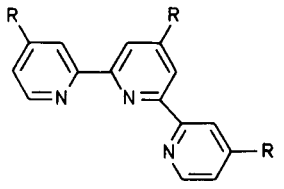
The Synthesis of Some 4,4′,4″-Trialkyl-2,2′:6′,2″-terpyridyls (1,2)

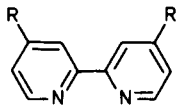
P. E. Rosevear and W. H. F. Sasse

CSIRO, Division of Applied Chemistry, Synthetic Chemistry Section,
P.O. Box 175, Chatswood, N.S.W., Australia 2067

Received February 16, 1971

2,2′:6′,2″-Terpyridyl (**1**) is widely used as a chelating agent (3) but few if any of its derivatives have been available for such applications. We have found that the 4,4′,4″-trialkyl-2,2′:6′,2″-terpyridyls (**2**), (**3**), (**4**), (**5**), and (**6**) are formed in useful yields when the corresponding 4-alkylpyridines are heated under reflux in the presence of a palladium-on-carbon catalyst (see Table I). The main products of these reactions are the 4,4′-dialkyl-2,2′-bipyridyls (**7**), (**8**), (**9**), (**10**), and (**11**), respectively, which are also valuable chelating agents (2).





1, R = H
2, R = CH_3
3, R = C_2H_5
4, R = $CH(CH_3)_2$
5, R = $(CH_2)_3$-CH_3
6, R = $(CH_2)_4$-CH_3

7, R = CH_3
8, R = C_2H_5
9, R = $CH(CH_3)_2$
10, R = $(CH_2)_3$-CH_3
11, R = $(CH_2)_4$-CH_3

TABLE I

Reaction of 4-Alkylpyridines with Palladium-on-Carbon: Percentage Yields of 4,4′-Dialkyl-2,2′-bipyridyls and 4,4′,4″-trialkyl-2,2′:6′,2″-terpyridyls (a)

Starting Material	Products	Catalyst	
		Degassed	Undegassed
4-Methylpyridine	**2**	1-2	1.5-3
	7	10-15	15-25
4-Ethylpyridine	**3**	3-5	2-3
	8	17-25	20-25
4-Isopropylpyridine	**4**	12-15	5-8
	9	40-50	20-30
4-*n*-butylpyridine	**5**	0.5-1.0	0.5-0.8
	10	5-10	10-15
4-*n*-Pentylpyridine	**6**	3-5	2-3
	11	13-20	15-20

(a) Conditions described in Experimental Part.

4,4′-Dialkyl-2,2′-bipyridyls are generally formed in better yields when degassed Raney nickel is used as catalyst (4) but from these reactions trialkylpyridines have not been isolated and the amount of 2,2′:6′,2″-terpyridyl formed from pyridine in the presence of degassed Raney nickel is less than 1% of the yield of 2,2′-bipyridyl produced (5). By comparison the yields of the terpyridyls obtained with palladium-on-carbon range from *ca.* 10 to 30% of the yields of the bipyridyls formed. However, the use of palladium-on-carbon in these reactions is more limited than that of degassed Raney nickel. Thus, at its boiling point pyridine gave less than 2% of 2,2′-bipyridyl (6,7) and terpyridyl was not detected. Similarly, several 3-substituted pyridines gave 5,5′-disubstituted 2,2′-bipyridyls in yields below 5% and terpyridyls could not be isolated (*cf.* 8).

In the present work several experimental parameters were varied in order to improve the yields of the terpyridyls. These included the concentration of the metal on the carrier, the carrier, the ratio catalyst/alkylpyridine, the time and temperature of the reaction, the use of ordinary and degassed palladium-on-carbon, the absence and presence of oxygen, and the presence of several hydrogen acceptors. The best yields were obtained by stirring a suspension of 5% palladium-on-carbon (1 g. per 25 ml. of alkylpyridine) in boiling alkylpyridine under reflux for 3 days. With several compounds improved yields were obtained when oxygen was excluded and when a degassed catalyst was used but this effect was not observed with all alkylpyridines. Cyclohexene and nitrobenzene inhibited the formation of terpyridines as did the addition of dialkylbipyridines at the beginning or during the reaction. Alumina and asbestos were inferior as carriers and even palladium-on-carbon varied in its efficiency from batch to batch. Most affected were the yields of those terpyridyls, that were formed in the lowest yields (Table I). Under the conditions described above, ordinary and degassed samples of carbon supported rhodium, platinum, iridium, and osmium did not produce detectable quantities of terpyridyls (7).

