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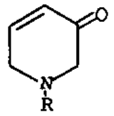
1,6-DIHYDRO-3(2*H*)-PYRIDINONES AS SYNTHETIC INTERMEDIATES. PHOTOCHEMICAL [2+2] CYCLOADDITION WITH VINYL ACETATE

Takeshi Imanishi, Yasuaki Wada, Makoto Inoue, and Miyoji Hanaoka*
Faculty of Pharmaceutical Sciences, Kanazawa University, Takara-machi, Kanazawa 920, Japan

Abstract —— Photochemical [2+2] cycloaddition of 1,6-dihydro-3(2*H*)-pyridinones (1a and 1b) with vinyl acetate gave the cycloadducts (2a and 2b). Utilizing this reaction as a key step, 1b was converted into the 4-substituted 1,6-dihydro-3(2*H*)-pyridinone (3) and the 4-substituted 3-piperidinone (4).

Photochemical [2+2] cycloaddition between α,β-enones and olefins has shown to be of great value[1] in synthesis of natural products since Corey and his co-workers demonstrated its utility in the total synthesis of (±)-caryophyllene.[2] In spite of a number of reports concerning the photocycloaddition between cycloalkenones and olefins or acetylenes, only a few reactions between azacyclic enone moiety and olefins have been examined. For example, 4-methoxy-2-pyridinone gave only the head-to-tail (HT) adduct on photoreaction with methyl vinyl ether,[3] and 1,3-dimethyluracil was found to yield the HT adduct as a sole product on the reaction with ethyl vinyl ether.[4]

As one of the continuous studies on 1,6-dihydro-3(2*H*)-pyridinones,[5] we have examined the photochemical [2+2] cycloaddition of 1 with vinyl acetate and now wish to report the behavior of the reaction and the transformation of 1b through the photocycloaddition step into the 4-substituted pyridinone (3) and into the



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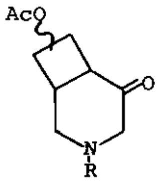
a R=SO_2Me
b R=CO_2Et



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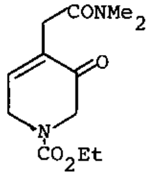

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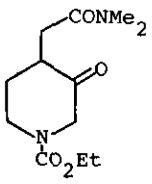

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4-substituted 3-piperidinone (4), both of which would be potential intermediates for the synthesis of the Corynanthe alkaloids.

Irradiation of a solution of 1a[6] and vinyl acetate in acetonitrile in the presence of acetone for 4 hr under ice-cooling gave the cycloadduct (2a) as a regio- and stereo-isomeric mixture in 86% yield. Ketalization of 2a with ethylene glycol followed by alkaline hydrolysis provided three products, 5 [62% yield; mp 134-136°], 6[7] [9% yield; mp 116-117°], and 7 [12% yield; mp 110.5-111.5°].[8] The ditetal (7) seems to be obtained from the head-to-head (HH) adduct (one component of 2a) through a retro-aldol reaction in the ketalization step. The photoreaction under other conditions gave the same products and the results are summarized in Table, which shows that the regioselectivity in this reaction is fairly constant and is affected by neither the sensitizer (acetone) nor the solvents.

