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N,N'-LINKED BIAZOLES. PART 7. OXIDATIVE DIMERIZATION OF N-UNSUBSTITUTED TETRAHYDROINDAZOLONES

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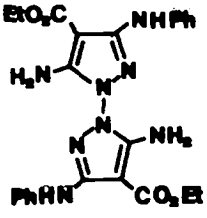
Abstract. The structure of the products obtained by oxidative dimerization of tetrahydroindazolones was established as being N(1)-C(3a') dimers. In one case a C(3a)-C(3a') dimer was also isolated, but N-N'-Linked dimers were never found, contrary to a previous report in the literature. A complete 13-carbon nmr study of the monomers and their fixed methylated derivatives was performed to determine the most abundant tautomer in each case, since the tautomerism study of tetrahydroindazolone and of its 4-ethoxycarbonyl derivative was needed to fully determine the structure of the dimers.

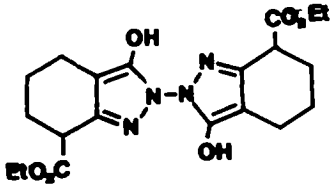
Introduction

Among the 153 different N,N'-Linked dimers of azoles, the 1,1'-bipyrazole system (1) proved to be one of the most difficult to obtain. Some old references[1] were found to be false,[2] and other more recent[3] are in fact much more complex than described.[4] Actually, only two remainig references describe the system, one by Schulz *et al.*[5] yielding the quite complicated structure (2), and the other reported by Skaric *et al.*, describing the dimerization of several ethoxycarbonyl derivatives of 4,5,6,7-tetrahydroindazolone with iodine. The structures assigned for the dimers, *i.e.* (3),[6] could open a practical way of access to (1) and its derivatives.

(1)



(2)

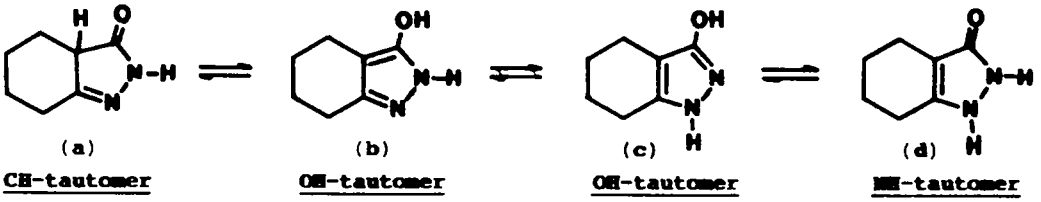


(3)

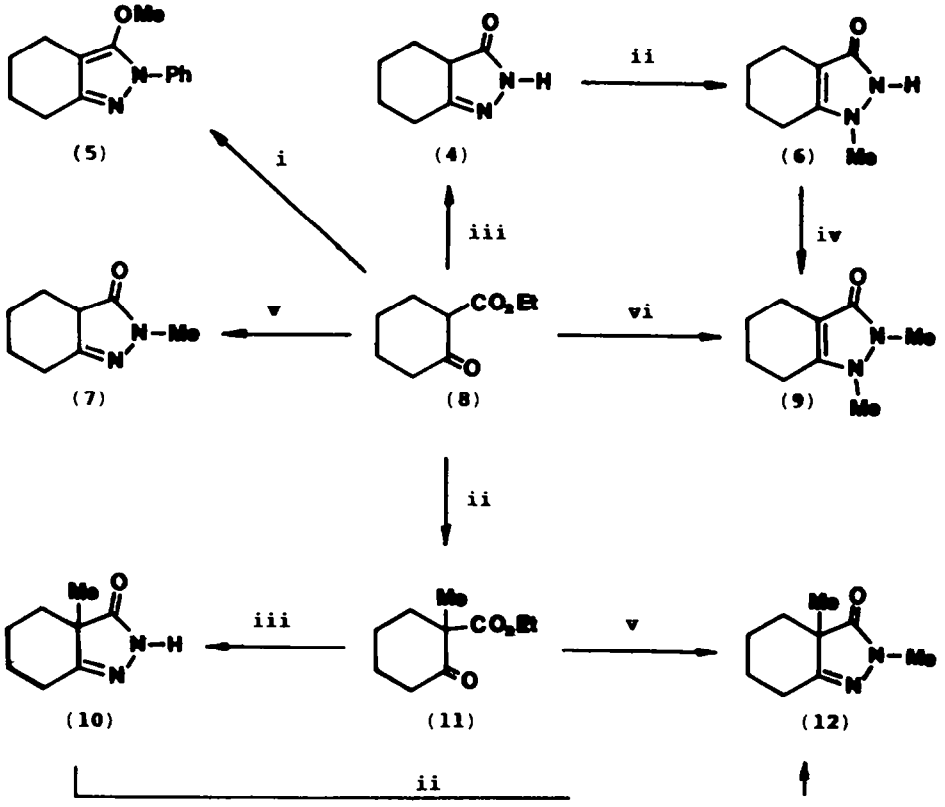
However, when the preparation of (3) was repeated, following the Skaric procedure,[6] a compound with a similar mp as described was found, but whose ^{13}C nmr spectrum was clearly inconsistent with the proposed structure. Owing to the unavailability of suitable crystals (the compound was a mixture of two diastereoisomers, see later), we decided to use ^{13}C nmr spectroscopy to establish its structure. Since the existence of tautomerism considerably complicates the study, it was also decided to carry out a careful study of the tautomerism of tetrahydroindazolones.

