Radical Decarboxylative Alkylation onto Heteroaromatic Bases with Trivalent Iodine Compounds

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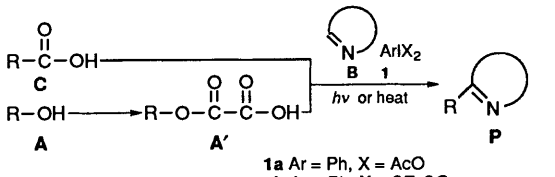
Heteroaromatic bases containing nitrogen atoms were easily alkylated with carboxylic acids in the presence of [bis(trifluoroacetoxy)iodo]benzene and [bis(trifluoroacetoxy)iodo]pentafluorobenzene *via* radical pathways. Similarly, the alkylation onto heteroaromatic bases was carried out with oxalic acid monoalkyl esters, which were prepared from alcohols and oxalyl dichloride, in the presence of the same trivalent iodine compounds. Moreover, this system was applied to the synthesis of *C*-nucleosides with the carboxylic acids bearing a sugar moiety.

Recently, the hypervalent iodine compounds have been found to be useful reagents in organic synthesis because of their powerful abilities as oxidants and C–C bond-forming reagents.[1] Among them, trivalent iodine compounds have become effective reagents in both these respects. In particular, the C–C bond-forming reactions are very important in organic synthesis. For example, the alkylation of heteroaromatic bases is a useful method in the preparation of natural products.[2] However, ionic methods are limited in their ability to prepare many kinds of alkylated heteroaromatic bases, *i.e.*, the reactivities with electrophiles (Friedel–Crafts type) or nucleophiles (addition) depend on the character of the heteroaromatic bases (electron density, *etc.*). On the other hand, alkylation onto heteroaromatic bases *via* a radical pathway has excellent possibilities, *i.e.*, chemoselectivity, regioselectivity, and mild conditions, *etc.* Hitherto, radical alkylations onto heteroaromatic bases have been well studied, especially by Minisci *et al.*[3] While, for trivalent iodine compounds, there are some studies on decomposition reactions,[4a] decarboxylative iodination of carboxylic acids,[4b] phenylation and alkylation of aromatic compounds,[4c] azido-phenylselenylation of double bonds,[4d] and rearrangement reactions from alcohols[4e] and amines.[4f] However, after a first study on the arylation and alkylation of aromatic rings by Karelsky and Minisci, respectively,[4c] detailed studies on the decarboxylative alkylation of heteroaromatic bases with trivalent iodine compounds (**1a**, **1b** and **1c**) starting from carboxylic acids **C** and alcohols **A** were never carried out. In preliminary communications,[5] we have shown that [bis(trifluoroacetoxy)iodo]benzene **1b** and [bis(trifluoroacetoxy)iodo]pentafluorobenzene **1c** reacted with carboxylic acids or oxalic acid monoalkyl esters in the presence of heteroaromatic bases to afford the corresponding alkylated products *via* radical decarboxylative pathways and this system was applied to the synthesis of *C*-nucleosides as shown in Scheme 1. We now report full details on these reactions and their extension to other, model systems.



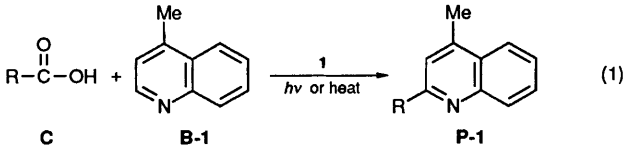
1a Ar = Ph, X = AcO
1b Ar = Ph, X = CF_3CO_2,
1c Ar = C_6F_5, X = CF_3CO_2,
R = 1°, 2°, 3°-alkyl and sugar moiety

Scheme 1

Results and Discussion

Carboxylic acids have often been utilized as a source of alkyl radicals by the oxidative decarboxylation with heavy-metal reagents [lead tetraacetate, silver nitrate, and mercury(II) oxide, *etc.*],[3] *N*-hydroxy-2-thiopyridone,[6a] *O*-acylbenzophenone oximes,[6b] photodecarboxylation[6c] and *N*-(acyloxy)phthalimides.[6d] Recently, it has been reported that (diacetoxyiodo)benzene (DAIB) **1a** reacted with carboxylic acids in the presence of iodine to give the corresponding alkyl iodide *via* a radical pathway.[4b] While, to be effective in the heteroaromatic substitution, the radical source must both produce alkyl radical species and have the character to oxidize the alkylated radical intermediates. Thus, the alkylation onto heteroaromatic compounds was carried out by using carboxylic acids, oxalic acid monoalkyl esters, and trivalent iodine compounds such as DAIB **1a**, [bis(trifluoroacetoxy)iodo]benzene **1b**, and [bis(trifluoroacetoxy)iodo]pentafluorobenzene **1c**.

1. *Alkylation onto Heteroaromatic Bases with Carboxylic Acids.*—The mixture of lepidine (4-methylquinoline) **B-1** and carboxylic acid **C** in the presence of a trivalent iodine compound **1** was refluxed in benzene or irradiated in dichloromethane to give the corresponding 2-alkyl-4-methylquinoline **P-1** as shown in eqn. (1). The reactivities of iodine(III) compounds **1a**, **1b** and



(1)

1c are shown in Table 1. The cyclohexylation of lepidine did not proceed effectively under irradiation or thermal conditions with compound **1a** (entries 1 and 2), while the reactions with compound **1b** gave 2-cyclohexyl-4-methylquinoline **P-1g** in moderate yields under irradiation or thermal conditions (entries 6 and 7).

Furthermore, compound **1c** was the most effective alkylating reagent under photochemical conditions (entries 8, 10 and 13), though it was not effective under refluxing conditions because of its thermal instability (entries 11 and 14). 2-Cyclohexyl-4-methylquinoline **P-1g** was obtained in the best yield when the proportions of carboxylic acid (**C**):heteroaromatic base (**B**):(diacyloxyiodo)arene (**1**) were 3:3:1 (Table 1). This alkylation reaction therefore requires an excess of both

Table 1 Alkylation of lepidine **B-1**

Entry	R in acid C	$ArIX_2$	(C:B:1) Proportions	Conditions[a]	Yield (%)[b] P-1
1	Cyclohexyl	**1a**	3:3:1	A	**P-1g** 3
2	Cyclohexyl	**1a**	3:3:1	B	4
3	Cyclohexyl	**1b**	1:1:1	A	1
4	Cyclohexyl	**1b**	3:1:1	A	1
5	Cyclohexyl	**1b**	1:3:1	A	26
6	Cyclohexyl	**1b**	3:3:1	A	50
7	Cyclohexyl	**1b**	3:3:1	B	52
8	Cyclohexyl	**1c**	3:3:1	B	72
9	1-Adamantyl	**1b**	3:3:1	A	**P-1a** 91
10	1-Adamantyl	**1c**	3:3:1	B	85
11	1-Adamantyl	**1c**	3:3:1	A	59
12	2-Phenylethyl	**1b**	3:3:1	A	**P-1h** 19
13	2-Phenylethyl	**1c**	3:3:1	B	28
14	2-Phenylethyl	**1c**	3:3:1	A	12

[a] A, Refluxed in benzene; B, irradiated in CH_2Cl_2 with low-pressure mercury lamp (15 W). [b] Yields were calculated based on compound **1**.

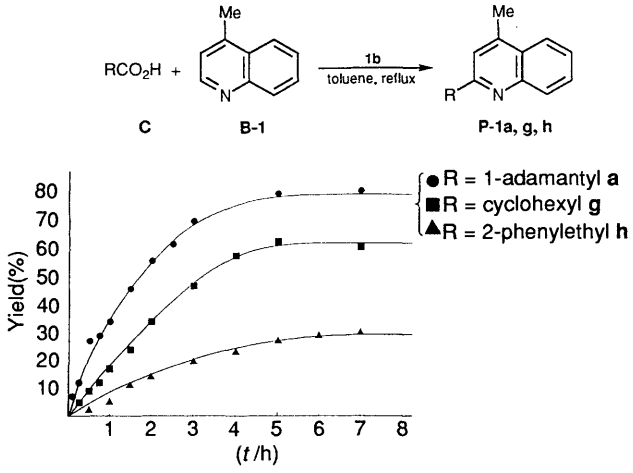
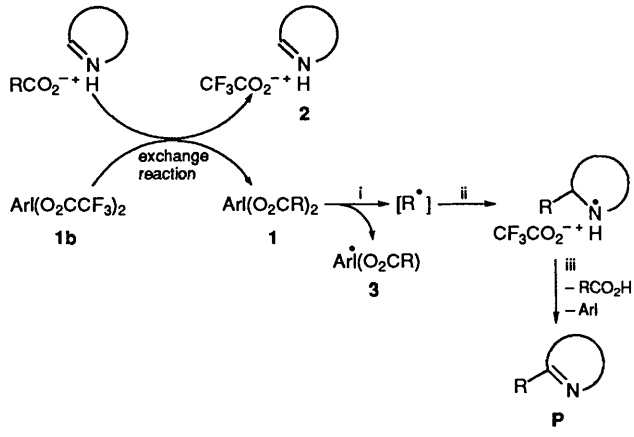


Fig. 1 Relative reactivities of RCO_2H C with $PhI(O_2CCF_3)_2$ **1b** in the presence of lepidine **B-1**



