other acids (**6e**: R^1=H, R^2=Me, R^3=Ts; and **6f**: R^1=R^2=Me, R^3=Ts) was analogously possible from the corresponding Grignard products (**2e** and **2f**), the intermediate such as **13** being conceivable during the course of the hydrolysis. Synthesis of the N-sulfonyl-1,2,3,4-tetrahydroisoquinoline derivatives (**14**) from **6** was accomplished by means of dicyclohexylcarbodiimide as shown in Table I, and among them, **14d** (R^1=R^2=H, R^3=Ms) was the model compound for the successful Wittig reaction on the N-sulfonyl lactam grouping,[6] aiming at the functionalization of the lactam-carbonyl in the six-membered ring.

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6) M. Natsume, M. Takahashi, K. Kiuchi, and H. Sugaya, *Chem. Pharm. Bull.* (Tokyo), **19**, 2648 (1971).

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Formation of 3-Cyano-1,4-dihydroquinolines and Their Conversion to Indole Derivatives

In order to extend our knowledge about the formation of stable dihydro heteroaromatic amines and to develop their application to the field of synthetic chemistry, we have taken up the quinoline series and at first refer to the Grignard reaction of 3-cyanoquinoline[1] (**1a**) and its alkyl derivative (**1b**), position of the cyano group in which corresponds to that of 4-cyanoisoquinolines reported in another paper.[2]

Two reaction sites, C-2 and C-4 positions, are conceivable in the quinolines, but the Grignard reaction proceeded exclusively at C-4 to afford a single product, though the dihydro addition product (**2**) was not so stable as that of isoquinoline derivatives, and it was necessary to convert **2** immediately either to the alkylated quinolines (**1b**,[3] mp 144—144.5°; **1c**, mp 77—78°; 68% and 72% yields from **1a**) by dehydrogenation with chloranil or to the N-tosyl derivatives (**3a**, mp 130—131°, 30% from **1a**; **3b**, mp 174—175.5°, 8% yield from **1b**), the latter being obtainable only by tosylation with powdered potassium hydroxide in hexamethylphosphoric triamide.[4] The position where the reaction took place was proved by the transformation of **1b** to lepidine (**4**) by alkaline hydrolysis of the cyano function, followed by decarboxylation. In contrast to obtaining **3b** in a poor yield due to the extremely unstable character of **2b**, it was quite surprising and inexplicable at the present time to realize that the dihydro product (**2c**), mp 140—141° was stable enough to be isolated in 57% yield and further methylated, benzoylated, or tosylated in a usual manner to form **3c**, mp 80—81.5°, **3d**, mp 126—126.5°, or **3e**, mp 125—126°, in respective yield of 63%, 60.5%, or 53%. The structure of 1,4-dihydroquinoline derivatives thus synthesized was supported by the

1) H.E. Jansen and J.P. Wibaut, *Rec. Trav. Chim.*, **56**, 709 (1937); H. Gilman and S.M. Spatz, *J. Am. Chem. Soc.*, **63**, 1553 (1941); F. Zymalkowski and P. Tinapp, *Ann.*, **699**, 98 (1966).
2) M. Natsume and M. Wada, *Chem. Pharm. Bull.* (Tokyo), **20**, 1589 (1972).
3) L. Marion and R.H.F. Manske, *Can. J. Chem.*, **24B**, 224 (1946).
4) F.L. Hahn and H. Walter [*Ber.*, **54B**, 1531 (1921)] prepared alcohol tosylates by using powdered potassium hydroxide in ether.