Tautomerism of tetrahydroindazolones

Surprisingly enough, although the tautomerism of pyrazolones is one of the paradigmatic cases of heterocyclic tautomerism,[7] ^{13}C nmr spectroscopy has been never systematically used as a tool for its study.[8] The tetrahydroindazolones of the present study are structurally more related to pyrazolones (as 3,4-tetramethylene derivatives) than to aromatic indazolones. As for N-unsubstituted pyrazolones, there exist four 'reasonable' tautomers of 4,5,6,7-tetrahydroindazolone (**4a**)-(**4d**):



The standard procedure for the study of tautomerism is to use a series of methyl derivatives as models.[7] The models for tetrahydroindazolone (**4a**)-(**4d**) and their syntheses are represented in Scheme 1, under one of their possible tautomeric forms.



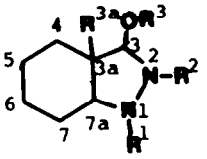
i) Ph-NH-NH_2 + $Me_3O^+BF_4^-$; ii) NaH, IMe ; iii) H_2N-NH_2, H_2O
iv) NaOH, IMe ; v) Me-NH-NH_2 ; vi) Me-NH-NH-Me .

Scheme 1

The ^{13}C nmr spectra of some pyrazolones has been reported,[9] but no systematic studies has yet been published. The chemical shifts of the tetrahydroindazolones of Scheme 1 are collected on Table 1. Both literature values[9] and DEPT experiments were used to assign the most significative signals. Although the assignment of methylene

carbons is only tentative, it is consistent with the values described for other tetrahydroindazoles.[2]

Table 1. ^{13}C Nmr chemical shifts of tetrahydroindazolones



No	Tautomer	Solvent	C_3	C_{3a}	C_{7a}	C_4	C_5	C_6	C_7	R^1	R^2	R^3	R^{3a}
4	4c	DMSO-d_6	158.5	98.6	139.8	18.9	21.3	22.3	22.9	--	--	--	--
5	5b	DMSO-d_6	149.9	99.1	149.1	20.2	22.7	23.1	23.9	--	*	59.8	--
6	6c	$CDCl_3$	158.8	99.9	140.3	18.9	21.3	22.5	22.7	34.2	--	--	--
6	6c	DMSO-d_6	157.3	99.0	139.2	19.2	20.9	22.4	22.7	34.5	--	--	--
7	7a	$CDCl_3$	174.8	47.9	162.7	27.5	24.1	28.4	29.0	--	30.9	--	--
7	7b	$CDCl_3$	161.8	101.8	146.7	18.8	21.9	22.1	22.6	--	30.4	--	--
7	7b	DMSO-d_6	157.6	99.8	147.1	19.0	22.3	22.3	22.6	--	31.1	--	--
9	9d	$CDCl_3$	166.2	107.0	152.4	18.7	21.7	22.1	22.2	33.8	28.6	--	--
9	9d	DMSO-d_6	165.4	104.9	152.6	18.9	21.3	22.0	22.2	33.8	28.5	--	--
10	10a	DMSO-d_6	180.8	46.5	166.2	34.3	20.0	26.1	28.0	--	--	--	17.0
12	12a	$CDCl_3$	178.7	48.4	166.9	35.0	20.5	26.6	28.6	--	30.8	--	17.0
12	12a	DMSO-d_6	177.9	47.6	166.2	34.5	20.0	25.9	28.2	--	30.4	--	17.2

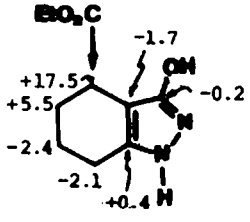
*C_i: 138.9; C_o: 121.6; C_m: 129.0; C_p: 125.9

