Alkylation of Pyridine-3,5-dicarboxamide and Pyridine-3,5-dicarbonitriles by Radical Substitution

Nobuhiro Kanomata, Hisashi Nagahara and Masaru Tada*

Department of Chemistry, School of Science and Engineering, Waseda University, Shinjuku-ku, Tokyo 169, Japan

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Structural modification of NAD(P) model compounds, *N,N,N',N'*-tetramethylpyridine-3,5-dicarboxamide (**1**), pyridine-3,5-dicarbonitrile (**2**), and 4-methylpyridine-3,5-dicarbonitrile (**3**), have been explored by the reaction with alkyl radicals such as the 1-adamantyl, *tert*-butyl, and isopropyl radicals. The alkyl substitutions of compounds **1**, **2**, and **3** with the 1-adamantyl and the *tert*-butyl radical gave both 2-mono and 2,6-disubstitution products, whereas the reaction of compound **2** with the isopropyl radical gave 2-mono **6c**, 2,4-di **7c**, 2,6-di **8c**, and 2,4,6-trisubstitution **9c** products.

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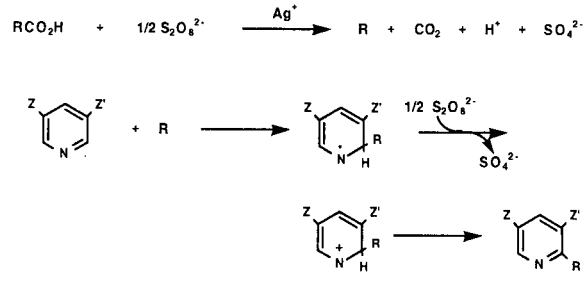
Minisci and his coworkers demonstrated that pyridine and quinoline derivatives react with an alkyl or an acyl radical in a nucleophilic manner to give the corresponding substitution products under acidic conditions [1]. We have also reported radical alkylation on the π-deficient nitrogen heterocycles such as pyridine-3-carboxamide [2], pyrazine-2,3-dicarbonitrile, and lumazine [3] (Scheme I). Pyridine-3-carboxamide plays a central role in the coenzyme NAD(P) of biological redox systems [4]. Chemical modification of the pyridine ring by bulky alkyl groups is of interest since it affords a variation in the model compound of NAD(P). The bulky substituent may interfere with the planarity of the multi-substituted pyridine ring and alter its redox characteristics. To get more insight on the alkyl modification of the pyridine ring, we tried radical alkylation of *N,N,N',N'*-tetramethylpyridine-3,5-dicarboxamide (**1**), pyridine-3,5-dicarbonitrile (**2**) [5], and 4-methylpyridine-3,5-dicarbonitrile (**3**) [6]. Those pyridine derivatives are expected to have higher reactivity to the alkyl radical than pyridine-3-carboxamide, since it has been established that the attack of an alkyl radical on *N*-heterocycles proceeds in a nucleophilic manner [1-3].

We performed the reaction of pyridines **1-3** with the 1-adamantyl, the *tert*-butyl, and the isopropyl radical which

Scheme I



was generated by Minisci oxidation [7] of the corresponding alkanoic acids (5 equivalents to **1-3**) by ammonium peroxodisulfate (2 or 4 equivalents to **1-3**) in the presence of a catalytic amount of silver nitrate (see Scheme I), and the results are summarized in Scheme II and Table 1. The reactions were carried out in ethanenitrile-water without the addition of sulfuric acid as conventionally employed by Minisci *et al.* [1]. Nevertheless the reaction mixtures became mildly acidic by the generation of sulfuric acid during the course of the reactions (see Scheme I). The reaction of alkyl radicals with compounds **1-3** having amide or cyano groups afforded alkyl substituted pyridines without hydrolysis under these reaction conditions.