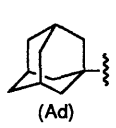
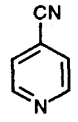
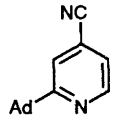
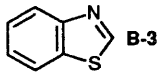
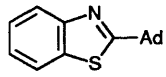
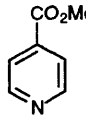
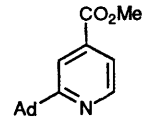
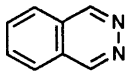
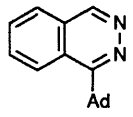
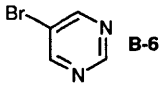
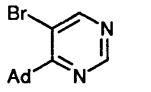
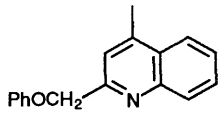
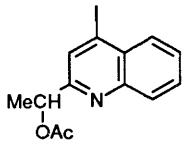
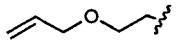
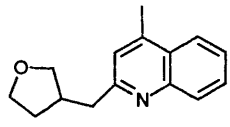
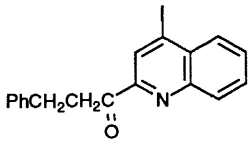
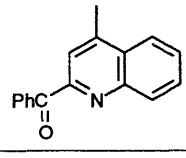
Scheme 2 *Reagents and conditions:* i, *hv* or reflux; ii, **2**; iii, oxidation, **3**

carboxylic acid and heteroaromatic base over trivalent iodine compound for this reaction to be carried out effectively. The excess of carboxylic acid and base used can be recovered. The reactivity of the carboxylic acid increases in the order of primary < secondary < tertiary carboxylic acids [entries 6, 9 and 12 under heating conditions (A), entries 8, 10 and 13 under irradiation conditions (B)], and, in particular, 2-adamantyl-4-methylquinoline **P-1a** was obtained in nearly quantitative yield when adamantane-1-carboxylic acid (tertiary) was used. The relative reactivities are shown in Fig. 1. Other examples of the alkylation employing the commercially available organoiodine reagent **1b**, various kinds of carboxylic acids, and heteroaromatic bases are shown in Table 2. Further, this reaction can successfully be applied for acylation of heteroaromatic base by using α-keto carboxylic acid (entries 9 and 10).

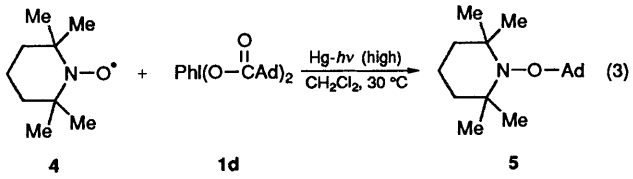
The nucleophilicity of the phenoxymethyl radical generated from phenoxyacetic acid increases due to electron donation from the oxygen atom at the α-position to the carbon radical centre, and therefore the yield of product was better than that with other primary carboxylic acids such as 3-phenylpropionic acid (entry 12 in Table 1). Other heteroaromatic bases such as methyl isonicotinate **B-4**, phthalazine **B-5**, 4-cyanopyridine **B-2**, 5-bromopyrimidine **B-6** and benzothiazole **B-3** can be easily alkylated (entries 1–5). When heteroaromatic bases having an electron-withdrawing group were used, the yield of product **P** increased a little.

This alkylation onto heteroaromatic bases proceeds *via* a radical reaction mechanism, as shown in Scheme 2. At the first step with compound **1b**, the exchange reaction of acyloxy anion and trifluoroacetate anion[7] occurs smoothly, though (diacyloxyiodo)benzene, [(acyloxy)(trifluoroacetoxy)iodo]benzene, and substrate **1b** may exist in equilibrium in the reaction medium. However, the results of entry 9 in Table 1 and entries 1 and 2 in Table 3 suggest that this reaction intermediate is (diacyloxyiodo)benzene, not [(acyloxy)(trifluoroacetoxy)-iodo]benzene. Namely, [(acyloxy)(trifluoroacetoxy)iodo]-benzene does not easily generate alkyl radicals until another trifluoroacetoxy group bonded to the iodine atom is replaced with an acyloxy group. Thus the origin of alkyl group in the product **P** came from an acyloxy group in (diacyloxyiodo)-benzene and the remaining acyloxy group was recovered as a carboxylic acid. This alkylation proceeds *via* a radical pathway, which was supported by both racemization and cyclization (5-*exo-trig* manner) experiments. Thus the almost racemized 2-(1-acetoxyethyl)-4-methylquinoline **P-1c** (6% ee) was obtained when *O*-acetyl-L-lactic acid was treated with lepidine and compound **1b**, and 4-methyl-2-(tetrahydro-3-furyl)methyl-quinoline **P-1d** instead of 2-[2-(allyloxy)ethyl)]-4-methyl-quinoline was obtained when 3-(allyloxy)propionic acid was treated with lepidine and compound **1b** under irradiation conditions at room temp. (entries 7 and 8 in Table 2). However, the yield of iodobenzene was lower (< 5%) probably because of the C–I bond cleavage. Moreover, the adamantyl radical, produced *via* the radical decarboxylation of adamantane-carbonyloxyl radical formed in turn by irradiation of [bis-(admantylcarbonyloxy)iodo]benzene could be trapped in 80% yield by 2,2,6,6-tetramethyl-1-piperidinyloxyl free radical

Table 2 Alkylation of heteroaromatic bases with carboxylic acids in the presence of organoiodine(III) compound **1b**[a]

Entry	R in C	B	Yield (%) of P	
1	 (Ad)	 **B-2**	 **P-2a**	88
2	Ad	 **B-3**	 **P-3a**	54
3	Ad	 **B-4**	 **P-4a**	68
4	Ad	 **B-5**	 **P-5a**	57
5	Ad	 **B-6**	 **P-6a**	27
6	$PhOCH_2$	**B-1**	 **P-1b**	61
7	(L)-MeCH(OAc)	**B-1**	 **P-1c**	20
8		**B-1**	 **P-1d**	13
9	$PhCH_2CH_2C(=O)$	**B-1**	 **P-1e**	56
10	PhC(=O)	**B-1**	 **P-1f**	46

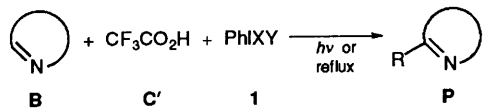
[a] Proportions of **C**:**B**:**1b** were 3:3:1 (mmol) and the mixture was refluxed in benzene.



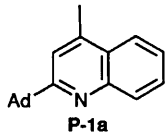
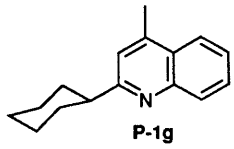
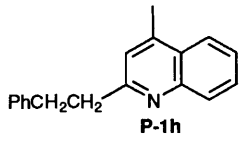
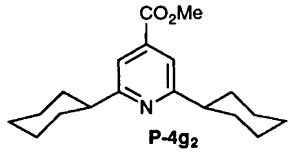
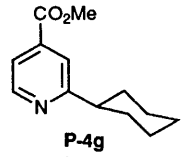
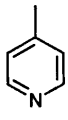
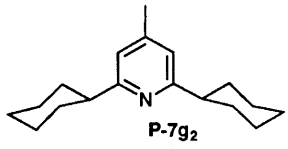
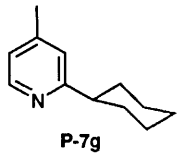
(TEMPO) **4** as shown in eqn. (3). Heteroaromatic bases such as 4-cyanopyridine **B-2** and methyl isonicotinate **B-4**, having two reactive positions, were not dialkylated at both C-2 and C-6 under the same reaction conditions with compound **1b** and the carboxylic acid. However, the dialkylation was achieved by use of another (diacyloxyiodo)benzene instead of compound **1b** and trifluoroacetic acid **C** [eqn. (2)]. When methyl isonicotinate **B-4** was used, the dialkylated compound **P-4g**$_2$ was obtained in 65% yield, and when γ-picoline **B-7** was used, the yields of dialkylated **P-7g**$_2$ and monoalkylated **P-7g** compounds were 20 and 46% yield, respectively. The reason why methyl isonicotinate **B-4** was dialkylated easily is that it is more reactive against nucleophilic alkyl radicals than γ-picoline.

The very important application with this method is the synthesis of *C*-nucleosides. Recently, many natural and unnatural *C*-nucleosides have been synthesized in multistep sequences because of their marked antiviral and antitumour activities.[8] Previously, in our laboratory *C*-nucleosides were synthesized *via* a radical pathway with *N*-hydroxy-2-thiopyridone and a carboxylic acid bearing a sugar moiety (Barton method).[9] It was the first report on the preparation of *C*-

Table 3 Alkylation with [(diacyloxy)- or (acyloxy)(trifluoroacetoxy)iodo]benzene



B C' 1 P

Entry	PhIXY	B	Conditions[a]	P and yield (%)[b]
1	X = Y = 1-Ad-CO_2	B-1	A[c]	 P-1a 81
2	X = 1-Ad-CO_2, Y = CF_3CO_2	B-1	A[d]	P-1a 41
3	X = Y = 	B-1	A[c]	 P-1g 46
4	X = Y = $PhCH_2CH_2$	B-1	A[c]	 P-1h 29
5	X = Y = 	B-4	C[e]	 $P\text{-}4g_2$ 65
				 P-4g trace
6	X = Y = 	B-4	B[e]	$P\text{-}4g_2$ 30 P-4g 11
7	X = Y = 	 B-7	C[e]	 $P\text{-}7g_2$ 20
				 P-7g 46

