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Selective Symmetric and Asymmetric Palladium-Catalyzed Dimerizations of Pyrimidinylmercuric Salts

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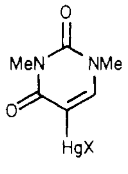
Palladium-catalyzed dimerization of 1,3-dimethyl-2,4-(1*H*,3*H*)-pyrimidinedion-5-ylmercuric salts[3] (**1**) occurs facilely to yield symmetric (1,1′,3,3′-tetramethyl-2,2′,4,4′-(1*H*,1′*H*,3*H*,3′*H*)-tetraoxo-5,5′-bipyrimidine, **2**) and/or asymmetric (1,1′,3,3′-tetramethyl-2,2′,4,4′(1*H*,1′*H*,3*H*,3′*H*)-tetraoxo-5,6′-bipyrimidine, **3**) dimers. These dimerization reactions occur under conditions which are superficially similar to conditions used for regio- and stereospecific coupling of **1** with glycals or other enol ethers.[3-5] For example, reaction of **1**, X = OAc, with 3,4,6-tri-*O*-acetyl-D-glucal[6] in the presence of 1 equiv of palladium(II) acetate and 2 equiv of lithium acetate resulted in high-yield coupling with C-nucleoside formation.[3,5] In contrast, when the acetate anion in this reaction mixture was replaced with chloride (i.e., **1**, X = Cl$^-$, PdCl$_2$ and LiCl were used), no coupling of **1** with glycal occurred;[5] instead, the glycal was recovered unchanged, and a mixture of pyrimidine dimers **2**[7-10] and **3**[11] was produced. Dimers **2** and **3** were formed also when acetate salts were used and no glycal was present. These results which indicate that selectivity among the several palladium-catalyzed reactions of **1** can be achieved by control of the nature of the anions present in the reaction mixture[5] prompted a study of palladium-catalyzed dimerization reactions of **1**. The results are summarized in Table I.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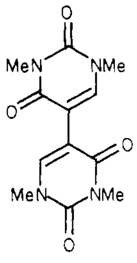
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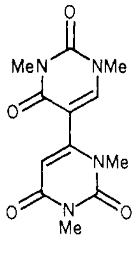
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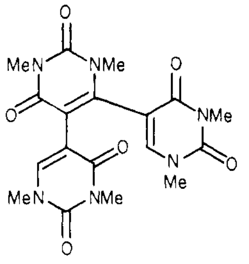
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Palladium-catalyzed dimerization of **1** was effective when either chloride or acetate anion was used although the selectivities for formation of the symmetric (**2**) and asymmetric (**3**) dimers are different. Use of the chloride anion favored formation of symmetric dimer **2** (experiments 1,2); acetate anion in the reaction mixture favored formation of asymmetric dimer **3** (experiment 5). The highest selectivity was achieved by use of acetate anion and either omitting the lithium salt (experiment 7) or (more effectively) replacing it with tetramethylammonium acetate (experiment 6). Under these conditions only asymmetric dimer

Table I. Palladium-Catalyzed Formation of Dimers of 1,3-Dimethyl-2,4(1*H*,3*H*)-pyrimidinedione in Acetonitrile Solution at Room Temperature[a]

	reactants, equiv						product yield,[b] %			
expt	PyHgX[c]	PyH[c]	PdX$_2$	LiX	Me$_4$NX	glycal[d]	2	3	4	other
				X = Cl						
1	1		1	2		1	47	25		
2	1		1	2			72	12		
3	1		1		2		20	42	16	
				X = OAc						
4	1		1	2		1				70–80[e]
5	1		1	2			23	19		
6	1		1		2			89		
7	1		1					48		
8	1		0.5					7		
9	1		0.5		1		4	47		
10	1	1	1		2		tr	6		
11		1	1				6	42		
12		1	0.5				tr	20		

