Generation of 1-aryl-3-methoxycarbonylnitrilimines and their reactions with unsaturated hydrocarbons

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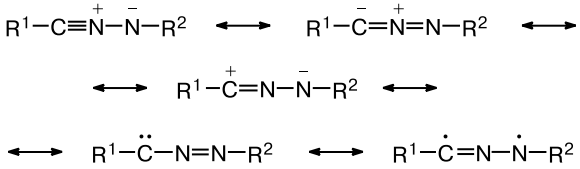
Thermolysis of 1-(4-methoxyphenyl)- and 1-(4-fluorophenyl)heptamethoxycarbonyl-3a,7a-dihydroindazoles at 135—140 °C resulted in the elimination of hexamethyl benzenehexacarboxylate and in the generation of 1-aryl-3-methoxycarbonylnitrilimines, which were trapped by alkenes and dienes to give the corresponding (1) pyrazolines *via* 1,3-dipolar cycloaddition and (2) 2-oxoalken-1-oic acid hydrazones *via* allylic proton migration to the nitrogen atom. The reaction with tetramethylethene unexpectedly yielded substituted 5-(1-hydroxy-1-methylethyl)- or 5-acetylpyrazolinecarboxylates as the main products. The formation of the latter compounds suggests initial abstraction of the H atom from tetramethylethene and probable participation of a water molecule that supplies one more oxygen atom to the reaction products.

Key words: 3a,7a-dihydroindazoles, nitrilimines, pyrazolines, hydrazones, 1,3-dipolar addition, oxidation, thermolysis.

Nitrilimines are highly reactive 1,3-dipoles and, like aliphatic diazo compounds, are widely used for the synthesis of pyrazolines, pyrazoles, and other heterocycles *via* 1,3-dipolar cycloaddition to unsaturated compounds.[1—5] The electronic state of nitrilimines can be represented by several resonance (propargyl, allene, allyl, carbene, and biradical) structures, the contribution of each structure being appreciably varied with the electronic properties of the substituents.[5—8]



Earlier,[9] we have discovered that a number of substituted 3a,7a-dihydroindazoles **1** undergo thermolysis at 130—140 °C with elimination of hexamethyl benzenehexacarboxylate and generation of the corresponding nitrilimines **2**, which are trapped by unsaturated substrates (methyl acrylate, ethyl vinyl ether, cyclopentene, and vinylcyclopropane) (Scheme 1). The reaction products included the expected pyrazolines and the corresponding pyrazoles. In the case of ethyl vinyl ether, the formation of 1-arylpyrazole-3-carboxylates can be due to easy elimination of ethanol, while the formation of pyrazoles in the reactions with other substrates should involve partial *in situ* oxidation of pyrazolines, possibly with nitrilimine itself.

It is known[10—12] that 3-alkoxycarbonyl-1-arylnitrilimines generated by base-catalyzed 1,3-dehydrochlorination of appropriate hydrazonyl chlorides readily react with electron-deficient unsaturated compounds and, to a much lower degree, with electron-donor olefins. In the latter case, nitrilimines mainly undergo cyclodimerization into substituted 1,2,4,5-tetrazines. Since the discovered way of generating nitrilimines differs from those described earlier,[10—14] it was interesting to study the thermolysis of 3a,7a-dihydroindazoles **1** in the presence of electron-saturated olefins and dienes containing methyl groups at the double bond. The formation of trapping products from nitrilimines generated by common methods has not been documented hitherto for such unsaturated compounds.

Results and Discussion

We used heptamethyl 1-(4-methoxyphenyl)- (**1a**) and 1-(4-fluorophenyl)-3a,7a-dihydroindazoleheptacarboxylates (**1b**) as sources of nitrilimines and 2,3-dimethylbut-1-ene (**3**), 2,3-dimethylbutadiene (**4**), 2,5-dimethylhexa-2,4-diene (**5**), and 2,3-dimethylbut-2-ene (**6**) as unsaturated compounds. Reactions were carried out in sealed tubes in an inert atmosphere as follows. Dihydroindazole **1a** was heated at 135—140 °C with a tenfold molar excess of an unsaturated compound in 1,4-dioxane. It turned out that the thermolysis of compound **1a** in the presence of dimethylbutene **3** or dimethylbutadiene **4** gives the expected pyrazoline **7** or **8** in 40 and 76% yields, respectively. Both

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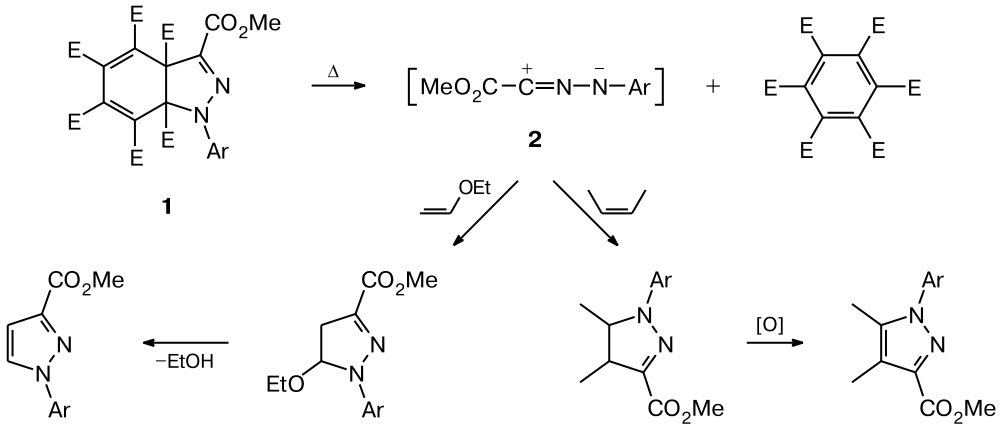
Scheme 1



E = CO_2Me; Ar = 4-FC_6H_4, 4-$MeOC_6H_4$

pyrazolines are regioselectively produced *via* the formation of a C—C bond between the nitrilimine and the terminal C atom of olefin **3** or diene **4** (Scheme 2). By-products of these transformations include acyclic hydrazones **9**—**11** and dihydropyridazine **12**, which most likely suggests asynchronous addition of nitrilimines to unsaturated compounds because of consecutive cleavage of the C—C and C—N bonds in the starting dihydroindazole **1a**. The initial C—C bonding to the alkene and the formation of betaine structure **A** or **B** can be followed either by heterocyclization into pyrazoline **7** or **8** or deprotonation of the alkene fragment during which the proton migrates to the negatively charged N atom to form unsaturated hydrazones **9**—**11** (see Scheme 2). The presence of six-membered heterocycle **12** among the reaction products can be attributed to the interconversions of betaine intermediates **B** and **C**.

Compounds **7**, **8**, **11**, and **12** were isolated in the individual state from the reaction mixtures by column chromatography on silica gel; their structures were determined from ^1H and ^{13}C NMR and mass spectra. Hydrazones **9** and **10** were analyzed as mixtures of isomers. In all the compounds obtained, the nitrilimine (**2a**) and hydrocarbon (**3** or **4**) fragments are retained.

Interestingly, the yield of unsaturated pyrazoline **8** is nearly twice as high as that of pyrazoline **7**. This fact can be due to both the higher reactivity of diene **4** (or the statistical factor reflecting twice as many similar double bonds in diene **4** compared to olefin **3**) and side transformations of the starting compounds and final products in the case of olefin **3**. The latter assumption is supported by surprisingly much stronger polymerization of the reaction mixture in the case of the reaction between compounds **1a** and **3** than between compounds **1a** and **4** under the same conditions.

