Acta Chemica Scandinavica, 1997: 51: 302–306
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ACTA
CHEMICA SCANDINAVICA
ISSN 0904-213X

Trialkylalanes in Palladium-Catalyzed *C*-Alkylations of Azines

Qingbo Lu, Ionel Mangalagiu, Tore Benneche* and Kjell Undheim

Department of Chemistry, University of Oslo, N-0315 Oslo, Norway

Lu, Q., Mangalagiu, I., Benneche, T. and Undheim, K., 1997. Trialkylalanes in Palladium-Catalyzed *C*-Alkylations of Azines. – Acta Chem. Scand. 51: 302–306.

Carbo-substitution with alkyl groups in halogenoazines is readily effected under the influence of Pd-catalysis with alanes as the donor of the alkyl group.

C-Alkylations in π-deficient azines have been effected by cross-coupling reactions of halogenoazines with organometallics catalyzed by transition metals.[1] Stannanes are especially useful organometallic reagents because of their ease of preparation and handling and their high reactivity in the presence of palladium catalysts.[2] The coupling reactions proceed well when the carbon bound to the metal in stannanes is sp^2- or sp-hybridized, but require more vigorous conditions, or may not proceed at all for the transfer of an alkyl group. It is highly desirable to find a general procedure to effect alkylation by coupling reactions that proceeds under mild and simple reaction conditions.

Transfer of alkyl groups from trialkylboranes to pyrazines has been reported to yield alkylpyrazines in moderate yields under relatively vigorous reaction conditions using Pd-catalysis.[3] Organozinc reagents can effect alkylation reactions as well as the transfer of vinyl or (hetero)aryl substituents using Pd-catalysis.[1,4]

Organoalanes have so far received relatively little attention as reagents for the transfer of alkyl groups to azines in metal-catalyzed carbo-substitutions.[1] The alkylalanes, however, would be expected to offer a wide range of useful applications since this class of reagents readily transfers an alkyl group from the aluminum to the palladium(II) complex which is formed after insertion of Pd(0) into a carbon–halogen or carbon–oxygen (e.g., triflate) bond; subsequent, rapid reductive elimination leads to an alkylated product.[5,6]

In the electrophilic positions in π-deficient azines we have previously established that the readily available chlorides are well suited to carbo-substitution reactions under the influence of Pd-catalysis.[7,8] In the benzenoid positions, i.e., in the pyrimidine 5-position or the benzene ring in quinazolines, the halogen should be a bromine or iodine; triflates will react in any position.[1,9]

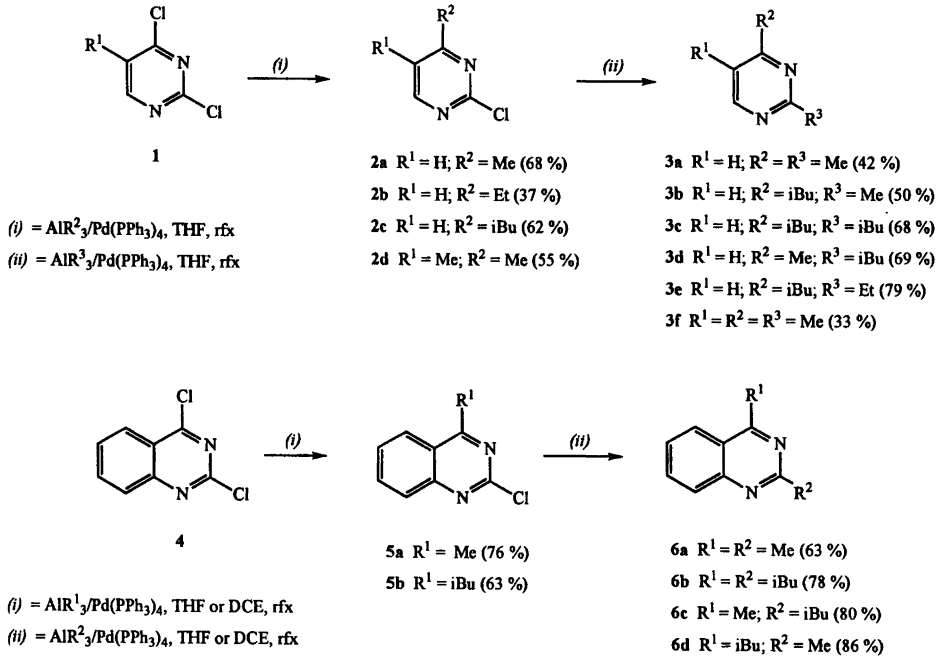
We have found that alkylalanes are excellent reagents for *C*-alkylations in azines under mild reaction conditions, and therefore of potential interest in modifications of biologically important azines, e.g., based on pyridine, pyrimidine, pteridine or purine ring systems. Simple alkylalanes are either commercially available or readily available by synthesis.[10] Previously it has been reported that 2-chloropyrazine and 2,5- and 2,6-dichloropyrazine can be dimethylated by trimethylalane,[11] that triflyloxypyridines and -quinazolines react with alkylalanes[5,12] and that 6-methyluridine nucleosides can be prepared from the corresponding 6-chloro precursor.[6]