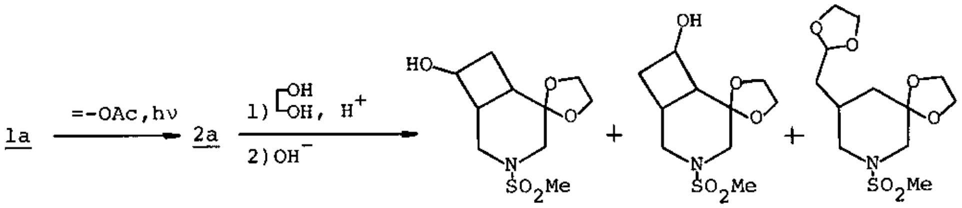

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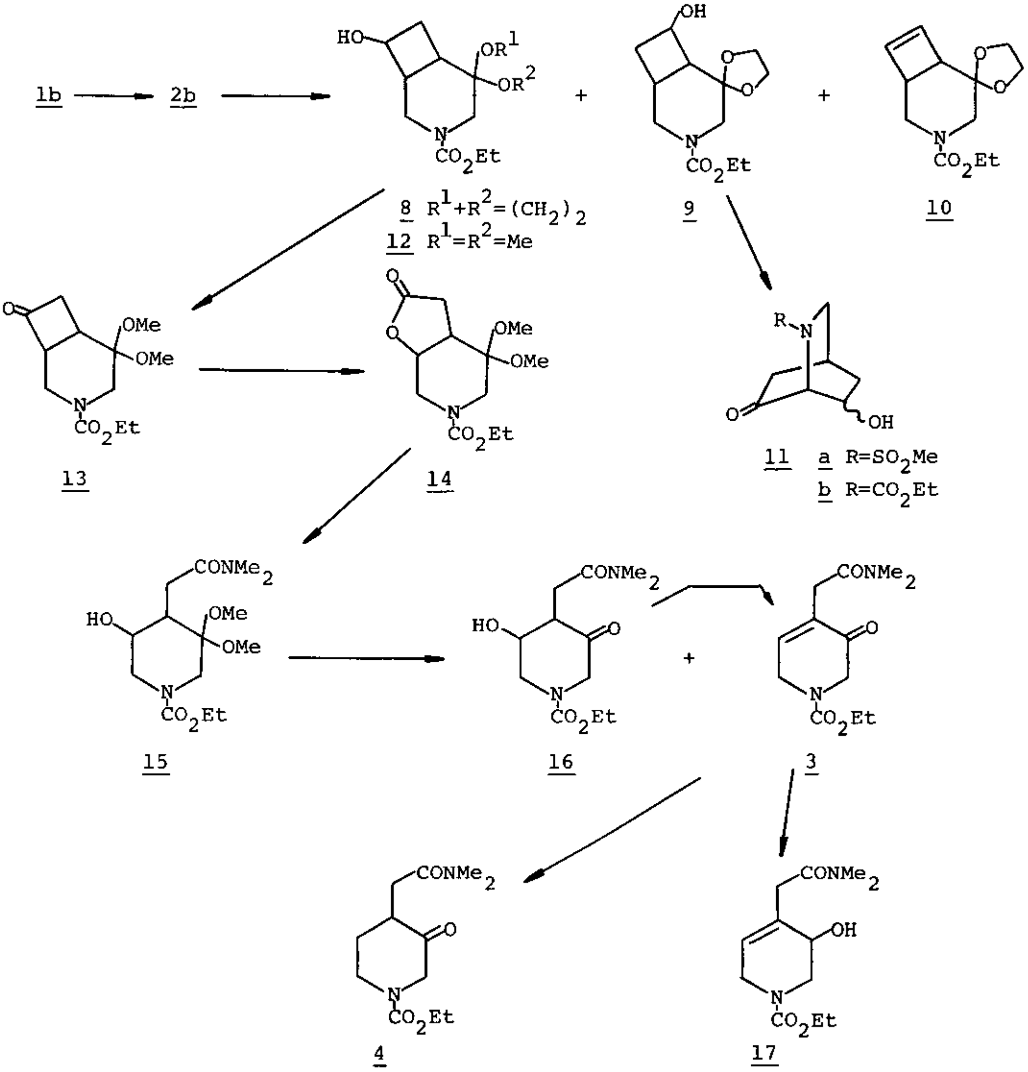
Table. Photochemical [2+2] Cycloaddition between 1a and Vinyl Acetate*

Conditions of Photoreaction			Products (%)			Ratio of
Solvent	Sens.	Time (hr)	5	6	7	HT-adduct/HH-adduct
MeCN	acetone	4	50	7.3	9.8	75/25
CH_2Cl_2	acetone	2.5	46	7.3	1.9	83/17
acetone	acetone	2.5	49	12	2.7	77/23
MeCN	none	4.5	44	15	3.8	70/30

* A solution of the enone (1a; 400 mg) and vinyl acetate (5 ml) in the slovent (150 ml) with the sensitizer (1 ml) was irradiated using a 100-W high pressure Hg lamp with Pyrex filter.