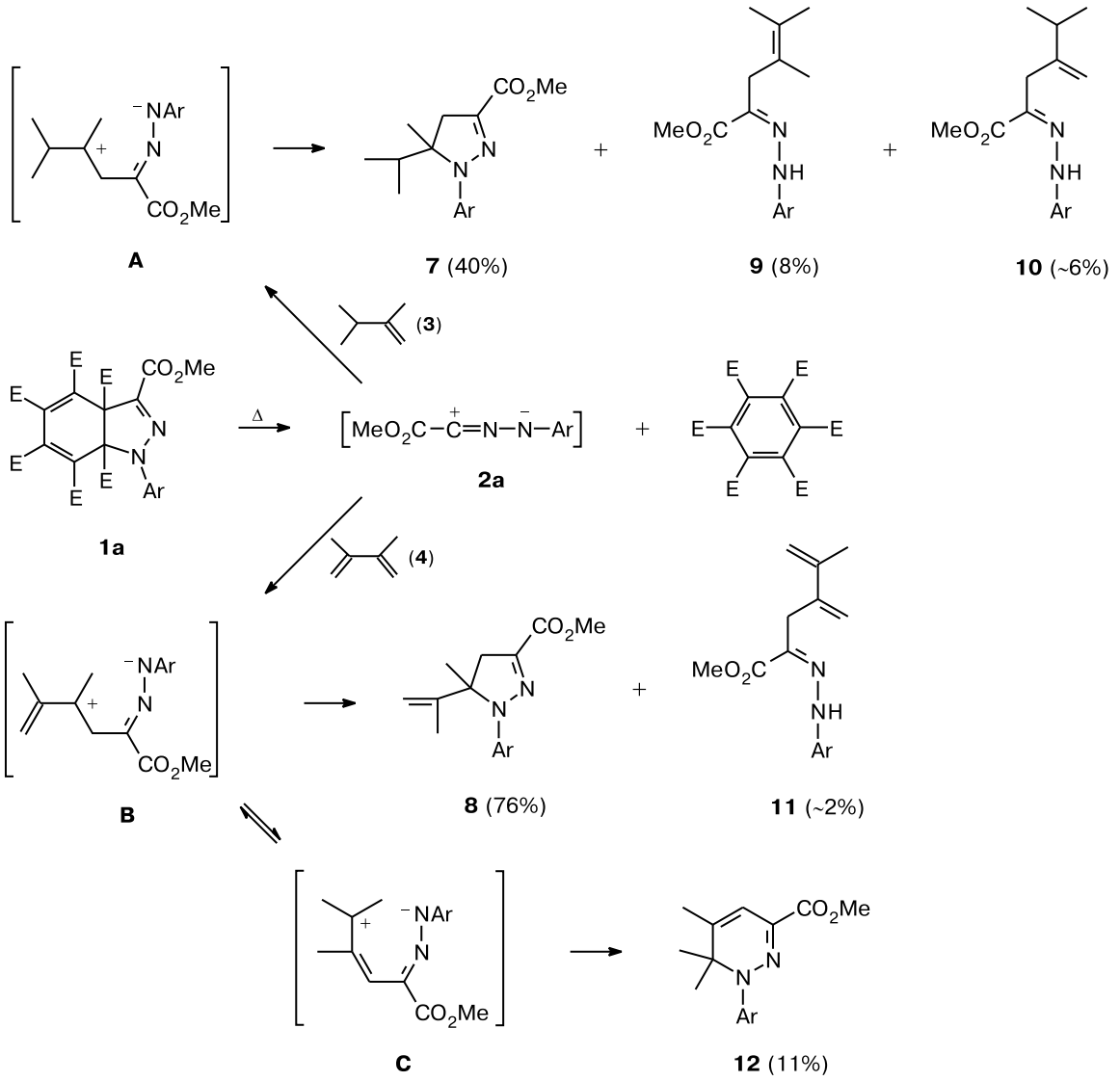
Formal trapping of nitrilimine **2a** by internal diene **5** also mainly gives 1,3-dipolar cycloaddition products. However, the steric effects preclude regioselective addition of the nitrilimine to the double bond, and the reaction produces pyrazoline **13a** and its regioisomer **14a** in a ratio of ~7.6 : 1. Both isomers (enriched to 95 and 90% either) were isolated by column chromatography on SiO_2. These regioisomers were distinguished by analyzing the chemical shifts of the ^{13}C NMR signals for the quaternary and protonated C atoms bound to the N(1) or C(3) atoms of the heterocycle. For pyrazoline **13a**, these signals appear at δ 49.9 and 72.1 (C(4) and C(5), respectively). For pyrazoline **14a**, the chemical shifts of the corresponding signals are δ 73.1 and 54.4. Apart from pyrazolines **13a** and **14a**, we isolated from the reaction mixture unsaturated hydrazone **15a** (Scheme 3), which is produced by addition of nitrilimine **2a** to the fragment HC= of diene **5** followed by migration of a methyl proton to nitrogen.

The ^1H and ^{13}C NMR spectra of hydrazone **15a** show signals for the aryl and ester groups, signals for the fragment $=CH_2$ and three methyl groups at the double bonds, and two signals for the fragments CH, which appear as broadened doublets at δ_H 4.3 and 5.5 with $J_{H,H}$ = 9.5 Hz. According to the HSQC experiment, the latter signals correspond to the signals at δ_C 47.3 and 124.6. In addition, the ^1H NMR spectrum contains a low-field (δ 12.1) broadened singlet for the proton of the fragment C=N—NH.

1-Fluorophenylnitrilimine **2b** reacts with diene **5** in a similar way to give pyrazolines **13b** and **14b** with a slightly lower regioselectivity (**13b** : **14b** = 5.7 : 1); the yield of unsaturated hydrazone **15b** was nearly three times as high (see Scheme 3).

It should be noted that 1,3-dipolar cycloaddition of nitrilimines to the multiple bonds of unsaturated compounds is not always regioselective, especially with conjugated and electron-deficient dipolarophiles as traps.[2,14—16] The formation of hydrazones **15a**,**b**, as well as the formation of compounds **9**—**12**, suggests a stepwise character of

Scheme 2

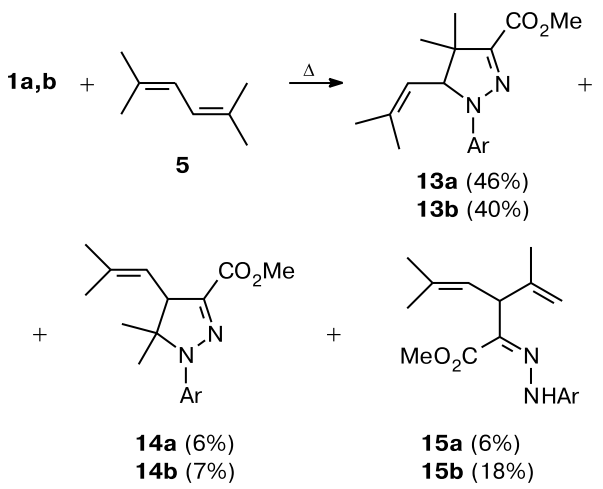


Ar = 4-$MeOC_6H_4$

the reaction of nitrilimine **2a** or **2b** with diene **5** and acquisition of a high positive charge by the hydrocarbon fragment upon the formation of the C—C bond. As distinct from, *e.g.*, the generation of nitrilimines by 1,3-dehydrochlorination of hydrazonoyl chlorides in the presence of alkenes, the thermolysis of dihydroindazoles **1a**,**b** produces no 1,2,4,5-tetrazines, which are nitrilimine cyclic dimers.

