123. *Synthetic Applications of Activated Metal Catalysts.   Part II.**
The Formation of Heterocyclic Diaryls.

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When pyridine is refluxed with a specially prepared Raney nickel catalyst, 2 : 2′-dipyridyl is formed in satisfactory yield.   Similar heterocyclic diaryls are formed from α-picoline, 4-ethylpyridine, nicotinic acid, quinoline, 6-methylquinoline, benzo[*f*]quinoline, and other related compounds.

Raney nickel is here reported as a useful catalyst for the preparation of heterocyclic diaryls.   For example, pyridine, when refluxed with the catalyst, affords 2 : 2′-dipyridyl in useful yield on evaporation (and recovery) of the unchanged base.   As 2 : 2′-dipyridyl and many related heterocyclic diaryls form characteristic metallic chelate compounds, the method should prove of value for the preparation of these valuable reagents.

In the preliminary experiments with pyridine, in which W7 Raney nickel [1] was used, the crude product was dark brown and was obtained only in small yield.   Attempts were therefore made to modify and improve the catalyst for the present purpose, by treating it in various ways to reduce the amount of adsorbed hydrogen.   The most satisfactory catalyst (see Experimental section) was obtained by heating W7 Raney nickel on a steam-bath in a vacuum.   Pyridine was then added to the essentially dry (and pyrophoric) catalyst, with care to exclude air until the nickel had been completely covered.   The addition of hydrogen acceptors (such as acetone and *cyclo*hexanone) to the reaction mixture was without influence on the yield, and a catalyst which had been deactivated with aqueous hydrogen peroxide was much less effective.   Under the best conditions so far found, the crude 2 : 2′-dipyridyl was obtained as pale yellow crystals which could be purified without difficulty.   From the liquors a little 2 : 2′ : 2″-terpyridyl was also obtained.   In some runs a small amount of an insoluble organonickel compound was obtained.   Pyrolysis of this material at atmospheric pressure gave a little volatile material which was identified as 2 : 2′-dipyridyl.   This was also obtained when the organonickel compound was dissolved in warm concentrated hydrochloric acid, and the solution basified.   It may be noted that

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* The paper, *J.*, 1954, 4162, is regarded as Part I.
[1] *Org. Synth.*, 1949, **29**, 24.

similar organonickel compounds were obtained in small quantity when a few other hetero-aromatic compounds were heated with the catalyst, but only when the latter had two free α-positions.

The reaction has also been examined with a number of related ring systems. Quinoline readily gave 2 : 2'-diquinolyl; and benzo[*f*]quinoline (II) gave 3 : 3'-di(benzo[*f*]quinolyl). Some 2 : 2'-di(benzo[*h*]quinolyl) was obtained from benzo[*h*]quinoline (III), but the yield was very poor and it is thought that steric hindrance may be involved here. It seems likely that dimerisation must be preceded by chemisorption of the nitrogen on to the

(I)   (II)   (III)   (IV)   (V)   (VI)
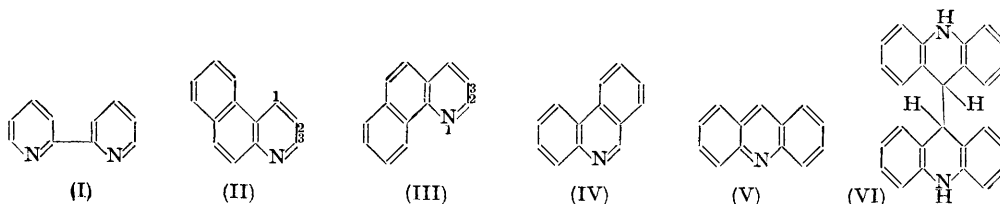
nickel surface (see Discussion below), and the benzo-ring would offer steric hindrance at this stage. Steric hindrance at the subsequent stage of dimerisation may be involved with phenanthridine (IV), for this substance was recovered unchanged. No tetrapyridyl could be obtained when dipyridyl was heated with the catalyst.

