**Summary**

It was found that the crystalline derivatives were readily obtainable when various hydrazine compounds were reacted with retinal. Many hydrazone-type derivatives of retinal were prepared and their physical properties, stability, toxicity and biopotency were examined.

All such derivatives are more stable than vitamin A palmitate, their toxicity being low, and some of them showed considerably higher vitamin A activity.

Retinal azine is obtained as crystals of m.p. 189° in a good yield when retinal is reacted with hydrazine-hydrate in the presence of an organic acid as a promotor. This compound is expected to have higher biological activity. *p*-Aminobenzoylhydrazone of retinal showed the biopotency equivalent to that of vitamin A.

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## 147. Issei Iwai and Junya Ide : Studies on Acetylenic Compounds. XXIII.*2 A New Ring Closure of 2-Propynyl Ethers.

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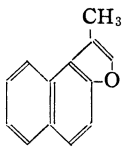
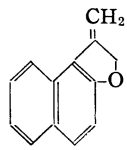
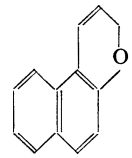
In the previous paper of this series, Okajima[1] reported the Claisen rearrangement of 3-phenoxy-1-propyne (I) and 3-(2′-naphthyloxy)-1-propyne (II). The Claisen rearrangement[2] of (I) had been investigated by Powell and Adams,[3] but no definite substance could be isolated either by refluxing diisopentyl ether (b.p. 170°) solution of (I) or by boiling (I) without solvent. Okajima reinvestigated the rearrangement of (I) in various conditions, but any definite substance was not obtained. On the other hand, by heating (II) at 208° for 20 minutes, he obtained only a small amount of pale yellow needles, m.p. 180°. Considering the naphthoic activity, he suggested one of the following structures for this compound from the results of elemental analysis and infrared spectrum :



(III)



(IV)



(V)

But a quantity of the sample was so small that he could not determine its structure.

In this paper, authors intend to clarify the chemical behavior of 3-(1′ or 2′-naphthyloxy)-1-propyne which are expected to give phenolic compounds by the Claisen rearrangement.

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*2 Part XXII. Y. Yura : This Bulletin, **10**, 376 (1962).
1) Y. Okajima : Yakugaku Zasshi, **80**, 315 (1960).
2) D.S. Tarbell : Org. Reactions **2**, Chap. 1 (1944).
3) S.G. Powell, R. Adams : J. Am. Chem. Soc., **42**, 652 (1920).

Sometimes, the solvents such as paraffin oil, tetralin, kerosene, N,N-dimethylaniline and N,N-diethylaniline were employed for the Claisen rearrengement.[3] These solvents often reduce a polymerized product, and especially basic solvents such as N,N-dimethyl- and N,N-diethyl-aniline give better yield comparing with hydrocarbons.

For the first time the rearrangement of (II) was carried out in N,N-dimethylaniline (b.p. 193°) under refluxing, and since almost of all starting material was recovered even by prolonged heating (3 hours), N,N-diethylaniline (b.p. 215~216°) was employed as a solvent in place of N,N-dimethylaniline. The solution was refluxed for 40 minutes and then benzene was added to the reaction mixture. After removal of N,N-diethylaniline with 5% hydrochloric acid, the benzene solution was extracted with 5% sodium hydroxide solution. Any phenolic substance, however, was not given from the alkaline extracts. By chromatographic purification of the residue obtained from benzene solution furnished white plates of m.p. 41~41.5° (A). The result of the elemental analysis of the crystals was in agreement with a calculated values for $C_{13}H_{10}O$, and its infrared spectrum showed no absorptions of triple bond, ethynyl group and hydroxyl group. The ultraviolet absorption maximum shifted to more bathochromic comparing with that of a starting material as shown in Fig. 1. In the presence of platinum dioxide, (A) was catalytically hydrogenated to give colorless oil of $b.p_{0.0001}$ 100~110° (bath temp.) after the absorption of 1 mole equivalent of hydrogen, which solidified on standing, m.p. 38.5~39.5° (B). The absorption maximum of the ultraviolet spectrum of (B) shifted to hypsochromic[4] in comparison with that of (A) as shown in Fig. 1.