In contrast to unsaturated compounds containing di- and trisubstituted double bonds, reactions of dihydroindazoles **1a** and **1b** with a tenfold molar excess of tetramethylethene (**6**) in dioxane under the same conditions gave products no analogs of which had been detected in the aforesaid experiments. The yields of the expected pyrazoline **16a** and hydrazones **17a**,**b** were low, while the major reaction products were compounds **18** and **19** containing additional oxygen atoms (Scheme 4). In the case of 1-(4-fluorophenyl)-3a,7a-dihydroindazole **1b**, pyrazoline **16b** was not obtained; instead, pyrazoline **20** and pyrazole **21** were detected, though in low yields (Scheme 5). All these compounds were isolated by column chromatography on SiO_2, and their structures were determined from spectroscopic data. For instance, ^1H and ^{13}C NMR studies revealed that alcohols **18a**,**b** and ketones **19a**,**b** formally contain the nitrilimine fragment (**2a** or **2b**) in the five-membered ring and the isolated alicyclic CH_2 group, which is manifested in the ^1H NMR spectra as two doublets with a geminal coupling constant of 18—19 Hz. Because of

Scheme 3



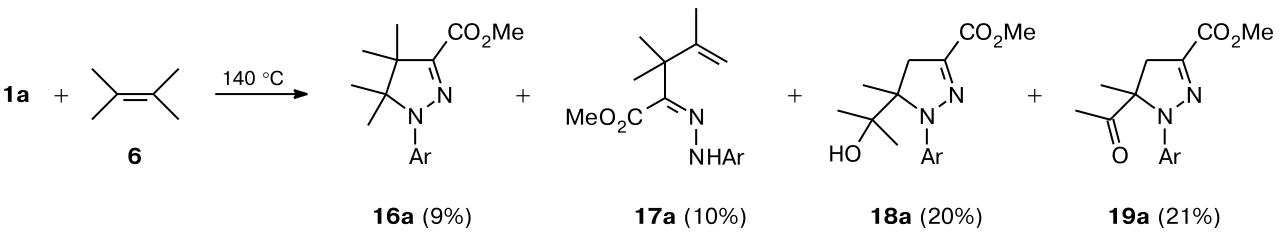
Ar = 4-$MeOC_6H_4$ (**a**), 4-FC_6H_4 (**b**)

steric hindrances, the ^1H and ^{13}C NMR spectra of tertiary alcohols **18a,b** show geminal nonequivalence of the methyl groups of the 1-hydroxy-1-methylethyl fragment.

To this point, we cannot provide a definite explanation of the formation of oxygen-containing compounds **18** and **19**. Since these products were detected immediately in the reaction mixture before its separation by column chromatography, one could assume that probable oxygen sources in an inert atmosphere inside a sealed tube are either ester groups or small amounts of water present in the reaction mixture. However, in any of the experiments, we isolated no compounds implying a transformation of the ester group. In addition, the amount of hexamethyl benzenehexacarboxylate was as high as in the other reactions of dihydroindazoles **1a**,**b**. At the same time, small amounts of water present in the reaction mixture can participate in relevant transformations. For instance, deliberate addition of an equimolar amount of water with respect to dihydroindazole **1a** to its reaction mixture with tetramethylethene slightly decreased the yields of compounds **16a** and **17a** but increased the yield of acetylpyrazoline **19a** from 21 to 32%.

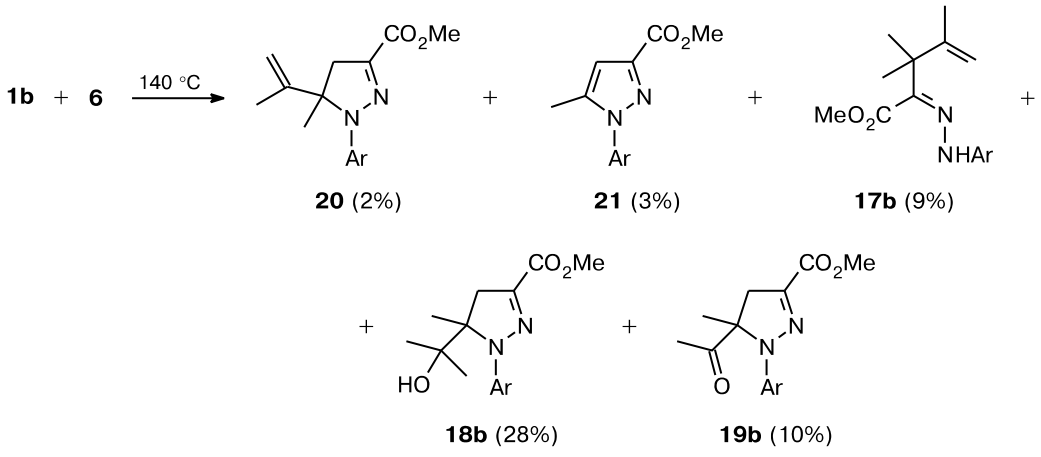
Apparently, tetramethylethene **6** with a sterically hindered double bond is a poor dipolarophile in reactions with nitrilimines, as well as with other 1,3-dipoles. However, generated nitrilimine **2** (or its precursor resulting from heterolytic or homolytic cleavage of a C—C or C—N

Scheme 4



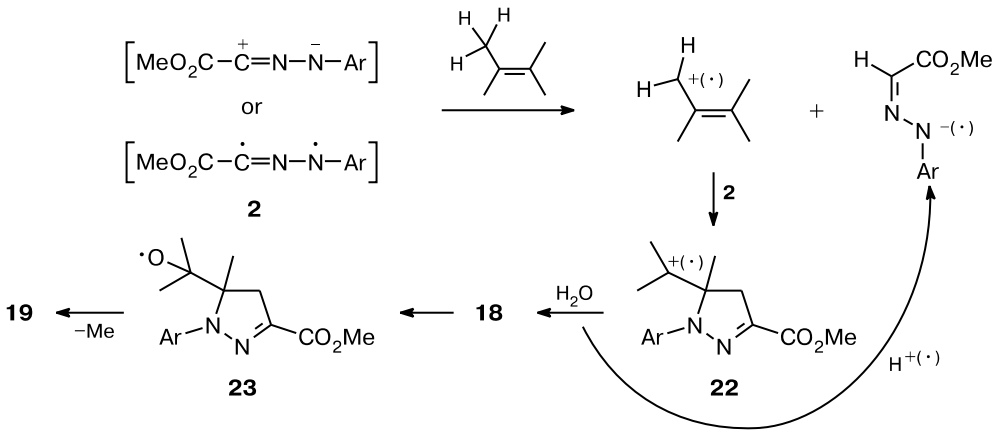
Ar = 4-$MeOC_6H_4$

Scheme 5



Ar = 4-FC_6H_4

Scheme 6



bond in the starting dihydroindazole **1**) can react with hydrazone **15** by removal of hydrogen from its methyl group. The resulting allylic cation (or radical) reacts with nitrilimine **2** to give heterocyclic intermediate cation (or radical) **22**, which is transformed into 5-(1-hydroxy-1-methylethyl)pyrazoline **18** upon a reaction with water (Scheme 6). Thus, the reaction of the generated nitrilimine with tetramethylethene is accompanied by formal reduction leading to a mixture of unidentified high-molecular-weight compounds.

According to previous data,[17—19] the formation of ketones from tertiary alcohols of similar structures can arise from cleavage of the C—C bond in 2-aryl-2-propyloxyl radicals, which provides explanation for the formation of acetylpyrazolines **19** as well. For this purpose, we should only assume that the scheme of transformations in the system nitrilimines **2a**,**b**—tetramethylethene involves the generation of 2-(pyrazol-5-yl)prop-2-yloxyl radicals **23**, which seems to be most probable when some of the reaction steps follow the radical mechanism.