The structures assigned to the new compounds rest on their abilities to form deep blue-red coloured chelates with

TABLE II

Characterization of New Compounds (a)

Compound	m.p. or b.p.	Calculated, % C	Calculated, % H	Calculated, % N	Found, % C	Found, % H	Found, % N	Mol. wt. (Mass Spectrometry)	Molecular Formula
2	186.5-187° (b)	78.51	6.22	15.26	78.31	6.19	15.38	275	$C_{18}H_{17}N_3$
3	89-91° (c)	79.46	7.30	13.24	79.58	7.38	12.95	317	$C_{21}H_{23}N_3$
4	88° (c)	80.18	8.13	11.69	80.02	8.22	11.67	359	$C_{24}H_{29}N_3$
5	33-35° (c)	80.75	8.78	10.47	80.60	8.45	10.25	401	$C_{27}H_{35}N_3$
6	50° (d)	81.21	9.32	9.47	80.93	9.32	9.48	443	$C_{30}H_{41}N_3$
9	88° (d)	79.96	8.39	11.66	80.10	8.33	11.85	240	$C_{16}H_{20}N_2$
10	171-172°/0.05 mm	80.55	9.01	10.44	80.54	9.00	10.45	268	$C_{18}H_{24}N_2$

(a) Analyses were performed by the Australian Microanalytical Service, Melbourne. (b) Crystallized from ethanol. (c) Crystallized from petrol, b.p. 60-80°, containing 5 vol. % aromatics. (d) Crystallized from methanol.

TABLE III

Pmr Spectral Data (a)

Compound	Chemical Shift	Multiplicity (b) (Apparent Coupling Constants in Hz)	Assignments
2	2.47	s (c)	CH_3-4, CH_3-4″
	2.50	t (0.7)	CH_3-4′
	7.12	ddq (0.7; 1.7; 4.9)	H-5, H-5″
	8.27	q (0.7)	H-3′, H-5′
	8.40	m	H-3, H-3″
	8.53	dd (0.6; 4.9)	H-6, H-6″
3	1.31	t (7.5) overlapping	CH_3 terminal rings
	1.43	t (7.5)	CH_3 central ring
	2.75	q (7.5) overlapping	CH_2 terminal rings
	2.87	q (7.5)	CH_2 central ring
	7.02	dd (4.9)	H-5, H-5″
	ca. 8.85	m	remaining protons
4	1.35	d (6.8) overlapping	CH_3 terminal rings
	1.37	d (6.8)	CH_3 central ring
	3.03	m	CH all rings
	7.22	ddd (5.05; 1.75; 0.5)	H-5, H-5″
	8.33	d (0.5)	H-3′, H-5′
	8.52	ddd (1.75; 0.65; 0.5)	H-3, H-3″
	8.63	dd (5.05; 0.65)	H-6, H-6″
5	0.97	t (d)	CH_3
	1.10-2.10	m	CH_3-(CH_2)$_2$-CH_2-
	2.60-3.00	m	Pyr-CH_2-
	7.16	dd (5.0; 1.8)	H-5, H-5″
	8.27	s (e)	H-3′, H-5′
	8.47	dd (1.7; 0.7)	H-3, H-3″
	8.58	dd (5.0; 0.7)	H-6, H-6″
6	0.92	m	CH_3
	1.15-2.05	m	CH_3-(CH_2)$_3$-
	2.76	m	Pyr-CH_2-
	7.13	dd (e) (5.0; 1.7)	H-5, H-5″
	8.30	s (e)	H-3′, H-5′
	8.45	s (e)	H-3, H-3″
	8.58	dd (5.0; 0.8)	H-6, H-6″

TABLE III (Continued)

9	1.30	d (6.8)	CH_3
	3.00	sep (e) (6.8)	CH
	7.17	ddd (5.1; 1.8; 0.5)	H-5, H-5′
	8.3	ddd (e) (1.8; 0.8; 0.5)	H-3, H-3′
	8.6	dd (e) (5.1; 0.8)	H-6, H-6′
10	0.93	t (d)	CH_3
	1.1-1.8	m	CH_3-(CH_2)$_2$-CH_2-
	2.69	t (e) (7.5)	Pyr-CH_2-
	7.11	dd (e) (5.0; 1.7)	H-5, H-5′
	8.28	dd (e) (1.7; 0.7)	H-3, H-3′
	8.58	dd (5.0; 0.7)	H-6, H-6′