The fixed derivatives (**5**), (**9**), (**10**), and (**12**) can be considered as model compounds for NH- [forms (**b**)-(**d**)] and CH-tautomers [form (**a**)]. Compound (**7**) exists in DMSO solely as an OH-tautomer, whereas in $CDCl_3$ both CH- and OH-tautomers are present, as in pyrazolones.[7] On the other hand, compound (**6**) was found to be an OH-tautomer both in $CDCl_3$ and DMSO. Finally, for the most complicated case of compound (**4**), the CH-tautomer was absent in DMSO (the compound was not soluble in $CDCl_3$). As it is well known,[7] the three other tautomers give rise to averaged signals. A comparison of the chemical shifts of (**4**) with those of (**5b**), (**6c**), (**7b**), and (**9d**) did not leave any doubt for the assignment of (**4c**) as the major tautomer in DMSO.

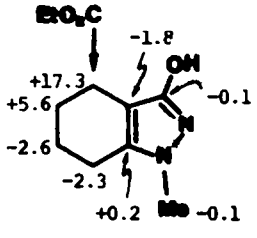
Synthesis and tautomerism of 4-ethoxycarbonyl-4,5,6,7-tetrahydroindazolones

Scheme 2 summarizes the reactions and compounds prepared in this series from diethyl 3-oxocyclohexane-1,2-dicarboxylate (**14**).[10] Although less complete than the series of Scheme 1, the results previously obtained in simpler cases can now be used successfully.

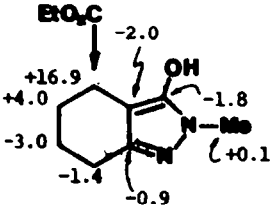
The ^{13}C chemical shifts are collected in Table 2. There was no effect of the ester group on the tautomerism (at least in DMSO), because the most stable tautomers were found to be the same in both series. The effect of the ester group substituent on the chemical shifts in DMSO was the following:



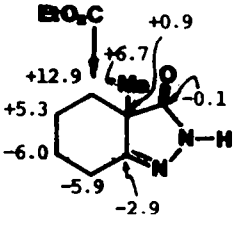
(**13c**) - (**4c**)



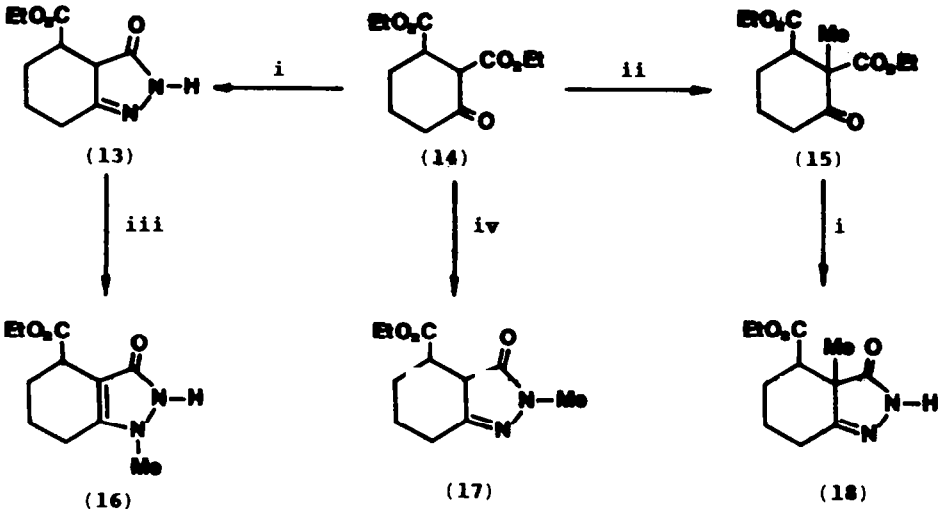
(**16c**) - (**6c**)



(**17b**) - (**7b**)

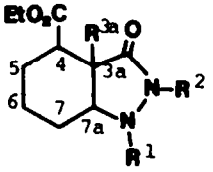


(**18a**) - (**10a**)



Scheme 2 : i) H_2N-NH_2 ; ii) NaH, IMe ; iii) NaH, Tos-OMe ; iv) Me-NH-NH_2 .