Thus, the observed unexpected formation of compounds **18**—**21** upon the thermolysis of 3a,7a-dihydroindazoleheptacarboxylates **1a**,**b** in the presence of tetramethylethene suggests a novel pathway of the chemical transformations of *in situ* generated 1-aryl-3-(methoxycarbonyl)nitrilimines (or their precursors resulting from cleavage of one bond in compounds **1a**,**b**), which can attack the allylic C—H bond of an alkene. It should be noted that conventional[12] generation of nitrilimine **2a** by 1,3-dehydrochlorination of the arylhydrazone $EtO_2CC(Cl)=N-NHC_6H_4OMe$-4 with triethylamine (80 °C, 4 h) in the presence of tetramethylethene yielded no trapping products at all, the main compound isolated being diethyl 1,4-bis(4-methoxyphenyl)-1,2,4,5-tetrazine-3,6-dicarboxylate (cyclic nitrilimine dimer).[11] Under similar conditions, the yield of pyrazoline **13a** from diene **5** was no higher than 5%. This indicates that nitrilimines generated from different sources are differently reactive. Apparently, the thermolysis of substituted 3a,7a-dihydroindazoles can involve homolytic cleavage of the C(3)—C(3a) and N(1)—C(7a) bonds followed by reactions of the generated nitrilimines **2a**,**b** (in the form of biradicals) with compound **6**.

Experimental

^1H and ^{13}C NMR spectra were recorded on Bruker AVANCE II 300 (300 and 75.5 MHz, respectively) and Bruker DRX-500 spectrometers (500 MHz and 125.3 MHz, respectively) in $CDCl_3$ containing 0.05% Me_4Si as the internal standard. The ^{19}F chemical shifts are referenced to CCl_3F. Homo- and heteronuclear 2D correlation experiments (COSY, HMBC, and HSQC) were used to assign NMR signals and distinguish between the isomers of the compounds obtained. GC-MS spectra were recorded on a Finnigan MAT DSQII instrument (EI, 70 eV, ion source—ion trap system temperature 200 °C) coupled with a Trace GC Ultra chromatograph (Thermo TR-5ms SQC column, 15 000×0.25 mm). High-resolution mass spectra (HRMS) were recorded on a Bruker micrOTOF II instrument (ESI, positive ion mode, capillary voltage 4500 V).[20] IR spectra were recorded on a Specord M-80 instrument in KBr pellets. Thin-layer chromatography was carried out on Silica gel 60 plates (Merck); spots were visualized under the iodine vapor. For preparative separation, column chromatography (silica gel 60, 0.040—0.063 mm, Merck) was used; the sample—sorbent ratio was ~1 : 100. Melting points were determined on a Nagema PHMK-05 instrument.

1-(4-Methoxyphenyl)- (**1a**) and 1-(4-fluorophenyl)-3,3a,4,5,6,7,7a-heptamethoxycarbonyl-3a,7a-dihydroindazoles (**1b**) (≥98% purity) were prepared as described earlier.[21] Unsaturated compounds were distilled in an inert atmosphere before use; solvents (reagent grade, >99.5%) were used without further purification.

Thermolysis of 3a,7a-dihydroindazoles (1a,b) in the presence of alkenes or dienes (general procedure). A mixture of heptamethyl 3a,7a-dihydroindazoleheptacarboxylate **1a** or **1b** (0.5 mmol) and an unsaturated compound (5 mmol) in 1,4-dioxane (0.4 mL) was heated in a sealed tube under argon at 135—140 °C for 8 h. The reaction mixture was analyzed using TLC and ^1H NMR spectroscopy. The main reaction products were isolated by column chromatography on SiO_2 with benzene—EtOAc (gradient

elution from 10 : 1 to 2 : 1) or $CHCl_3$—EtOAc (5 : 1) as an eluent. Hexamethyl benzenehexacarboxylate always emerged from the column behind the corresponding pyrazolines and hydrazones.

Methyl 5-isopropyl-1-(4-methoxyphenyl)-5-methyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate (7), methyl 2-[(4-methoxyphenyl)hydrazono]-4,5-dimethylhex-4-enoate (9), and methyl 2-[(4-methoxyphenyl)hydrazono]-5-methyl-4-methylidenehexanoate (10). A reaction of dihydroindazole **1a** (315 mg) with 2,3-dimethylbut-1-ene (**3**) (0.42 g) gave compound **7** (58 mg, 40%) and an inseparable (under these conditions) mixture of hydrazones **9** and **10** (20 mg, 14%; 1.3 : 1 (^{1}H NMR)), colorless oil. MS (EI), m/z (I_{rel} (%)): 290 $[M]^+$ (30), 275 $[M - Me]^+$ (2), 247 (10), 231 (10), 215 (30), 122 (100), 108 (14), 95 (20).

Compound **7**, colorless oil. Found (%): C, 65.73; H, 7.45; N, 9.68. $C_{16}H_{22}N_2O_3$. Calculated (%): C, 66.18; H, 7.64; N, 9.65. MS (EI), m/z (I_{rel} (%)): 290 $[M]^+$ (30), 259 $[M - OMe]^+$ (10), 247 (70), 215 (100), 203 (20), 188 (30), 148 (50), 122 (50), 107 (35), 92 (53), 77 (75), 64 (40), 59 (45). IR, ν/cm^{-1}: 2968, 1696 (COO), 1508 (C=N). ^{1}H NMR ($CDCl_3$), δ: 0.93, 0.95 (both d, 3 H each, 2 Me, ^3J = 7.0 Hz); 1.33 (s, 3 H, Me); 2.25 (septet, 1 H, HCMe$_2$, ^3J = 7.0 Hz); 2.70, 3.18 (both d, 1 H each, $H_2C(4)$, ^2J = 17.8 Hz); 3.78, 3.84 (both s, 3 H each, 2 OMe); 6.82 (d, 2 H, H_m, ^3J = 9.0 Hz); 7.21 (d, 2 H, H_o, ^3J = 9.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 17.4, 17.5 (2 Me); 25.3 (Me); 34.5 (CH); 39.1 (CH_2); 51.7 (CO_2Me); 55.3 (OMe); 75.9 (C(5)); 113.9 (C_m); 121.7 (C_o); 135.7, 135.8 (C_{ipso}, C(3)); 156.3 (C_p); 163.6 (COO).

Compound **9**. ^{1}H NMR ($CDCl_3$), δ: 1.66, 1.70, 1.76 (all br.s, 3 H each, 3 Me); 3.24 (br.s, 2 H, CH_2); 3.76, 3.78 (both s, 3 H each, 2 OMe); 6.86 (m, H_m, this signal coincides with a similar signal for compound **10**); 7.11 (d, 2 H, H_o, ^3J = 9.0 Hz); 12.0 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 18.2, 20.6, 20.9 (3 Me); 37.4 (CH_2); 51.3 (CO_2Me); 55.7 (OMe); 114.7, 114.9 (C_m, C_o); 124.5, 125.9 (C(4), C(5)); 126.8 (C(2)); 137.8 (C_{ipso}); 155.0 (C_p); 164.5 (COO).

Compound **10**. ^{1}H NMR ($CDCl_3$), δ: 1.08 (d, 6 H, 2 Me, ^3J = 7.0 Hz); 2.33 (br.septet, 1 H, CH, ^3J = 7.0 Hz); 3.21 (t, 2 H, CH_2, ^4J = 1.3 Hz); 3.75, 3.77 (both s, 3 H each, 2 OMe); 4.65, 4.80 (both m, 1 H each, =CH_2); 6.86 (m, H_m, this signal coincides with a similar signal for compound **9**); 7.14 (d, 2 H, H_o, ^3J = 9.0 Hz); 12.1 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 21.7 (2 Me); 33.8 (C(5)); 37.8 (C(3)); 51.2 (CO_2Me); 55.6 (OMe); 108.0 (=CH_2); 114.8, 114.9 (C_m, C_o); 125.9 (C(2)); 137.6 (C_{ipso}); 155.1 (C_p); 164.4 (COO).

Methyl 1-(4-methoxyphenyl)-5-methyl-5-(prop-1-en-2-yl)-4,5-dihydro-1*H*-pyrazole-3-carboxylate (8), methyl 2-[(4-methoxyphenyl)hydrazono]-5-methyl-4-methylidenehex-5-enoate (11), and methyl 1-(4-methoxyphenyl)-5,6,6-trimethyl-1,6-dihydropyridazine-3-carboxylate (12). A reaction of dihydroindazole **1a** (316 mg) with 2,3-dimethylbutadiene (**4**) (0.41 g) gave compounds **8** (109 mg, 76%), **11** (3 mg, ~2%), and **12** (16 mg, 11%).