The emphasis in this work has been to explore and establish the selectivity towards carbo-substitution in the electrophilic 2- and 4-positions, when they are occupied by a chlorine atom, and a further comparison with a benzenoid position carrying a bromine substituent. We find that selectivity for the 4-position both in 2,4-dichloropyrimidines (**1**) and 2,4-dichloroquinazolines (**4**) can be effected with trimethyl-, triethyl- and triisobutyl-alanes under the influence of tetrakis(trisphenylphosphine)palladium as catalyst (Scheme 1). The reactions proceed under reflux conditions in THF or in 1,2-dichloroethane (DCE). On a small scale no adverse reaction between DCE and the alanes was observed. Larger scale work may require another solvent.

The preference for coupling in the 4-position is maintained even when an alkyl group is placed next to the 4-chloro substituent. Thus 5-methyl-2,4-dichloropyrimidine gives the 4-methyl derivatives (**2d**) in 55% yield when coupled with trimethylalane.

Only minor amounts (<10%) of 2,4-dialkyl-substituted pyrimidines or quinazolines are formed in the coupling reactions. With triethyl-and triisobutyl-alane, however, reductions can take place as observed in the synthesis of **2b** and **2c**. In the former case 25% of the crude product was 2-chloropyrimidine, while in the latter case 37% 2-isobutylpyrimidine was isolated. Presumably β-elimination in the alanes leads to the corresponding

* To whom correspondence should be addressed.



Scheme 1.

hydrido derivatives, which are responsible for the reduction. Formation of 2-isobutylpyrimidine probably results from an initial reduction in the 4-position followed by a coupling in the 2-position.

In the presence of another mole-quivalent or more of an alane, products which carry the same or a different alkyl group in the 2-position (**3** or **6**) are formed.

In 5-bromo-2-chloropyrimidine (**7**) coupling takes place selectively in the 5-position (Scheme 2). As before the coupling reactions are accompanied by reduction when triethyl- or triisobutyl-alane are used. 2-Chloropyrimidine is formed in about 30% yield in both cases (**8b** and **8c**).

Under the reaction conditions used in this study, selectivity for monosubstitution in 6-bromo-2,4-dichloroquinazoline (**9**) was not fully achieved (Scheme 2). The main product was formed by substitution of the chlorine in the 4-position (**10**), the minor product from substitution of the 6-bromo substitutent (**11**). The products were readily separated by flash chromatography and were reacted separately with additional amounts of alanes under similar conditions. In this manner trimethyl- (**12a**) and triisobutyl-quinazoline (**12b**) were obtained. Under similar conditions, 5-bromo-2-chloro-4-methyl- or -isobutyl-quinazoline (**10**) gave the products (**13**) carrying the same alkyl group in the 2,6-positions. In the final example, 2,4-dichloro-6-isobutylquinazoline was 2,4-dimethylated (**14**) by trimethylalane.