Table 2. ^{13}C Nmr chemical shifts of 4-CO_2Et tetrahydroindazolones in DMSO-d_6

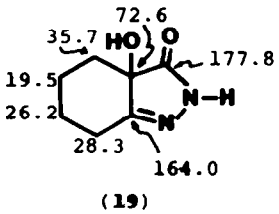


No	Tautomer	C_3	C_{3a}	C_{7a}	C_4	C_5	C_6	C_7	R^1	R^3	R^{3a}
13	**13c**	158.3	96.9	140.2	36.4	26.8	19.9	20.8	--	--	--
16	**16c**	157.2	97.2	139.4	36.5	26.5	19.8	20.4	34.4	--	--
17	**17b**	155.8	97.8	146.2	35.9	26.3	19.3	21.2	--	31.2	--
18	**18a**	180.7	47.4	163.3	47.2	25.3	20.1	22.1	--	--	23.7

Ester groups: **13** (173.8, 59.6, 13.9); **16** (173.8, 59.7, 14.0); **17** (173.0, 59.9, 13.8; **18** (171.5, 60.0, 13.6).

Dimerization of 4,5,6,7-tetrahydroindazolone (4)

The oxidation of (**4**) was carried out in toluene with iodine as oxidant (Skaric conditions). The yield of dimers was poor at room temperature, but it growed up to 60% (crude material) working at reflux during 60 hours. Column chromatography afforded two compounds, (**19**) and (**20**), in 12.5% and 20% yield, respectively.

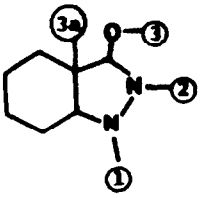


(**19**)

Compound (**19**), mp 203-204°C had a molecular peak at m/z 154, and ir bands at 3220, 1720, 1700, and 1630 cm^{-1}, very similar to those of (**10**) (3200, 1700, and 1670 cm^{-1}). The ^{13}C nmr spectrum (values on the formula) suggested a structure related to (**10**) but with an electronegative group at 3a instead of a methyl group. Such a structure has been previously described by Veibel[11] (mp 195-197°C). To avoid any doubt, Veibel synthesis was repeated and both compounds proved identical.

Compound (**20**) was a dimer ($C_{14}H_{18}N_4O_2$, analysis and molecular peak at m/z 274). However, the dimerization of (**4**) can yield up to ten dimers, from which several could be under different tautomeric forms (Table 3).

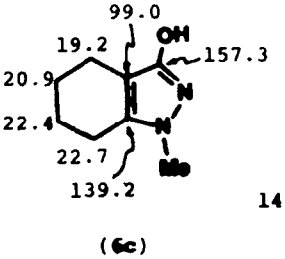
Table 3. Structure of the possible dimers.



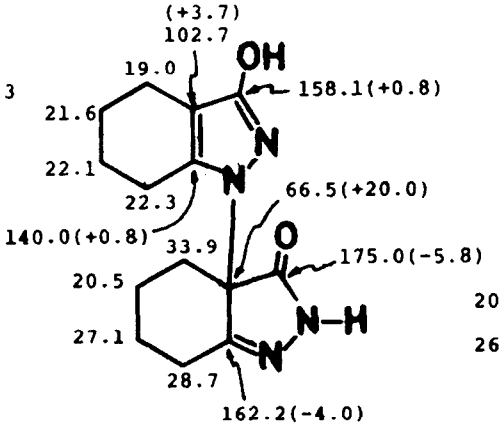
1-1	Sym	3 taut									
1-2	Asym	6 taut	2-2*	Sym	6 taut						
1-3	Asym	4 taut	2-3	Asym	6 taut	3-3	Sym	3 taut			
1-3a	Asym	2 taut	2-3a	Asym	3 taut	3-3a	Asym	2 taut	3a-3a	Sym	1 taut

*Skaric-type structure.

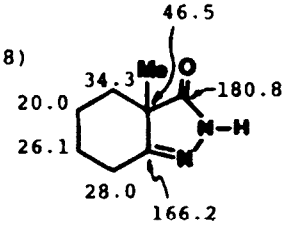
Considering that tautomers are *sensu strictu* different compounds, it was necessary to choose between 36 structures (without considering diastereoisomers in the case of 3a-linked dimers). ^{13}C Nmr spectroscopy allowed us to solve this rather complicated problem in an elegant way. The fact that the spectra in DMSO show fourteen signals excluded the 'symmetrical' structures 1-1, 2-2(Skaric-type), and 3-3 (Table 3), since pyrazolonic tautomers, with the exception of the CH one [which was not observed in DMSO except for the CH-blocked tautomers (**10a**) and (**12a**), see Table 1], give rise to averaged signals for the tautomeric mixture. The remaining 3a-3a 'symmetrical' structure, though blocked in its tautomerism, could be in fact a mixture of two diastereoisomers (up to 14 signals), but this possibility was ruled out since only one 'carbonyl' signal (at 175.0 ppm) was observed (for the authentical 3a-3a dimer, see below). The signals at 175.0 ppm ($C_{3'}$) and 162.2 ppm ($C_{7a'}$) points to a C_{3a} substituted structure, only compatible with 1-3a, 2-3a, and 3-3a dimers [compare with (**10**) and (**12**), Table 1]. The chemical shift of C_{3a} (at 66.5 ppm) excluded the 3-3a structure, for which a more deshielded signal should be expected [compare with (**19**)]. Finally, the comparison with the chemical shifts of (**6c**) and (**7b**) (Table 1) allowed the definitive selection of the 1-3a structure (**20ca**)(the differences with regard to model compounds are included in parentheses).