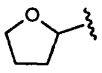
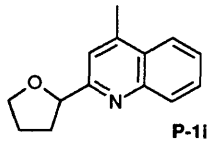
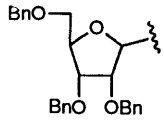
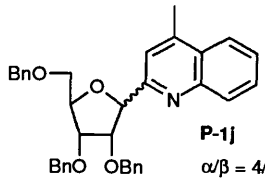
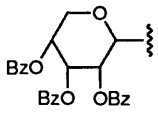
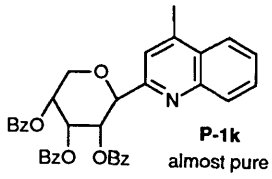
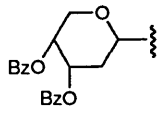
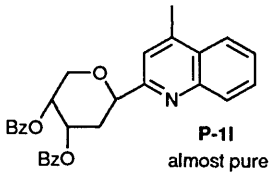
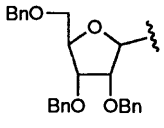
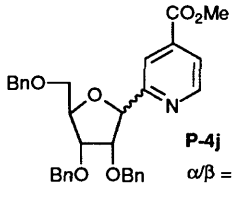
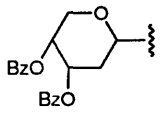
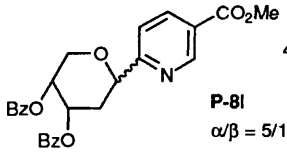
[a] Condition: A, refluxed in benzene; B, irradiated in CH_2Cl_2 with low-pressure mercury lamp; C, irradiated with high-pressure mercury lamp. [b] Yields were calculated based on compound **1**. [c] Proportions of **C'**:**B**:**1** were 3:3:0.5 (mmol). [d] Proportions of **C'**:**B**:**1** were 3:3:1 (mmol). [e] Proportions of **C'**:**B**:**1** were 0.5:0.5:2 (mmol).

nucleosides *via* a radical-coupling method. Here, the present method was applied to the preparation of *C*-nucleosides.*

Preliminarily, we carried out a model reaction with tetrahydrofuran-2-carboxylic acid and lepidine to find the best reaction conditions and some results are shown in Table 4. 4-Methyl-2-(tetrahydro-2-furyl)quinoline **P-1i** was obtained in 22% yield with compound **1b** and in 29% yield with compound **1c** under irradiation conditions. On the other hand, under thermal conditions it was obtained in only 12% yield with compound **1b**. Thus, compound **1c** was the most effective

* During this work, the preparation of *C*-nucleosides with 2,3;4,6-di-*O*-isopropylidene-D-*lyxo*-hex-2-ulosonic acid and methyl 2,3-*O*-isopropylidene-β-D-ribofuranosiduronic acid, and (diacetoxyiodo)benzene in the presence of heteroaromatic bases was reported.[10]

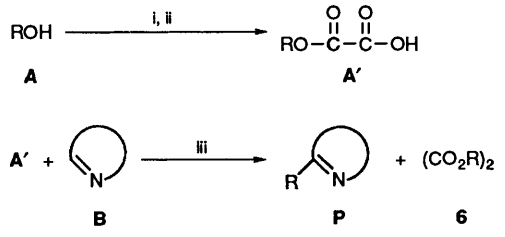
Table 4 Preparation of *C*-nucleosides with compound **1c**[a]

Entry	R (C)	B	P and yield (%)
1		B-1	 29 **P-1l**
2		B-1	 34 **P-1j** α/β = 4/6
3		B-1	 39 **P-1k** almost pure β form
4		B-1	 56 **P-1l** almost pure β form
5		B-4	 19 **P-4j** α/β = 7/3
6		B-8	 42 **P-8l** α/β = 5/1

[a] Irradiated in CH_2Cl_2 with low-pressure mercury lamp. Proportions of **C**:**B**:**1** were 2:2:0.4.

alkylating reagent and this result suggested its applicability to the synthesis of *C*-nucleosides. In practice, the corresponding *C*-nucleosides were obtained by the reaction of compound **1c** and carboxylic acids bearing sugar moieties. There was little selectivity between α and β forms when 2,5-anhydro-3,4,6-tri-*O*-benzyl-D-*ribo*-hexonic acid was used, while the stereoselectivities with 2,6-anhydro-4,5-di-*O*-benzoyl-3-deoxy-D-*erythro*-hexonic acid depended on the heteroaromatic base used (entries 2–6). Another advantage of the benzoyl group is that the deprotection is very easy. Thus, benzoyl groups were easily deprotected with NH_3 in dry methanol in quantitative yield, while the deprotection of benzyl groups did not succeed with use of PdO and cyclohexene under hydrogen because of the formation of many undesired products. However, these results suggest that the present method makes possible the preparation of *C*-nucleosides and *C*-glycosides from the reaction of heteroaromatic bases and carboxylic acids bearing a sugar moiety.

2. *Alkylation onto Heteroaromatic Bases starting from Alcohols.*—The alkylation onto heteroaromatic bases was carried out with the oxalic acid monoalkyl esters, prepared from alcohols as starting materials, in the presence of trivalent iodine compounds such as compounds **1a**, **1b** and **1c** (see Scheme 3). Hitherto, for the generation of an alkyl radical from



Scheme 3 *Reagents and conditions:* i $(COCl)_2$; ii, water; iii, **1**, reflux in benzene or toluene

alcohol, the methods with xanthates, xanthate analogues, and oxalate esters with tributyltin hydride have been well studied.[11] However, the alkylation onto heteroaromatic bases with these systems does not proceed because tributyltin hydride is a reducing agent. As mentioned before, the radical source must have oxidative ability for the alkylation of heteroaromatic bases to proceed.

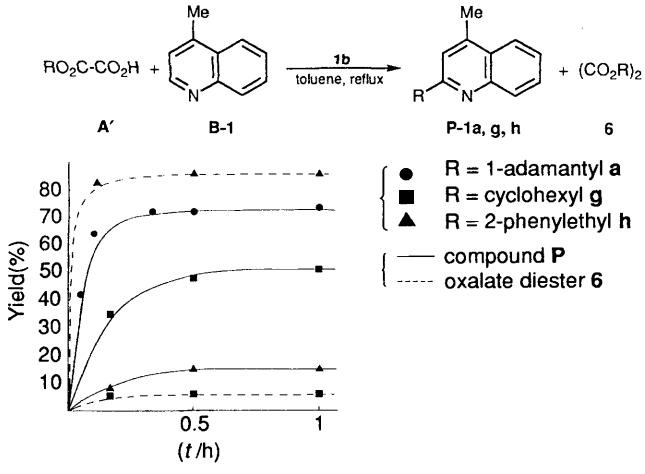
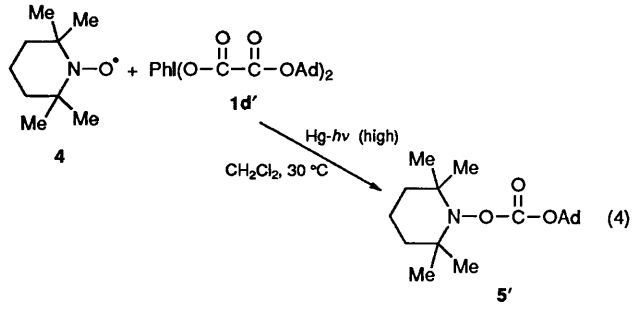


Fig. 2 Relative reactivities of RO_2C–CO_2H A′ with $PhI(O_2CCF_3)_2$ **1b** in the presence of lepidine **B-1**

The first report of alkylation onto heteroaromatic bases with oxalic acid monoester starting from alcohols was reported by us previously.[5] The results and reaction conditions with oxalic acid monoester and **1** are summarized in Table 5. The proportions of **A′**:**B**:**1** (3:3:1) were suitable for this reaction, as in the case with carboxylic acids. Compound **1b** was the most effective alkylating agent among the three trivalent iodine compounds (entries 1, 3 and 4). Further, since heat was required to accelerate the bimolecular decarboxylation, toluene was a better solvent than benzene (entries 1 and 2). The reactivities of the half-esters **A′** prepared from primary, secondary and tertiary alcohols are illustrated in Fig. 2. As shown in Fig. 2, these reactions are complete within 1 h and the reactivities of compounds **A′** increase in the order primary < secondary < tertiary esters. Oxalate diester **6** was predominantly formed by the radical coupling of the alkoxycarbonyl radical formed together with compound **P** from a primary ester **A′**, because the bond-dissociation energy of its carbon–oxygen bond is higher than those of secondary and tertiary alcohol derivatives (entries 8 and 9). When the mixture of heteroaromatic base and oxalic acid monoalkyl ester was refluxed in toluene without an iodine(III) compound **1**, oxalate diester **6** was not formed. This fact indicates that the oxalate diester obtained was formed *via* the coupling of alkoxycarbonyl radical generated from monoester **A′** and **1**, not *via* thermal disproportionation of **A′** alone. Further, the formation of alkoxycarbonyl radical was further supported by the trapping experiment with TEMPO to give carbonate derivative **5′** in 84% yield as shown in eqn. (4). These results again suggest that



the reaction proceeds *via* a radical pathway. When the chiral compound was used as the monoester compound **A′**, the corresponding single isomer was obtained due to its steric hindrance (entry 10). Other heteroaromatic bases, such as