With acridine (V), both the α-positions are blocked and this compound gave an apparently anomalous result. Some 9 : 10-dihydroacridine was formed, but 9 : 9' : 10 : 10'-tetrahydro-9 : 9'-diacridinyl (VI) was also obtained. This is the only example of a γγ'-dimerisation which has been found.

*iso*Quinoline decomposed extensively (with evolution of much ammonia) when heated with Raney nickel, and little success could be achieved. When carried out in xylene solution the reaction gave an almost black organonickel product. This was pyrolysed at atmospheric pressure, and the sublimate gave a little 3 : 3'-di*iso*quinolyl.

The reaction has also been investigated with a few substituted derivatives. α-Picoline gave 6 : 6'-dimethyl-2 : 2'-dipyridyl, albeit in poor yield; and collidine was recovered unchanged. An alkyl group in the γ-position seems to have no inhibiting effect, for 4-ethylpyridine gave a very satisfactory yield of 4 : 4'-diethyl-2 : 2'-dipyridyl. No dimer could be obtained from 2-aminopyridine, or from 3 : 5-dibromopyridine. In the latter case it is of interest that dehalogenation did not occur to any extent under the conditions used.

Similar results were obtained with two quinoline derivatives : 6-methylquinoline gave 6 : 6'-dimethyl-2 : 2'-diquinolyl in satisfactory yield, but quinaldine was recovered unchanged. In the latter, no free α-position is available, and steric hindrance to chemisorption at the catalyst surface may also be a factor.

Nicotinic acid was also dimerised in aqueous sodium carbonate to give a dicarboxydi-pyridyl, probably 5 : 5'-dicarboxy-2 : 2'-dipyridyl. Similarly, in xylene solution, ethyl nicotinate gave a diethoxycarbonyldipyridyl, probably 5 : 5'-diethoxycarbonyl-2 : 2'-dipyridyl. In this case a little of an organonickel compound was also formed, which on hydrolysis with alcoholic potassium hydroxide gave 5 : 5'-dicarboxy-2 : 2'-dipyridyl.

Discussion.—The literature [2] records several methods for the preparation of 2 : 2'-di-pyridyl by heating pyridine with various catalysts; but it is unlikely that the present method involves a simple dehydrogenation. The experimental conditions are mild, a temperature of about 115—150° being involved. It has also been found that platinised asbestos does not catalyse the formation of dipyridyl from pyridine even on 48 hours' refluxing, and it seems that the adsorbed hydrogen on the nickel catalyst must be essential to the reaction.

Pyridine and similar heteroaromatic compounds are known to be catalyst " poisons "

[2] *E.g.*, (*a*) Willink and Wibaut, *Rec. Trav. chim.*, 1935, **54**, 275; (*b*) Wibaut, Willink, and Nieuwenhuis, *ibid.*, p. 804; Hein and Retter, *Ber.*, 1928, **61**, 1790; Morgan and Burstall, *J.*, 1932, 20.

in hydrogenation reactions [3] and it seems to be accepted that such compounds use the nitrogen " lone pair " to form a covalent bond with the catalyst.[4] It is reasonable to suppose that such a bond is formed as the first stage in the present reaction. It is significant that the reaction proceeds only to a small extent when the approach to the nitrogen atom is sterically hindered, as in benzo[*h*]quinoline (III).

It is tentatively suggested that the next step may involve the addition of one atom of hydrogen (presumably to the nitrogen) to give a radical with a free valency at the α- or γ-position. When two such free radicals are formed sufficiently close to one another on the catalyst surface, then overlap of the singly occupied atomic orbitals can occur only at the α-positions. In this way a tetrahydrodiaryl would be formed, and this would be expected to lose hydrogen rather easily to give the observed diaryls. Diaryls are not formed from heteroaromatic compounds (collidine, quinaldine) in which the α-positions are blocked. Similarly no diaryl was formed from phenanthridine, and in this case the close approach of two molecules at the α-positions is hindered by the adjacent benzene rings. In the case of acridine (in which both α-positions are blocked) steric hindrance presumably weakens the nitrogen–catalyst bond, and the tetrahydrodiaryl must be formed *in solution* and not on the surface of the catalyst. This tetrahydrodiaryl is, of course, considerably more stable than the tetrahydrodiaryls postulated as intermediates in other cases.