Compound **8**, colorless oil. Found (%): C, 66.72; H, 7.19; N, 9.59. $C_{16}H_{20}N_2O_3$. Calculated (%): C, 66.65; H, 6.99; N, 9.72. IR, ν/cm^{-1}: 2952, 1696 (COO), 1508 (C=N). MS (EI), m/z (I_{rel} (%)): 288 $[M]^+$ (100), 273 $[M - Me]^+$ (12), 247 (22), 241 (20), 215 (45), 122 (66), 107 (45), 92 (22), 77 (30). ^{1}H NMR ($CDCl_3$), δ: 1.51 (s, 3 H, Me at C(5)); 1.82 (br.s, 3 H, Me); 2.99, 3.20 (both d, 1 H each, $H_2C(4)$, ^2J = 18.0 Hz); 3.77, 3.87 (both s, 3 H each, 2 OMe); 5.05, 5.11 (both m, 1 H each, =CH_2); 6.79 (d, 2 H, H_m, ^3J = 9.1 Hz); 7.23 (d, 2 H, H_o, ^3J = 9.1 Hz). ^{13}C NMR ($CDCl_3$), δ: 19.2, 22.7 (2 Me); 46.6 (C(4)); 52.1 (CO_2Me); 55.5 (OMe); 73.4 (C(5)); 112.4 (=CH_2); 114.2 (C_m); 117.7 (C_o); 135.6, 136.0 (C_{ipso}, C(3)); 147.9 (=C); 155.3 (C_p); 163.6 (COO).

Compound **11**, oil. MS (EI), m/z (I_{rel} (%)): 288 $[M]^+$ (20), 215 (5), 200 (8), 152 (5), 137 (35), 122 (100), 107 (22), 95 (16). HRMS (ESI): $[M + H]^+$, calculated for $C_{16}H_{21}N_2O_3$ 289.1547, found: 289.1553. ^{1}H NMR ($CDCl_3$), δ: 1.95 (d, 3 H, Me, ^4J = 1.3 Hz); 3.47 (s, 2 H, CH_2); 3.77, 3.78 (both s, 3 H each, 2 OMe); 4.92, 5.00 (both m, 1 H each, =C(6)H_2); 5.18, 5.22 (both br.s, 1 H each, H_2C=C(4)); 6.85 (d, 2 H, H_m, ^3J = 9.0 Hz); 7.11 (d, 2 H, H_o, ^3J = 9.0 Hz); 12.1 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 21.4 (Me); 36.7 (C(3)); 51.4 (CO_2Me); 55.7 (OMe); 113.2, 113.8 (H_2C=C(4), C(5)); 114.8, 114.9 (C_m, C_o); 125.2 (C(2)); 137.5 (C_{ipso}); 142.76, 145.39 (C(4), C(5)); 155.2 (C_p); 164.5 (COO).

Compound **12**, oil. The product was further purified by preparative TLC to give an analytically pure sample, R_f 0.75 (benzene : EtOAc = 2 : 1). MS (EI), m/z (I_{rel} (%)): 288 $[M]^+$ (10), 273 $[M - Me]^+$ (100), 199 (10), 148 (9), 107 (6), 92 (8), 77 (10). HRMS (ESI): $[M + Na]^+$, calculated for $C_{16}H_{20}N_2O_3Na$ 311.1366, found: 311.1364. IR, ν/cm^{-1}: 3004, 2956, 1696 (COO), 1508 (C=N). ^{1}H NMR ($CDCl_3$), δ: 1.20 (s, 6 H, 2 Me); 1.89 (d, 3 H, Me, ^4J = 1.4 Hz); 3.80, 3.81 (both s, 3 H each, 2 OMe); 6.35 (q, 1 H, =CH, ^4J = 1.4 Hz); 6.85 (d, 2 H, H_m, ^3J = 9.0 Hz); 7.22 (d, 2 H, H_o, ^3J = 9.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 18.8 (Me); 23.5 (2 Me); 52.1 (CO_2Me); 55.6 (OMe); 59.3 (C(6)); 113.7 (C(4)); 113.8 (C_m); 130.3 (C_o); 133.2 (C(3)); 137.5, 137.8 (C_{ipso}, C(5)); 158.7 (C_p); 164.8 (COO).

Methyl 1-(4-methoxyphenyl)-4,4-dimethyl-5-(2-methylprop-1-enyl)- (13a) and methyl 1-(4-methoxyphenyl)-5,5-dimethyl-4-(2-methylprop-1-enyl)-4,5-dihydro-1*H*-pyrazole-3-carboxylates (14a) and methyl 2-[(4-methoxyphenyl)hydrazono]-5-methyl-3-(prop-1-en-2-yl)hex-4-enoate (15a). A reaction of dihydroindazole **1a** (315 mg) with 2,5-dimethylhexa-2,4-diene (**5**) (0.55 g) followed by separation of the products by column chromatography (SiO_2, $CHCl_3$—EtOAc, 5 : 1) gave pyrazoline **13a** (72 mg, 46%; the content of isomeric pyrazoline **14a** is <5%), pyrazoline **14a** (10 mg, 6%; the content of isomeric pyrazoline **13a** is <10%), and hydrazone **15a** (12 mg), which was further purified by TLC (C_6H_6—EtOAc, 9 : 1). The yield of compound **15a** was ~6%.

Compound **13a**, colorless oil. Found (%): C, 68.43; H, 8.40; N, 8.68. $C_{18}H_{24}N_2O_3$. Calculated (%): C, 68.33; H, 7.65; N, 8.85. GC-MS (EI), m/z (I_{rel} (%)): 316 $[M]^+$ (70), 301 $[M - Me]^+$ (62), 285 $[M - OMe]^+$ (8), 189 (42), 174 (35), 149 (58), 121 (100). IR, ν/cm^{-1}: 2959, 1696 (COO), 1616 w, 1520 m, 1508 (C=N), 1436. ^{1}H NMR ($CDCl_3$), δ: 1.20, 1.40 (both s, 3 H each, Me_2C(4)); 1.77, 1.79 (both d, 3 H each, =CMe$_2$, ^4J = 1.4 Hz); 3.78, 3.84 (both s, 3 H each, 2 OMe); 4.54 (d, 1 H, H(5), ^3J = 9.9 Hz); 5.09 (dsp, 1 H, =CH, ^3J = 9.9 Hz, ^4J = 1.4 Hz); 6.82 (d, 2 H, H_m, ^3J = 9.2 Hz); 7.10 (d, 2 H, H_o, ^3J = 9.2 Hz). ^{13}C NMR ($CDCl_3$), δ: 18.5, 25.9 (=CMe$_2$); 20.1, 26.0 (Me$_2$C(4)); 49.9 (C(4)); 51.7 (CO_2Me); 55.5 (OMe); 72.1 (C(5)); 114.3 (C_m); 117.4 (C_o); 118.6 (=CH); 137.4 (C_{ipso}); 137.7 (=C); 144.5 (C(3)); 155.1 (C_p); 163.0 (COO).

