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PHOTOCHEMICAL REACTION OF CHOLESTEROL ANALOGS WITH A CARBENE-GENERATING SUBSTITUENT ON THE SIDE CHAIN

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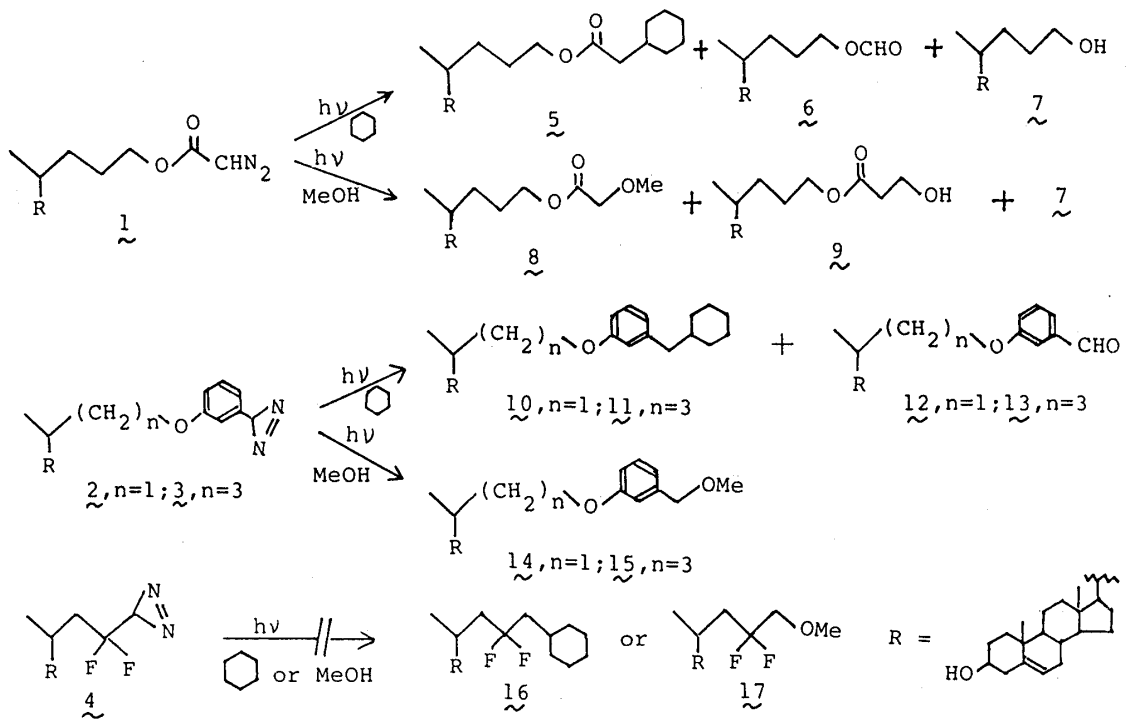
Photolysis of cholesterol analogs with a diazoacetate or aryldiazirine substituent on the side chain effectively gave C-H or O-H insertion products.

KEYWORDS-cholesterol analog; photoaffinity label; diazoacetate; aryldiazirine; carbene insertion

In the preceding paper,[1] we described the synthesis of the diazoacetate 1, the aryldiazirines 2 and 3, and the fluorodiazirine 4 as photoaffinity-labelled analogs of cholesterol. Before these compounds are subjected to interaction with phospholipids in artificial or biological membranes, it is essential to know their photochemical properties. Described here are the results of photolysis of 1-4 in a solution of cyclohexane or methanol, which can be considered as models of the hydrophobic portions of a phospholipid and water, respectively.

When the diazoacetate 1 in cyclohexane solution was irradiated with a low pressure mercury lamp for 10 min, the three products 5, 6 and 7 were obtained, after chromatography on silica gel, in 55%, 17% and 19% yield, respectively. The structures of these compounds as well as other irradiation products described below were straightforwardly determined by spectroscopy.[2] Analogous photolysis of 1 in methanol solution for 6 min gave the three products 7, 8 and 9 in 9%, 70% and 10% yield, respectively. The major products 5, 8 and 9 in the irradiation processes were the results of the photogenerated carbene insertion into the solvents. The mechanism of formation of the formate 6 and the alcohol 7 is unclear, although analogous products had been observed on photolysis of cholesteryl diazoacetate.[3] Photolysis of the aryldiazirines 2 and 3 was carried out with a high pressure mercury lamp irradiating through a Pyrex filter. Irradiation of 2 in cyclohexane solution for 50 min gave the two products 10 and 12 in 61% and 26% yield, respectively, whereas photolysis in methanol solution for 60 min yielded 14 in 90% yield as almost the sole product. Similarly, the other aryldiazirine 3 produced(in cyclohexane) 11 and 13 in 63% and 26% yield, respectively, or (in methanol) 15 in 90% yield. Clearly C-H insertion into cyclohexane and O-H insertion into methanol are again the principal photochemical reactions. On the other hand, on irradiation of the fluorodiazirine 4 with a



a high pressure mercury lamp through a Pyrex filter, no appreciable carbene insertion products 16 or 17 was produced. This result is reminiscent of Khorana's observation[4] that photolysis of 3-(1,1-difluorooctyl)-3H-diazirine showed no insertion into C-H or O-H bonds.

In summary, the present results suggest that the diazoacetate 1 and the aryldiazirines 2 and 3 are promising probes for investigating cholesterol-phospholipid interaction in artificial and/or biological membranes.

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REFERENCES AND NOTES

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2) For example, the compound 5 showed IR($CHCl_3$) 1715cm^{-1}(ester); ^{1}H-NMR($CDCl_3$, 270MHz): 2.17(2H, d, J=6Hz, $COCH_2$-⬡), 4.03ppm(2H, td, J=6.5 and 3.5Hz, 24-H_2); m/z of the trimethylsilyl ether derivative, 556(M^+), 500(M-56), 466(M-trimethylsilanol, base peak), 427(M-129), 129.
3) S. A. Kailbough and E. R. Thornton, J. Am. Chem. Soc., 105, 3283(1983).
4) B. Erni and H. G. Khorana, J. Am. Chem. Soc., 102, 3888(1980).

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