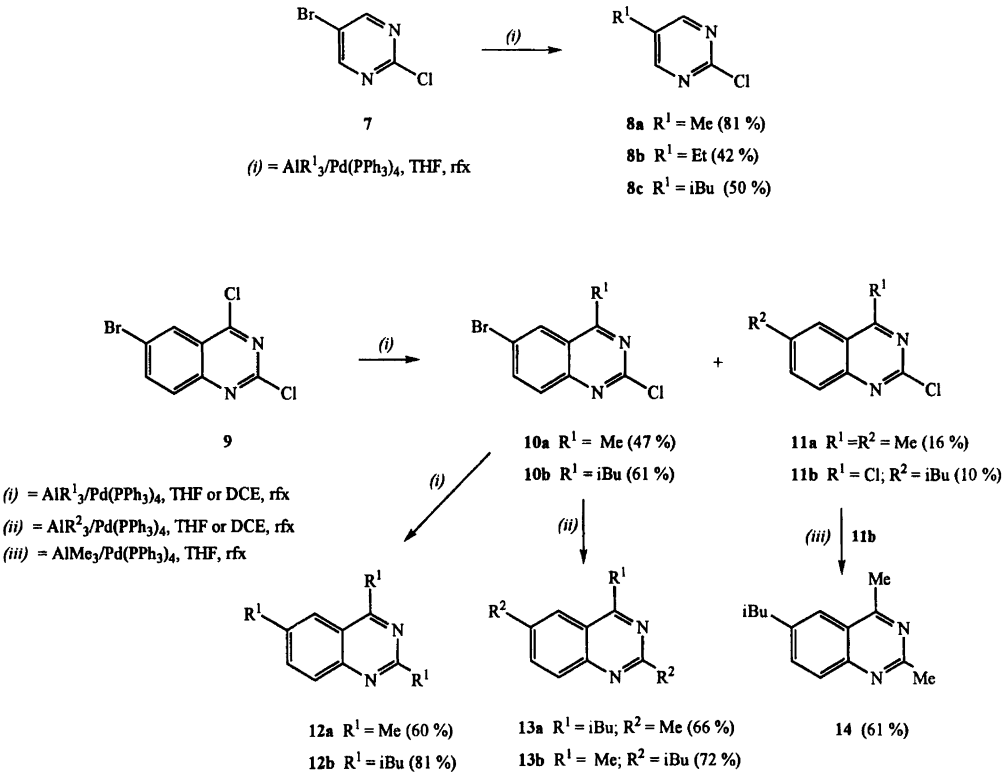
Experimental

Mass spectra were recorded under electron impact conditions at 70 eV. The spectra are presented as *m/z* (% rel. int.). The ^{1}H NMR spectra were recorded at 200 or 300 MHz and the ^{13}C NMR spectra at 50 MHz. All NMR spectra were run for samples in $CDCl_3$. Coupling constant are given in Hz. The alanes used were commercially available solutions in THF.

Compounds reported in the literature. 2-Chloro-4-methylpyrimidine (**2a**),[13] 2-chloro-4,5-dimethylpyrimidine (**2d**),[14] 2,4-dimethylpyrimidine (**3a**),[15] 2,4,5-trimethylpyrimidine (**3f**),[16] 2,4-dichloroquinazoline (**4**),[17] 2-chloro-4-methylquinazoline (**5a**),[18] 2,4-dimethylquinazoline (**6a**),[19] 2-chloro-5-methylpyrimidine (**8a**),[20] 2-chloro-5-ethylpyrimidine (**8b**).[21]

General procedure for alkylation of the pyrimidines **1** *and* **7**, *and the quinazolines* **4** *and* **9**. Trimethyl-, triethyl- or triisobutyl-alane (1.2 mmol for monoalkylation, 4 mmol for dialkylation) and 7 mol% tetrakis(triphenylphosphine)palladium were added under nitrogen to a solution of the halogenoazine (1.0 mmol) in dry THF (3 ml) or DCE (3 ml), and the mixture heated under reflux for 24 h. The reaction was quenched by addition of water (10 ml), and the mixture extracted with diethyl ether. The ethereal solution was washed, dried ($MgSO_4$), and evaporated. The products were isolated by flash chromatography on silica using hexane–EtOAc.

2-Chloro-4-ethylpyrimidine (**2b**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 4:1.^{1}H NMR : δ 1.25 (t, CH_3, *J* 7.61), 2.74 (q, CH_2), 7.09 (d, H5, *J* 5.17), 8.44 (d, H6, *J* 5.09). ^{13}C NMR: δ 12.96 (CH_3), 31.00 (CH_2), 117.72 (C5), 158.45 (C6), 160.41 (C4), 174.83 (C2). MS: 142 (M^+, 50), 141 (100), 128 (3), 114 (11), 105 (27), 79 (31), 62 (12), 53 (28).



Scheme 2.