Compound **14a**, colorless oil. GC-MS (EI), m/z (I_{rel} (%)): 316 $[M]^+$ (65), 301 $[M - Me]^+$ (20), 200 (25), 175 (15), 163 (100), 148 (95), 122 (15), 92 (15), 77 (20). ^{1}H NMR ($CDCl_3$), δ: 1.21, 1.23 (both s, 3 H each, Me_2C(5)); 1.76 (d, 3 H, *Z*-Me, ^4J = 1.3 Hz); 1.79 (d, 3 H, *E*-Me, ^4J = 1.3 Hz); 3.80, 3.82 (both s, 3 H each, 2 OMe); 3.83 (d, 1 H, H(4), ^3J = 10.6 Hz); 5.11 (dsp, 1 H, =CH, ^3J = 10.6 Hz, ^4J = 1.3 Hz); 6.84 (d, 2 H, H_m, ^3J = 9.0 Hz); 7.17 (d, 2 H, H_o, ^3J = 9.0 Hz). ^{13}C NMR

($CDCl_3$), δ: 18.1 (*Z*-Me); 21.6, 25.3 ($\underline{Me_2}C(5)$); 26.1 (*E*-Me); 51.9 ($CO_2\underline{Me}$); 54.4 (C(4)); 55.5 (OMe); 73.1 (C(5)); 114.0 (C_m); 118.6 (=CH); 124.5 (C_o); 135.7 (C_{ipso}); 136.1 (=C); 141.4 (C(3)); 157.3 (C_p); 163.4 (COO).

Compound **15a**, colorless oil. HRMS (ESI): $[M + H]^+$, calculated for $C_{18}H_{25}N_2O_3$ 317.1860, found: 317.1856. ^1H NMR ($CDCl_3$), δ: 1.69, 1.77 (both d, 3 H each, 2 Me at C(5), ^4J = 1.5 Hz); 1.75 (t, 3 H, Me, ^4J = 1.3 Hz); 3.78, 3.79 (both s, 3 H each, 2 OMe); 4.29 (br.d, 1 H, H(3), ^3J = 9.5 Hz); 4.77 (m, 2 H, $=CH_2$); 5.51 (dsp, 1 H, H(4), ^3J = 9.5 Hz, ^4J = 1.5 Hz); 6.87 (d, 2 H, H_m, ^3J = 9.0 Hz); 7.12 (d, 2 H, H_o, ^3J = 9.0 Hz); 12.1 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 18.1 (*Z*-Me); 21.4 (Me); 26.1 (*E*-Me); 47.3 (C(3)); 51.4 ($CO_2\underline{Me}$); 55.7 (OMe); 110.6 ($=CH_2$); 114.8, 115.0 (C_o, C_m); 124.6 (C(4)); 127.9, 132.3 (C(2′), C(5)); 137.8 (C_{ipso}); 147.1 (C(2)); 155.1 (C_p); 164.3 (COO).

Methyl 1-(4-fluorophenyl)-4,4-dimethyl-5-(2-methylprop-1-enyl)- (13b) and methyl 1-(4-fluorophenyl)-5,5-dimethyl-4-(2-methylprop-1-enyl)-4,5-dihydro-1*H*-pyrazole-3-carboxylates (14b) and methyl 2-[(4-fluorophenyl)hydrazono]-5-methyl-3-(prop-1-en-2-yl)hex-4-enoate (15b). A reaction of dihydroindazole **1b** (0.31 g) with 2,5-dimethylhexa-2,4-diene (**5**) (0.55 g) gave regioisomeric pyrazolines **13b** and **14b** (71 mg, 47%) in a ratio of 5.7 : 1 (^1H NMR) and hydrazone **15b** (28 mg, 18%). For the mixture of isomers **13b** and **14b**, found (%): C, 66.68; H, 7.10; N, 8.72. $C_{17}H_{21}FN_2O_2$. Calculated (%): C, 67.09; H, 6.95; N, 9.20.

Compound **13b**. GC-MS (EI), *m/z* (I_{rel} (%)): 304 $[M]^+$ (46), 289 $[M - Me]^+$ (100), 273 $[M - OMe]^+$ (4), 257 (5), 245 (5), 229 (5), 177 (24), 176 (28), 162 (16), 161 (8), 136 (8), 122 (8), 110 (16), 109 (20), 95 (40). ^1H NMR ($CDCl_3$), δ: 1.23, 1.39 (both s, 3 H each, 2 Me at C(4)); 1.78, 1.80 (both d, 3 H each, $=C\underline{Me_2}$, ^4J = 1.4 Hz); 3.85 (s, 3 H, OMe); 4.54 (d, 1 H, H(5), ^3J = 9.8 Hz); 5.07 (dsp, 1 H, =CH, ^3J = 9.8 Hz, ^4J = 1.4 Hz); 6.92, 7.11 (both m, 2 H each, H_o, H_m). ^{13}C NMR ($CDCl_3$), δ: 18.4, 25.9 ($=C\underline{Me_2}$); 20.1, 26.0 (2 Me at C(4)); 50.0 (C(4)); 51.7 ($CO_2\underline{Me}$); 71.8 (C(5)); 115.4 (d, C_m, $^2J_{C,F}$ = 22.5 Hz); 117.1 (d, C_o, $^3J_{C,F}$ = 8.0 Hz); 120.3 (=CH); 137.9 (=C); 139.8 (d, C_{ipso}, $^4J_{C,F}$ = 2.4 Hz); 145.5 (C(3)); 158.3 (d, C_p, $^1J_{C,F}$ = 241 Hz); 162.8 (COO).

Compound **14b**. GC-MS (EI), *m/z* (I_{rel} (%)): 304 $[M]^+$ (34), 289 $[M - Me]^+$ (16), 273 $[M - OMe]^+$ (4), 257 (5), 248 (4), 245 $[M - COOMe]^+$ (5), 229 (5), 152 (34), 151 (86), 136 (100), 110 (16), 109 (18), 95 (50). ^1H NMR ($CDCl_3$), δ: 1.24, 1.27 (both s, 3 H each, $Me_2C(4)$); 1.76, 1.79 (both d, 3 H each, $=C\underline{Me_2}$, ^4J = 1.4 Hz); 3.83 (s, 3 H, OMe); 3.84 (d, 1 H, H(5), ^3J = 10.0 Hz); 5.09 (dsp, 1 H, =CH, ^3J = 10.0 Hz, ^4J = 1.4 Hz); 6.97, 7.20 (both m, 2 H each, H_o, H_m). ^{13}C NMR ($CDCl_3$), δ: 18.1, 26.1 ($=C\underline{Me_2}$); 21.7, 25.3 ($\underline{Me_2}C(4)$); 51.8 ($CO_2\underline{Me}$); 54.8 (C(4)); 72.8 (C(5)); 115.9 (d, C_o, $^3J_{C,F}$ = 8.0 Hz); 116.2 (d, C_m, $^2J_{C,F}$ = 22.4 Hz); 118.2 (=CH); 136.4 (=C); 138.8 (d, C_{ipso}, $^4J_{C,F}$ = 2.4 Hz); 142.2 (C(3)); 160.1 (d, C_p, $^1J_{C,F}$ = 243 Hz); 163.3 (COO).

Compound **15b**, colorless crystals, m.p. 46—47 °C ($CHCl_3$). Found (%): C, 66.95; H, 6.86; N, 9.27. $C_{17}H_{21}FN_2O_2$. Calculated (%): C, 67.09; H, 6.95; N, 9.20. MS (EI), *m/z* (I_{rel} (%)): 304 $[M]^+$ (38), 289 $[M - Me]^+$ (10), 257 (10), 162 (20), 134 (32), 110 (100), 95 (40), 83 (65). IR, ν/cm^{-1}: 3260 (NH), 2972, 2916, 1676 (C=O), 1612, 1544, 1516 (C=N), 1436. ^1H NMR ($CDCl_3$), δ: 1.70, 1.78 (both d, 3 H each, $Me_2C(5)$, ^4J = 1.5 Hz); 1.75 (t, 3 H, Me, ^4J = 1.2 Hz); 3.79 (s, 3 H, OMe); 4.30 (br.d, 1 H, H(3), ^3J = 9.6 Hz); 4.78 (m, 2 H, $=CH_2$); 5.48 (dsp, 1 H, H(4), ^3J = 9.6 Hz, ^4J = 1.5 Hz); 6.99 (m, 2 H, H_m); 7.11 (m, 2 H, H_o); 12.1 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 18.1 (*Z*-Me); 21.5 (Me); 26.1 (*E*-Me); 47.3 (C(3)); 51.6 ($CO_2\underline{Me}$); 110.8 ($=CH_2$); 114.7 (C_o, $^3J_{C,F}$ = 7.7 Hz); 115.9 (C_m, $^2J_{C,F}$ = 23.2 Hz); 124.3 (C(4)); 129.1, 132.6 (C(2′), C(5)); 140.2 (C_{ipso}, $^4J_{C,F}$ = 2.3 Hz); 146.9 (C(2)); 158.3 (C_p, $^1J_{C,F}$ = 240 Hz); 164.2 (COO). ^{19}F NMR ($CDCl_3$), δ: −123.3 (tt, CF, $^3J_{H,F}$ = 8.7 Hz, $^4J_{H,F}$ = 4.2 Hz).