(**6c**)



(**20ca**)

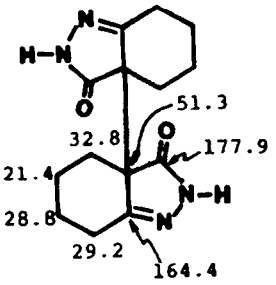


(**10a**)

Since the 3a-substituted substructure is a blocked tautomer of type (a), only the upper 1-substituted substructure could present tautomerism. As it was the case with compound (**6**), the hydroxy tautomer was preferred in DMSO.

In addition to the study of the oxidation of the tetrahydroindazolone (**4**) with iodine, we investigated also the use of lead dioxide as oxidant. Pirkle[12] has described the formation of N-N bonds in the dimerization of urazoles and

pyrazolidin-3,5-diones by means of this reagent. When Pirkle oxidation method was applied to tetrahydroindazolone (**4**) two dimers of the same formula ($C_{14}H_{18}N_4O_2$) were obtained. After column separation, one of them (23%) was found to be identical in every respect to (**20**). The structure (**21**) was assigned to the second dimer (17%) on the basis of its ^{13}C nmr spectra. The number of signals (seven) and the chemical shifts are only compatible with a 3a-3a 'symmetrical' structure. Other literature examples account for the formation of C-C dimers by oxidation of pyrazolin-5-ones with mild oxidants.[13,14]

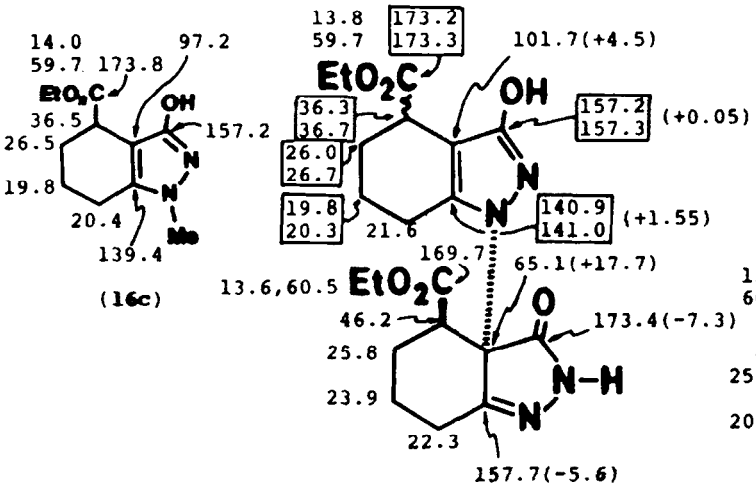


(**21aa**)

The two chiral centres at C_{3a} and $C_{3a'}$ can give raise to diastereoisomerism. However, no splitting of the carbon signals was observed at 50 MHz, suggesting that only one diastereoisomeric pair was present. Inspection of space-filling molecular models (CPK) indicated that the *meso* form was sterically favored over the racemic one.

Dimerization of 4-ethoxycarbonyl-4,5,6,7-tetrahydroindazolone (13)

In our hands, the Skaric reaction with (**13**) furnished a solid (15% yield) whose properties were found identical to those described for compound (**3**). The compound melted at 86-88°C (lit.[6] 89-90°C), but analytical HPLC revealed a 60:40 mixture of two isomers. We were unable to separate both compounds. Mass spectrometry and microanalysis agree with a dimer ($C_{20}H_{26}N_4O_6$, m/z 418), but the ^{13}C nmr spectrum showed no less than 26 signals, many like ill-resolved 'doublets', *i.e.*, at almost identical chemical shifts. Considering that only OH-tautomers of type (**b**) are observed in DMSO, the Skaric structure (**3**) can be ruled out even if all the carbon signals were splitted (maximum 20 signals). Only a structure (**22ca**), similar to (**20**), accounts for the observed behaviour.