Table 5 Alkylation of heteroaromatic bases with oxalate monoesters **A′**

Entry	R in **A′**	Aromatic base	$ArIX_2$	Conditions[b]	Products and yields (%)[a] P		$(CO_2R)_2$
1	1-Adamantyl	**B-1**	**1b**	A	**P-1a**	62	—
2	1-Adamantyl	**B-1**	**1b**	B	**P-1a**	72[c]	—
3	1-Adamantyl	**B-1**	**1a**	A	**P-1a**	31	—
4	1-Adamantyl	**B-1**	**1c**	C	**P-1a**	19	—
5	1-Methylcyclohexyl	**B-1**	**1b**	A	4-Methyl-2-(1-methylcyclohexyl)quinoline **P-1m**	54	—
6	Cyclohexyl	**B-1**	**1b**	A	**P-1g**	43	20
7	Cyclohexyl	**B-1**	**1b**	B	**P-1g**	52[c]	6[c]
8	2-Phenylethyl	**B-1**	**1b**	A	**P-1h**	13	86
9	2-Phenylethyl	**B-1**	**1b**	B	**P-1h**	15[c]	88[c]
10	(−)-Menthyl	**B-1**	**1b**	B	2-Menthyl-4-methylquinoline **P-1n**	41[d]	trace
11	1-Adamantyl	**B-4**	**1b**	A	**P-4a**	58	—
12	1-Adamantyl	**B-5**	**1b**	A	**P-5a**	33	—
13	1-Adamantyl	**B-3**	**1b**	A	**P-3a**	28	6
14	1-Adamantyl	**B-2**	**1b**	A	**P-2a**	47	12
15	1-Methylcyclohexyl	**B-4**	**1b**	A	Methyl 2-(1-methylcyclohexyl)isonicotinate **P-7m**	36	—
16	Cyclohexyl	**B-4**	**1b**	B	**P-4g**	39	22
17	Cyclohexyl	**B-5**	**1b**	B	1-Cyclohexylphthalazine **P-5g**	36	23

[a] Yields were calculated based on $ArIX_2$. [b] A, Refluxed in benzene; B, refluxed in toluene; C, irradiated in CH_2Cl_2 at room temp. with low-pressure mercury lamp. Proportions of **A**:heteroaromatic base:**1** were 3:3:1. [c] Yields were determined by GLC. [d] $[\alpha]_D^{24}$ −63.31 (*c* 0.861, $CHCl_3$).

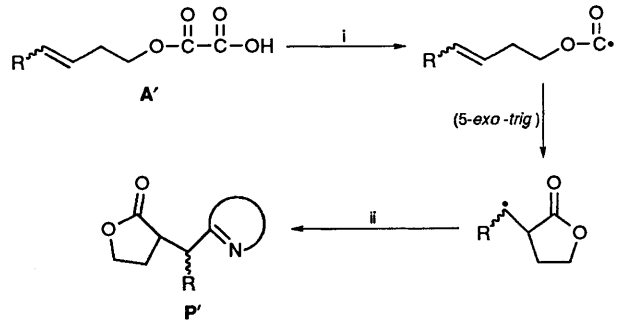
Table 6 Lactonization with lepidine **B-1** as shown in Scheme 4

Entry	A', R	$ArIX_2$	Conditions[a]	P, Yield (%)[b]
1	(*Z*)-Et	**1b**	C	42 (52:48)[c]
2	(*Z*)-Et	**1c**	C	30 (50:50)[c]
3	(*Z*)-Et	**1b**	B	14 (50:50)[c]
4	(*Z*)-Et	**1b**	A	17 (51:49)[c,d]
5	(*E*)-Et	**1b**	C	47 (62:38)[c]

[a] Proportions of A': lepidine: $ArIX_2$ were 3:3:1. A, refluxed in benzene; B, irradiated in CH_2Cl_2 with low-pressure mercury lamp; C, irradiated in CH_2Cl_2 with high-pressure mercury lamp. [b] The yields were calculated based on compound **1**. [c] Ratio of the diastereoisomeric mixture. [d] Oxalate diester was obtained in 7% yield.

methyl isonicotinate **B-4**, phthalazine **B-5** and benzothiazole **B-3**, were also alkylated easily.

When oxalic acid monohex-3-enyl ester was used in the presence of compound **1b** and lepidine **B-1**, the lepidine moiety bearing a lactone moiety at C-2 was obtained in 42% yield (diastereoisomeric mixture 52:48) starting from mono-(*Z*)-hex-3-enyl ester of oxalic acid and in 47% yield (62:38) starting from the *E*-form (Table 6). The alkoxycarbonyl radical generated *via* monomolecular decarboxylation cyclized in a 5-*exo*-*trig* manner and reacted with heteroaromatic bases to give product **P'** (Scheme 4). In these reactions, only a trace of oxalate diester



Scheme 4 *Reagents and conditions:* i, **1**, *hv* or reflux; ii, **B**

was obtained. This lactonization occurred more readily under irradiation conditions than under thermal conditions, by retarding the second decarboxylation of the formed alkenoxycarbonyl radical (entries 1 and 5 in Table 6).

In conclusion, this method is very useful for the alkylation of heteroaromatic bases from both carboxylic acids and alcohols as starting materials and furthermore is applicable to the synthesis of *C*-nucleosides.

Experimental

Microanalyses were performed with a Perkin-Elmer 240B and 2400 elemental analysers at the Chemical Analysis Center of Chiba University. IR and ^1H NMR spectra were measured with Hitachi-215, JEOL-MH100, JEOL-JNM-FX270, JEOL-GSX-400 and JEOL-GSX500 spectrometers. ^{13}C NMR spectra were measured with a JEOL-JNM-FX270 spectrometer. *J*-Values are given in Hz. Mass spectra were measured with Hitachi M-60 and JEOL-HX110 spectrometers. Optical rotations ($[\alpha]_D$-values given in units of 10^{-1} deg cm^2 g^{-1}) were measured on a JASCO-DIP-370 polarimeter. Wakogel C-200 was used for column chromatography, Kieselgel 60 F_{254} (Merck) was used for TLC, and Wakogel B-5F was used for preparative TLC (PTLC).

Materials.—The trivalent iodine compounds (diacetoxyiodo)benzene **1a** and [bis(trifluoroacetoxy)iodo]benzene **1b** and simple organic chemicals were commercially available. [Bis(trifluoroacetoxy)iodo]pentafluorobenzene **1c** was prepared according to the procedure described in the literature.[12]

Alkylation onto Heteroaromatic Bases with Carboxylic Acids (General Procedure).—The reaction was carried out with molar proportions of 3:3:1 (carboxylic acid: heteroaromatic base: trivalent iodine compound) and the two methods are described below.

Method 1. To a solution of trivalent iodine compound **1** in dry benzene (5 cm^3) were added the appropriate carboxylic acid and heteroaromatic base under argon and the mixture was refluxed for 8–10 h.

Method 2. To a solution of trivalent iodine compound **1** in dry dichloromethane (5 cm^3) in a quartz cell were added the appropriate carboxylic acid and heteroaromatic base under argon and the mixture was irradiated with a low-pressure mercury lamp (15 W) at room temp. for 8–10 h.

Each reaction mixture was then washed with saturated aq. sodium hydrogen carbonate. Then the aqueous layer was extracted with dichloromethane once and the combined organic layer was dried over $MgSO_4$. After the removal of solvent under reduced pressure, the residual oil was purified by column chromatography on silica gel with CH_2Cl_2 as eluent.

Spectral and analytical data of compounds prepared were as follows and most authentic samples were easily prepared by Minisci's procedure with a peroxide system.[3]

2-Cyclohexyl-4-methylquinoline **P-1g**. Oil; ν_{max}(neat)/cm^{-1} 3050, 2910, 2845, 1600, 1450 and 770; δ_H(100 MHz; CCl_4) 1.10–2.00 (10 H, m, cyclohexyl), 2.47 (3 H, s, Me), 2.30–2.80 (1 H, m, cyclohexyl CH), 6.75 (1 H, s, base 3-H), 7.00–7.40 (2 H, m, base 6- and 7-H), 7.50 (1 H, d, *J* 9.0, base 5-H) and 7.75 (1 H, d, *J* 9.0, base 8-H); *m/z* (EI) M^+ 225 (Found: C, 85.3; H, 8.6; N, 6.5. $C_{16}H_{19}N$ requires C, 85.28; H, 8.50; N, 6.22%).

2-(1-Adamantyl)-4-methylquinoline **P-1a**. M.p. 120.3–122.0 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 3040, 2880, 2840, 1590, 1440 and 760; δ_H(100 MHz; CCl_4) 1.80 (6 H, br s, adamantyl), 2.07 (9 H, br s, adamantyl), 2.60 (3 H, s Me), 7.15 (1 H, s, base 3-H), 7.30–7.60 (2 H, m, base 6- and 7-H), 7.80 (1 H, d, *J* 9.0, base 5-H) and 7.90 (1 H, d, *J* 9.0, base 8-H); *m/z* (EI) M^+ 277 (Found: C, 86.4; H, 8.3; N, 5.2. $C_{20}H_{23}N$ requires C, 86.59; H, 8.36; N, 5.05%).

4-Methyl-2-(2-phenylethyl)quinoline **P-1h**. Oil; ν_{max}(neat)/cm^{-1} 3050, 2900, 1600, 1445, 770 and 710; δ_H(100 MHz; CCl_4) 2.60 (3 H, s, Me), 3.14 (4 H, br s, CH_2CH_2), 6.96 (1 H, s, base 3-H), 7.15 (5 H, s, Ph), 7.30–7.70 (2 H, m, base 6- and 7-H), 7.85 (1 H, d, *J* 9.0, base 5-H) and 8.00 (1 H, d, *J* 9.0, base 8-H); *m/z* (EI) M^+ 247 (Found: C, 86.9; H, 7.1; N, 5.5. $C_{18}H_{17}N$ requires C, 87.41; H, 6.93; N, 5.66%).