<div align="center">EXPERIMENTAL</div>

Preparation of Catalyst.—Nickel–aluminium alloy (125 g.) was added in portions to a solution of sodium hydroxide (160 g.) in water (600 c.c.) during 7—10 min. The reaction was carried out in a 2-l. conical flask immersed in an ice-bath and equipped with a very efficient stirrer, to control frothing (no alcohol was added to reduce frothing). The temperature quickly reached 80—85° and, as soon as the addition of alloy was complete, the cooling-bath was removed, stirring being continued to control the frothing. When the temperature began to fall the flask was immersed in a boiling-water bath, gentle stirring being continued for 30 min. The stirrer was then stopped and distilled water (600 c.c.) added. The supernatant liquid was decanted and the catalyst then washed by decantation with distilled water (8 × 500 c.c.). The wet catalyst was then transferred to a 3-necked flask fitted with a condenser (closed at the top with a stopper), a dropping funnel, and a connection to the water-pump. The flask was slowly evacuated and warmed on a water-bath, care being taken to avoid losses of catalyst by frothing. After 2 hr. at 100°/*ca.* 20 mm. the flask was removed from the steam-bath. The pyridine (or other heterocyclic derivative) was then added, *via* the dropping funnel, to the evacuated flask, care being taken to avoid access of air until the catalyst had been thoroughly wetted. The stopper was then removed and the mixture refluxed.

Pyridine.—Pyridine (250 c.c.) was refluxed in the presence of nickel catalyst prepared as above. After 11 hr. the catalyst was filtered off (pyrophoric !) and quickly washed with a little hot pyridine. Unchanged pyridine (225 c.c., plus washings) was then removed by distillation, and the residue extracted with boiling light petroleum (b. p. 60—80°). In some runs a small amount (up to 0·5 g.) of an insoluble organonickel compound was removed at this stage. The petroleum solution was purified by passage through a column of alumina, the solvent evaporated, and the resulting product recrystallised from light petroleum (b. p. 40°). The 2 : 2'-dipyridyl (20 g.) formed colourless prisms, m. p. and mixed m. p. 70·5—71·5°.

From sixteen experiments under varying experimental conditions, a yield of 60 g. of dipyridyl was obtained and recrystallised. From the combined mother-liquors a little 2 : 2' : 2″-terpyridyl (1·0 g.) was obtained. After recrystallisation from light petroleum it had m. p. 88° (lit., 88—89°) (Found : C, 77·1; H, 4·7; N, 18·1. Calc. for $C_{15}H_{11}N_3$: C, 77·2; H, 4·75; N, 18·0%).

Quinoline.—Quinoline (100 g.) was refluxed at 12 mm. for 14 hr. with nickel catalyst (from 125 g. of alloy). Removal of the unchanged quinoline gave the crude product (5·0 g.) which was recrystallised once from ethanol. The 2 : 2'-diquinolyl formed colourless plates, m. p. and mixed m. p. 193—194° (lit., 194·5—195·5°).

Benzo[*f*]*quinoline.*—A solution of benzo[*f*]quinoline (47 g.) in sulphur-free xylene (230 c.c.) was refluxed over nickel catalyst (from 125 g. of alloy) for 5 hr. The separated catalyst was washed with boiling xylene (500 c.c.), after which the combined filtrates were concentrated to

[3] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446; Elsner and Paul, *J.*, 1953, 3156.
[4] Maxted, *Adv. Catalysis*, 1951, **3**, 129.

250 c.c. The pale yellow crystals which separated (2·0 g.) were collected and recrystallised from xylene. 3 : 3′-Di(*benzo*[f]*quinolyl*) formed pale yellow needles, m. p. 300° (Found : C, 87·55; H, 4·7; N, 8·0. C₂₆H₁₆N₂ requires C, 87·6; H, 4·5; N, 7·9%). It gave a yellow solution in mineral acid and its xylene solution showed a blue fluorescence. The addition of cuprous ions to its solution in ethanol gave a chelate compound of the same colour as that given by 2 : 2′-di-quinolyl.