[a] Experiments utilized 1–10 mmol of pyrimidine reactants in 20–100 mL of acetonitrile. The reaction mixtures were stirred at room temperature until thin-layer chromatographic analysis of aliquots indicated the reactions had ceased. Reaction times varied from 30 min when ammonium salts were present to 2–3 days when no ammonium ion was used and chloride anions were used. [b] For experiments 1–5 yields are based on isolation of products. For the remainder of the experiments, yields are based on reversed-phase high-pressure liquid chromatographic (HPLC) analysis of products following NaBH$_4$ treatment of the reaction mixture; for experiment 6 the isolated yield was 72% in contrast to the HPLC yield of 89%. [c] Py = 1,3-Dimethyl-2,4(1*H*,3*H*)-pyrimidinedion-5-yl. [d] 3,4,6-Tri-*O*-acetyl-D-glucal.[6] [e] 1,3-Dimethyl-5-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*erythro*-hex-2-enopyranosyl)-2,4(1*H*,3*H*)-pyrimidinedione, or if hydrogen sulfide is used to precipitate metal salts an approximately 1:1 mixture of this compound and 5-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-1,3-dimethyl-2,3(1*H*,3*H*)-pyrimidinedione.[5]

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(11) Mp 295 °C. Anal. Found for $C_{12}H_{14}N_4O_4$: C, 52.0; H, 5.21; N, 20.0. ^{1}H NMR (CDCl$_3$) δ 3.31, 3.39, 3.43, 3.52 (NMes), 5.67 (C-6H), 7.42 (C-5H).

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3 was isolated. No conditions were found which resulted in exclusive formation of symmetric dimer **2**. The selectivity for asymmetric dimer formation resulting from use of the tetramethylammonium cation is evident on comparison of experiments 2 and 3. Replacement of lithium chloride by tetramethylammonium chloride resulted in a change in dimer formation from a ratio of symmetric (**2**) to asymmetric (**3**) of 6:1 (Li^+, experiment 2) to 1:2 (Me_4N^+, experiment 3). Under the latter conditions, trimer **4**[12] was produced in addition to the dimers.

Use of less than stoichiometric quantities of palladium salt resulted in diminished yields (experiments 8, 9, 12). It is noteworthy that 1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione[13] underwent dimerization in the presence of palladium acetate (experiments 11, 12), essentially as effectively as the corresponding mercuric derivative (**1**).

The results of this study underscore the striking selectivity of transition-metal-catalyzed reactions and emphasize the need to develop a deeper understanding of factors which determine selection among permissible reaction pathways.

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(12) Mp >350 °C. Anal. Found for $C_{18}H_{20}N_6O_6$: C, 51.9; H, 5.01; N, 20.1. ^1H NMR ($CDCl_3$) δ 3.26, 3.29, 3.33, 3.53, 3.63 (NMes), 7.08, 7.59 (pyrimidine Hs).

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N-Alkylformamidyl Radicals. Identification and Electronic Structure[1]

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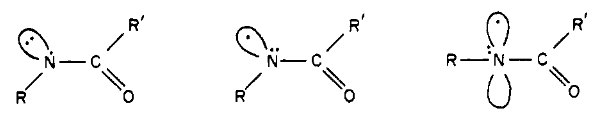
We[3,4] and others[5] have recently shown by EPR spectroscopy that *N*-alkylcarboxamidyl radicals, RNC(O)R′, have the π electronic configuration (**1**) in their ground state rather than the bent (**2**) or linear (**3**) σ_N configurations, thus ending many years of somewhat inconclusive arguments based on the results of theoretical calculations.[6] For the related *N*-alkylformamidyl radicals, R$\dot{\mathrm{N}}$C(O)H, there is no experimental information, though Danen and Neugebauer in their 1975 review[14] note that the EPR spectrum of such a radical "would be very informative by virtue of the large coupling constant a^H(CHO) anticipated for a σ_N configuration (i.e., **5**)...but attempts to generate $(CH_3)_3C\dot{N}C(O)H$ either in solution or in adamantane matrix have not been fruitful". The EPR experience we had gained with R$\dot{\mathrm{N}}$C(O)R′ radicals gave us confidence that we would be able to observe R$\dot{\mathrm{N}}$C(O)H radicals provided R was sufficiently bulky. Such proved to be the case, and our results provide unequivocal proof that R$\dot{\mathrm{N}}$C(O)H radicals have the same electronic ground state as R$\dot{\mathrm{N}}$C(O)R′ radicals, i.e., the π configuration, **4**.