2-Chloro-4-isobutylpyrimidine (**2c**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 4:1. ^{1}H NMR: δ 0.86 (d, 2 × CH_3, *J* 7.61), 1.96–2.13 (m, CH), 2.55 (d, CH_2, *J* 7.24), 7.16 (d, H5, *J* 5.08), 8.41 (d, H6, *J* 5.08). ^{13}C NMR: δ 22.28 (CH_3), 28.61 (CH), 46.59 (CH_2), 119.25 (C5), 158.52 (C6), 160.83 (C4), 173.46 (C2). MS (EI) 170 (M^+, 1), 169 (5), 155 (26), 130 (34), 128 (100), 92 (16), 65 (5), 43 (7), 41 (10). Anal. $C_8H_{11}ClN_2$: C, H. HRMS: *M*: 170.0618. Calc. for $C_8H_{11}ClN_2$: 170.0611.

4-Isobutyl-2-methylpyrimidine (**3b**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 4:1. ^{1}H NMR: δ 0.86 (d, 2 × CH_3, *J* 6.63), 1.96–2.10 (m, CH), 2.51 (d, CH_2, *J* 7.241), 2.64 (2-CH_3), 6.85 (d, H5, *J* 5.12), 8.42 (d, H6, *J* 5.16). ^{13}C NMR: δ 22.93 (CH_3), 26.65 (CH_3), 29.12 (CH), 47.34 (CH_2), 117.26 (C5), 155.39 (C6), 166.67 (C4), 168.73 (C2). MS (EI): 150 (M^+, 3), 149 (8), 135 (22), 109 (8), 108 (100), 93 (3), 81 (4), 67 (4). HR MS: *M*: 150.1167. Calc. for $C_9H_{14}N_2$:150.1157.

2,4-Diisobutylpyrimidine (**3c**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 4:1. ^{1}H NMR ($CDCl_3$): δ 0.89 (d, 2 × CH_3, *J* 2.89), 0.93 (d, 2 × CH_3, *J* 2.89), 2.01–2.29 (m, CH), 2.57 (d, CH_2, *J* 7.28), 2.77 (d, CH_2, *J* 7.32), 6.90 (d, H5, *J* 5.13), 8.49 (d, H6, *J* 5.13). ^{13}C NMR: δ 22.97 (CH_3), 23.05 (CH_3), 29.27 (CH), 29.32 (CH), 47.38 (CH_2), 48.83 (CH_2), 117.45 (C5), 155.34 (C6), 168.67 (C4), 169.37 (C2). MS (EI): 192 (M^+, 3), 191 (12), 177 (44), 150 (100), 135 (22), 108 (34), 93 (7), 68 (15). HR MS: *M*: 191.1555. Calc. for $C_{12}H_{20}N_2$: 191.1548.

2-Isobutyl-4-methylpyrimidine (**3d**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 4:1. ^{1}H NMR: δ 0.89 (d, 2 × CH_3, *J* 6.64), 2.12–2.26 (m, CH), 2.44 (4-CH_3), 2.72 (d, CH_2, *J* 7.33), 6.91 (d, H5, *J* 5.13), 8.44 (d, H6, *J* 5.13). ^{13}C NMR: δ 23.01 (CH_3), 24.80 (4-CH_3), 29.18 (CH), 48.75 (CH_2), 117.27 (C5), 155.39 (C6), 165.64 (C4), 169.27 (C2). MS (EI): 150 (M^+, 4), 149 (3), 135 (18), 109 (8), 108 (100), 94 (5), 67 (10). HRMS: *M*: 150.11567. Calc. for $C_9H_{14}N_2$: 150.1157.

2-Ethyl-4-isobutylpyrimidine (**3e**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 4:1. ^{1}H NMR: δ 0.83 (d, 2 × CH_3, *J* 6.67), 1.24 (d, CH_2CH_3), 1.93–2.04 (m, CH), 2.48 (d, CH_2 in iBu, *J* 7.28), 2.85 (q, CH_2CH_3), 6.82 (d, H5, *J* 5.12), 8.41 (d, H6, *J* 5.13). ^{13}C NMR: δ 13.22 (C8), 22.69 (C11), 28.81 (C10), 32.95 (C7), 47.12 (C9), 117.49 (C5), 155.70 (C6), 169.04 (C4), 171.09 (C2). MS (EI): 164 (M^+, 3), 163 (9), 149 (22), 141 (4), 122 (100), 108 (3), 94 (4), 67 (5). HRMS: *M*: 164.1308. Calc. for $C_{10}H_{16}ClN_2$: 164.1313.