Scheme II

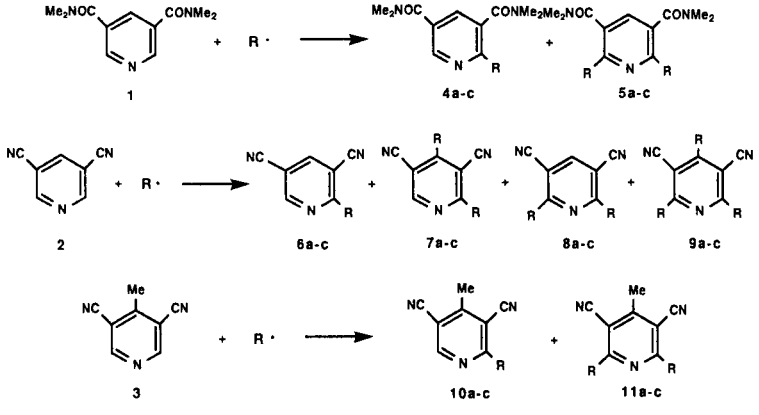


Table 1

Product Yields from the Reaction of Pyridines **1-3** with Alkyl Radicals

Starting Material	R	$[S_2O_8^{-2}]$/[1]-[3]	Product/Yield (%)		Total Yield (%)
1	Ad	2.0	**4a**/91	**5a**/ 8	99
1	Ad	4.0	**4a**/13	**5a**/44	57
1	*t*-Bu	2.0	**4b**/ 6	---	6
1	*t*-Bu	4.0	**4b**/39	---	39
1	*i*-Pr	2.0	**4c**/45	**5c**/26	71
1	*i*-Pr	4.0	**4c**/26	**5c**/47	73
2	Ad	4.0	--- ---	**8a**/76 ---	76
2	*t*-Bu	4.0	**6b**/48 ---	**8b**/38 ---	86
2	*i*-Pr	4.0	**6c**/ 7 **7c**/36	**8c**/24 **9c**/13	70
3	Ad	2.0	**10a**/58	**11a**/16	74
3	Ad	4.0	---	**11a**/73	73
3	*t*-Bu	2.0	**10b**/70	**11b**/ 1	71
3	*t*-Bu	4.0	**10b**/60	**11b**/24	84
3	*i*-Pr	2.0	**10c**/60	**11c**/14	74
3	*i*-Pr	4.0	**10c**/50	**11c**/35	85

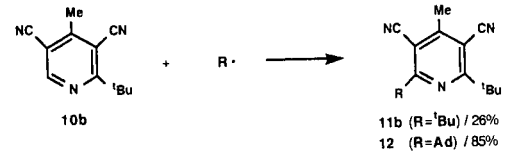
Structural assignment of the substitution products was made straight forwardly on the basis of the characteristic ^{1}H-nmr spectroscopic data (see Experimental). The ^{1}H-nmr spectra of the products replaced the signals due to the aromatic hydrogens with the signals due to the alkyl substituents.

The reaction of the 1-adamantyl radical with compounds **1-3** afforded the 2-(1-adamantyl)pyridines **4a** and **10a** and 2,6-di(1-adamantyl)pyridines **5a**, **8a**, and **11a**. Pyridines **1-3** afforded 2,6-disubstitution products rather than 2,4-disubstitution products. This result can be accounted for by the intrinsically higher reactivity of the 2 as well as the 6-position and the large steric requirement of the adamantyl radical for the narrow space of the 4-position. Evidently, compounds **2** and **3** are more reactive than compound **1** because of the greater steric space at the 4-position and the greater electronegative properties of the cyano group. Thus the reaction of **1** with excess amounts of the adamantyl radical gave only the 2,6-disubstitution products **5a**. The reactivity of the *tert*-butyl radical is lower as compared to the 1-adamantyl radical. The reaction of **1** with the *tert*-butyl radical afforded 2-*tert*-butylpyridines **4b** in at the most 39% yields, and no disubstitution product was obtained. In contrast pyridine-3,5-dicarbonitriles **2** and **3** gave both 2-(*tert*-butyl)- **6b** and **10b** and 2,6-di(*tert*-butyl)pyridines **8b** and **11b** in good yield. The reaction of compounds **1-3** with the isopropyl radical gave 2-monosubstitution products **4c**, **6c**, and **10c** and 2,6-disubstitution products **5c**, **8c**, and **11c**. In addition, the reaction of **2** with the isopropyl radical gave 2,4-disubstitution product **7c** and 2,4,6-trisubstitution products **8c** and **9c**.