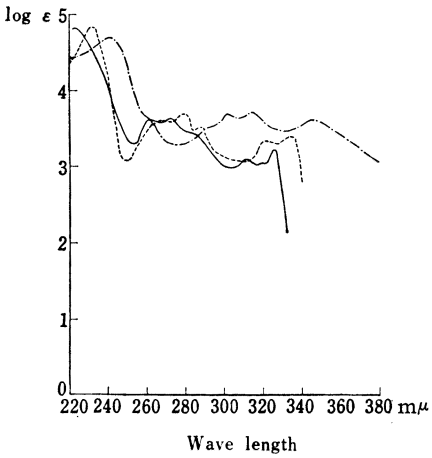
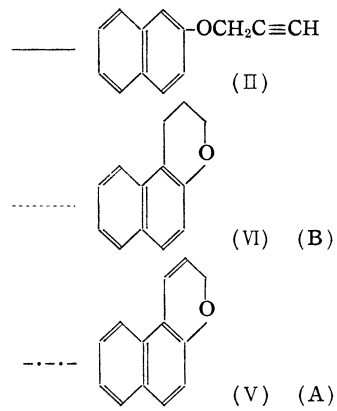
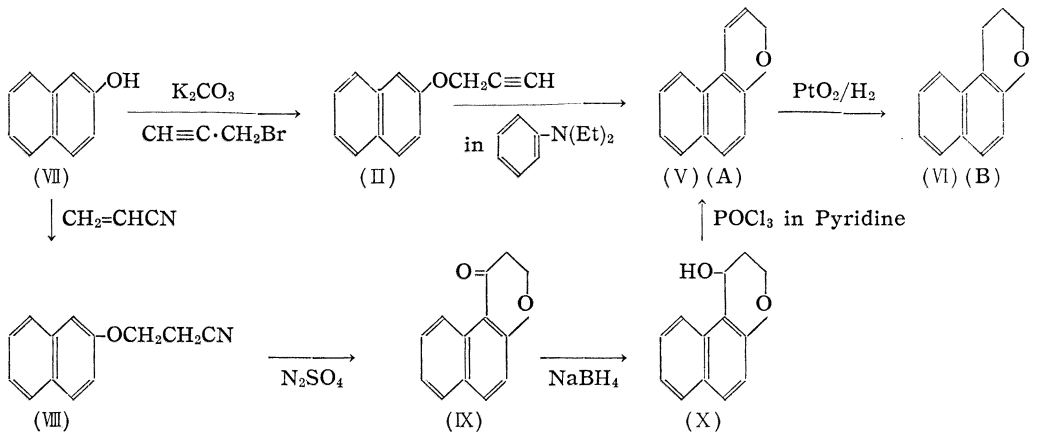



Fig. 1.




From these results, it was supposed that ring-closure reaction occurred and an unsaturated bond adjacent to a naphthalene nucleus was newly formed. On the other hand, 1-methyl-naphtho[2,1-*b*]furan (III), m.p. 59°, was already synthesized by Stoemer,[5] but the characteristics of (A) were quite different from those of (III). Moreover, if (A) was 1-methylene-1,2-dihydronaphtho[2,1-*b*]furan (IV), (A) would be changed into (III) by treating with mineral acid, but (III) was not obtained by this treatment from (A). Therefore, the most probable structure for (A) appeared to be 3*H*-naphtho[2,1-*b*]pyran (V), which was shythesized by the following route :

4) R. A. Friedel, M. Orchin : "Ultraviolet Spectra of Aromatic Compounds" John Wiley & Sons, Inc. (1951).
5) R. Stoemer : Ann., **312**, 491 (1900).