2-Chloro-4-isobutylquinazoline (**5b**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 7:3. ^{1}H NMR: δ 0.95 (d, 2 × CH_3, *J* 6.67), 2.23–2.50 (m, CH), 2.94 (d, CH_2, *J* 7.32), 7.48–7.56 (m, H6), 7.78–7.85 (m, H5, H7), 7.95 (dd, H8, *J* 7.98, *J* 0.98). ^{13}C NMR: δ 22.49 (CH_3), 28.73

(CH), 48.78 (CH_2), 122.90 (C6), 126.80 (C7), 126.93 (C5), 127.82 (C8), 133.83 (C4a), 150.17 (C4), 160.08 (C8a), 167.04 (C2). MS (EI): 222/220 (M^+, 2/7), 198 (68), 163 (100), 129 (33), 102 (69), 83 (14), 75 (28).

2,4-Diisobutylquinazoline (**6b**). Reaction solvent: DCE. Eluent: hexane–ethyl acetate 7:3. ^{1}H NMR: δ 0.95 (d, $2\times CH_3$ in 4-iBu, *J* 6.54), 0.96 (d, $2\times CH_3$ in 2-iBu, *J* 6.49), 2.20–2.38 (m, $2\times$CH), 2.93 (d, CH_2 in 4-iBu, *J* 7.26), 3.08 (d, CH_2 in 2-iBu, *J* 7.25), 7.45–7.54 (m, H6), 7.74–7.81 (m, H7), 7.93 (dd, H5, *J* 8.42, *J* 1.43), 8.04 (dd, H8, *J* 8.42, *J* 1.46). ^{13}C NMR: δ 22.50 (CH_3 in 4-iBu), 22.72 (CH_3 in 2-iBu), 28.75 (CH in 4-iBu), 29.18 (CH in 2-iBu), 43.24 (CH_2 in 4-iBu), 48.82 (CH_2 in 2-iBu), 122.22 (C6), 124.73 (C7), 126.22 (C5), 128.54 (C8), 133.07 (C4a), 150.23 (C4), 166.12 (C8a), 170.56 (C2). MS (EI): 242 (M^+, 5), 227 (6), 200 (15), 186 (46), 171 (32), 158 (14), 144 (100), 130 (5), 103 (5).

2-Isobutyl-4-methylquinazoline (**6c**). Reaction solvent: DCE. Eluent: hexane–ethyl acetate 7:3.^{1}H NMR: δ 0.98 (d, $2\times CH_3$, *J* 6.59), 2.30–2.48 (m, CH), 2.91 (4-CH_3), 2.92 (d, CH_2, *J* 7.32), 7.50–7.58 (m, H6), 7.82–7.91 (m, H7), 7.95 (d, H5, *J* 7.45), 8.04 (d, H8, *J* 8.06), ^{13}C NMR: δ 23.08 (CH_3 in iBu), 29.14 (CH), 49.12 (CH_2), 62.53 (4-CH_3), 123.55 (C6), 124.40 (C7), 126.12 (C5), 127.98 (C8), 132.83 (C4a), 148.62 (C4), 161.35 (C8a), 168.43 (C2), MS (EI): 200 (M^+, 13), 185 (16), 158 (100), 144 (8), 130 (4), 103 (5), 91 (8), 77 (6).

4-Isobutyl-2-methylquinazoline (**6d**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 7:3. ^{1}H NMR: δ 0.96 (d, $2\times CH_3$ in iBu, *J* 6.64), 2.19–2.40 (m, CH), 2.82 (2-CH_3), 3.06 (d, CH_2, *J* 7.33), 7.45–7.53 (m, H6), 7.73–7.81 (m, H-7), 7.89 (d, H5, *J* 8.43), 8.03 (d, H8, *J* 8.42). ^{13}C NMR: δ 23.34 (CH_3 in iBu), 27.09 (2-CH_3), 29.90 (CH), 43.608 (CH_2), 121.46 (C6), 124.35 (C7), 125.81 (C5), 127.77 (C8), 132.72 (C4a), 149.54 (C4), 162.55 (C8a), 169.92 (C2). MS (EI): 200 (M^+, 15), 185 (18), 158 (100), 143 (9), 103 (6), 97 (6), 91(9), 76 (7).