The efficiency of radical substitution onto pyridines was rationalized by both steric and electronic effects of the π-deficient heteroaromatics and of the alkyl radicals. Ionization potentials of alkyl radicals decreases in the order of isopropyl, *tert*-butyl, and the 1-adamantyl radical [8], and the energy of the lowest SOMO level must increase in the opposite order. This feature is responsible for the high reactivity of the 1-adamantyl radical. However, the reaction of the *tert*-butyl radical with compound **1** afforded substitution products in lower yield than the isopropyl radical. This feature is accounted for by the dissipation of the *tert*-butyl radical such as liberation of the *tert*-butyl cation from the sterically crowded intermediate adduct (see Scheme I) and generation of isobutylene from the *tert*-butyl radical before the addition onto pyridine rings. Pyridine-3-carboxamide reacted with the *tert*-butyl radical to give 6-(*tert*-butyl)pyridine-3-carboxamide exclusively [2], and the same case also applies to pyridine-3,5-dicarbonitrile (**1**). Thus the cyano group in **2** and **3** brings about stronger reactivity with less steric hindrance and more electronegativity than the amide group. Unexpectedly, the 1-adamantyl radical which seems to have similar steric bulkiness as the *tert*-butyl radical showed the highest reactivity, which indicates superior activation by the SOMO level, and also shows the lack of radical dissipation by hydrogen elimination as seen in the *tert*-butyl radical.

Pyridine-3,5-dicarbonitriles **2** and **3** behave as good radicophiles since they are activated by two cyano groups. Considering that disubstitution proceeds stepwise, the first alkylation onto compounds **2** and **3** takes place to considerable extent, thus the total yields of mono- and dialkylation products are high (70-86%). Since a cyano group is sterically compact enough to allow an alkylation on both the 2 and 6-positions, the ease of the second substitution on pyridines seem to be affected by the SOMO level of the attacking radical. Actually 2-*tert*-butyl-4-methylpyridine-3,5-dicarbonitrile (**10b**) reacted with the 1-adamantyl radical to give 2-(1-adamantyl)-6-*tert*-butyl-4-methylpyridine-3,5-dicarbonitrile (**12**) in 85% yield (Scheme III), but the reaction of **10b** with the *tert*-butyl radical afforded the di-*tert*-butyl derivative **11b** only in 26% yield with a recovery of **10b** in 66% yield. The reaction of the isopropyl radical with compound **2** took place both at the 2- (6-) and the 4-positions. The substitution at the 4-position of compound **2** becomes feasible since the isopropyl radical has a lower steric requirement, and the total yield of products **7c** and **9c** (49%) exceeds the total yield of **6c** and **8** (31%).

Scheme III



In conclusion, radical alkylation of pyridine derivatives having an amide group at the 3- and 5-positions gave 2-mono or 2,6-disubstitution products. The pyridine-3,5-dicarbonitrile derivatives are more reactive than the corresponding amide derivatives, and the reaction with the isopropyl radical gave 2-mono, 2,4-di, 2,6-di, and 2,4,6-trisubstitution products. The amide group activates the pyridine ring to a lesser extent due to a larger steric requirement and less electronegative character, whereas the cyano group activates the pyridine ring by acting in opposition wth regard to those a steric and electronic features. Among 1-adamantyl, *tert*-butyl, and isopropyl radicals, the adamantyl radical is the most reactive due to its high level of SOMO. The *tert*-butyl radical is reactive to a sterically non-crowded site as seen in the alkylation onto the 2- as well as the 6-position of compounds **2** and **3**.

EXPERIMENTAL

The ir spectra were recorded on a Perkin-Elmer 1600 spectrometer. The ^{1}H-nmr spectra were recorded on a JEOL PMX60si (60 MHz) and chemical shifts are given in ppm (δ) relative to tetramethylsilane. Mass spectra and high-resolution mass spectra were measured by a Shimadzu GCMS QP-1000 and a JEOL JMS-DX300 spectrometer respectively. Melting points were measured by a Gallenkamp melting point apparatus and were not corrected. Elemental analyses were performed at the Science and Engineering Research Laboratory of Waseda University. Pyridine-3,5-dicarbonitrile [5], and 4-methylpyridine-3,5-dicarboxylic acid [6] were prepared by the reported procedures.

Preparation of *N,N,N',N'*-Tetramethylpyridine-3,5-dicarboxamide (**1**).