Reaction of compound 1a with 2,3-dimethylbut-2-ene (6). The products obtained from dihydroindazole **1a** (316 mg) and tetramethylethene (**6**) (0.42 g) were separated by column chromatography on SiO_2 ($CHCl_3$—EtOAc, 5 : 1). They include methyl 1-(4-methoxyphenyl)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate (**16a**) (13 mg, 9%), methyl 2-[(4-methoxyphenyl)hydrazono]-3,3,4-trimethylpent-4-enoate (**17a**) (14 mg, 10%), methyl 5-(2-hydroxyprop-2-yl)-1-(4-methoxyphenyl)-5-methyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate **(18a)** (30 mg, 20%), and methyl 5-acetyl-1-(4-methoxyphenyl)-5-methyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate (**19a**) (30 mg, 21%).

Compound **16a**, colorless oil. HRMS (ESI): $[M + Na]^+$, calculated for $C_{16}H_{22}N_2O_3Na$ 313.1523, found: 313.1523. MS (EI), *m/z* (I_{rel} (%)): 290 $[M]^+$ (85), 275 $[M - Me]^+$ (100), 259 $[M - OMe]^+$ (10), 231 $[M - COOMe]^+$ (22), 216 (22), 163 (40), 148 (74), 121 (20), 92 (20). IR, ν/cm^{-1}: 2976, 2958, 1696 (C=O), 1508 (C=N), 1436. ^1H NMR ($CDCl_3$), δ: 1.10 (s, 6 H, $Me_2C(4)$); 1.23 (s, 6 H, $Me_2C(5)$); 3.80, 3.84 (both s, 3 H each, 2 OMe); 6.85 (d, 2 H, H_m, ^3J = 9.0 Hz); 7.17 (d, 2 H, H_o, ^3J = 9.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 19.5, 19.8 ($\underline{Me_2}C(4)$, C(5)); 50.6 (C(4)); 51.7 ($CO_2\underline{Me}$); 55.5 (OMe); 74.9 (C(5)); 113.9 (C_m); 125.5 (C_o); 135.9 (C_{ipso}); 145.4 (C(3)); 157.6 (C_p); 163.4 (COO).

Compound **17a** (~95% purity), oil. MS (EI), *m/z* (I_{rel} (%)): 290 $[M]^+$ (80), 275 $[M - Me]^+$ (25), 259 $[M - OMe]^+$ (5), 231 $[M - COOMe]^+$ (10), 215 (10), 149 (12), 135 (20), 121 (100), 108 (35), 95 (50), 84 (90). IR, ν/cm^{-1}: 3268 (NH), 3020, 1702 (C=O), 1670, 1542, 1518, 1438. ^1H NMR ($CDCl_3$), δ: 1.37 (s, 6 H, $Me_2C(3)$); 1.67 (t, 3 H, Me, ^4J = 1.2 Hz); 3.72, 3.78 (both s, 3 H each, 2 OMe); 4.75 (q, 2 H, $=CH_2$, ^4J = 1.2 Hz); 6.87 (d, 2 H, H_m, ^3J = 9.1 Hz); 7.13 (d, 2 H, H_o, ^3J = 9.1 Hz); 12.0 (NH). ^{13}C NMR ($CDCl_3$), δ: 20.3 (Me); 27.2 ($\underline{Me_2}C(3)$); 45.2 (C(3)); 50.8 ($CO_2\underline{Me}$); 55.7 (OMe); 108.4 ($=CH_2$); 114.7, 114.8 (C_o, C_m); 132.3 (C(4)); 138.1 (C_{ipso}); 152.1 (C(2)); 154.9 (C_p); 164.5 (COO).

Compound **18a**, yellowish oil. Found (%): C, 62.52; H, 7.33; N, 8.67. $C_{16}H_{22}N_2O_4$. Calculated (%): C, 62.73; H, 7.24; N, 9.14. MS (EI), *m/z* (I_{rel} (%)): 306 $[M]^+$ (5), 275 $[M - OMe]^+$ (3), 247 $[M - COOMe]^+$ (50), 215 (100); 203 (8); 188 (15), 148 (50), 132 (12); 121 (15); 107 (20); 92 (40); 84 (40); 77 (65); 59 (100). IR, ν/cm^{-1}: 3608 (OH), 2980, 2958, 1696 (C=O), 1508 (C=N), 1449. ^1H NMR ($CDCl_3$), δ: 1.21, 1.25 (both s, 3 H each, 2 Me); 1.45 (s, 3 H, MeC(5)); 1.76 (br.s, 1 H, OH); 2.90, 3.25 (both d, $H_2C(4)$, ^2J = 18.0 Hz); 3.76, 3.81 (both s, 3 H each, 2 OMe); 6.81 (d, 2 H, H_m, ^3J = 9.0 Hz); 7.32 (d, 2 H, H_o, ^3J = 9.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 21.5 ($\underline{Me}C(5)$); 25.6, 25.7 (2 Me); 43.6 (C(4)); 51.9 ($CO_2\underline{Me}$); 55.3 (OMe); 75.5 (C(5)); 78.4 (C—OH); 113.7 (C_m); 125.8 (C_o); 136.8, 136.9 (C(3), C_{ipso}); 157.3 (C_p); 163.3 (COO).

Compound **19a**, colorless crystals, m.p. 101—102 °C ($CHCl_3$). Found (%): C, 62.12; H, 6.60; N, 9.38. $C_{15}H_{18}N_2O_4$. Calculated (%): C, 62.06; H, 6.25; N, 9.65. MS (EI), *m/z* (I_{rel} (%)): 290 $[M]^+$ (14), 247 $[M - Ac]^+$ (65), 215 (100), 188 (20), 160 (10), 148 (32), 107 (12), 92 (22), 77 (30). IR, ν/cm^{-1}: 1716 (COO), 1700 (C=O), 1652, 1616, 1540, 1508 (C=N), 1464. ^1H NMR ($CDCl_3$), δ: 1.48 (s, 3 H, MeC(5)); 2.23 (s, 3 H, Me); 3.09, 3.35 (both d, $H_2C(4)$, ^2J = 17.9 Hz); 3.77, 3.90 (both s, 3 H each, 2 OMe); 6.81 (d, 2 H, H_m, ^3J = 9.0 Hz); 6.99 (d, 2 H, H_o, ^3J = 9.0 Hz).

^{13}C NMR ($CDCl_3$), δ: 19.9 (MeC(5)); 24.8 (Me); 45.3 (C(4)); 52.3 (CO_2Me); 55.6 (OMe); 76.6 (C(5)); 114.7 (C_m); 117.0 (C_o); 134.9, 135.7 (C(3), C_{ipso}); 155.6 (C_p); 162.8 (COO); 206.7 (C=O).