2-(1-Adamantyl)-4-cyanopyridine **P-2a**. M.p. 134.5–136.1 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 2870, 2825, 1580, 1540, 1450 and 845; δ_H(100 MHz; CCl_4) 1.60–2.20 (15 H, m, adamantyl), 7.25 (1 H, d, *J* 6.0, base 5-H), 7.40 (1 H, s, base 3-H) and 8.67 (1 H, d, *J* 6.0, base 6-H); *m/z* (EI) M^+ 238 (Found: C, 80.9; H, 7.4; N, 11.9. $C_{16}H_{18}N_2$ requires C, 80.63; H, 7.61; N, 11.75%).

2-(1-Adamantyl)benzothiazole **P-3a**. M.p. 102.3–104.2 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 2900, 2850, 1450 and 1370; δ_H(100 MHz; CCl_4) 1.75 (6 H, br s, adamantyl), 2.05 (9 H, br s, adamantyl), 7.10–7.40 (2 H, m, base 5- and 6-H) and 7.60–7.90 (2 H, m, base 4- and 7-H); *m/z* (EI) M^+ 269 (Found: C, 75.6; H, 7.2; N, 5.4. $C_{17}H_{19}NS$ requires C, 75.79; H, 7.11; N, 5.20%).

Methyl 2-(1-Adamantyl)isonicotinate **P-4a**. M.p. 36.5–38.0 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 2890, 2840, 1725, 1295, 1220 and 770; δ_H(100 MHz; CCl_4) 1.70–2.30 (15 H, m, adamantyl), 3.90 (3 H, s, Me), 7.55 (1 H, d, *J* 6.0, base 5-H), 7.75 (1 H, s, base 3-H) and 8.68 (1 H, d, *J* 6.0, base 6-H); *m/z* (EI) M^+ 271 (Found: C, 75.3; H, 7.85; N, 5.4. $C_{17}H_{21}NO_2$ requires C, 75.24; H, 7.80; N, 5.16%).

1-(1-*Adamantyl*)*phthalazine* **P-5a**. M.p. 122.1–123.0 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 2900, 2840, 1450 and 1370; δ_H(100 MHz; CCl_4) 1.80–2.60 (15 H, m, adamantyl), 7.80–8.10 (3 H, m, base 6-, 7- and 8-H), 8.65–8.85 (1 H, m, base 5-H) and 9.43 (1 H, s, base 4-H); *m/z* (EI) M$^+$ 264 (Found: C, 82.1; H, 7.7; N, 10.6. $C_{18}H_{20}N_2$ requires C, 81.77; H, 7.63; N, 10.60%).

4-(1-*Adamantyl*)-5-*bromopyrimidine* **P-6a**. M.p. 109–110.4 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 2900, 2840, 1450 and 1370; δ_H(100 MHz; CCl_4) 1.60–2.40 (15 H, m, adamantyl), 8.55 (1 H, br s, base 6-H) and 8.86 (1 H, s, base 2-H) (Found: C. 57.1; H, 5.8; N, 9.5. $C_{14}H_{17}BrN_2$ requires C, 57.35; H, 5.84; N, 9.56%).

4-*Methyl*-2-(*phenoxymethyl*)*quinoline* **P-1b**. Oil; ν_{max}(neat)/cm^{-1} 3040, 1660, 1500, 1245, 1220 and 765; δ_H(100 MHz; CCl_4) 2.60 (3 H, s, Me), 5.16 (2 H, s, CH_2), 6.60–7.60 (8 H, m, Ph and base 3-, 6- and 7-H), 7.70 (1 H, d, *J* 9.0, base 5-H) and 7.90 (1 H, d, *J* 9.0, base 8-H); *m/z* (EI) M$^+$ 249 (Found: C, 81.5; H, 6.1; N, 5.55. $C_{17}H_{15}NO$ requires C, 81.90; H, 6.06; N, 5.62%).

2-(1-*Acetoxyethyl*)-4-*methylquinoline* **P-1c**. Oil; ν_{max}(neat)/cm^{-1} 2960, 2920, 1740, 1600, 1370, 1245, 1080 and 770; δ_H(100 MHz; CCl_4) 1.60 (3 H, d, *J* 6.0, Me), 2.05 (3 H, s, MeCO), 2.60 (3 H, s, Me), 5.90 (1 H, q, *J* 6.0, CH), 7.10 (1 H, s, base 3-H), 7.20–7.60 (2 H, m, base 6- and 7-H), 7.76 (1 H, d, *J* 9.0, base 5-H) and 7.90 (1 H, d, *J* 9.0, base 8-H) (Found: C, 73.5; H, 6.4; N, 6.4. $C_{14}H_{15}NO_2$ requires C, 73.34; H, 6.59; N, 6.11%).

4-*Methyl*-2-[(*tetrahydro*-3-*furyl*)*methyl*]*quinoline* **P-1d**. Oil; ν_{max}(neat)/cm^{-1} 2900, 2840, 1600, 1445, 1050 and 765; δ_H(100 MHz; CCl_4) 1.10–2.20 (3 H, m, furan 3-H and 4-H_2), 2.62 (3 H, s, Me), 2.75–3.00 (2 H, m, CH_2), 3.30–4.00 (4 H, m, OCH_2 × 2), 6.95 (1 H, s, base 3-H), 7.20–7.65 (2 H, m, base 6- and 7-H), 7.80 (1 H, d, *J* 9.0, base 5-H) and 7.90 (1 H, d, *J* 9.0, base 8-H); *m/z* (EI) M$^+$ 227 (Found: C, 74.2; H, 7.1; N, 5.9. $C_{15}H_{17}NO$ requires C, 74.05; H, 7.04; N, 5.76%).

4-*Methyl*-2-(3-*phenylpropionyl*)*quinoline* **P-1e**. M.p. 72.2–73.1 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 3010, 2910, 1685, 1450, 1380, 765 and 700; δ_H(100 MHz; CCl_4) 2.05 (2 H, t, *J* 7.5, CH_2), 2.60 (3 H, s, Me), 3.30 (2 H, t, *J* 7.5, CH_2), 6.90–8.00 (9 H, m, Ph and base 3-, 5-, 6- and 7-H) and 8.10 (1 H, d, *J* 9.0, base 8-H) (Found: C, 82.6; H, 6.6; N, 4.8. $C_{19}H_{17}NO$ requires C, 82.88; H, 6.22; N, 5.09%).

2-*Benzoyl*-4-*methylquinoline* **P-1f**. M.p. 106.5–107.4 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 1660, 1590, 1220, 770 and 690; δ_H(100 MHz; $CDCl_3$) 2.73 (3 H, s, Me) and 7.32–8.34 (10 H, m, Ph and base); *m/z* (EI) M$^+$ 247 (Found: C, 82.3; H, 5.05; N, 5.7. $C_{17}H_{13}NO$ requires C, 82.56; H, 5.30; N, 5.67%).

Relative Reactivity of Tertiary, Secondary and Primary Carboxylic Acids.—To a solution of [bis(trifluoroacetoxy)-iodo]benzene **1b** (1 mmol) in dry benzene (5 cm^3) were added the appropriate carboxylic acid (3 mmol) (adamantane-1-carboxylic acid, cyclohexanecarboxylic acid, or 3-phenylpropionic acid) and lepidine **B-1** (3 mmol). Then, *p*-terphenyl (1 mmol) was added to the solution as an internal standard and the obtained mixture was refluxed. Then, a portion (0.2 cm^3) of the reaction mixture was extracted by syringe every 15 min and poured into a mixture of ethyl acetate and saturated aq. sodium hydrogen carbonate. Products were analysed by GLC.

Synthesis of C-Nucleosides.—The reaction was carried out with molar proportions of 5 : 5 : 1 (sugar carboxylic acid : heteroaromatic base : trivalent iodine compound). [Bis(trifluoroacetoxy)iodo]pentafluorobenzene **1c** was used as the trivalent iodine compound. To a solution of trivalent iodine compound in dry dichloromethane (5 cm^3) in a quartz cell were added the appropriate sugar carboxylic acid and heteroaromatic base under argon and the mixture was irradiated with a low-pressure mercury lamp at room temp. for 8–10 h. After the reaction, the solvent was removed under reduced pressure and the residue, in ethyl acetate, was washed with saturated aq. sodium hydrogen carbonate. Then the aqueous layer was extracted with ethyl acetate (× 3) and the combined organic layer was dried over $MgSO_4$. After the removal of solvent under reduced pressure, the residual oil was purified by PTLC on silica gel [ethyl acetate–hexane (1 : 2–1 : 1)].

In order to recover the starting sugar carboxylic acid, the aqueous layer was acidified to pH ~ 1 by 2 mol dm^{-3} HCl and the organic layer was extracted with diethyl ether (× 3). The recovered sugar carboxylic acid was used again to synthesize further *C*-nucleoside.