To a suspension of pyridine-3,5-dicarbonyl dichloride [9] (2.03 g, 10 mmoles) in chloroform (40 ml) was added a 40% aqueous solution of dimethylamine (20 ml) at 0° in a nitrogen atmosphere, and the reaction mixture was vigorously stirred for 4 hours in an ice-water bath. The reaction mixture was then allowed to separate into chloroform and aqueous layers, and the latter layer was extracted with chloroform. The combined organic layer was washed with brine and aqueous sodium bicarbonate. After evaporation of the solvent *in vacuo*, the crude product **1** (0.96 g) was obtained in 40% yield.

Compound **1** was recrystallized from ethanol-hexane and melted at 120-122°; ir (chloroform): 2990, 1645, 1410, 1210 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 3.06 (12H, broad s), 7.80 (1H, t, J = 2.0 Hz), 8.07 (2H, d, J = 2.0 Hz); ms: (20 eV) m/z (relative intensity) = 221 (M$^+$, 100%).

Anal. Calcd. for $C_{11}H_{15}N_3O_2$: C, 59.71; H, 6.83; N, 18.99. Found: C, 59.45; H, 6.77; N, 18.92.

General Procedure for the Reaction of Pyridine Derivatives **1-3** with Alkyl Radicals.

To a solution of **1-3** (0.5 mmole), alkanoic acid (2.5 mmoles), and silver nitrate (0.1 or 0.2 mmole) in a 1:1 mixture of ethanenitrile-water (1 ml) was added dropwise an aqueous solution (0.5 ml) of ammonium peroxodisulfate (1.0 or 2.0 mmole) under nitrogen at 80°. After further stirring for 2 hours at 80°, the reaction mixture was treated with concentrated aqueous ammonia (0.5 ml) and extracted with chloroform. The extract was washed with saturated aqueous sodium bicarbonate, dried over sodium sulfate, and concentrated *in vacuo*. The residue was separated by preparative tlc on silica gel plates to give the alkylated products. The solvent system for the separation and further purification procedure are described in the paragraph of the following section. Some products including minor ones were difficult to purify for satisfactory elemental analyses (< 0.4%), but those were essentially pure from analytical tlc and ^{1}H-nmr spectroscopic analyses. High resolution mass spectral data for molecular ions were obtained for those products. Yields of the products are summarized in Table 1.

The Reaction of *N,N,N',N'*-Tetramethylpyridine-3,5-dicarboxamide (**1**) with the 1-Adamantyl Radical.

N,N,N',N'-Tetramethyl-2-(1-adamantyl)pyridine-3,5-dicarboxamide (**4a**) and *N,N,N',N'*-tetramethyl-2,6-di(1-adamantyl)pyridine-3,5-dicarboxamide (**5a**) were separated by preparative tlc on silica gel with ethanol-ethyl acetate (1:5).

Compound **4a** was recrystallized from ethanol and decomposed at 296-297°; ir (chloroform): 2909, 1628, 1596 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.65-1.92 (6H, m), 1.93-2.10 (9H, m), 2.83 (3H, s), 3.07 (6H, s), 3.11 (3H, s), 7.44 (1H, d, J = 2.1 Hz), 8.68 (1H, d, J = 2.1 Hz); ms: (20 eV): m/z (relative intensity) = 355 (M$^+$, 100%).

Mass Calcd. for $C_{21}H_{29}N_3O_2$: m/z = 355.2260. Found: m/z = 355.2286.

Compound **5a** was recrystallized from ethanol and decomposed at 288-291°; ir (chloroform): 2907, 1624, 1586 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.63-1.92 (12H, m), 1.97-2.22 (18H, m), 2.55 (6H, s), 3.08 (6H, s), 7.00 (1H, s); ms: (20 eV) m/z (relative intensity) = 489 (M$^+$, 60%), 354 (100%).

Mass Calcd. for $C_{31}H_{43}N_3O_2$: m/z = 489.3355. Found: m/z = 489.3337.

The Reaction of Pyridine-3,5-dicarbonitrile (**2**) with 1-Adamantyl Radical.

2,6-Di(1-adamantyl)pyridine-3,5-dicarbonitrile (**8a**) was isolated by column chromatography on silica gel using chloroform-hexane (1:1) as an eluent. The compound was recrystallized from benzene-ethanol (1:1) and melted at 250-252°; ir (chloroform): 2908, 2230, 1584 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.61-1.94 (12H, m), 1.94-2.31 (18H, m), 7.97 (1H, s); ms: (20 eV) m/z (relative intensity) = 397 (M$^+$, 100%).