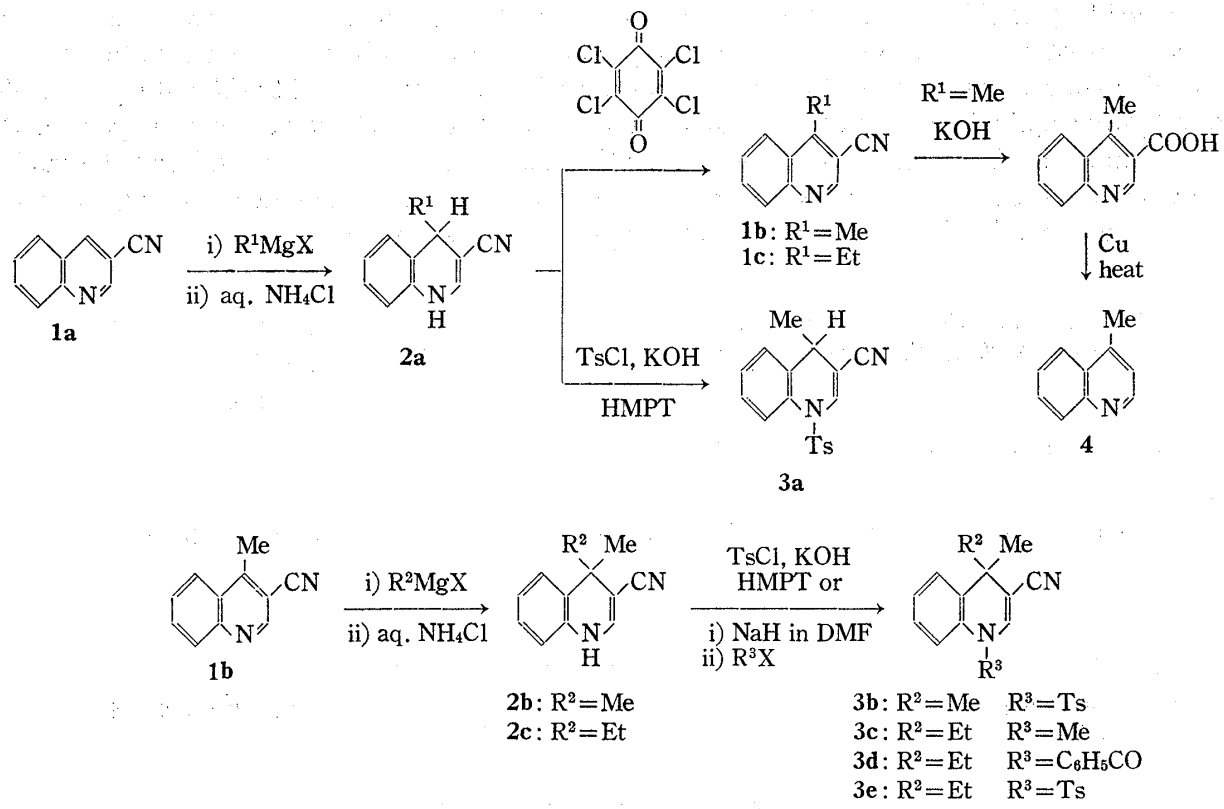

Chart 1

Table I. IR and NMR Spectral Data of 3-Cyano-1,4-dihydroquinolines

	IR (KBr) cm^{-1}		NMR ($CDCl_3$) δ from TMS					
	CN	C=C	2-H	CH_3	4-H	4-CH_3	4-CH_2CH_3	4-CH_2CH_3
2c	2196	1644 3298 (NH)	*a*)	—	—	1.56, s	1.76, q[b)]	0.79, t[b)]
3a	2216	1640	7.58, s	2.40[c)]	3.42, q[b)]	0.94, d[b)]	—	—
3b	2223	1642	7.71, s	2.39[c)]	—	1.27, s	—	—
3c	2195	1643	6.83, s	3.20[d)]	—	1.53, s	1.73, q[b)]	0.75, t[b)]
3d	2210	1644 1688 (CO)	7.71, s	—	—	1.61, s	1.89, q[b)]	0.84, t[b)]
3e	2220	1651	7.81, s	2.37[c)]	—	1.33, s	1.65, q[b)]	0.47, t[b)]

a) in the aromatic protons *b*) J=7 Hz *c*) methyl protons of the tosyl group
d) methyl protons of the N-Me group

infrared (IR) and nuclear magnetic resonance (NMR) spectra as shown in Table I.