(**16c**) (**22ca**) (**18a**)

The differences in chemical shifts with the model compounds (values in parentheses) are quite similar to those found in dimer (**20ca**). Comparison of structures (**20**) and (**22**) allows for the calculation of the effects produced by the ethoxycarbonyl substituent: they are of the same magnitude as those calculated previously for the (**16c**)-(**6c**) and (**18a**)-(**10a**) pairs. Despite the fact that some signals of (**22**) have been only tentatively assigned, there is no doubt that the compound described by Skaric (and probably the rest of dimers described in the same paper)[6] is a 1-3a dimer existing in DMSO as a (**ca**) tautomer. Another remarkable fact is that the splitting of the signals affects exclusively the 1-substituted-3-hydroxy-4,5,6,7-

tetrahydroindazole substructure. There are three chiral centres in (**22**): C_4 , $C_{4'}$, and $C_{3a'}$, thus four diastereoisomeric pairs are to be expected. The fact that only two were obtained indicates that two of the chiral centres exist under only one relative configuration. The observed partial splitting of the ^{13}C signals and the examination of molecular models lead us to propose that substituents in positions 3a' and 4' are in a *trans* relative position; only the substituent in C_4 changes its configuration.

Conclusion

Our previous studies on the dimerization of pyrazole derivatives under different oxidation levels (2-pyrazolines or pyrazoles) demonstrated that, unless there are no other alternatives, N-N bonds were not formed[2] or, at least, were not the only products formed.[4] The present study shows that, in the case of tetrahydroindazolones (pyrazolones), a N-C or even a C-C bond is also preferred. The formation of N-C dimers has been observed in the preceeding papers of this series.[2,4] As we have already indicated, C-C bond formation has been reported for pyrazolones.[14] In full accord with this behaviour, when position 3a was substituted and position 2 free, as in compound (**10**), the dimerization reaction (either by iodine or lead dioxide) failed, indicating that the radical obtained by the oxidation of (**4**) and (**13c**) is delocalized mainly over N_1 and C_{3a}.

EXPERIMENTAL

Melting points are uncorrected. Ir spectra were registered on a Pye Unicam SP 1100 instrument, and uv spectra were determined in ethanol on a Perkin Elmer 124 spectrophotometer (values in parentheses refer to log ε). ^1H- and ^{13}C-nmr spectra were recorded on a Bruker WM 200 SY instrument, and mass spectra (electronic impact mode) on a Hewlett-Packard 5985. Column chromatography was performed on silica gel (Merck, 70-230 mesh). The following compounds were obtained according to known procedures: 4,5,6,7-tetrahydro-(3aH)indazolin-3-one (**4**),[15] 2-methyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (**7**),[16] 1,2-dimethyl-4,5,6,7-tetrahydroindazolin-3-one, (**9**),[17] 3a-methyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (**10**),[18] 4-ethoxycarbonyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (**13**),[6] and 3-hydroxy-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (**19**).[11] Except for the methoxy-derivative (**5**), the rest of new compounds gave satisfactory analyses for C, H, and N, within a ±0.3% error.

2-Phenyl-3-methoxy-4,5,6,7-tetrahydroindazole (5). A solution of phenylhydrazine (0.7 g) in ethanol (5 ml) was added dropwise to a well stirred solution of ethyl 2-oxocyclohexancarboxylate (**8**)(1.0 g) in ethanol (20 ml), and the mixture was stirred at room temperature for 24 hours. Evaporation of the solvent and recrystallization of the resulting solid afforded 2-phenyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (0.8 g, 63%), mp 180°C (lit.[19] mp 180°C). A solution of this compound in dichloromethane (10 ml), containing one drop of triethylamine, was slowly added under argon to a suspension of an equimolecular amount of trimethyloxonium tetrafluorborate in dichloromethane (10 ml), and the mixture was stirred at room temperature for 24 hours. Solid sodium bicarbonate was added, and the mixture was filtered and evaporated. The resulting oil was then triturated with diethyl ether to separate any residual starting material, which remained as a solid, and was filtered off. The ether solution was evaporated, and the residue submitted to column chromatography (dichloromethane). Among various unidentified products, a few amount of (**5**) was isolated (14%), as a colorless oil, which decomposed on standing. Ms: m/z 228 (M^+, 100%), 213, 200, and 185; ^1H nmr ($CDCl_3$): 1.3 (m, 4H), 1.8 (m, 2H), 2.7 (m, 2H), 3.95 (s, 3H), 7.24 (m, 1H), 7.39 (m, 2H), and 7.63 (m,

2H) ppm.