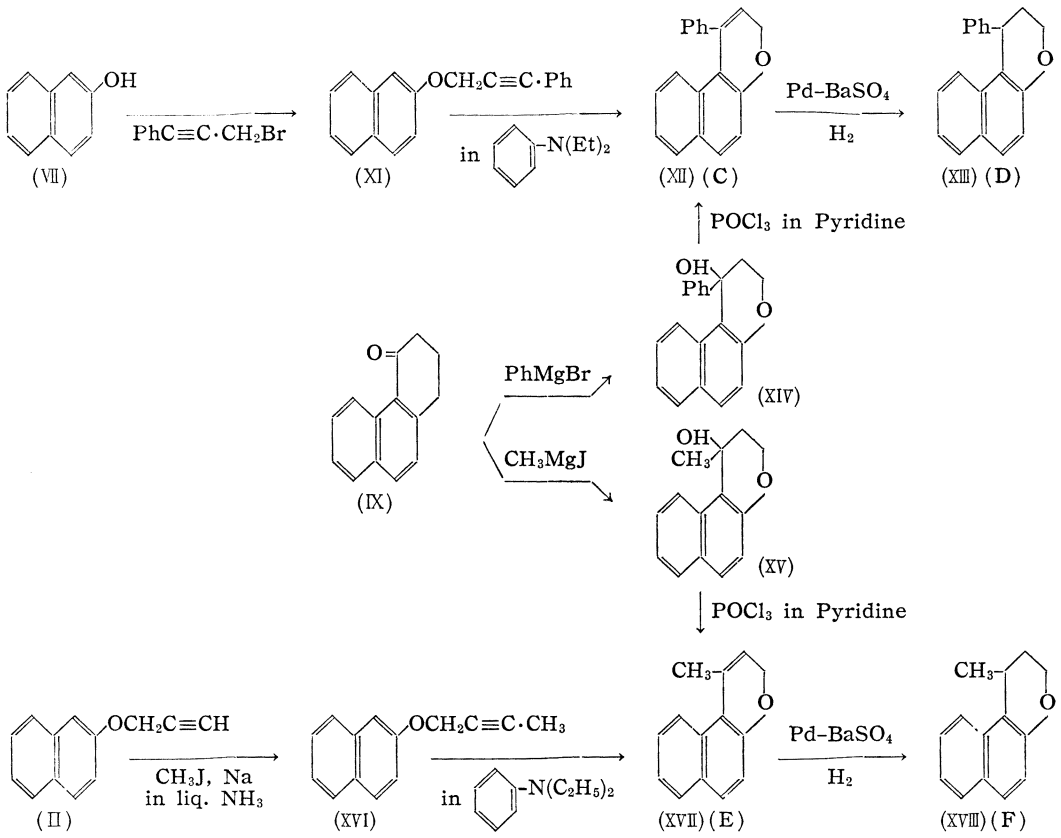



2,3-Dihydro-1*H*-naphtho[2,1-*b*]pyran-1-one (IX) was prepared according to the method of Levine, *et al.*[6] (IX) was reduced to 2,3-dihydro-1*H*-naphtho[2,1-*b*]pyran-1-ol, m.p. 108° (X) with sodium borohydride. The structure of (X) was confirmed by elemental analysis and the infrared spectrum. Dehydration of (X) with phosphorous oxychloride in pyridine produced colorless needles of m.p. 40~41° (V) which showed no absorption of hydroxyl group in the infrared spectrum and no depression in melting point on admixture with (A). Moreover, the infrared and ultraviolet spectra of (V) and (A) were coincided each other. From these results, it was concluded that (II) did not undergo the expected Claisen rearrangement but the ring-closure reaction to give (V). The compound (V), however, is different from the substance of m.p. 180° which has been obtained by Okajima from (II) by heating without solvent.

Furthermore, this type of the reaction was also examined on methyl and phenyl derivatives of (II). 1-Phenyl-3-(2′-Naphthyloxy)-1-propyne which was prepared from 2-naphthol and 1-phenyl-3-bromo-1-propyne according to the method of Okajima, gave pale orange needles (C), m.p. 118~119° in good yield (95%) by refluxing in N,N-diethylaniline. The elemental analysis of the product was in agreement with the caluculated values for $C_{19}H_{14}O$. The compound (C) showed no depression on the mixed melting point with 1-phenyl-3*H*-naphtho[2,1-*b*]pyran (XII) derived from (IX) by the Grignard reaction followed by dehydration. Catalytic hydrogenation of (C) over platinum dioxide afforded colorless needles of m.p. 134~135° (D) after the absorption of one equivalent mole of hydrogen. By the results of mixed melting point, infrared and ultraviolet spectra of both compounds. (D) was identified as 1-phenyl-2,3-dihydro-1*H*-naphtho[2,1-*b*]pyran (XIII) which obtained from (XII) by catalytic hydrogenation over platinum dioxide.

Similarly, refluxing diethylaniline solution of 1-(2′-naphthyloxy)-2-butyne (XVI) m.p. 69~70° which was prepared from sodium acetylide of (II) by methylation with methyl iodide in liquid ammonia, gave a pale yellow oil, (E) $b.p._{0.05}$ 104~112° (bath temp.). The infrared and ultraviolet spectra of (E), whose analytical values corresponded to $C_{14}H_{12}O$, were identical with that of 1-methyl-3*H*-naphtho[2,1-*b*]pyran (XVII), prepared from (IX) by the same procedure as (XII) employing methylmagnesium iodide in place of phenylmagnesium bromide. The catalytic hydrogenation of (E) over palladium-barium sulfate furnished colorless plates (F) m.p. 59~60° after the absorption of one mole equivalent of hydrogen. The elemental analysis of (F) was in agreement with the calculated values for $C_{14}H_{14}O$, which showed no depression in melting point with 1-methyl-2,3-dihydro-1*H*-naphtho[2,1-*b*]pyran (XVIII) obtained by catalytic hydrogenation of (XVII).

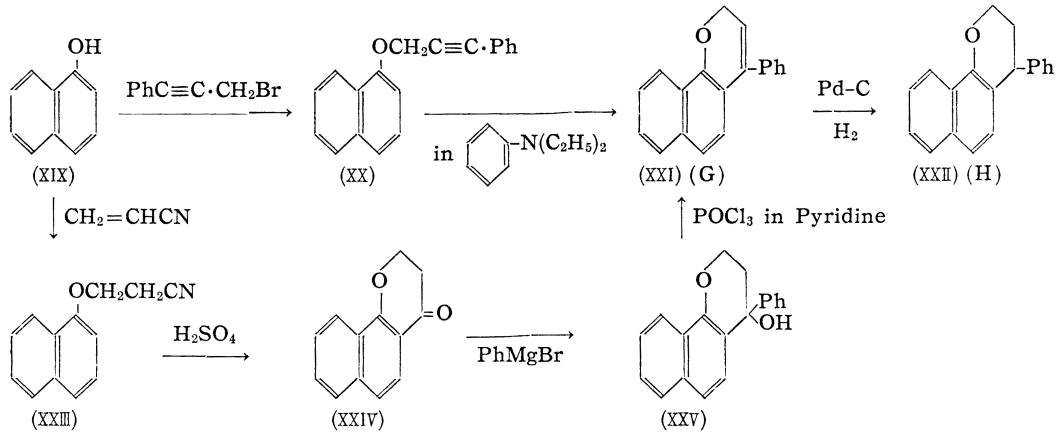
6) A. Levine, G. Bryant : J. Am. Chem. Soc., **69**, 2341 (1947).