The ozonolysis of 3-cyano-1-tosyl-1,4-dihydroquinolines was examined in the hope of ready solvolysis of both acid cyanide and N-formyltosylamide moieties in the anticipated product (**5** or its equivalent) and of making possible the conversion from the quinolines to indole derivatives, which will provide us with a new approach to the synthesis of indole alkaloids from quinolines. The result from **3b** and **3e** exceeded our expectation and 3,3-dialkyl-1-tosyloxindoles (**6b**), mp 133.5—135°, IR ν_{CO}^{KBr} 1758 cm^{-1}, and (**6c**), mp 95—96°, IR ν_{CO}^{KBr} 1758 cm^{-1}, were obtained directly in a high yield by brief bubbling of ozone into the dichloromethane solution of **3b** or **3e** under ice-cooling and subsequent treatment of the ozonide with 5% hydrochloric acid containing methanol under reflux for a short period, and the structure was supported by the alternative transformation, characterizing the α-ketols (**7a**), mp 142—143°, IR ν_{CO}^{KBr} 1718 cm^{-1}, NMR ($CDCl_3$) δ: 6.06 (H at C-2); (**7b**), a syrupy mixture of

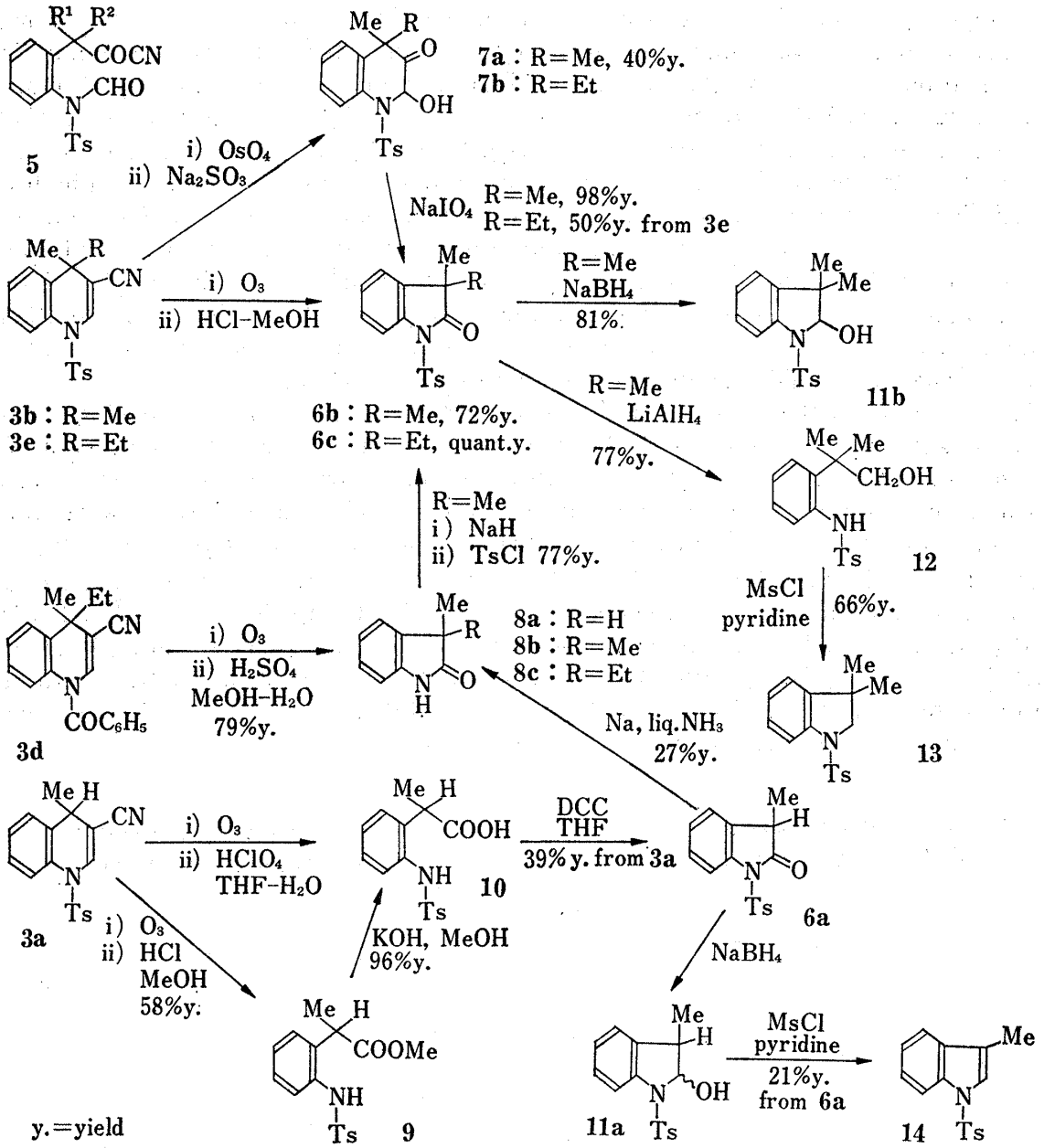

Chart 2

two isomers due to the configuration of the hydroxyl group, at the intermediary stage. The direct comparison of **6b** with the N-tosylated product of 3,3-dimethyloxindole[5] (**8b**) furnished the conclusive evidence for the structure of the ozonolysis product. For the purpose of securing oxindole itself from the quinoline derivative, **3d** was selected as the suitable substrate for the ozonolysis and a similar procedure as above, but not using hydrochloric acid because of the accompanying chlorination at the benzene portion, produced the oxindole derivative (**8c**), mp 142—143°, in a very good yield.

When the same treatment as to **3b** and **3e** was applied to **3a**; an ester (**9**), syrup, IR ν_{max}^{film} cm^{-1}: 3275 (NH), 1740 (CO); NMR ($CDCl_3$) δ: 1.24 (3H, d, J=7 Hz, >CH-C<u>H</u>$_3$), 3.64 (1H, q, J=7 Hz, >C<u>H</u>-CH_3), 3.63 (3H, s, -COOC<u>H</u>$_3$), was found to be the main product in this case, contrary to the direct preparation of the *gem*-dialkyloxindoles. **9** could be hydrolyzed to the corresponding carboxylic acid (**10**), and yet the preparative method for **6a** was achieved