Anal. Calcd. for $C_{27}H_{31}N_3$: C, 81.57; H, 7.86; N, 10.57. Found: C, 81.92; H, 7.93; N, 10.43.

The Reaction of 4-Methylpyridine-3,5-dicarbonitrile (**3**) with the 1-Adamantyl Radical.

2-(1-Adamantyl)-4-methylpyridine-3,5-dicarbonitrile (**10a**) and 2,6-di(1-adamantyl)-4-methylpyridine-3,5-dicarbonitrile (**11a**) were separated by tlc on silica gel with ether-hexane (1:5).

Compound **10a** was recrystallized from ethanol and melted at 187-188°; ir (chloroform): 2909, 2854, 2236, 1574, 1446 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.72-1.98 (6H, m), 1.98-2.39 (9H, m), 2.78 (3H, s), 8.85 (1H, s); ms: (20 eV) m/z (relative intensity) = 277 (M$^+$, 100%).

Anal. Calcd. for $C_{18}H_{19}N_3$: C, 77.95; H, 6.90; N, 15.15. Found: C, 77.74; H, 7.04; N, 15.01.

Compound **11a** was recrystallized from benzene-ethanol (2:1)

and melted at 273-274°; ir (chloroform): 2907, 2224, 1558 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.67-1.97 (12H, m), 1.97-2.36 (18H, m), 2.74 (3H, s); ms: (20 eV) m/z (relative intensity) = 411 (M^+, 100%).

Anal. Calcd. for $C_{28}H_{33}N_3$: C, 81.71; H, 8.08; N, 10.21. Found: C, 81.42; H, 8.23; N, 10.10.

The Reaction of *N,N,N',N'*-Tetramethylpyridine-3,5-dicarboxamide (**1**) with the *tert*-Butyl Radical.

N,N,N',N'-Tetramethyl-2-*tert*-butylpyridine-3,5-dicarboxamide (**4b**) was isolated by tlc on silica gel with ethanol-ether (1:2). This compound was recrystallized from ethanol and melted at 155-156°; ir (chloroform): 2962, 1632, 1597 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.38 (9H, s), 2.82 (3H, s), 3.03 (3H, s), 3.05 (6H, s), 7.45 (1H, d, J = 1.8 Hz), 8.63 (1H, d, J = 1.8 Hz); ms: (20 eV) m/z (relative intensity) = 277 (M^+, 57%), 164 (100%).

Anal. Calcd. for $C_{15}H_{23}N_3O_2$: C, 64.94; H, 8.36; N, 15.16; m/z = 277.1790. Found: C, 64.52; H, 8.56; N, 14.99; m/z = 277.1835.

The Reaction of Pyridine-3,5-dicarbonitrile (**2**) with the *tert*-Butyl Radical.

2-*tert*-Butylpyridine-3,5-dicarbonitrile (**6b**) and 2,6-di-*tert*-butylpyridine-3,5-dicarbonitrile (**8b**) were separated by tlc on silica gel with ether-hexane (1:10).

Compound **6b** was recrystallized from hexane by cooling the solution and melted at 48-49°; ir (chloroform): 2976, 2244, 1595 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.56 (9H, s), 8.17 (1H, d, J = 1.7 Hz), 8.88 (1H, d, J = 1.7 Hz); ms: (20 eV) m/z (relative intensity) = 185 (M^+, 10%), 170 (100%).

Anal. Calcd. for $C_{11}H_{11}N_3$: C, 71.31; H, 5.99; N, 22.70. Found: C, 71.44; H, 5.96; N, 22.72.

Compound **8b** was recrystallized from ethanol and melted at 133-134°; ir (chloroform): 2974, 2234, 1588 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.52 (18H, s), 8.08 (1H, s); ms: (20 eV) m/z (relative intensity) = 241 (M^+, 28%), 226 (100%).

Anal. Calcd. for $C_{15}H_{19}N_3$: C, 74.64; H, 7.94; N, 17.42; m/z = 241.1579. Found: C, 74.08; H, 7.83; N, 17.24; m/z = 241.1591.

The Reaction of 4-Methylpyridine-3,5-dicarbonitrile (**3**) with the *tert*-Butyl Radical.

2-*tert*-Butyl-4-methylpyridine-3,5-dicarbonitrile (**10**) and 2,6-di-*tert*-butyl-4-methylpyridine-3,5-dicarbonitrile (**11b**) were separated by tlc on silica gel with ether-hexane (1:7).