Furthermore, the similar reaction of 1-phenyl-3-(1′-naphthyloxy)-1-propyne (XX) was examined. Refluxing of N, N-diethylaniline solution of (XX) gave pale yellow needles of m.p. 97~98° (G) in good yield (70%), whose elemental analysis was in agreement with the calculated values for $C_{19}H_{14}O$. The infrared spectum of (G) showed no absorption of a triple bond and the absorption maxima of ultraviolet spectrum of (G) shifted bathochromically comparing with (XX). Oxidative degradation of (G) with potassium permanganate afforded phthalic acid and benzoic acid. Therefore, the ring-closure must occur to 2-position but not to $\alpha'$-position of naphthalene nucleus.

On the other hand, 4-phenyl-2*H*-naphtho[1,2-*b*]pyran (XXI) was synthesized by another route. There are many reports[7~9] concerning to the preparation of 2,3-dihydro-4*H*-naphtho[1,2-*b*]pyran-4-one (XXIV). In this case, (XXIV) was prepared from 1-naphthol (XIX) by cyanoalkylation followed by treating with sulfuric acid according to the method of Colonre, *et al.*[10] An authentic sample of (XXI) was synthesized from (XXIV) by Grignard reaction and followed by dehydration. The compound (G) showed no depression in melting point on admixture with (XXI). The infrared and ultraviolet spectra of both compounds superimposed to each other. Catalytic hydrogenation of (G) over palladium-carbon catalyst afforded dihydro compound (H) of m.p. 99~100° which was identified as 4-phenyl-3,4-dihydro-2*H*-naphtho[1,2-*b*]pyran (XXII) of m.p. 100~100.5° obtained by hydrogenation of (XXI).

7) P. Pfeiffer, J. Grimmer : Ber., **50**, 921~924 (1917).
8) St. von Kostonecki, G. Froemsdorff : Ber., **35**, 860 (1902).
9) D. Chakravato, J. Dutta : J. Indian Chem. Soc., **16**, 639 (1939).
10) J. Colonre, A. Guyot : Bull. soc. chim. France, **1958**, 325 (1958).




Propargyl ethers of 2-naphthol was expected to give 1-substituted 2-naphthol derivatives by the Claisen rearrangement caused by naphthoid activity, same as the case of allylic ether of 2-naphthol. On the contrary to our expectation, the former compounds give 3*H*-naphtho[2,1-*b*]pyran derivatives. And it is found that phenyl propargyl ether of 1-naphthol also gives 2*H*-naphtho[1,2-*b*]pyran derivatives.

From these results, it is concluded that the derivatives of naphthyl propargyl ether undergo a new ring-closure reaction to give naphthopyran derivatives. The yield of 1-phenyl-3*H*-naphtho[2,1-*b*]pyran from the corresponding ether exceeded to that of 4-phenyl-2*H*-naphtho[1,2-*b*]pyran from the corresponding 1-naphthyl ether. This fact wolud be resulted by $\delta^-$-effect of carbon-atom due to the naphthoid activity.

## Experimental*3

**3*H*-Naphtho[2,1-*b*]pyran (V) from (II)**——A solution of 5 g. of 2-naphthyl 2-propynyl ether (I) in 20 cc. of N,N-diethylaniline was refluxed for 40 min. To the dark red colored reaction mixture was added 20 cc. of benzene, and washed with 5% HCl. The benzene solution was washed with $H_2O$ and dried over $Na_2SO_4$. Concentration under reduced pressure gave a brown gummy substance which was taken up in benzene and chromatographed over Walen neutral alumina (grade II). From benzene eluate were obtained 1.93 g. (40%) of pale yellow needles m.p. 40~41.5°, which recrystallized from EtOH to m.p. 41~41.5°. *Anal.* Calcd. for $C_{13}H_{10}O$ : C, 85.69; H, 5.53; O, 8.78. Found : C, 85.96; H, 5.61; O, 8.43. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 242 (4.66), 261 (3.64) (shoulder), 290 (3.51) (shoulder), 301 (3.66), 314 (3.69), 347 (3.59).

**3*H*-Naphtho[2,1-*b*]pyran (V) from (X)**——To a solution of 3 g. of (X) in 40 cc. of pyridine was added dropwise 13 cc. of $POCl_3$ with stirring under cooling with ice-water. After the addition, the reaction mixture was boiled under refluxing for 1 hr., and poured into 100 g. of crushed ice after cooling. The precipitate was filtered and a recrystallized from 95% EtOH to give pale yellow needles, m.p. 40.5~41.5° (2 g., 66%). *Anal.* Calcd. for $C_{13}H_{10}O$ : C, 85.69; H, 5.53; O, 8.78. Found: C, 85.69; H, 5.61; O, 8.70. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 242 (4.69), 261 (3.63) (shoulder), 291 (3.49) (shoulder), 301 (3.67), 314 (3.67), 348 (3.61).