4-*Methyl*-2-(*tetrahydro*-2-*furyl*)*quinoline* **P-1i**. Oil; ν_{max}(neat)/cm^{-1} 1590 and 1060; δ_H(270 MHz; $CDCl_3$) 1.96–2.13 (3 H, m, CH_2), 2.42–2.60 (1 H, m, CH_2), 2.72 (3 H, s, Me), 4.05 (1 H, dd, *J* 14.0 and 7.0, OCH_2), 4.18 (1 H, dd, *J* 14.0 and 7.1, OCH_2), 5.14 (1 H, t, *J* 7.0, OCH), 7.45 (1 H, s, base 3-H), 7.52 (1 H, br t, *J* 8.2, base 6-H), 7.68 (1 H, br t, *J* 8.2, base 7-H), 7.97 (1 H, br d, *J* 8.2, base 5-H) and 8.05 (1 H, br d, *J* 8.2, base 8-H) [Found: HRMS (FAB) (M + H)$^+$ 214.1227. $C_{14}H_{16}NO$ requires (*M* + H), 214.1231] (Found: C, 78.5; H, 6.95; N, 6.5. $C_{14}H_{15}NO$ requires C, 78.84; H, 7.09; N, 6.57%).

4-*Methyl*-2-(2′,3′,5′-*tri*-O-*benzyl*-D-*ribofuranosyl*)*quinoline* **P-1j**. (α form): Oil; $[\alpha]_D^{23}$ −29.3 (*c* 0.58, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2840, 1590, 1445, 1350, 1205, 1120, 1085, 1045, 1025, 910, 740 and 700; δ_H(400 MHz; $CDCl_3$) 2.68 (3 H, d, *J* 0.6, Me), 3.67 (1 H, dd, *J* 10.8 and 4.2, 5′-H), 3.84 (1 H, dd, *J* 10.8 and 2.6, 5′-H), 3.97 (1 H, d, *J* 11.7, OCH_2), 4.14 (1 H, d, *J* 11.7, OCH_2), 4.28 (1 H, dd, *J* 8.6 and 4.0, 3′-H), 4.42 (1 H, d, *J* 11.9, OCH_2), 4.44 (1 H, m, 2′-H), 4.54–4.57 (1 H, m, 4′-H), 4.56 (1 H, d, *J* 11.9, OCH_2), 4.56 (1 H, d, *J* 12.1, OCH_2), 4.64 (1 H, d, *J* 12.1, OCH_2), 5.36 (1 H, d, *J* 2.8, 1′-H), 6.80 (2 H, d, *J* 7.0, *o*-Ph), 6.99–7.10 (3 H, m, Ph), 7.25–7.35 (10 H, m, Ph), 7.55 (1 H, ddd, *J* 8.2, 7.0 and 1.3, base 6-H), 7.68 (1 H, br s, base 3-H), 7.71 (1 H, ddd, *J* 8.2, 7.0 and 1.3, base 7-H) and 7.99–8.02 (2 H, m, base 5- and 8-H); δ_C(67.8 MHz; $CDCl_3$) 18.7 (base Me), 70.1 (C-5′), 72.6 (OCH_2), 73.2 (OCH_2), 73.5 (OCH_2), 79.4 (C-2′), 80.0 (C-3′), 80.4 (C-4′), 84.5 (C-1′), 121.3, 123.8, 125.9, 129.0 and 129.4 (base C-3, -5, -6, -7 and -8), 127.3, 127.5, 127.6, 127.8, 127.9, 128.0, 128.3 and 128.4 (Ph and base C-4a), 137.7 (Cq, Ph), 137.8 (Cq, Ph), 138.3 (Cq, Ph), 147.1 (Cq, base C-8a), 144.2 (Cq, base C-4) and 159.1 (Cq, base C-2); NOE (1′-H–3′-H) was observed; *m/z* (FAB) (M + H)$^+$ 546.

(β form): M.p. 67–68 °C (from EtOH); $[\alpha]_D^{23}$ +127.1 (*c* 0.43, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2850, 1585, 1440, 1345, 1200, 1080, 1120, 905, 735 and 700; δ_H(400 MHz; $CDCl_3$) 2.48 (3 H, d, *J* 0.7, Me), 3.73 (1 H, dd, *J* 10.8 and 3.8, 5′-H), 3.90 (1 H, dd, *J* 10.8 and 2.9, 5′-H), 4.05 (1 H, dd, *J* 7.1 and 5.1, 3′-H), 4.28 (1 H, dd, *J* 5.1 and 3.3, 2′-H), 4.38 (1 H, d, *J* 11.9, OCH_2) 4.45–4.49 (1 H, m, 4′-H), 4.57 (1 H, d, *J* 10.3, OCH_2), 4.60 (1 H, d, *J* 10.3, OCH_2), 4.65 (1 H, d, *J* 11.9, OCH_2), 4.77 (1 H, d, *J* 12.1, OCH_2), 4.84 (1 H, d, *J* 12.1, OCH_2), 5.38 (1 H, d, *J* 3.3, 1′-H), 7.21–7.33 (13 H, m, Ph), 7.39–7.41 (2 H, m, Ph), 7.40 (1 H, br s, base 3-H), 7.53 (1 H, ddd, *J* 8.4, 7.0 and 0.9, base 6-H), 7.70 (1 H, ddd, *J* 8.3, 7.0 and 0.9, base 7-H), 7.94 (1 H, dd, *J* 8.4 and 0.9, base 5-H) and 8.08 (1 H, br d, *J* 8.3, base 8-H); δ_C(67.8 MHz; $CDCl_3$) 18.6 (base Me), 69.8 (C-5′), 71.4 (OCH_2), 72.0 (OCH_2), 73.4 (OCH_2), 77.1 (C-2′), 81.1 (C-3′), 81.3 (C-4′), 85.5 (C-1′), 119.5, 123.7, 125.9, 129.8 and 129.0 (base C-3, -5, -6, -7 and -8), 127.5, 127.6, 127.7, 127.9, 128.2, 128.3 and 128.4 (Ph and base C-4a), 137.9 (Cq, Ph), 138.0 (Cq, Ph), 138.4 (Cq, Ph), 144.8 (Cq, base C-4), 147.5 (Cq, base C-8a) and 160.1 (Cq, base C-2); NOE (1′-H–4′-H) was observed; *m/z* (FAB) (M + H)$^+$ 546 (Found: C, 78.95; H, 6.6; N, 2.5. $C_{36}H_{35}NO_4$ requires C, 79.24; H, 6.47; N, 2.57%).

Methyl 2-(2′,3′,5′-*tri*-O-*benzyl*-D-*ribofuranosyl*)*isonicotinate* **P-4j**. (α form): Oil; $[\alpha]_D^{23}$ +54.3 (*c* 0.45, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3000, 2840, 1720, 1300, 1210, 1100, 740 and 700;

δ_H(500 MHz; $CDCl_3$) 3.65 (1 H, dd, *J* 10.7 and 3.9, 5'-H), 3.82 (1 H, dd, *J* 10.7 and 2.5, 5'-H), 3.93 (3 H, s, Me), 4.05 (1 H, d, *J* 11.8, OCH_2), 4.23 (1 H, d, *J* 11.8, OCH_2), 4.29 (1 H, dd, *J* 8.5 and 4.1, 3'-H), 4.38 (1 H, m, 4'-H), 4.43 (1 H, d, *J* 11.8, OCH_2), 4.50 (1 H, dd, *J* 4.1 and 2.8, 2'-H), 4.54 (1 H, d, *J* 12.1, OCH_2), 4.55 (1 H, d, *J* 11.8, OCH_2), 4.62 (1 H, d, *J* 12.1, OCH_2), 5.31 (1 H, d, *J* 2.8, 1'-H), 6.89 (2 H, d, *J* 6.1, Ph), 7.12–7.17 (3 H, m, Ph), 7.26–7.35 (10 H, m, Ph), 7.75 (1 H, dd, *J* 5.0 and 1.4, base 5-H), 8.18 (1 H, d, *J* 1.4, base 3-H) and 8.64 (1 H, d, *J* 5.0, base 6-H); δ_C(67.8 MHz; $CDCl_3$) 52.6 (Me), 69.8 (C-5'), 72.6 (OCH_2), 73.2 (OCH_2), 73.5 (OCH_2), 79.0 (C-2'), 80.0 (C-3'), 80.3 (C-4'), 83.7 (C-1'), 121.6 (base C-5), 121.9 (base C-3), 127.4, 127.6, 127.7, 127.8, 127.9, 128.1, 128.3 and 128.4 (Ph), 137.6 (Cq, Ph), 137.7 (Cq, Ph), 137.8 (Cq, Ph), 138.2 (Cq, base C-4), 149.0 (base C-6), 160.2 (Cq, base C-2) and 165.8 (Cq, CO); NOE (1'-H–3'-H) was observed; *m/z* (FAB) $(M + H)^+$ 540 (Found: C, 73.15; H, 6.2; N, 2.6. $C_{33}H_{33}NO_6$ requires C, 73.45; H, 6.16; N, 2.60%).