Reaction of compound 1b with 2,3-dimethylbut-2-ene (6). The products obtained from dihydroindazole **1b** (0.31 g) and tetramethylethene (**6**) (0.42 g) were separated by column chromatography on SiO_2 (benzene—EtOAc, gradient elution from 9 : 1 to 2 : 1). They include methyl 2-(4-fluorophenyl)hydrazono-3,3,4-trimethylpent-4-enoate (**17b**) (13 mg, 9%), methyl 1-(4-fluorophenyl)-5-(2-hydroxyprop-2-yl)-5-methyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate (**18b**) (41 mg, 28%), methyl 5-acetyl-1-(4-fluorophenyl)-5-methyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate (**19b**) (14 mg, 10%), and minor amounts of methyl 1-(4-fluorophenyl)-5-methyl-5-(prop-1-en-2-yl)-4,5-dihydro-1*H*-pyrazole-3-carboxylate (**20**) (3.0 mg, 2%) and methyl 1-(4-fluorophenyl)-5-methyl-1*H*-pyrazole-3-carboxylate (**21**) (3.6 mg, 3%).

Compound **17b** (~93% purity), oil. MS (EI), *m/z* (I_{rel} (%)): 278 $[M]^+$ (50), 263 $[M - Me]^+$ (55), 231 (100), 203 (15), 177 (8), 150 (10), 136 (14); 123 (18), 110 (90), 95 (30), 83 (70). ^{1}H NMR ($CDCl_3$), δ: 1.39 (s, 6 H, $Me_2C(3)$); 1.67 (br.s, 3 H, Me); 3.76 (s, 3 H, OMe); 4.75 (m, 2 H, $=CH_2$); 7.00 (m, 2 H, H_m); 7.13 (m, 2 H, H_o); 11.9 (NH). ^{13}C NMR ($CDCl_3$), δ: 20.3 (Me); 27.1 ($Me_2C(3)$); 45.4 (C(3)); 51.0 (CO_2Me); 108.7 ($=CH_2$); 114.6 (C_o, ^3J = 7.5 Hz); 115.9 (C_m, ^2J = 22.5 Hz); 133.6 (C(4)); 140.5 (C_{ipso}, ^4J = 3.0 Hz); 151.8 (C(2)); 156.2 (C_p, ^1J = 242 Hz); 164.4 (COO). ^{19}F NMR ($CDCl_3$), δ: −123.7 (tt, CF, $^3J_{H,F}$ = 8.6 Hz, $^4J_{H,F}$ = 4.1 Hz).

Compound **18b**, yellowish oil. Found (%): C, 60.96; H, 6.54; N, 9.46. $C_{15}H_{19}FN_2O_3$. Calculated (%): C, 61.21; H, 6.51; N, 9.52. MS (EI), *m/z* (I_{rel} (%)): 294 $[M]^+$ (6), 263 $[M - OMe]^+$ (5), 235 $[M - CO_2Me]^+$ (45), 203 (100), 191 (15), 136 (30), 95 (30). IR, ν/cm^{-1}: 3612 (OH); 2980, 2956, 1704 (C=O), 1560, 1508 (C=N), 1448. ^{1}H NMR ($CDCl_3$), δ: 1.26, 1.28 (both s, 3 H each, 2 Me); 1.49 (s, 3 H, MeC(5)); 1.70 (br.s, 1 H, OH); 2.95, 3.27 (both d, $H_2C(4)$, ^2J = 18.0 Hz); 3.86 (s, 3 H, OMe); 6.97 (m, 2 H, H_m); 7.46 (m, 2 H, H_o). ^{13}C NMR ($CDCl_3$), δ: 21.6 (MeC(5)); 25.8, 26.1 (2 Me); 44.3 (C(4)); 52.2 (CO_2Me); 75.9 (C(5)); 78.4 (C—OH); 115.3 (C_m, ^2J = 22.3 Hz); 125.0 (C_o, ^3J = 7.7 Hz); 138.0 (C(3)); 140.0 (C_{ipso}, ^4J = 2.9 Hz); 160.1 (C_p, ^1J = 244 Hz); 163.3 (COO). ^{19}F NMR ($CDCl_3$), δ: −123.9 (tt, CF, $^3J_{H,F}$ = 8.7 Hz, $^4J_{H,F}$ = 4.1 Hz).

Compound **19b**, colorless crystals, m.p. 156—157 °C ($CHCl_3$). Found (%): C, 60.30; H, 5.36; N, 10.03. $C_{14}H_{15}FN_2O_3$. Calculated (%): C, 60.43; H, 5.43; N, 10.07. MS (EI), *m/z* (I_{rel} (%)): 278 $[M]^+$ (12), 235 (62), 203 (100); 191 (14), 148 (10), 136 (25), 109 (10), 95 (30). IR, ν/cm^{-1}: 3020, 1720 (COO), 1700 (C=O), 1560, 1508 (C=N), 1448. ^{1}H NMR ($CDCl_3$), δ: 1.51 (s, 3 H, MeC(5)); 2.25 (s, 3 H, MeCO); 3.12, 3.38 (both d, $H_2C(4)$, ^2J = 18.1 Hz); 3.90 (s, 3 H, OMe); 7.00 (m, 4 H, H_m, H_o). ^{13}C NMR ($CDCl_3$), δ: 19.7 (MeC(5)); 24.7 (MeCO); 45.5 (C(4)); 52.5 (CO_2Me); 76.3 (C(5)); 116.2 (C_m, ^2J = 22.7 Hz); 116.7 (C_o, ^3J = 7.7 Hz); 136.8 (C(3)); 137.5 (C_{ipso}, ^4J = 2.8 Hz); 158.6 (C_p, ^1J = 243 Hz); 162.6 (COO). ^{19}F NMR ($CDCl_3$), δ: −121.8 (tt, CF, $^3J_{H,F}$ = 8.2 Hz, $^4J_{H,F}$ = 4.9 Hz).

Compound **20**, enriched to ~80%. GC-MS (EI), *m/z* (I_{rel} (%)): 276 $[M]^+$ (60), 261 $[M - Me]^+$ (10), 235 (38), 229 (25), 203 (98), 191 (15), 176 (10), 136 (25), 109 (58), 95 (100). ^{1}H NMR ($CDCl_3$), δ: 1.53 (s, 3 H, MeC(5)); 1.80 (Me); 3.02, 3.21 (both d, $H_2C(4)$, ^2J = 18.1 Hz); 3.87 (s, 3 H, OMe); 5.07, 5.12 (both m, 1 H each, $=CH_2$); 6.92 (m, 2 H, H_m); 7.24 (m, 2 H, H_o).

Compound **21**, oil. HRMS (ESI): $[M + Na]^+$, calculated for $C_{12}H_{11}FN_2O_2Na$ 257.0697, found: 257.0691. MS (EI), *m/z* (I_{rel} (%)): 234 $[M]^+$ (78), 219 $[M - Me]^+$ (5), 203 $[M - OMe]^+$ (100), 176 (45), 160 (22), 135 (25), 109 (15), 95 (45). IR, ν/cm^{-1}: 2956, 2928, 1724 (COO), 1516 (C=N), 1452. ^{1}H NMR ($CDCl_3$), δ: 2.31 (s, 3 H, Me); 3.94 (s, 3 H, OMe); 6.74 (br.s, 1 H); 7.17 (m, 2 H, H_m); 7.43 (m, 2 H, H_o). ^{13}C NMR ($CDCl_3$), δ: 12.4 (Me); 52.2 (OMe); 109.3 (C(4)); 116.2 (C_m, ^2J = 23.2 Hz); 127.5 (C_o, ^3J = 8.6 Hz); 135.3 (C_{ipso}, ^4J = 3.1 Hz); 140.8 (C(5)); 143.7 (C(3)); 162.5 (C_p, ^1J = 248 Hz); 163.0 (COO). ^{19}F NMR ($CDCl_3$), δ: −111.8 (tt, CF, $^3J_{H,F}$ = 9.4 Hz, $^4J_{H,F}$ = 5.7 Hz).

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