**2,3-Dihydro-1*H*-naphtho[2,1-*b*]pyran (VI)**——A solution of 1.333 g. of 3*H*-naphtho[2,1-b]pyran (V) in 20 cc. of EtOH was shaken in $H_2$ at an ordinary pressure over 200 mg. of $PtO_2$ and 227 cc. of $H_2$ uptake was observed (90% of calcd. amount at 27°) for 30 min. After removal of the catalyst, the solvent was distilled under reduced pressure. The colorless oily residue, $b.p_{0.0006}$ 100~110° (bath temp.), was crystallized to give white needles, m.p. 38.5~39.5. *Anal.* Calcd. for $C_{13}H_{12}O$ : C, 84.75; H, 6.57; O, 8.68. Found : C, 84.81; H, 6.78; O, 8.41. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 233 (4.85), 258 (3.45) (shoulder), 268 (3.61), 278 (3.69), 289 (3.57), 320 (3.34), 334 (3.39).

**2,3-Dihydro-1*H*-naphtho[2,1-b]pyran-1-one (IX)**——Starting from 300 g. of 2-naphthol, 120 g. of white powder, m.p. 44~45°, was obtained according to the method of Levine *et al.*[6] *Anal.* Calcd.

*3 All m.p.s are uncorrected.

for $C_{13}H_{10}O_2$ : C, 77.98; H, 6.04; O, 15.98. Found : C, 77.63; H, 6.01; 16.36. O, UV $\lambda_{max}^{EtOH}$ mμ (log ε): 221 (4.52), 236 (4.34) (shoulder), 264 (3.94), 311 (3.89), 344 (3.68). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$ : 1675 (=CO).

**2,3-Dihydro-1*H*-naphtho[2,1-*b*]pyran-1-ol (X)**——A solution of 20.0 g. of (IX) and 1.843 g. of $NaBH_4$ in 125 cc. of EtOH was allowed to stand at room temperature for 15 hr. After the excess $NaBH_4$ was decomposed with AcOH, almost EtOH was removed under reduced pressure. The residue was poured into crushed ice and white precipitate appeared was filtered and recrystallized from $CCl_4$ to give white needles, m.p. 109~109.5° (18 g.). *Anal.* Calcd. for $C_{13}H_{12}O_2$ : C, 77.98; H, 6.04; O, 15.98. Found : C, 77.76; H, 6.13; O, 16.11. IR $\nu_{max}^{CCl_4}$ : 3300~3400 $cm^{-1}$ (OH). UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 231 (4.80), 257 (3.45) (shoulder), 265 (3.59), 276 (3.66), 287 (3.54), 318 (3.28), 333 (3.38).

**1-Phenyl-3-(2′-naphthyloxy)-1-propyne (XI)**——A solution of 20 g. of 1-phenyl-3-bromo-1-propyne, 15 g. of 2-naphthol and 15 g. of $K_2CO_3$ in 80 cc. of $Me_2CO$ was boiled under reflux for 8 hr. After cooling an inorganic substance was filtered, $Et_2O$ was added to the filtrate and washed successively with 5% NaOH solution, water, and dried over $Na_2SO_4$. The removal of $Et_2O$ afforded 19 g. of viscous oil which solidified on scratching. Recrystallization from petr. benzin gave colorless powder, m.p. 92~93°. *Anal.* Calcd. for $C_{19}H_{14}O$ : C, 88.34; H, 5.46; O, 6.20. Found : C, 88.40; H, 5.75; O, 5.85. IR $\nu_{max}^{CCl_4}$ : 2230 $cm^{-1}$ (-C≡C-). UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 225 (5.15), 272 (4.06), 312 (3.40), 318 (3.39), 327 (3.57).

**1-Phenyl-3*H*-naphtho[2,1-*b*]pyran (XII) from (XI)**——A solution of 2 g. of (XI) in N,N-diethylaniline (40 cc.) was boiled under reflux for 4.5 hr. After removal of N,N-diethylaniline under reduced pressure, 100 cc. of $Et_2O$ was added to the residue and washed succesively with 5% HCl, 5% NaOH, solution, water and dried over $Na_2SO_4$. The removal of $Et_2O$ gave brown viscous oil (1.9 g.) which solidified on scratching. Recrystallization from 99% EtOH afforded pale orange needles m.p. 118~119°. *Anal.* Calcd. for $C_{19}H_{14}O$ : C, 88.34; H, 5.46; O, 6,20. Found : C, 87.77; H, 5.40; O, 6.83. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 244 (4.57), 302 (3.69), 313 (3.70), 345 (3.65).

**1-Phenyl-3*H*-naphtho[2,1-*b*]pyran (XII) from (XIV)**——To a solution of 2.5 g. of (XIV) in 35 cc. of dehyd. pyridine was added dropwise 10 cc. of $POCl_3$ with stirring under cooling with ice-water. The reaction mixture was refluxed for 1.5 hr. After cooling, it was poured into 80 g. of crushed ice. The precipitate was filtered and recrystallized from 95% EtOH to pale orange needles, m.p. 118~119°. *Anal.* Calcd. for $C_{19}H_{14}O$ : C, 88.34; H, 5.46; O, 6.20. Found : C, 88.14; H, 5.91; O, 5.95. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 224 (4.58), 301 (3.70), 313 (3.72), 345 (3.64).