1-Methyl-4,5,6,7-tetrahydro-(2H)indazolin-3-one (6). The method of Chupp[16] afforded in our hands a mixture of (**6**)(22%) and the dimethyl-derivative (**9**)(50%). For the exclusive preparation of (**6**), the following procedure was undertaken: 4,5,6,7-tetrahydro-(3aH)indazolin-3-one (**4**)[15] (0.30 g) was added to a suspension of sodium hydride (0.055 g) in dry tetrahydrofuran (10 ml). The reaction mixture was stirred at room temperature for 10 min, and then iodomethane (0.5 ml) was added, and the reaction was further stirred for one hour. Water (3 ml) and diethyl ether (20 ml) were added, and the aqueous layer was separated and washed with an additional amount of diethyl ether (15 ml). The combined ether extracts were washed with water and brine, dried over magnesium sulphate, and evaporated, to give 0.17 g (51%) of (**6**), mp 176-179°C (lit.[16] 178-181°C).

2,3a-Dimethyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (12).[20]
Method A: Methylhydrazine (0.13 g) was added dropwise to a solution of ethyl 1-methyl-2-oxocyclohexancarboxylate (**11**)[21] and the mixture was refluxed for 5 hours. The solvent was evaporated and the crude oil was purified by column chromatography (diethyl ether) to give (**12**)(0.30 g, 67%). Ir(neat): 1710 and 1615 cm^{-1}; Uv: 247 nm; Ms: m/z 166 (M^+, 100%), 151, 138, 123, and 109; ^1H nmr (DMSO-d_6): 1.14 (s, 3H), 1.1-2.3 (m, 8H), and 3.14 (s, 3H) ppm.
Method B: A solution of 3a-methyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (**10**) (0.30 g) in anhydrous tetrahydrofuran (4 ml) was added dropwise under argon to a stirred suspension of sodium hydride (0.10 g) in tetrahydrofuran (4 ml). After 30 min, iodomethane (0.5 ml) was added, and the reaction was stirred overnight, and then poured into water (10 ml). The solution was extracted with diethyl ether, and the organic layer was washed with brine, dried over magnesium sulphate, and evaporated, to give (**12**)(0.15 g, 91%), identical in every respect to the compound obtained by Method A.

4-Ethoxycarbonyl-1-methyl-4,5,6,7-tetrahydro-(2H)indazolin-3-one (16).
4-Ethoxycarbonyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (**13**)[6] (0.15 g) was added at room temperature to a stirred suspension of sodium hydride (0.02 g) in dry tetrahydrofuran (10 ml). After 15 min, methyl 4-toluenesulphonate (0.135 g) was added, and the reaction was stirred at room temperature for 24 hours. Water (3 ml) and diethyl ether (15 ml) were added and the layers were separated. The aqueous phase was further extracted with diethyl ether, and the combined organic fractions were washed with water and brine, dried over magnesium sulphate, and concentrated to dryness, yielding (**16**)(0.72 g, 45 %), mp 178-180°C (diethyl ether-hexane). Ir(nujol): 3200-2300, 1740, 1610, 1540, 1520, and 1160 cm^{-1}; Uv: 207(3.95), 230 (3.93), and 257(sh)(3.28) nm; Ms: m/z 224 (M^+, 14%), 151 (100%), 136, and 107; ^1H nmr (DMSO-d_6): 1.15 (t, 3H), 1.75 (m, 4H), 2.46 (m, 2H), 3.37 (m, 1H), 3.42 (s, 3H), 4.02 (q, 2H), and 9.38 (br s, 1H) ppm.

4-Ethoxycarbonyl-2-methyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (17).
Methylhydrazine (0.10 g) was added dropwise to a solution of diethyl 3-oxocyclohexan-1,2-dicarboxylate (**14**)[10] (0.50 g) in ethanol (5 ml). The reaction mixture was stirred at room temperature for 24 hours. The solvent was evaporated and the crude product washed with hexane to give (**17**)(0.22 g, 47%), mp 144-146°C (ethyl acetate-hexane). Ir(nujol): 3100-2100, 1740, 1600, and 1550 cm^{-1}; Uv: 206 (3.84) and 251(3.94) nm; Ms: m/z 224 (M^+, 36%), 176, 151 (100%), 150, 135, and 107; ^1H nmr (DMSO-d_6): 1.16 (t, 3H), 1.6-1.8 (m, 4H), 2.4-2.5 (m, 3H), 3.28 (s, 3H), 4.03 (q, 2H), and 10.55 (br s, 1H) ppm.