On the other hand, the photocycloaddition using the ethyl urethane (1b)[5a] in acetonitrile containing the sensitizer followed by ketalization with ethylene glycol and alkaline hydrolysis gave three products, 8 (52%), 9[7] (9.6%), and 10 [2.0%; ν 1680, 1650; δ 5.63(1H,dt,J=10,2), 5.88(1H,dt,J=10,3)]. The dimethyl ketal analog (12) of 8, obtained from 1b in overall 50% yield, was oxidized with PCC to give the ketone (13) in 62% yield. The Baiyer-Villiger oxidation[9] of 13 with *m*-chloroperbenzoic acid in methylene chloride at room temperature for 2.5 days afforded the disired lactone [<u>14</u>; δ 4.5-4.8(1H,m)], which reacted with dimethylamine in methanol to yield the amide (<u>15</u>) in 61% yield from <u>13</u>. On acid



hydrolysis with 2% hydrochloric acid in acetone at 45° for 1 hr <u>15</u> gave the hydroxy ketone (<u>16</u>) in 68% yield along with the dehydrated product (<u>3</u>) [12%; ν 1700, 1680, 1630; δ 1.26(3H,t,*J*=7), 2.92(3H,s), 3.05(3H,s), 3.27(2H,d,*J*=1.5), 4.12(2H,q,*J*=7), 6.85(1H,broad t,*J*=3.5); *m/e* 254(M^+), 153(base)]. The former was easily transformed into the latter with *p*-toluenesulfonic acid in boiling benzene in 77% yield. The enone (<u>3</u>), however, was obtained directly (86% yield) on hydrolysis of <u>15</u> with 2% hydrochloric acid in acetone at 60° for 3.5 hr.

Catalytic hydrogenation of 3 over 5% palladium on carbon in methanol furnished the saturated ketone (4)[10] [87%; ν 1720sh, 1680, 1635; δ 1.23(3H,t,*J*=7), 2.90(3H,s), 3.00(3H,s), 4.08(2H,q,*J*=7); *m/e* 256(M^+), 211(base)], while reduction of 3 with sodium borohydride in methanol yielded the alcohol (17)[97%; ν 3360, 1680, 1620; δ 1.25(3H,t,*J*=7), 2.93(3H,s), 3.03(3H,s), 3.23(2H,broad s), 4.13(2H,q,*J*=7), 5.05 (1H,m)]. Thus, the dihydropyridinone (1b) was converted into 3, 4, or 17 *via* photochemical [2+2] cycloaddition as a key step. Synthetic efforts for the Corynanthe family, e.g. hirstine, using these compounds are in progress.

REFERENCES AND NOTES

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5. a) T. Imanishi, I. Imanishi, and T. Momose, *Syn. Commun.*, 1978, 8, 99; b) T. Imanishi, H. Shin, M. Hanaoka, T. Momose, and I. Imanishi, *Heterocycles*, 1980, 14, 1111; c) T. Imanishi, H. Shin, N. Yagi, and M. Hanaoka, *Tetrahedron Lett.*, 1980, 21, 3285; d) T. Imanishi, N. Yagi, and M. Hanaoka, *ibid.*, 1981, 22, 667; e) T. Imanishi, A. Nakai, N. Yagi, and M. Hanaoka, *Chem. Pharm. Bull.*, 1981, 29, 901; f) T. Imanishi, N. Yagi, H. Shin, and M. Hanaoka, *Tetrahedron Lett.*, 1981, 22, 4001.
6. Prepared from 1,2,3,6-tetrahydropyridine according to the method in ref. 5a.
7. The HH-adduct (6 or 9) was able to be transformed into the known 2-azabicyclo[2.2.2]octanone[5c] (11) by the acid hydrolysis.
8. In the course of this work K. Mori and M. Sasaki [*Tetrahedron*, 1980, 36, 2197]. have reported a similar HT-adduct/HH-adduct ratio in the photocycloaddition between 3-methyl-2-cyclopentenone and vinyl acetate.
9. Oxidation of 13 with alkaline hydrogen peroxide [*cf.* M.J. Bogdanowicz, T. Ambelang, and B.M. Trost, *Tetrahedron Lett.*, 1973, 923] was found to be fruitless.
10. N-Acylated 3-piperidinones have been alkylated exclusively at C_2-position *via* enamines. *cf.* T. Masamune, H. Hayashi, M. Takasugi, and S. Fukuoka, *J. Org. Chem.*, 1972, 37, 2343; P. Krogsgaard-Larsen and H. Hjeds, *Acta Chem. Scand., Ser. B*, 1976, 30, 884.

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