**1-Phenyl-2,3-dihydro-1*H*-naphtho[2,1-*b*]pyran (XIII)**——A solution of 500 mg. of 1-phenyl-3*H*-naphtho[2,1-*b*]pyran (XII) in 20 cc. of EtOH was shaken in $H_2$ at an ordinary pressure over 66 mg. of $PtO_2$ and 47 cc. of $H_2$ uptake was observed (99.9% of calcd. amount at 25.5°) for 20 min. After removal of the catalyst, the solvent was distilled off under reduced pressure to give a viscous residue. A treatment of it with charcoal gave colorless needles, m.p. 134~135° (from EtOH). *Anal.* Calcd. for $C_{19}H_{16}O$ : C, 87.66; H, 6.15; O, 6.19. Found : C, 87.88; H, 6.33; O, 5.97. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 234 (4.81), 258 (3.58) (shoulder), 267 (3.71), 277 (3.45), 289 (3.67), 320 (3.42), 334 (3.54).

**1-Phenyl-2,3-dihydro-1*H*-naphtho[2,1-*b*]pyran-1-ol (XIV)**——To the Grignard solution prepared from 3.9 g. of Mg and 15.7 cc. of bromobenzene in 70 cc. of dehyd. $Et_2O$ was added dropwise 26.0 g. of (IX) in 80 cc. of dehyd. $Et_2O$ under cooling with ice-water during 40 min. Then the reaction mixture was refluxed for 3 hr. with continuous stirring. After cooling the reaction mixture was decomposed with sat. $NH_4Cl$ solution, the organic layer was separated and the aqueous layer was extracted with $Et_2O$. The combined organic layer washed successively with 5% HCl, 10% $NaHCO_3$ and water until neutral to litmus, and dried over $Na_2SO_4$. The evaporation of $Et_2O$ under reduced pressure and recrystallization from $CCl_4$ gave white powder, m.p. 159~160°. *Anal.* Calcd. for $C_{19}H_{16}O_2$ : C, 82.57; H, 5.86; O, 11.57. Found : C, 82.64; H, 5.58; O, 11.78. IR $\nu_{max}^{CCl_4}$ : 3500 $cm^{-1}$ (OH).

**4-(2′-Naphthyloxy)-2-butyne (XVI)**——4.1 g. of Na was added in small pieces to 200 cc. of liq. $NH_3$ and then 28.0 g. of 3-(2′-naphthyloxy)-1-propyne (II) in 100 cc. of dehyd. $Et_2O$ was added dropwise. After stirring 1.5 hr. at −40°, 28.4 g. of MeI in 100 cc. of $Et_2O$ was added dropwise during 40 min. The reaction mixture was stirred for 4 hr. at −45° and 9 g. of $NH_4Cl$ was added in many portions, and allowed to stand overnight under cooling by dry ice-$Me_2CO$. Liq. $NH_3$ was allowed to evaporate at room temperature under continuous stirring. The reaction mixture was poured into 60 g. of crushed ice, the organic layer was separated and the aqueous layer was extracted with $Et_2O$. The combined extract was washed successively with dil. $H_2SO_4$, 10% $NaHCO_3$ solution and water until neutral to litmus and dried over $Na_2SO_4$. The solvent was distilled under reduced pressure. The residue solidified on cooling and scratching. Recrystallization three times from 99% EtOH gave thin yellow needles, m.p. 69~70°, yield, 6 g. *Anal.* Calcd. for $C_{14}H_{12}O$ : C, 85.68; H, 6.16; O, 8.16. Found : C, 85.63; H, 6.21; O, 8.12. IR $\nu_{max}^{CCl_4}$ : 2240 $cm^{-1}$ (-C≡C-). UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 226 (4.76), 254 (3.38) (shoulder), 262 (3.50), 271 (3.54), 282 (3.37) (shoulder), 313 (3.03), 319 (2.98), 327 (3.15).

**1-Methyl-3*H*-naphtho[2,1-*b*]pyran (XVII) from (XVI)**—— The solution of 2.0 g. of 4-(2′-naphthyloxy)-2-butyne (XVI) in 40 cc. of dehyd. N,N-diethylaniline was boiled under reflux for 4 hr. and solvent was removed under reduced pressure. The residue was dissolved in 30 cc. of $Et_2O$ and was washed

successively with 5% HCl, 10% $NaHCO_3$ solution, water and dried over $Na_2SO_4$. After removal of the solvent under reduced pressure, the vacuo distillation gave a pale yellow oil, b.$p_{0.015}$ 104~112° (bath temp.) (49%). *Anal.* Calcd. for $C_{14}H_{12}O$ : C, 85.68; H, 6.16; O, 8.16. Found : C, 85.92; H, 5.93; O, 8.15. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 243 (4.65), 282 (3.61) (shoulder), 301 (3.68), 312 (3.57), 346 (3.64).