Compound **10b** was recrystallized from ethanol and melted at 78-79°; ir (chloroform): 2973, 2254, 1570 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.57 (9H, s), 2.82 (3H, s), 8.97 (1H, s); ms: (20 eV): m/z (relative intensity) = 199 (M^+, 52%), 184 (100%).

Anal. Calcd. for $C_{12}H_{13}N_3$: C, 72.63; H, 6.56; N, 20.90. Found: C, 72.33; H, 5.57; N, 21.09.

Compound **5d** was recrystallized from ethanol and melted at 111-112°; ir (chloroform): 2973, 2227, 1562 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.61 (18H, s), 2.77 (3H, s); ms: (20 eV) m/z (relative intensity) = 255 (M^+, 54%), 240 (100%).

Anal. Calcd. for $C_{16}H_{21}N_3$: C, 75.25; H, 8.29; N, 16.46. Found: C, 75.49; H, 8.49; N, 16.26.

The Reaction of 2-*tert*-Butyl-4-methylpyridine-3,5-dicarbonitrile (**10b**) with the 1-Adamantyl Radical.

The reaction conditions and workup procedure are mostly the same as the general procedure for the reaction of **1-3**. 2-(1-Adamantyl)-6-*tert*-butyl-4-methylpyridine-3,5-dicarbonitrile (**12**) was isolated in 85% yield by column chromatography using ether-hexane (1:5) as an eluent. Compound **12** was recrystallized from ethanol and melted at 151-152°; ir (chloroform): 2971, 2908, 2224, 1560 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.50 (9H, s), 1.64-1.92 (6H, m), 1.92-2.33 (9H, m), 2.73 (3H, s); ms: (70 eV) m/z (relative intensity) = 333 (M^+, 100%).

Anal. Calcd. for $C_{22}H_{27}N_3$: C, 79.23; H, 8.17; N, 12.61. Found: C, 79.01; H, 8.33; N, 12.48.

The Reaction of 2-*tert*-Butyl-4-methylpyridine-3,5-dicarbonitrile (**10b**) with the *tert*-Butyl Radical.

The reaction conditions and workup procedure are mostly the same as the general procedure for the reaction of compound **1-3**. Compound **11b** was obtained in 26% yield by tlc on silica gel with ether-hexane (1:7) besides the recovered **10b** (66%).

The Reaction of *N,N,N',N'*-Tetramethylpyridine-3,5-dicarbonitrile (**2**) with the Isopropyl Radical.

N,N,N',N'-Tetramethyl-2-isopropylpyridine-3,5-dicarboxamide (**4c**) and *N,N,N',N'*-tetramethyl-2,6-diisopropylpyridine-3,5-dicarboxamide (**5c**) were separated by tlc on silica gel with ethanol-ethyl acetate (1:2).

Compound **4c** was recrystallized from ethanol-hexane by cooling the solution and melted at 167-168°; ir (chloroform): 1630 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.29 (6H, d, J = 6.0 Hz), 2.77-2.94 (1H, m), 2.83 (3H, s), 3.01 (4H, s), 3.10 (3H, s), 7.44 (1H, d, J = 2.0 Hz), 8.61 (1H, d, J = 2.0 Hz); ms: (70 eV) m/z (relative intensity) = 263 (M^+, 97%), 72 (100%).

Anal. Calcd. for $C_{14}H_{21}N_3O_2$: C, 63.84; H, 8.04; N, 15.96; m/z = 263.1634. Found: C, 63.34; H, 8.25; N, 15.84; m/z = 263.1613.

Compound **5c** was recrystallized from ethanol-hexane by cooling the solution and melted at 160-162°; ir (chloroform): 1632 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.26 (12H, d, J = 6.0 Hz), 2.64-3.00 (2H, m), 2.81 (6H, s), 3.06 (6H, s), 7.17 (1H, s); ms: (70 eV): m/z (relative intensity) = 305 (M^+, 39%), 206 (100%).

Mass Calcd. for $C_{17}H_{27}N_3O_2$: m/z = 305.2103. Found: m/z = 305.2103.

The Reaction of Pyridine-3,5-dicarbonitrile (**2**) with the Isopropyl Radical.