2-Chloro-5-isobutylpyrimidine (**8c**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 4:1 ^{1}H NMR: δ 0.84–0.87 (d, $2\times CH_3$), 1.73–1.86 (m, CH), 2.42 (d, CH_2, *J* 7.24) 8.37 (s, H4,6). ^{13}C NMR ($CDCl_3$): δ 21.87 (CH_3), 29.64 (CH), 38.55 (CH_2), 132.78 (C5), 159.09 (C2), 159.71 (C4, C6). MS (EI) 172 (M+2, 13), 170 (M^+, 39), 130 (31), 128 (100), 100 (9), 92 (12), 65 (7), 43 (68), 39 (25), 27 (9). HRMS: *M*: 170.0616. Calc. for $C_8H_9ClN_2$: 170.0611.

6-Bromo-2-chloro-4-methylquinazoline (**10a**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 7:3. ^{1}H NMR: δ 2.88 (CH_3), 7.77 (d, H8, *J* 9.36), 7.92 (dd, H7, *J* 9.36, *J* 2.24), 8.18 (d, H5, *J* 2.24), ^{13}C NMR: δ 22.35 (CH_3), 120.98 (C6), 123.21 (C7), 126.95 (C8), 129.16 (C5), 137.51 (C4a), 149.00 (C4), 155.98 (C8a), 169.95 (C2), MS (EI): 260/258 (M^+, 27/100), 243 (9), 221 (17), 192 (43), 156 (11), 116 (15), 89 (13), 75 (18).

6-Bromo-2-chloro-4-isobutylquinazoline (**10b**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 7:3. ^{1}H NMR: δ 1.00 (d, $2\times CH_3$, *J* 6.64), 2.22–2.42 (m, CH), 3.06 (d, CH_2, *J* 7.24), 7.87 (d, H8, *J* 8.87), 8.03 (dd, H7, *J* 8.87, *J* 2.20), 8.38 (d, H5, *J* 2.20). ^{13}C NMR: δ 23.331 (CH_3), 29.70 (CH), 43.44 (CH_2), 120.91 (C6), 122.64 (C7), 127.560 (C8), 128.96 (C5), 138.97 (C4a), 150.11 (C4), 154.48 (C8a), 172.97 (C2). MS (EI): 302/300 (M^+, 4/11), 278 (100), 258 (89), 243 (71), 180 (20), 100 (31), 81 (10), 75 (25), 50 (18).

2-Chloro-4,6-dimethylquinazoline (**11a**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 7:3. ^{1}H NMR: δ 2.54 (6-CH_3), 2.88 (4-CH_3), 7.69 (dd, H7, *J* 8.50, *J* 2.28), 7.78–7.83 (m, H5, H8), ^{13}C NMR: δ 22.295 (6-CH_3), 22.473 (4-CH_3), 122.165 (C7), 123.44 (C5), 127.13 (C8), 136.28 (C4a), 137.38 (C6), 148.96 (C4), 154.89 (C8a), 170.01 (C2).

2,4-Dichloro-6-isobutylquinazoline (**11b**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 7:3. ^{1}H NMR: δ 0.93 (d, $2\times CH_3$, *J* 6.59), 1.88–2.06 (m, CH), 2.69 (d, CH_2, *J* 6.96), 7.80 (d, H8, *J* 9.04), 7.93 (dd, H7, *J* 9.04, *J* 2.26), 8.22 (d, H5, *J* 2.26), ^{13}C NMR: δ 22.88 (CH_3), 28.85 (CH), 43.01 (CH_2), 122.76 (C7), 126.88 (C8), 129.36 (C5), 137.41(C4a), 147.65 (C6), 157.24 (C4), 169.99 (C2), MS (EI): 256 (M^+, 2), 241 (2), 214 (26), 172 (100), 157 (13), 131 (10), 103 (4), 89 (9).

2,4,6-Trimethylquinazoline (**12a**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 7:3. ^{1}H NMR: δ 2.49 (6-CH_3), 2.77 (4-CH_3), 2.82 (2-CH_3), 7.73–7.74 (d, H7, *J* 8.51), 7.60 (dd, H6, *J* 8.51, *J* 1.83), 7.76 (d, H5, *J* 1.83), ^{13}C NMR: δ 22.26 (6-CH_3), 22.36 (4-CH_3), 26.87 (2-CH_3), 121.49 (C7), 123.10 (C5), 127.24 (C8), 134.95 (C6), 135.74 (C4a), 147.50 (C4), 161.59 (C8a), 166.13 (C2), MS (EI): 172 (M^+, 100), 157 (49), 149 (16), 131(36), 116 (7), 103 (4), 89 (19), 63 (7).