Benzo[h]*quinoline.*—A solution of benzo[*h*]quinoline (35 g.) in xylene (170 c.c.) was refluxed with nickel catalyst (from 92 g. of alloy) for 12 hr. The crude product (0·1 g.) was recrystallised from xylene. The resulting 2 : 2′-di(*benzo*[h]*quinolyl*) formed pale yellow needles, m. p. 280° (Found : C, 87·25; H, 4·7; N, 8·0. C₂₆H₁₆N₂ requires C, 87·6; H, 4·5; N, 7·9%). It gave a yellow solution in mineral acids, and its xylene solution showed a blue fluorescence. It did not form a chelate compound with cuprous ions under conditions in which di(benzo[*f*]quinolyl) does.

Acridine.—A solution of acridine (75 g.) in xylene (200 c.c.) was refluxed with nickel catalyst (from 150 g. of alloy) for 5 hr. The mixture became yellow at once and a white precipitate soon appeared. This was collected together with the catalyst, and washed with boiling xylene (200 c.c.). Concentration of the combined filtrates gave 9 : 10-dihydroacridine (9 g.) which, after recrystallisation from ethanol, had m. p. 171—173° (lit., 172—173°). It was identified by oxidation with aqueous potassium dichromate and sulphuric acid to acridine, m. p. 109—110°. The filtrate from this material was evaporated to dryness and the residue chromatographed in light petroleum (b. p. 60—80°) on alumina. In this way a little acridine (2·0 g.), m. p. 110°, was recovered.

The contaminated catalyst was extracted for 3 days (Soxhlet) with pyridine. Filtration of the cooled extract gave 9 : 9′ : 10 : 10′-tetrahydro-9 : 9′-diacridinyl (12 g.). Lehmstedt and Hundertmark's method [5] gave material of m. p. 247—248° (lit., 249°, for higher-melting isomeride). It was characterised by treatment with sulphuric acid to give 1 : 2-di-(2-diphenylyl-amino)ethylene oxide, which after recrystallisation from ethanol had m. p. 165° (Lehmstedt and Hundertmark [5] given m. p. 165°). On evaporation of the pyridine a dark residue was obtained which on chromatography gave acridine (5 g.), m. p. 109—110°. Re-examination of the catalyst showed that it still contained a considerable amount of tetrahydrodiacridinyl.

iso*Quinoline.*—A solution of redistilled *iso*quinoline (100 g.) in xylene (70 c.c.) was refluxed over nickel catalyst (from 125 g. of alloy) for 5 hr., considerable evolution of ammonia being noted. Evaporation of the filtrate (70 g. of *iso*quinoline recovered) gave a dark organonickel product which was pyrolysed (dull red heat) at atmospheric pressure. Extraction of the sublimate with benzene, and purification of the extract by chromatography on alumina, gave 3 : 3′-di*iso*quinolyl (0·10 g.). After recrystallisation from benzene it had m. p. 195—196° (lit., 197—198°), and gave an intense orange chelate compound with ferrous ion in agreement with the literature.[6] (1 : 1′-Di*iso*quinolyl has m. p. 162—163° and does not form a chelate compound.)

α-*Picoline.*—The redistilled base (230 c.c.) was refluxed for 8 hr. with a catalyst (from 125 g. of alloy). After recrystallisation from light petroleum (b. p. 40°) the 6 : 6′-dimethyl-2 : 2′-di-pyridyl (0·85 g.) had m. p. 88—90° (Willink *et al.*[2a] give 89·5—90·5°). The picrate had m. p. 167—169° (lit., 170—171°).