(a) Spectra were measured with a Varian A60 spectrometer using *ca.* 10% solutions in deuteriochloroform containing TMS. The chemical shifts are given as ppm. The intensities agree with the assignments and have been omitted. (b) s, singlet; d, doublet; t, triplet; q, quartet; sep, septet; m, multiplet; dd, doublet of doublets; ddd, doublet of doublet of doublets. (c) Broadened singlet (half width 1.7 Hz). (d) Distorted signal. (e) Broadened signal.

ferrous ions and on their spectral properties which are summarized in the experimental part.

EXPERIMENTAL (9)

Catalysts.

Several batches of 5 and 10% palladium-on-carbon, 5%-platinum-on-carbon, and 5% rhodium-on-carbon were obtained commercially (Engelhardt Industries). Iridium-on-carbon, osmium-on-carbon and catalysts on asbestos and alumina were obtained as described (7).

General Procedures.

(a) With Ordinary Catalysts.

The catalyst (1 g.) and the alkylpyridine (25 ml.) were heated for three days under reflux while being stirred. The reaction mixture was treated with boiling benzene, filtered, and distilled to give benzene, alkylpyridine, and dialkylbipyridyl. The residue was chromatographed on silicic acid (Mallinckrodt; 100 mesh; A. R.; deactivated with 10% water). The terpyridyls were eluted with 1:1- to 2:1 benzene/petrol (b.p. 60-80°).

(b) With Degassed Catalysts.

The catalyst was placed into a round bottom flask which was equipped with two connections to a vacuum system, a dropping funnel, and a thermometer. The flask was slowly evacuated to *ca.* 0.03 mm and heated to 200° (internal temperature) at a rate which did not cause loss of the catalyst through frothing. After being kept at 200° ± 2° for 20 minutes the flask was allowed to cool to room temperature. The connections to the vacuum system were closed and the alkylpyridine (25 ml. per g. of catalyst) was added through the dropping funnel without admitting air. After the catalyst had been wetted thoroughly with air the flask was opened to the atmosphere and treated as described under (a) except that "oxygen free" dry nitrogen was slowly passed through the apparatus during the reaction.

The properties of the 4,4′-dialkyl-2,2′-bipyridyls (**7**), (**8**), and (**11**) have been described (5,10); details for the new compounds are given in Tables II and III.

Acknowledgment.

We thank Mr. P. J. Collin for the pmr spectra and Professor J. S. Shannon for the mass spectra.

REFERENCES

(1) Synthetical Applications of Activated Metal Catalysts. XXVII. Preceding paper in this series: J. C. Carey and W. H. F. Sasse, *Aust. J. Chem.*, **21**, 207 (1968).

(2) A patent application based on the present results has been filed.

(3a) W. W. Brandt, F. P. Dwyer and E. C. Gyarfars, *Chem. Rev.*, **54**, 957 (1954); (b) F. P. Dwyer and D. P. Mellor, "Chelating Agents and Metal Chelates" Academic Press, New York, N. Y., and London, England, 1964.

(4a) W. H. F. Sasse and C. P. Whittle, *J. Chem. Soc.*, 1347 (1961); (b) W. H. F. Sasse, *Org. Synth.*, **46**, 5 (1966).

(5a) G. M. Badger and W. H. F. Sasse, *J. Chem. Soc.*, 616 (1956); (b) W. H. F. Sasse and C. P. Whittle, *Aust. J. Chem.*, **16**, 31 (1963).

(6) H. Rapoport, R. Iwamoto and J. R. Tretter, *J. Org. Chem.*, 25, 372 (1960).

(7) G. D. F. Jackson, W. H. F. Sasse and C. P. Whittle, *Aust. J. Chem.*, **16**, 1126 (1963).

(8) G. M. Badger and W. H. F. Sasse, in "Advances in Heterocyclic Chemistry" Vol. 2, A. R. Katritzky, Ed., Academic Press, New York, N. Y. and London, England, 1963, p. 179.

(9) Melting points were determined with a Leitz Hot Stage Microscope 350. The mass spectra were measured with an Atlas CH-4 spectrometer.

(10) C. P. Whittle, Ph. D. Thesis, University of Adelaid, 1962.