans-1-benzoyl-2,2-diffuoro-3-phenylcyclopropane (XI)⁹ in triglyme is heated under reflux for 11 h 3-fluoro-2,5diphenylfuran (XII), m.p. $66-66\cdot5^{\circ}$ (76%, 96% allowing for recovered starting material), is formed. This product was identified similarly to (VII), (IX), and (X); particularly important evidence was the u.v. spectrum, λ_{max} (EtOH) 228, 236sh, 311 (infl.), 319, 325, and 340sh nm. (log ϵ 4.26, $4\cdot11$, $4\cdot50$, $4\cdot53$, $4\cdot57$, and $4\cdot33$), which is similar to that reported for 2,5-diphenylfuran¹⁰ and unlike that for 2,4diphenylfuran.10



Several polyfluorofurans have recently been described.⁷ These compounds rapidly decomposed. Furan (X), although initially colourless, becomes brown within a day and furan (XII) becomes yellow within a few days. The steroidal furans (VII) and (IX), however, show no sign of decomposition after several months.

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- † No systematic attempts were made to maximise yields.
- We find that 2-phenylfuran has λ_{max} (EtOH) 218, 223sh, 272sh, 279, 290sh nm. (log ϵ 3.97, 3.91, 4.26, 4.28, 4.10). ¶ Professor H. Wynberg kindly informs us that 3-phenylfuran has λ_{max} (96% EtOH) 253 nm (log ϵ 4.03).

¹ Ylides react with unsaturated systems to afford products formally derived by or via 1,4-addition, see e.g., B. Holt and P. A. Lowe, Tetrahedron Letters, 1966, 683; H. G. Lehmann, *ibid.*, 1968, 607; T. A. Harris, C. M. Harris, and J. C. Cleary, *ibid.*, 1968, 1427; P. Bravo, G. Gaudiano, and A. Umani-Ronchi, *ibid.*, 1969, 679; and E. Breuer and D. Melumad, *ibid.*, 1969, 1875.

² P. Hodge, J. A. Edwards, and J. H. Fried, Tetrahedron Letters, 1966, 5175.
 ³ D. L. Storm and T. A. Spencer, Tetrahedron Letters, 1967, 1865. See also, T. A. Spencer, R. M. Villarica, D. L. Storm, T. D. Weaver, R. J. Friary, J. Posler, and P. R. Shafer, J. Amer. Chem. Soc., 1967, 89, 5497.

S. T. Murayama and T. A. Spencer, Tetrahedron Letters, 1969, 4479.

⁵ Compound (VI) was recovered unchanged after a solution in triglyme had been heated under reflux for 1 hr.

⁶ E.g., C. Beard, B. Berkoz, N. H. Dyson, I. T. Harrison, P. Hodge, L. H. Kirkham, G. S. Lewis, D. Giannini, B. Lewis, J. A. Edwards, and J. H. Fried, *Tetrahedron*, 1969, 25, 1219.
⁷ J. Burdon, G. E. Chivers, and J. C. Tatlow, J. Chem. Soc. (C), 1970, 2146.
⁸ Similar fragmentations occur with other Δ²-steroids. See e.g., ref. 2 and H. Budzikiewicz, C. Djerassi, and D. H. Williams in "Structure Elucidation of Natural Products by Mass Spectrometry," vol. 2, Holden-Day Inc., San Francisco, 1964, pp. 98—101. ⁹ M. Derenberg and P. Hodge, unpublished work.

¹⁰ S. M. King, Č. R. Bauer, and R. E. Lutz, J. Amer. Chem. Soc., 1951, 73, 2253.