1 R,R′ = alkyl   **2** R,R′ = alkyl   **3** R,R′ = alkyl

4 R = alkyl, R′ = H   **5** R = alkyl, R′ = H   **6** R = alkyl, R′ = H

N-Alkylformamidyls having R = *t*-$BuCH_2$, $(t\text{-}Bu)_2CH$, and *t*-Bu were observed[15] upon photolysis under oxygen-free conditions of their parent *N*-chloroformamides in cyclopropane solvent in the cavity of a Varian E-104 EPR spectrometer.[3,4,16] The identity of these radicals and the conclusion that they have the π electronic ground state, **4**, is established by comparison of their EPR parameters with those of the corresponding R$\dot{\mathrm{N}}$C(O)CH_3 radicals as measured at or near the same temperatures[3,4] (see Table I). Because the temperature ranges over which the formamidyls could be detected were somewhat limited, we are unable to apply the detailed arguments about structure that were employed previously.[3,4] Nevertheless, the excellent agreement between the *g* and a^N values for each pair of radicals, and between the magnitudes of $a^H\beta$ for R = *t*-$BuCH_2$ and $(t\text{-}Bu)_2CH$, establishes that R$\dot{\mathrm{N}}$C(O)H and R$\dot{\mathrm{N}}$C(O)R′ radicals have the same electronic structure, i.e., **4** and **1**, respectively. Furthermore, the relatively low *g* value plus the enhanced values of a^N and a^H(CHO) for *t*-Bu$\dot{\mathrm{N}}$C(O)H implies that this radical is substantially more "twisted" than the

Table I. EPR Parameters for Some RNC(O)H and Related R$\dot{\mathrm{N}}$C(O)CH_3 Radicals

radical	*T*, K	*g*	a^N, G	$a^H\beta$(R), G	a^H(CHO), G	a^D(CDO),[a] G	a^{13C}(CHO),[b] G	$a^{13C}(CH_3)$,[c] G
t-$BuCH_2NC(O)H$	158	2.0054	14.8	40.7	10.3	1.4	11.0	
	188	2.0054	14.7	39.3	d	1.4		
t-$BuCH_2\dot{N}C(O)CH_3$[e,f]	161	2.0051	15.1	40.3				2.4
	190		15.0	39.2				
$(t\text{-}Bu)_2CH\dot{N}C(O)H$	159	2.0056	14.4	12.4	7.4	*g, h*	11.4[g,i]	
	199	2.0056	14.4	11.7	7.5	*g, h*		
	228	2.0056	14.3	11.3		*g, h*		
$(t\text{-}Bu)_2CH\dot{N}C(O)CH_3$[e]	153	2.0056	14.7	12.6				*j*
	193		*i*	12.3				
	233		*i*	12.1				
t-$Bu\dot{N}C(OH)$	194	2.0044	16.1		21.5	3.4	k	
t-$Bu\dot{N}C(O)CH_3$[e,l]	173	2.0044	15.8					4.6

[a] By photolysis of RN(Cl)C(O)D. [b] By photolysis of $RN(Cl)^{13}C(O)H$. [c] By photolysis of $RN(Cl)^{13}C(O)CH_3$. [d] Not measured; only *t*-$BuCH_2NC(O)D$ examined at this temperature. [e] Reference 4. [f] The other *t*-$BuCH_2\dot{N}C(O)R'$ radicals have similar parameters:[4] e.g., R′ = Et at 161 K, $g = 2.0053$, $a^N = 14.9$G, $a^H\beta = 40.3$ G; R′ = *t*-Bu at 153 K, $g = 2.0053$, $a^N = 15.2$ G, $a^H\beta = 40.9$ G. [g] Not fully resolved. [h] Line width, $\Delta H_{pp} = 3.4$ G. [i] Obtained from total spectral width. [j] Not measured. [k] Spectral intensity too poor to allow analysis. [l] The other *t*-$Bu\dot{N}C(O)R'$ radicals have similar parameters: e.g., R′ = Et at 169 K, $g = 2.0045$, $a^N = 15.6$ G R′ = *t*-Bu at 143 K, $g = 2.0049$, $a^N = 15.7$ G.

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