4-*Ethylpyridine.*—The base (100 g.) was refluxed with catalyst (from 125 g. of alloy) for 17 hr. After removal of unchanged 4-ethylpyridine the residue was dissolved in benzene, a small amount (0·85 g.) of an organonickel compound being removed. The benzene extract yielded 4 : 4′-*diethyl*-2 : 2′-*dipyridyl* (15 g.), b. p. 210°/30 mm., m. p. 38—40° (Found : C, 79·2; H, 7·4; N, 13·4. C₁₄H₁₆N₂ requires C, 79·2; H, 7·6; N, 13·2%). With ferrous ions it gave a chelate compound having the same colour as that from dipyridyl.

Phenanthridine, Collidine, 2-Aminopyridine, Quinaldine, 3 : 5-Dibromopyridine and 2 : 2′-Di-pyridyl.—These compounds gave no dimeric product when refluxed with the catalyst.

6-*Methylquinoline.*—The base (97 g.) was refluxed (at 20 mm.) with the catalyst (from 125 g. of alloy) for 14 hr. The resulting 6 : 6′-*dimethyl*-2 : 2′-*diquinolyl* (2 g.), recrystallised from benzene, formed colourless needles, m. p. 267° (Found : C, 84·1; H, 5·7; N, 9·95. C₂₀H₁₆N₂ requires C, 84·4; H, 5·7; N, 9·85). With cuprous ions it gave a chelate compound having the same colour as that from diquinolyl.

Sodium Nicotinate.—A solution of nicotinic acid (50 g.) in water containing a slight excess of sodium carbonate was refluxed for 8 hr. with the nickel catalyst (from 125 g. of alloy). There was a slight evolution of ammonia. After filtration, the catalyst was repeatedly extracted with

[5] Lehmstedt and Hundertmark, *Ber.*, 1930, **63**, 1229.
[6] Case, *J. Org. Chem.*, 1952, **17**, 471.

hot aqueous sodium carbonate. The filtrate was neutralised, and the resulting precipitate purified by dissolution in sodium carbonate and reprecipitation with acid. A much less soluble acid (1·0 g.) was separated from the unchanged nicotinic acid during this purification. It was further purified by several dissolutions in alkali and reprecipitations with acid. 5 : 5'(?)-*Dicarboxy-2 : 2'-dipyridyl* was obtained as a white amorphous powder, m. p. >400° (Found : C, 59·0; H, 3·3; N, 11·4; O, 26·5. $C_{12}H_8O_4N_2$ requires C, 59·0; H, 3·3; N, 11·5; O, 26·2%). It was soluble in acids and bases, but insoluble in all common organic solvents. It could not be sublimed at 300°/0·01 mm. When suspended in ethanol it gave no chelate compound with ferrous ions, presumably because of its insolubility. Pyrolysis at a dull red heat gave 2 : 2'-dipyridyl, identified by comparison with an authentic specimen. (Willink *et al.*[2a] give m. p. 268—269° for 3 : 3'-dicarboxy-2 : 2'-dipyridyl.)

Ethyl Nicotinate.—A solution of the ester (53 g.) in xylene (220 c.c.) was refluxed over the catalyst (from 125 g. of alloy) for 21 hr. The catalyst was removed and washed with ethanol, and the ethanol removed from the combined filtrates by distillation. After being kept overnight the colourless product was collected and recrystallised from ethanol. 5 : 5'(?)-*Diethoxycarbonyl-2 : 2'-dipyridyl* (4·85 g.) formed colourless needles, m. p. 148—149° (Found : C, 64·3; H, 5·4; N, 9·4. $C_{16}H_{16}O_4N_2$ requires C, 64·0; H, 5·4; N, 9·3%). It gave a purple chelate compound with ferrous ions.

The unchanged ethyl nicotinate (30 g.) was removed by distillation, and the residue extracted with boiling benzene. After chromatography, the benzene extract yielded a further 0·25 g. of the diester. The benzene-insoluble portion (2·75 g.) was an organonickel compound, which at a dull red heat gave a small amount of volatile organic material, which gave a positive ferroin reaction. Another portion was boiled with ethanolic potassium hydroxide and filtered. The resulting residue was soluble in mineral acid and gave a positive test for nickel with dimethylglyoxime. The light brown filtrate was treated with charcoal and then neutralised to give dicarboxy-2 : 2'-dipyridyl, identical with that obtained above.