A mixture of isopropyl substituted products was separated by preparative tlc on silica gel with ether-hexane (1:7). The first (the least polar) band from tlc afforded 2,4,6-triisopropylpyridine-3,5-dicarbonitrile (**9c**). The second band included 2,4-diisopropylpyridine-3,5-carbonitrile (**7c**), and 2,6-diisopropylpyridine-3,5-dicarbonitrile (**8c**). The third band afforded 2-isopropylpyridine-3,5-dicarbonitrile (**6c**). A mixture of compounds **7c** and **8c** was further separated by tlc on silica gel with benzene-hexane (1:1).

Compound **6c** was obtained as an oil and boiled at 88.4°/10.9 mm Hg; ir (chloroform): 2975, 2243, 1596 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.33 (6H, d, J = 6.6 Hz), 3.52 (1H, sep, J = 6.6 Hz), 8.03 (1H, d, J = 1.9 Hz), 8.82 (1H, d, J = 1.9 Hz); ms: (20 eV) m/z (relative intensity) = 171 (M^+, 21%), 156 (100%).

Anal. Calcd. for $C_{10}H_9N_3$: C, 70.16; H, 5.30; N, 24.54. Found: C, 69.98; H, 5.27; N, 24.50.

Compound **7c** was recrystallized from hexane by cooling the solution and melted at 51-52°; ir (chloroform): 2976, 2234, 1568 cm^{-1}; ^{1}H-nmr deuteriochloroform): δ 1.36 (6H, d, J = 6.7 Hz), 1.55 (6H, d, J = 7.0 Hz), 3.39-3.86 (2H, m), 8.87 (1H, s); ms: (20 eV) m/z (relative intensity) = 213 (M^+, 40%), 198 (100%).

Anal. Calcd. for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70. Found: C, 73.17; H, 7.17; N, 19.46.

Compound **8c** was recrystallized from hexane by cooling the solution and melted at 46-47°; ir (chloroform): 2974, 2234, 1592 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.34 (12H, d, J = 6.6 Hz), 3.55 (2H, sep, J = 6.6 Hz), 8.07 (1H, s); ms: (20 eV) m/z (relative intensity) = 213 (M^+, 55%), 198 (100%).

Anal. Calcd. for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70. Found: C, 72.91; H, 6.99; N, 19.44.

Compound **9c** was recrystallized from hexane by cooling the solution and melted at 86-87°; ir (chloroform): 2974, 2230, 1562 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.30 (12H, d, J = 6.2 Hz), 1.51 (6H, d, J = 6.9 Hz), 3.56 (2H, sep, J = 6.2 Hz), 3.61 (1H, sep, J = 6.9 Hz); ms: (20 eV): m/z (relative intensity) = 255 (M^+, 37%), 240 (100%).

Mass Calcd. for $C_{16}H_{21}N_3$: m/z = 255.1735. Found: m/z = 255.1726.

The Reaction of 4-Methylpyridine-3,5-dicarbonitrile (**3**) with the Isopropyl Radical.

A mixture of 2-isopropyl-4-methylpyridine-3,5-dicarbonitrile (**10c**) and 2,6-diisopropyl-4-methylpyridine-3,5-dicarbonitrile (**11c**) was separated by tlc on silica gel with ether-hexane (1:4).

Compound **10c** was recrystallized from ethanol and melted at 97-98°; ir (chloroform): 2975, 2234, 1578 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.35 (6H, d, J = 6.6 Hz), 2.76 (3H, s), 3.60 (1H, sep, J = 6.6 Hz), 8.83 (1H, s); ms: (70 eV): m/z (relative intensity) = 185 (M^+, 25%), 170 (100%).

Anal. Calcd. for $C_{11}H_{11}N_3$: C, 71.31; H, 5.99; N, 22.70. Found: C, 71.61; H, 5.90; N, 22.42.

Compound **11c** was recrystallized from hexane and melted at 38-40°; ir (chloroform): 2973, 2229, 1570 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.33 (12H, d, J = 6.2 Hz), 2.72 (3H, s), 3.54 (2H, sep, J = 6.2 Hz); ms: (70 eV) m/z (relative intensity) = 227 (M^+, 27%), 212 (100%).

Anal. Calcd. for $C_{14}H_{17}N_3$: C, 73.96; H, 7.54; N, 18.49. Found: C, 73.91; H, 7.69; N, 18.27.

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