5) K. Brunner, *Monatsh.*, **18**, 98 (1897); *cf. Org. Syntheses*, Collected Vol. 4, 657.

by decomposing the ozonide from **3a** with an acid, avoiding hydrochloric acid, in non-methanolic solvent to afford **10**, which was further cyclized with dicyclohexylcarbodiimide (DCC) in an anhydrous solvent; and the cleavage of N-tosyl group with sodium in liquid ammonia to obtain **8a**[6] proved the structure of **6a**, mp 97—98°, IR ν_{CO}^{KBr} 1758 cm^{-1}; NMR ($CDCl_3$) δ: 1.38 (3H, d, J=7.5 Hz), 2.41 (3H, s, tosyl-C<u>H</u>$_3$), 3.49 (1H, q, J=7.5 Hz). In the case of 3,3-dialkyloxindole derivative, heating a methanolic solution of **6b** with potassium hydroxide did hydrolyze it to produce a salt of the carboxylic acid relating to **10**, whereas the free acid could not exist in the open chain form and **6b** was recovered in 92% yield by acidification, when 3-position of oxindole was occupied by two alkyl groups. This fact implies that the *peri* interaction of these substituents with the hydrogen at C-4 induces the rotation of α, α-dialkylacetic acid side chain to a limited extent so as to make the carboxylic acid close enough to the sulfonamide, producing a spontaneous ring closure.

We next studied the behavior of N-tosyloxindole derivatives toward reducing reagents, mostly to metal hydrides, and a marked difference was observed between sodium borohydride and lithium aluminum hydride by the fact that the former reagent could stop the reduction of **6a** and **6b** partially at the hydroxyl stage to produce **11a**, mp 157—158°, a mixture of two isomers due to the configuration of hydroxyl group, and **11b**, mp 128.5—129°, NMR ($CDCl_3$) δ: 0.90 (3H, s), 1.33 (3H, s), 5.34 (1H, s, >N-C<u>H</u>-OH). On the other hand, the latter hydride reduced **6b** completely to the open chain alcohol (**12**), mp 155—155.5°, NMR ($CDCl_3$) δ: 1.31 (6H, s), 3.69 (2H, s), which formed N-tosylindoline (**13**), mp 126—127.5°, NMR ($CDCl_3$) δ: 1.13 (6H, s), 3.63 (2H, s), during O-mesylation reaction. **11a** was dehydrated with mesyl chloride in pyridine to furnish an indole derivative (**14**), mp 113.5—114°, whose structure was verified by an unequivocal synthesis from skatole.

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