**1-Methyl-3*H*-naphtho[2,1-*b*]pyran (XVII) from (XV)**——To a solution of 5 g. of 1-methyl-2,3-dihydro-1*H*-naphtho[2,1-b]pyran-1-ol (XV) in 35 cc. of dehyd. pyridine was added dropwise 13 cc. of $POCl_3$ under cooling with ice-water. Then the reaction mixture was refluxed for 3 hr. and poured into 80 g. of crushed ice and extracted with $Et_2O$. The ethereal solution was washed successively with 5% $H_2SO_4$, water and dried over $Na_2SO_4$. After removal of $Et_2O$, the residue was submitted to vacuo distillation to give a pale yellow oil, b.$p_{0.02}$ 105~110° (bath temp.). *Anal.* Calcd. for $C_{14}H_{12}O$: C, 85.68; H, 6.16; O, 8.16. Found : C, 85.58; H, 6.04; O, 8.38. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 243 (4.71), 291 (3.63) (shoulder), 301 (3.74), 311 (3.64) (shoulder), 347 (3.71).

**1-Methyl-2,3-dihydro-1*H*-naphtho[2,1-*b*]pyran (XVIII)**——A solution of 503 mg. of (XVII) in 20 cc. of EtOH was shaken in $H_2$ at an ordinary pressure over 500 mg. of Pd-$BaSO_4$ and 600 cc. of $H_2$ was absorbed (96% of calcd. amount at 25°). After removal of the catalyst, the solvent was distilled off. After standing overnight, the residue solidified. Recrystallization of it from EtOH gave colorless needles, m.p. 59~60°. *Anal.* Calcd. for $C_{14}H_{14}O$ : C, 84.81; H, 7.12; O, 8.17. Found : C, 84.72; H, 7.29; O, 7.99. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 233 (4.85), 258 (3.46) (shoulder), 267 (3.63), 277 (3.70), 288 (3.58), 320 (3.33), 334 (3.42).

**1-Methyl-2,3-dihydro-1*H*-naphtho[2,1-*b*]pyran-1-ol (XV)**——To the Grignard solution prepared from 4 g. of Mg and 25.6 g. of MeI in 90 cc. of dehyd. $Et_2O$ was added dropwise 32.7 g. of (IX) in 120 cc. of dehyd. $Et_2O$ during 1.5 hr. and the reaction mixture was stirred for 3 hr. and decomposed with sat. $NH_4Cl$ solution. The usual process and recrystallization from $CCl_4$ furnished white needles, m.p. 117~118°. *Anal.* Calcd. for $C_{14}H_{14}O$ : C, 78.48; H, 6.59; O, 14.93. Found : C, 78.79; H, 6.59; O, 14.62. IR $\nu_{max}^{CCl_4}$ : 3540 $cm^{-1}$ (OH). UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 232 (4.83), 256 (3.53), 266 (3.64), 277 (3.70), 288 (3.58), 306 (3.09) (shoulder), 318 (3.36), 332 (3.39).

**1-Phenyl-3-(1′-naphthyloxy)-1-propyne (XX)**——A solution of 20 g. of 1-phenyl-3-bromo-1-propyne, 15 g. of 1-naphthol and 16 g. of $K_2CO_3$ in 90 cc. of $Me_2CO$ was refluxed for 10 hr. After cooling and filtering inorganic substance, the filtrate was evaporated, and the residue was dissolved in 90 cc. of $Et_2O$ and washed successively with 5% NaOH solution and water and then dried over $Na_2SO_4$. The solvent was evaporated and the residue was chromatographed on alumina. From petr. ether-benzene (10:1) there was obtained 18 g. of colorless prisms, m.p. 65.6~66.5°. *Anal.* Calcd. for $C_{19}H_{14}O$ : C, 88.34; H, 5.46; O, 6.20. Found : C, 88.46; H, 5.47; O, 6.07. IR $\nu_{max}^{CCl_4}$ : 2240 $cm^{-1}$ (-C≡C-). UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 231 (4.65), 282 (3.78), 290 (3.79), 305 (3.54) (shoulder), 320 (3.25).

**4-Phenyl-2*H*-naphtho[1,2-*b*]pyran (XXI) from (XX)**——A solution of 2 g. of (XX) in 40 cc. of N,N-diethylaniline was refluxed for 4.5 hr. and the solvent was distilled under reduced pressure. The residue was dissolved in 100 cc. of $Et_2O$ and washed successively with 5% HCl, 5% NaOH solution and water, and dried over $Na_2SO_4$. Evaporation of the solvent and treatment with charcoal gave crude solid, which was recrystallized from EtOH to afford colorless plates, m.p. 97~98 (50%). *Anal.* Calcd. for $C_{19}H_{14}O$ : C, 88.34; H, 5.46; O, 6.20. Found : C, 88.36; H, 5.56; O, 6.08. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 226 (4.65), 248 (4.51) (shoulder), 262 (4.43), 271 (4.42), 328 (3.57) (shoulder), 338 (3.61), 352 (3.56).