2,4,6-Triisobutylquinazoline (**12b**). Reaction solvent: DCE. Eluent: hexane–ethyl acetate 10:1. ^{1}H NMR: δ 0.95 (d, $6\times CH_3$), 1.83–2.07 (m, CH in 6-iBu), 2.19–2. 47 (m, CH in 2- and 4-iBu), 2.64 (d, CH_2 in 6-iBu *J* 7.33), 2.91 (d, CH_2 in 4-iBu, *J* 7.37), 3.07 (d, CH_2 in 2-iBu *J* 7.28), 7.61 (dd, H7, *J* 8.46, *J* 1.10), 7.75 (d, H5, *J* 1.10), 7.85 (d, H8, *J* 8.46). ^{13}C NMR: δ 22.92 (CH_3 in 6-iBu), 23.12 (CH_3 in 4-iBu), 23.37 (CH_3 in 4-iBu), 29.34 (CH in 6-iBu), 29.71(CH in 4-iBu), 30.75 (CH in 2-iBu), 43.54 (CH_2 in 6-iBu), 45.88 (CH_2 in 4-iBu), 49.10 (CH_2 in 2-iBu), 121.64 (C7), 123.37 (C5), 127.60 (C8), 134.47 (C6), 139.22 (C4a), 148.24 (C8a), 164.46 (C4), 168.94 (C2), MS (EI): 298 (M^+, 25), 283 (23), 256 (100), 214 (36), 197 (8), 171 (16), 149 (16), 130 (12), 103 (5), 78 (4).

4-Isobutyl-2,6-dimethylquinazoline (**13a**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 3:2. ^{1}H NMR: δ 0.98 (d, $2\times CH_3$, *J* 6.62), 2.22–2.50 (m, CH), 2.53

(6-CH_3), 2.82 (2-CH_3), 3.05 (d, CH_2, *J* 7.29), 7.63 (dd, H7, *J* 8.53, *J* 1.42), 7.75–7.83 (m, H5, H8), ^{13}C NMR: δ 22.25 (6-CH_3), 23.16 (CH_3 in iBu), 26.81 (2-CH_3), 29.60 (CH), 43.45 (CH_2), 121.73 (C7), 123.29 (C5), 127.64 (C8), 135.10 (C6), 135.80 (C4a), 148.36 (C8a), 162.04 (C4), 169.46 (C2).

2,6-Diisobutyl-4-methylquinazoline (**13b**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 7:3. THF. ^{1}H NMR: δ 0.86 (d, 2 × CH_3 in 6-iBu, *J* 6.76), 1.04 (d, 2 × CH_3 in 2-iBu, *J* 6.68), 2.09–2.29 (m, CH in 2- and 6-iBu), 2.82 (4-CH_3), 3.17 (d, CH_2 in 6-iBu, *J* 7.50), 4.20 (d, CH_2 in 2-iBu, *J* 7.39), 7.63 (d, H8, *J* 9.11), 7.79 (dd, H7, *J* 9.11, *J* 2.20), 8.10 (d, H5, *J* 2.20). ^{13}C NMR: δ 20.01 (2 × CH_3 in 6-iBu), 22.34 (2 × CH_3 in 2-iBu), 27.63 (CH in 6-iBu), 30.10 (CH in 2-iBu), 45.31 (CH_2 in 6-iBu), 70.00 (CH_2 in 2-iBu), 70.70 (4-CH_3), 117.00 (C7), 127.02 (C8), 121.73 (C5), 130.22 (C6), 136.42 (C4a), 149.40 (C8a), 161.07 (C4), 169.86 (C2).

6-Isobutyl-2,4-dimethylquinazoline (**14**). Reaction solvent: THF. Eluent: hexane–ethyl acetate 3:2. ^{1}H NMR: δ 0.93 (d, 2 × CH_3, *J* 6.60), 1.89–2.08 (m, CH), 2.66 (d, CH_2, *J* 7.04), 2.81 (4-CH_3), 2.87 (2-CH_3), 7.66 (dd, H7, *J* 9.02, *J* 1.40), 7.74 (d, H5, *J* 1.40), 7.83 (d, H8, *J* 9.02).

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Received April 1, 1996.