(β form): Oil; $[\alpha]_D^{23}$ +15.6 (*c* 0.15, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3000, 1715, 1290, 1200, 740 and 700; δ_H(500 MHz; $CDCl_3$) 3.68 (1 H, dd, *J* 10.7 and 4.1, 5'-H), 3.83 (1 H, dd, *J* 10.7 and 3.0, 5'-H), 3.83 (3 H, s, Me), 4.00 (1 H, dd, *J* 7.2 and 5.0, 3'-H), 4.18 (1 H, dd, *J* 5.0 and 3.3, 2'-H), 4.41 (1 H, d, *J* 11.8, OCH_2), 4.43–4.45 (1 H, m, 4'-H), 4.56 (1 H, d, *J* 11.8, OCH_2), 4.59 (1 H, d, *J* 12.1, OCH_2), 4.67 (1 H, d, *J* 12.1, OCH_2), 4.68 (1 H, d, *J* 12.1, OCH_2), 4.76 (1 H, d, *J* 12.1, OCH_2), 5.28 (1 H, d, *J* 3.3, 1'-H), 7.23–7.36 (15 H, m, Ph), 7.73 (1 H, dd, *J* 5.0 and 1.4, base 5-H), 8.18 (1 H, d, *J* 1.4, base 3-H) and 8.73 (1 H, d, *J* 5.0, base 6-H); δ_C(67.8 MHz; $CDCl_3$) 52.5 (Me), 69.5 (C-5'), 71.6 (OCH_2), 72.1 (OCH_2), 73.3 (OCH_2), 77.5 (C-2'), 81.1 (C-3'), 81.5 (C-4'), 84.6 (C-1'), 120.5 (base C-5), 121.7 (base C-3), 127.4, 127.5, 127.7, 127.8, 127.9, 128.2 and 128.3 (Ph), 137.8 (Cq, Ph), 137.9 (Cq, Ph), 138.0 (Cq, Ph), 138.3 (Cq, base C-4), 149.9 (base C-6), 161.3 (Cq, base C-2), and 165.7 (Cq, CO); NOE (1'-H–4'-H) was observed; *m/z* (FAB) $(M + H)^+$ 540.

2-(3',4'-*Di*-O-*benzoyl*-2-*deoxy*-D-erythro-pentapyranosyl)-4-*methylquinoline* **P-1l**. (β form): M.p. 149–151 °C (from EtOH); $[\alpha]_D^{24}$ 15.6 (*c* 1.08, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 1720, 1590, 1450, 1265, 1105, 770 and 725; δ_H(500 MHz; $CDCl_3$) 2.34 (1 H, ddd, *J* 14.7, 11.3 and 2.5, 2'-H), 2.68 (1 H, ddd, *J* 14.7, 4.1 and 2.5, 2'-H), 2.75 (3 H, s, Me), 4.23 (1 H, t, *J* 10.2, 5'-H^b), 4.30 (1 H, dd, *J* 10.2 and 5.2, 5'-H^a), 5.18 (1 H, dd, *J* 11.3 and 2.5, 1'-H), 5.48 (1 H, ddd, *J* 10.2, 5.2 and 3.0, 4'-H), 5.96 (1 H, m, 3'-H), 7.35 (2 H, t, *J* 7.7, Ph), 7.49–7.59 (4 H, m, Ph and base 3-H), 7.56 (1 H, dd, *J* 8.3 and 7.2, base 6-H), 7.63 (1 H, t, *J* 7.7, Ph), 7.70 (1 H, dd, *J* 8.5 and 7.2, base 7-H), 7.92 (2 H, d, *J* 7.7, Ph), 8.00 (1 H, d, *J* 8.3, base 5-H), 8.06 (1 H, d, *J* 8.5, base 8-H) and 8.17 (2 H, d, *J* 7.7, Ph); NOEs (3'-H–Me, 5'-H^a–Me, 5'-H^b–Me) were observed; *m/z* (FAB) $(M + H)^+$ 468 (Found: C, 74.0; H, 5.4; N, 2.9. $C_{29}H_{25}NO_5$ requires C, 74.50; H, 5.39; N, 3.00%).

Methyl 6-(3',4'-*Di*-O-*benzoyl*-2'-*deoxy*-D-erythro-*pentopyranosyl*)*nicotinate* **P-8l**. (α-form): M.p. 135–137 °C (from MeOH); $[\alpha]_D^{24}$ +87.4 (*c* 0.29, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 1710, 1590, 1450, 1270, 1105, 1015, 770 and 715; δ_H(500 MHz; $CDCl_3$) 2.14 (1 H, ddd, *J* 14.7, 11.3 and 2.5, 2'-H^b), 2.67 (1 H, ddd, *J* 14.7, 4.2 and 2.6, 2'-H^a), 3.96 (3 H, s, CO_2Me), 4.18 (1 H, t, *J* 10.6, 5'-H^b), 4.29 (1 H, dd, *J* 10.6 and 4.7, 5'-H^a), 5.09 (1 H, dd, *J* 11.3 and 2.6, 1'-H), 5.42 (1 H, ddd, *J* 10.6, 4.7 and 3.1, 4'-H), 5.92 (1 H, m, 3'-H), 7.37 (2 H, dd, *J* 3.1 and 1.5, Ph), 7.51 (3 H, m, Ph, base 5-H), 7.62 (2 H, tt, *J* 7.4 and 1.5, Ph), 7.90 (2 H, dd, *J* 8.4 and 1.3, Ph), 8.14 (2 H, dd, *J* 8.4 and 1.4, Ph), 8.35 (1 H, dd, *J* 8.1 and 2.1, base 4-H) and 9.14 (1 H, dd, *J* 2.1, and 0.8, base 2-H); NOEs (1'-H–3'-H, 1'-H–5'-H^a, 1'-H–5'-H^b) were observed [Found: HRMS (FAB) $(M + H)^+$ 462.1547. $C_{26}H_{24}NO_7$ requires $(M + H)$ 462.1551] (Found: C, 67.55; H, 4.95; N, 3.2. $C_{26}H_{23}NO_7$ requires C, 67.67; H, 5.02; N, 3.04%).

4-*Methyl*-2-(2',3',4'-*Tri*-O-*benzoyl*-D-*ribopyranosyl*)*quinoline* **P-1k**. (β form): M.p. 136–139 °C (from EtOH); $[\alpha]_D^{30}$ −122.5 (*c* 0.13, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2950, 1720, 1595, 1270, 1100, 770 and 720; δ_H(500 MHz; $CDCl_3$) 2.71 (3 H, s, Me), 4.24 (1 H, dd, *J* 11.0 and 9.9, 5'-H), 4.33 (1 H, dd, *J* 11.0 and 5.0, 5'-H), 5.32 (1 H, br d, *J* 7.8, 1'-H), 5.67 (1 H, ddd, *J* 9.9, 5.0 and 3.0, 4'-H), 5.85 (1 H, br d, *J* 7.8, 2'-H), 6.36 (1 H, d, *J* 3.0, 3'-H), 7.22–7.65 (12 H, m, Ph, base 3-, 6- and 7-H), 7.80 (2 H, d, *J* 7.7, Ph), 7.91–7.96 (4 H, m, Ph, base 5- and 8-H) and 8.15 (2 H, d, *J* 7.7, Ph) [Found: HRMS (FAB) $(M + H)^+$ 588.2015. $C_{36}H_{30}NO_7$ requires $(M + H)$ 588.2020] (Found: C, 73.35; H, 5.2; N, 2.1. $C_{36}H_{29}NO_7$ requires C, 73.58; H, 4.97; N, 2.38%).

Dialkylation onto Heteroaromatic Bases with (*Diacyloxyiodo*)*benzene* (*General Procedure*).—To a solution of (diacyloxyiodo)benzene (2 mmol) in dry dichloromethane (5 cm^3) were added trifluoroacetic acid and heteroaromatic base under argon. Then the mixture was irradiated with a high-pressure mercury lamp for 10 h. The reaction mixture was washed with saturated aq. sodium hydrogen carbonate and the aqueous layer was extracted with dichloromethane (×3). The organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by PTLC.

Methyl 2-*cyclohexylisonicotinate* **P-4g**. Oil; ν_{max}(neat)/cm^{-1} 2890, 2810, 1720, 1425, 1280, 1220, 1105 and 760; δ_H(100 MHz; CCl_4) 1.20–2.20 (10 H, m, cyclohexyl), 2.50–2.90 (1 H, m, cyclohexyl CH), 3.88 (3 H, s, Me), 7.60 (1 H, s, base 3-H), 7.51 (1 H, d, *J* 6.1, base 5-H) and 8.58 (1 H, d, *J* 6.1, base 6-H); *m/z* (EI) M^+ 219 (Found: C, 71.1; H, 8.0; N, 6.1. $C_{13}H_{17}NO_2$ requires C, 71.20; H, 7.82; N, 6.39%).

Methyl 2,6-*dicyclohexylisonicotinate* **P-4g$_2$**. Oil; ν_{max}(neat)/cm^{-1} 2895, 2830, 1720, 1555, 1435, 1230 and 770; δ_H(100 MHz; CCl_4) 1.00–2.20 (20 H, m, cyclohexyl × 2), 2.46–2.81 (2 H, m, cyclohexyl CH × 2), 3.86 (3 H, s, Me) and 7.42 (2 H, s, base 3- and 5-H); *m/z* (EI) M^+ 301 (Found: C, 75.5; H, 9.0; N, 4.5. $C_{19}H_{27}NO_2$ requires C, 75.71; H, 9.03; N, 4.65%).

2-*Cyclohexyl*-4-*methylpyridine* **P-7g**. Oil; ν_{max}(neat)/cm^{-1} 2880, 1440 and 850; δ_H(100 MHz; CCl_4) 1.10–2.10 (10 H, m, cyclohexyl), 2.30 (3 H, s, Me), 2.40–2.70 (1 H, m, cyclohexyl CH), 6.90 (1 H, s, base 3-H), 6.87 (1 H, d, *J* 6.0, base 5-H) and 8.35 (1 H, d, *J* 6.0, base 6-H); *m/z* (EI) M^+ 175 (Found: C, 82.5; H, 9.9; N, 7.8. $C_{12}H_{17}N$ requires C, 82.23; H, 9.78; N, 7.99%).