4-Ethoxycarbonyl-3a-methyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (18). A solution of hydrazine hydrate (98%)(0.058 g) in ethanol (5 ml) was added to a solution of

diethyl 2-methyl-3-oxocyclohexan-1,2-dicarboxylate (**15**)[10] (0.030 g) in ethanol (5 ml). The reaction mixture was refluxed for 15 hours. The solvent was evaporated and the crude product was purified by column chromatography (dichloromethane-ethanol 9:1) to give (**18**)(0.124 g, 47%), mp 143-146°C. Ir(nujol): 3220-3110, 1740, 1725, 1620, and 1200 cm^{-1}; Uv: 243(4.14) nm; Ms: m/z 224 (M^+, 56%), 179, 178, 151, 150 (100%), and 122; ^1H nmr (DMSO-d_6): 1.10 (t, 6H), 1.16 (s, 3H), 1.3-2.9 (m, 7H), 3.97 (q, 2H), and 4.00 (q, 2H) ppm.

Dimerization of 4,5,6,7-tetrahydro-(3aH)indazolin-3-one (4).

Method A: To a suspension of (**4**) (1.0 g) in dry toluene (250 ml) was added iodine (3.2 g). The reaction mixture was refluxed for 60 hours, and the solvent was evaporated *in vacuo*. The crude product was treated with diethyl ether (500 ml) and water (40 ml), and then solid sodium metabisulphite was added in portions until the iodine colour had completely disappeared. The organic layer was separated and sequentially washed with a saturated solution of sodium bicarbonate, water and brine, and dried over magnesium sulphate. The solvent was eliminated *in vacuo* and the crude product was purified by column chromatography (ratio of compound *vs.* silica gel 0.1:40)(dichloromethane-ethanol 8:1) to give (**19**)(0.125 g, 12.5%), mp 203-204°C (ethyl acetate-petroleum ether)(lit.[11] 195-197°C) and (**20**)(0.200 g, 20%), mp 222-224°C. Ir(nujol): 3280, 1720, 1620, 1540, and 1510 cm^{-1}; Uv: 202, 237, and 254 (sh) nm; Ms: m/z 274 (M^+, 11%), 137 (100%), and 110; ^1H nmr (pyridine-d_5): 1.4-3-0 (m, 16H), 9.75 (s, 1H), and 11.28 (s, 1H) ppm.

Method B: To a suspension of (**4**)(0.750 g) and anhydrous sodium sulphate (4.0 g) in benzene-acetone (6:1)(150 ml) lead dioxide (1.4 g) was added. The reaction mixture was stirred at room temperature for 24 hours and then centrifugated at 3500 rpm for 15 min. The solution was evaporated and the crude product was purified by column chromatography (ratio of compound *vs.* silica gel 0.1:30)(dichoromethane-ethanol-hexane 6:1:6) to give (**20**)(0.175 g, 23%) identical to the compound obtained by Method A, and (**21**)(0.133 mg, 17%), mp 213-215°C(dec)(ethyl acetate-hexane). Ir (nujol): 3280, 1720, 1700, 1640, 1540, and 1510 cm^{-1}; Uv: 250(3.75) nm; Ms: m/z 274 (M^+, 6%), 139, 138, and 137 (100%); ^1H nmr (DMSO-d_6): 1.0-2.9 (m, 16H) and 11.2 (s, 2H) ppm.

Dimerization of 4-ethoxycarbonyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (13).

When the Skaric procedure[6] was followed, a 40% of starting material (**13**) was recovered, and 15% of 1,3a'-bi-4-ethoxycarbonyl-4,5,6,7-tetrahydro-(3aH)indazolin-3-one (**22**) was obtained. Mp 86-88°C (diethyl ether-hexane)(lit.[6] for a N-N dimeric structure, mp 89-90°C). Ir(KBr): 3340, 2950, 1735, 1608, 1540, 1490, 1450, 1375, and 1195 cm^{-1} (lit.[6] 2941, 1724, 1608, 1534, 1486, 1445, 1366, and 1190 cm^{-1}); Uv: 208(3.52), 237(3.55), and 258 (sh)(3.24) nm [lit.[6] 204.9(3.41), 238(3.65), and 257.4 (sh)(3.42)]; Ms: m/z 418 (M^+, 1.1%), 345, 211, 210, 209, 208, 137 (100%), and 136; ^1H nmr (DMSO-d_6): 1.16 (t, 6H), 1.3-2.8 (m, 14H), 4.04 (q, 4H), 9.97 (br s, 1H), and 11.22 (br s, 1H) ppm.

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