**4-Phenyl-3,4-dihydro-2*H*-naphtho[1,2-*b*]pyran (XXII)**——A solution of 360 mg. of (XXI) in 8 cc. of EtOH was shaken in $H_2$ at an ordinary pressure over 100 mg. of Pd-$BaSO_4$ and 34.5 cc. of $H_2$ uptake was observed (100.8% of calcd. amount at 25.5°) for 35 min. After removal of the catalyst, the solvent was distilled under reduced pressure. The residue solidified on standing overnight, which was recrystallized from petr. ether to give colorless needles, m.p. 99~100. *Anal.* Calcd. for $C_{19}H_{16}O$: C, 87.66; H, 6.15; O, 6.19. Found : C, 87.86; H, 6.07; O, 6.07. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 239 (4.70), 263 (3.43) (shoulder), 270 (3.53) (shoulder), 288 (3.70) (shoulder), 296 (3.73), 311 (3.62), 325 (3.51).

**2,3-Dihydro-4*H*-naphtho[1,2-*b*]pyran-4-one (XXIV)**——Starting from 100 g. of 1-naphthol, 12 g. of white plates, m.p. 104~105 (from EtOH) were obtained by the method of Colonre and Guyot[10], *Anal.* Calcd. for $C_{13}H_{10}O_2$ : C, 78.77; H, 5.09; O, 16.14. Found : C, 78.83; H, 5.35; O, 15.92. IR $\nu_{max}^{CCl_4}$ :1680 $cm^{-1}$ (C=O). UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 252 (4.57), 260(4.14), 280 (3.91), 290 (3.92), 348 (3.70) (shoulder), 358 (3.74).

**4-Phenyl-2*H*-naphtho[1,2-*b*]pyran (XXI) from (XXIV) via (XXV)**——The compound (XXV) was prepared from (XXIV) by the same procedure as of (XIV). But crude substance was only given, and this substance seemed to be a mixture of (XXV) and dehydrated substance of (XXV). IR $\nu_{max}^{CCl_4}$ : 3500 $cm^{-1}$ (OH).

To a solution of 2 g. of crude (XXV) in 35 cc. of dehyd. pyridine was added dropwise 10 cc. of $POCl_3$ with stirring under ice-cooling. Then the reaction mixture was refluxed for 2 hr. the same process as 1-phenyl-3*H*-naphtho[2,1-*b*]pyran and recrystallization from EtOH gave 1.4 g. of colorless plates of m.p. 96.5~97.5. *Anal.* Calcd. for $C_{19}H_{14}O$ : C, 88.34; H, 5.46; O, 6.20. Found : C, 88.36; H, 5.56; O, 6.08. UV $\lambda_{max}^{EtOH}$ mμ (log ε) : 226 (4.74), 248 (4.58) (shoulder), 262 (4.49), 271 (4.37), 328 (3.65) (shoulder), 338 (3.68), 350 (4.62).

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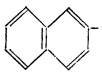
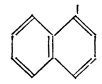
## Summary

It has been reported that 2-naphthyl allylic ethers undergo the Claisen rearrangement to give naphthol derivatives. 2-naphthyl propargyl ether derivatives,  -O·$CH_2C{\equiv}C$-R (R=H, $CH_3$, Ph.), replacing the double bond of allylic ethers by a triple bond, do not undergo the Claisen rearrangement but a new ring-closure to give 3*H*-naphtho[2,1-*b*]pyran derivatives. Moreover, 1-naphthyl derivatives, 
also undergo the same ring-closure to give 4-phenyl-2*H*-naphtho[1,2-*b*]pyran. The structures of new pyran derivatives obtained by the new ring-closure were confirmed by the melting point, infrared and ultraviolet spectra of the authentic samples which were synthesized by another routes.

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**148. Takanobu Itai and Shigeru Sako :** Potential Anti-cancer Agents. V. 3,6-Disubstituted 4-Nitropyridazine 1-Oxides and their Derivatives.

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On the nitration of 3-methoxy- and 3,6-dimethoxy-pyridazine 1-oxides had been reported by Itai and Igeta,[1] Igeta,[2,3] and by Nakagome.[4] In our third paper[5] of this series, syntheses of 3,6-dialkoxy-4-nitropyridazine 1-oxides and their anti-cancer actions were reported. Synthesis of 3-alkoxy-6-chloropyridazine 1-oxides were given in our fourth paper.[6] Now, nitration of 3-methoxy- and 3-hydroxy-6-chloropyridazine 1-oxides and reactions of their products will be reported in this paper.

On hydrolysis of 3-methoxy-6-chloropyridazine 1-oxide (Ia) with 5% sodium hydroxide, 6-chloro-3-pyridazinol 1-oxide (Ib) was produced. Nitration of these two compounds was carried out with sulfuric acid-nitric acid at 50°, which occurred rather easily, but was more difficult than for 3-methoxy- or 3,6-dimethoxypyridazine 1-oxides. As nitration did not occur of 3-methoxypyridazine, it was clear that contribution of

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6) *Idem* : *Ibid.*, **10**, 989 (1962).