2,6-*Dicyclohexyl*-4-*methylpyridine* **P-7g$_2$**. Oil; ν_{max}(neat)/cm^{-1} 2900, 2840, 1600, 1440, 1180 and 850; δ_H(100 MHz; CCl_4) 1.20–2.00 (20 H, m, cyclohexyl × 2), 2.25 (3 H, s, Me), 2.30–2.80 (2 H, m, cyclohexyl CH × 2) and 6.70 (2 H, s, base 3- and 5-H); *m/z* (EI) M^+ 257 (Found: C, 83.8; H, 10.6; N, 5.4. $C_{18}H_{27}N$ requires C, 83.98; H, 10.57; N, 5.44%).

Oxalic Acid Monoalkyl Esters (*General Procedure*).—To a solution of an alcohol (10 mmol) in dichloromethane (20 cm^3) was added an excess of oxalyl dichloride (30 mmol) in dichloromethane (10 cm^3) at room temperature. The reaction was carried out until the evolution of HCl gas ceased. The reaction mixture was evaporated to remove volatile materials and water was added to hydrolyse the residue. The organic layer was extracted with dichloromethane (×3) and the obtained organic layer was dried over $MgSO_4$. After the removal of the solvent, the residue was purified by column chromatography on silica gel [eluent $CHCl_3$–AcOEt (3:1)].

Alkylation onto Heteroaromatic Bases starting from Alcohols (*General Procedure*).—The reaction was carried out with molar proportions of 3:3:1 (oxalic acid monoalkyl ester–heteroaromatic base–trivalent iodine compound). To a solution of trivalent iodine compound in dry benzene or toluene (5 cm^3) were added the appropriate oxalic acid monoalkyl ester and heteroaromatic base. Then the mixture was refluxed under argon. The reaction mixture was worked up by the same procedure as described above.

4-*Methyl*-2-(1-*methylcyclohexyl*)*quinoline* **P-1m**. Oil; ν_{max}(neat)/cm^{-1} 2900, 2830, 1590, 1440 and 760; δ_H(100 MHz; CCl_4) 1.30 (3 H, s, Me), 1.20–1.80 (8 H, m, cyclohexyl), 2.20–2.55 (2 H, m cyclohexyl CH), 2.60 (3 H, s, Me), 7.25 (1 H, s, base 3-H), 7.25–7.75 (2 H, m, base 6- and 7-H), 7.87 (1 H, d, *J* 9.1, base 5-H) and 8.06 (1 H, d, *J* 9.1, base 8-H); *m*/*z* (EI) M$^+$ 239 (Found: C, 85.3; H, 8.9; N, 6.1. $C_{17}H_{21}N$ requires C, 85.30; H, 8.84; N, 5.85%).

2-(−)-*Menthyl*-4-*methylquinoline* **P-1n**. Oil; ν_{max}(neat)/cm^{-1} 2900, 1595, 1440 and 765; δ_H(270 MHz; $CDCl_3$) 0.75 (3 H, d, *J* 7.2, menthyl Me), 0.82 (3 H, d, *J* 7.2, menthyl Me), 0.91 (3 H, d, *J* 6.7, menthyl Me), 1.02–1.95 (9 H, m, menthyl CH and CH_2), 2.68 (3 H, d, *J* 0.6, base Me), 2.91 (1 H, td, *J* 11.1 and 2.5, menthyl CH), 7.16 (1 H, br s, base 3-H), 7.49 (1 H, ddd, *J* 8.7, 6.8 and 1.4, base 6-H), 7.66 (1 H, ddd, *J* 8.7, 6.8 and 1.4, base 7-H), 7.94 (1 H, dd, *J* 8.7 and 1.4, base 5-H) and 8.10 (1 H, br d, *J* 8.7, base 8-H); *m*/*z* (EI) M$^+$ 281 (Found: C, 84.7; H, 10.4; N, 4.75. $C_{20}H_{27}N$ requires C, 85.35; H, 9.67; N, 4.98%).

Methyl 2-(1-*methylcyclohexyl*)*isonicotinate* **P-7m**. Oil; ν_{max}(neat)/cm^{-1} 2890, 2825, 1720, 1430, 1290, 1260 and 760; δ_H(100 MHz; CCl_4) 1.24 (3 H, s, Me), 1.10–1.84 (8 H, m, cyclohexyl), 2.08–2.50 (2 H, m, cyclohexyl CH), 3.96 (3 H, s, OMe), 7.64 (1 H, d, *J* 6.1, base 5-H), 7.89 (1 H, s, base 3-H) and 8.78 (1 H, d, *J* 6.1, base 6-H); *m*/*z* (EI) M$^+$ 233 (Found: C, 71.4; H, 8.0; N, 5.9. $C_{14}H_{19}NO_2$ requires C, 72.07; H, 8.21; N, 6.01%).

3-[1-(4-*Methylquinolyl*)*propyl*]-4,5-*dihydrofuran*-2(3H)-*one* (*less polar*) **P'-1** (R = Et). Oil; ν_{max}(neat)/cm^{-1} 2930, 2900, 1750, 1590, 1440, 1370, 1155, 1020 and 765; δ_H(400 MHz; $CDCl_3$) 0.89 (3 H, t, *J* 7.4, Me), 2.07–2.24 (3 H, m, CH_2 and CH_2), 2.34–2.44 (1 H, m, CH_2), 2.68 (3 H, d, *J* 0.6, base Me), 3.07 (1 H, td, *J* 9.2 and 6.8, CHCO), 3.30 (1 H, q, *J* 6.8, CH), 4.13–4.17 (2 H, m, OCH_2), 7.17 (1 H, br s, base 3-H), 7.53 (1 H, td, *J* 8.3 and 1.1, base 6-H), 7.68 (1 H, ddd, *J* 8.3, 7.7 and 1.1, base 7-H), 7.96 (1 H, dd, *J* 8.3 and 1.1, base 5-H) and 8.03 (1 H, br d, *J* 7.7, base 8-H) (Found: C, 75.6; H, 6.9; N, 5.0. $C_{17}H_{19}NO_2$ requires C, 75.81; H, 7.11; N, 5.20%).

(*More polar*). Oil; ν_{max}(neat)/cm^{-1} 2900, 1750, 1595, 1440, 1370, 1150, 1020 and 765; δ_H(500 MHz; $CDCl_3$) 0.87 (3 H, t, *J* 7.3, Me), 1.82 (1 H, dtd, *J* 14.8, 7.3 and 5.0, CH_2), 2.07–2.16 (1 H, m, CH_2), 2.34–2.41 (2 H, m, CH_2), 2.70 (3 H, d, *J* 0.8, base Me), 3.17 (1 H, td, *J* 9.6 and 5.0, CHCO), 3.28 (1 H, dt, *J* 10.2 and 5.0, CH), 4.12–4.21 (2 H, m, OCH_2), 7.19 (1 H, br s, base 3-H), 7.52 (1 H, ddd, *J* 8.3, 6.9 and 1.4, base 6-H), 7.67 (1 H, ddd, *J* 8.3, 6.9 and 1.4, base 7-H), 7.97 (1 H, dd, *J* 8.3 and 1.4, base 5-H) and 8.04 (1 H, br d, *J* 8.3, base 8-H) (Found: C, 75.9; H, 6.9; N, 5.2).

Comparison of Relative Reactivity of Tertiary, Secondary and Primary Oxalic Acid Monoalkyl Esters.—To a solution of compound **1b** (1 mmol) in dry toluene (5 cm^3) was added the appropriate oxalic acid monoalkyl ester **A'** (3 mmol) and lepidine **B-1** (3 mmol). Then, *p*-terphenyl (1 mmol) was added to the solution as an internal standard and the obtained mixture was refluxed. The analysis of products was carried out by the same procedure as that using carboxylic acid.

Reaction to Trap Alkyl Radicals and Alkoxycarbonyl Radicals with TEMPO.—A mixture of TEMPO (1 mmol) and (diacyloxyiodo)benzene {or [bis(alkoxyoxalyloxy)iodo]benzene} (1 mmol) in dry dichloromethane (5 cm^3) was irradiated at 30 °C. After the reaction, the mixture was worked up in the usual way.

N-(1-*Adamantyloxy*)-2,2,6,6-*tetramethylpiperidine* **5**. M.p. 87–90 °C (from MeOH); ν_{max}(KBr)/cm^{-1} 2850, 1440, 1345, 1130, 1050, 920 and 710; δ_H(270 MHz; $CDCl_3$) 1.00–1.65 (12 H, m, adamantyl and CH_2 × 3), 1.08 (6 H, s, Me × 2), 1.18 (6 H, s, Me × 2), 1.85–1.95 (6 H, m, adamantyl) and 2.13 (3 H, br s, adamantyl) [Found: HRMS (FAB): (M + H)$^+$ 292.2640. $C_{19}H_{34}NO$ requires (M + H) 292.2639].

N-(1-*Adamantyloxycarbonyloxy*)-2,2,6,6-*tetramethylpiperidine* **5'**. Oil; ν_{max}(neat)/cm^{-1} 2860, 1720, 1440, 1340, 1210, 1180 and 1025; δ_H(270 MHz; $CDCl_3$) 1.10 (6 H, s, Me × 2), 1.15 (6 H, s, Me × 2), 1.30–1.80 (11 H, m, adamantyl and CH_2 × 3) and 2.10–2.18 (10 H, m, adamantyl) [Found: HRMS (FAB) (M + H)$^+$ 336.2539. $C_{20}H_{34}NO_3$ requires (M + H) 336.2537].

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